TABLE I

ALKYL HALF ESTER OF *cis*-3,6-ENDOMETHYLENE-Δ^4-TETRAHYDROPHTHALIC ACID

R	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Acid no. Calcd.	Acid no. Found
CH_3[a]	101–102	$C_{10}H_{12}O_4$	61.21	61.35	6.17	6.08	196	195
C_2H_5	74–75	$C_{11}H_{14}O_4$	62.68	63.12	6.72	6.63	210	212
n-C_3H_7	71–72	$C_{12}H_{16}O_4$	64.31	64.44	7.19	7.10	224	226
n-C_4H_9	65–66	$C_{13}H_{18}O_4$	65.56	65.63	7.62	7.22	238	240
n-C_5H_{11}	51–52	$C_{14}H_{20}O_4$	66.64	66.95	7.99	7.73	252	254
n-C_6H_{13}	52–53	$C_{15}H_{22}O_4$	67.68	68.00	8.33	7.98	266	270
n-C_7H_{15}	43–44	$C_{16}H_{24}O_4$	68.59	68.88	8.63	8.28	280	279
n-C_8H_{17}	32–33	$C_{17}H_{26}O_4$	69.32	69.24	8.99	9.05	294	290
n-C_9H_{19}	45–46	$C_{18}H_{28}O_4$	70.10	70.01	9.15	9.13	308	310
n-$C_{10}H_{21}$	50–51	$C_{19}H_{30}O_4$	70.77	71.10	9.38	9.38	322	321
n-$C_{11}H_{23}$	53–54	$C_{20}H_{32}O_4$	71.39	71.60	9.62	9.46	336	333
n-$C_{12}H_{25}$	52–53	$C_{21}H_{34}O_4$	71.96	72.13	9.78	9.61	350	356
n-$C_{13}H_{27}$	53–54	$C_{22}H_{36}O_4$	72.46	72.08	9.95	9.98	364	365
n-$C_{14}H_{29}$	59–60	$C_{23}H_{38}O_4$	73.24	73.17	10.12	10.44	378	373
n-$C_{15}H_{31}$	59–60	$C_{24}H_{40}O_4$	73.42	73.26	10.27	10.18	392	389
n-$C_{16}H_{33}$	63–64	$C_{25}H_{42}O_4$	73.84	73.70	10.41	10.44	406	402
n-$C_{17}H_{35}$	63–64	$C_{26}H_{44}O_4$	74.24	73.98	10.54	10.48	420	414
n-$C_{18}H_{37}$	69–70	$C_{27}H_{46}O_4$	74.61	74.46	10.67	10.64	435	432

[a] Prepared by Morgan, Tipson, Lowy and Baldwin, THIS JOURNAL, 66, 404 (1944).

discontinued and the temperature rose spontaneously to 160° and was maintained at this degree by intermittent application of heat for 15 minutes. After cooling the oily half esters were purified by dissolving them in 10% sodium carbonate solution, followed by filtration. The filtrate was extracted twice with ether and acidified with 10% hydrochloric acid. The aqueous solution was decanted and the oily residue dissolved in benzene. After filtering the benzene solution was washed with water and extracted with 10% sodium bicarbonate solution. The extract was made acid with 10% hydrochloric acid and the free acid ester which separated was washed with water and dissolved in benzene. After drying over sodium sulfate the solvent was removed by distillation under vacuum. The half esters were further purified by dissolving them in petroleum ether and freezing them out by immersion in an acetone–Dry Ice mixture. This procedure was repeated until a constant melting compound was obtained after drying for 24 hours in a vacuum.

The Half Esters Tridecyl through Octadecyl.—A mixture of the appropriate alcohol and equivalent molar amount of the anhydride was heated for 12 hr. at 125°. The mixture was stirred occasionally during the heating to give a homogeneous liquid. The cooled mixture was poured into an excess of 10% sodium carbonate and stirred until the solid dissolved. The solution was extracted with benzene and filtered through a wetted filter. An excess of 10% hydrochloric acid was then added and the oily precipitate was allowed to harden, then filtered and dried. The product was recrystallized from petroleum ether until constant melting after drying 24 hr. in vacuum.

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The Si–C Bond Distance in $Si(CH_3)_4$

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A reinvestigation of tetramethylsilane by electron diffraction[1] has led to the result Si–C = 1.888 ± 0.02 Å. (previous report[2]: 1.93 ± 0.03 Å.), in agreement with the values found for carborundum[3] (1.88–1.90 Å.), the three other methylsilanes[4] (1.87 Å.), and $Si_2(CH_3)_6$[5] (1.90 ± 0.02 Å.).

The observed diffraction pattern, which has eleven rings extending to $s = 32$, is well represented by the simplified intensity curve calculated with appropriate temperature factors for a symmetrical (T_d) model with the methyl groups in the staggered orientation, as held by independent 1.3 kcal./mole threefold potential barriers,[6] and with Si–C = 1.89, Si–H = 1.10, and ∠ Si–C–H = 110°; the average of the deviations $|(s_{calcd}/s_{obsd}) - (s_{calcd}/s_{obsd})|$ is 0.005 for the eleven well-located and reasonably symmetrical features used for the scale determination. Models with opposed methyl groups are unsatisfactory, both in the position and qualitative aspects of the first five or six rings, and it seems certain that the methyl groups are indeed predominantly staggered.

The final results are: ∠Si–C–H, 110 ± 3°; C–H, 1.10 ± 0.05 Å.[7]; and Si–C, 1.888 ± 0.02 Å.[7]

(1) See K. Hedberg and A. J. Stosick, THIS JOURNAL, **74**, 954 (1952), for details of the methods used.

(2) L. O. Brockway and H. O. Jenkins, *ibid.*, **58**, 2036 (1936).

(3) N. W. Thibault, *Am. Mineral.*, **29**, 249, 327 (1944); L. S. Ramsdell, *ibid.*, **29**, 431 (1944); **30**, 519 (1945).

(4) L. O. Brockway and A. C. Bond, Second Int. Cong. Cryst., Stockholm (1951), Abstr. ED 12.

(5) L. O. Brockway and N. R. Davidson, THIS JOURNAL, **63**, 3287 (1941).

(6) J. G. Aston, R. M. Kennedy and G. H. Messerly, *ibid.*, **63**, 2343 (1941).

(7) Including 0.8% estimated limit of scale error.

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Antitubercular Studies. III. Hydroxylamines and Thiosemicarbazones

BY PRICE TRUITT, E. H. HOLST AND MARGARET ROBBINS

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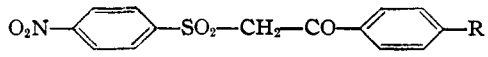
Our interest in antitubercular studies has led us to synthesize a number of compounds with varying structures for testing against tuberculosis. Among these substances there have been O-substituted

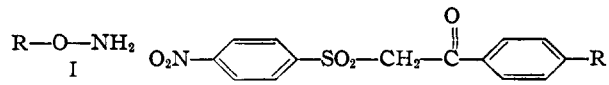
TABLE I



R	M.p., °C.	Yield, %	Solvent recryst.	Crystals	Formula	Nitrogen, % Calcd.	Found
Br[a]	173	80	Ethanol	Powder	$C_{15}H_{13}BrN_4O_2S_2$	13.18	12.92
Br	221-222	75	Ethanol	Flakes	$C_{15}H_{13}BrN_4O_4S_2$	12.25	12.42
Cl	202	91	Ethanol-acetone	Needles	$C_{15}H_{13}ClN_4O_4S_2$	13.57	13.53
CH_3	197	71	*n*-Butanol	Needles	$C_{16}H_{16}N_4O_4S_2$	14.32	14.30
(*b*)	198 (dec.)	62	Ethanol	Needles	$C_9H_{11}N_3O_2S_2$	16.34	16.37

[a] This compound was the sulfide corresponding to the formula above. [b] β-(2-Thenoyl)-propionic acid thiosemicarbazone.

derivatives of hydroxylamine (I) and thiosemicarbazones of α-(4-nitrophenylsulfonyl)-acetophenones (II).



I
R = alkyl, etc.

II
R = CH_3, Cl, Br

Although compounds of type (I) have been reported, no report of antitubercular testing or activity has been noted. However, certain hydroxamic acids have been reported to possess antituberculous properties.[1,2] Gardner and co-workers,[3] however, report that compounds of this type have little value as antitubercular agents.

The continued interest in thiosemicarbazones as possible antitubercular agents[4,5] prompted us to attempt the preparation of thiosemicarbazones (II) of a number of α-(4-nitrophenylsulfonyl)-acetophenones and of some of the corresponding amines and sulfides.[6]

None of the amines which correspond to II could be prepared by any variation of the general procedure of preparation. Although a reaction was observed and a product isolated with each of the amines, the product could not be purified sufficiently for correct analysis.

Since a quantity of β-(2-thenoyl)-propionic acid was at hand from other work, the thiosemicarbazone of this ketoacid was prepared.

The thiosemicarbazones did not possess significant antitubercular properties. However, two of the O-substituted hydroxylamines gave the following antitubercular activities: O-benzylhydroxylamine hydrochloride, active at 5 mg. %; O-2-phenoxyethylhydroxylamine hydrochloride, active at 1.25 mg. %. Both of these derivatives were active at 10 mg. % in the presence of bovine serum. The LD_{50} (mice) for these substances were 0.36 mg./g. and 0.26 mg./g., respectively. The hydroxylamines also exhibited a slight pressor activity.

Experimental

o-2-Phenoxyethyl Acetoxime.—This material was prepared by the condensation of 2-phenoxyethyl bromide and the sodium salt of acetoxime; b.p. 126–128° (4 mm.), $n^{20}D$ 1.5120.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.4; H, 7.82; N, 7.25. Found: C, 68.5; H, 7.91; N, 7.34.

O-2-Phenoxyethyl Hydroxylamine Hydrochloride.[7]—O-2-Phenoxyethyl acetoxime was hydrolyzed by refluxing for four hours with 10% hydrochloric acid. A 63% yield of product was obtained, m.p. 172° (dec.).

Anal. Calcd. for $C_8H_{12}ClNO_2$: Cl, 18.7; N, 7.39. Found: Cl, 18.6; N, 7.52.

O-Benzylhydroxylamine Hydrochloride.—This compound was prepared as above, m.p. 230–235° (dec.). Behrend[8] reported this salt to melt at 226–235° (dec.).

O-Isoamyl Acetoxime.—This oxime was prepared in 50% yield as in previous experiments; b.p. 154–155° (66–69° (25 mm.)), $n^{20}D$ 1.4230.

Anal. Calcd. for $C_8H_{17}NO$: N, 9.78. Found: N, 9.61.

O-Isoamylhydroxylamine Hydrochloride.—Hydrolysis of the above oxime with 10% hydrochloric acid gave a 28% yield of desired product, m.p. 173–174° (dec.).

Anal. Calcd. for $C_8H_{17}ClNO$: Cl, 25.4; N, 10.0. Found: Cl, 25.5; N, 10.3.

O-2-(4-Ethoxyphenoxy)-ethyl Acetoxime.—The desired substance was obtained in 18% yield by the prior procedure, b.p. 150–153° (5 mm.).

Anal. Calcd. for $C_{13}H_{19}NO$: N, 6.86. Found: N, 6.95.

O-2-(4-Ethoxyphenoxy)-ethylhydroxylamine Hydrochloride.—The acid hydrolysis of the corresponding acetoxime gave a 35% yield of the expected salt, m.p. 188–192° (dec.).

Anal. Calcd. for $C_{10}H_{16}ClNO_3$: Cl, 15.2; N, 6.01. Found: Cl, 15.4; N, 6.20.

The following general procedure was used to prepare the thiosemicarbazones (II) and the data are recorded in Table I.

A solution of 5 g. of the ketone, 1.26 g. of thiosemicarbazide and 3 ml. of concd. sulfuric acid in 125 ml. of 95% ethanol was refluxed for six hours. The mixture was filtered while hot and the filtrate allowed to cool overnight. The lemon-yellow to cream-colored product was recrystallized from the appropriate solvent.

(1) T. Urbanski, *Nature*, **166**, 267 (1950).
(2) T. Urbanski, S. Slopek and S. Venulet, *ibid.*, **168**, 29 (1951).
(3) T. S. Gardner, E. Wenir and F. A. Smith, THIS JOURNAL, **73**, 5455 (1951).
(4) J. Bernstein, *et al.*, *ibid.*, **73**, 906 (1951).
(5) H. Bauer, *ibid.*, **73**, 5862 (1951).
(6) P. Truitt, R. Stead, L. M. Long and W. J. Middleton, *ibid.*, **71**, 3511 (1949).
(7) P. Truitt, L. M. Long and M. Mattison, *ibid.*, **70**, 1989 (1948).
(8) Behrend, *Ann.*, **257**, 207 (1890).

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The Stereochemistry of the Reaction of γ-Methoxy Acids with Thionyl Chloride

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The stereochemical relationship between (+)-γ-methoxyvaleric acid (I) and the (+)-methyl alkyl carbinols, which has recently been determined,[1] permits one to determine the stereochemistry of the reaction of the γ-methoxy acids with thionyl chloride. It has previously been shown that the γ-alkoxybutyric acids (II) give γ-chloro-

(1) W. E. Doering and R. W. Young, THIS JOURNAL, **74**, 2997 (1952).