

TABLE I

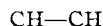
2-METHYL-2-MONOALKYLAMINOPROPYL FUROATE AND 2-THIOPHENECARBOXYLATE HYDROCHLORIDES^a $\text{RCOOCH}_2\text{C}(\text{CH}_3)_2\text{-NHR}'\cdot\text{HCl}$

R	R'	M.p., °C. (uncor.)	Formula	Calcd.	Chlorine, %	Found ^b
2-Furan	<i>n</i> -C ₃ H ₇	184-185	C ₁₂ H ₂₀ O ₃ NCI	13.54	13.32	13.29
2-Furan	<i>n</i> -C ₄ H ₉	146-147	C ₁₃ H ₂₂ O ₃ NCI	12.86	12.58	12.63
2-Furan	<i>n</i> -C ₅ H ₁₁	144-145	C ₁₄ H ₂₄ O ₃ NCI	12.24	12.12	12.00
2-Thiophene	<i>n</i> -C ₃ H ₇	165-166	C ₁₂ H ₂₀ O ₂ NCIS	12.76	12.87	12.81
2-Thiophene	<i>n</i> -C ₄ H ₉	175-176	C ₁₃ H ₂₂ O ₂ NCIS	12.15	12.25	12.30
2-Thiophene	<i>n</i> -C ₅ H ₁₁	130-131	C ₁₄ H ₂₄ O ₂ NCIS	11.59	11.54	11.49

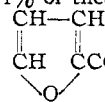
^a These compounds will be tested for anesthetic activity by Dr. H. B. Haag of the Medical College of Virginia and the results reported elsewhere. ^b Analyses by R. L. Kersey.

ride and was isolated as the disulfate. Each of the 2-methyl-2-monoalkylaminopropyl aromatic carboxylates, in the process of purification, was converted into the free base, dissolved in isopropyl ether and precipitated as the salt by the addition of hydrogen chloride or concentrated sulfuric acid.

Experimental



$\text{CCOOCH}_2\text{C}(\text{CH}_3)_2\text{NHC}_4\text{H}_9\cdot\text{HCl}$, 2-(2-Methyl-2-*n*-butylaminopropyl) Thiophenecarboxylate Hydrochloride.—To 13.1 g. (0.1 mole) of 2-methyl-2-*n*-butylamino-1-propanol was added 13.4 ml. (0.15 mole) of concentrated hydrochloric acid. The solution was evaporated to dryness in a vacuum. To the amino alcohol hydrochloride thus formed was added 14.6 g. (0.1 mole) of thiophenecarboxylic chloride.⁶ The mixture was heated on an oil-bath at 100° for 15 minutes, at 130° for 15 minutes and at 150° for 15 minutes. The reaction mixture was taken up in 50 ml. of alcohol, the solution was poured into 100 ml. of *N* sodium hydroxide solution and the oil which separated was dissolved in isopropyl ether. The ethereal solution was saturated with dry hydrogen chloride. The solid formed was filtered with suction, washed with isopropyl ether and recrystallized to constant melting point from alcohol and isopropyl ether. The yield of purified 2-methyl-2-*n*-butylaminopropyl 2-thiophenecarboxylate hydrochloride was 7 g. or 24% of theory.



$\text{CCOOCH}_2\text{C}(\text{CH}_3)_2\text{NHC}_4\text{H}_9\cdot\text{HCl}$, 2-Methyl-2-*n*-butylaminopropyl Furoate Hydrochloride.—Tenth molar quantities of 2-methyl-2-*n*-butylamino-1-propanol and furoyl chloride were heated, as above. The reaction product was dissolved in 50 ml. of ethanol and poured into 100 ml. of *N* sodium hydroxide solution. The free base separating was dissolved in isopropyl ether and precipitated as the crystalline hydrochloride by the addition of hydrogen chloride. 2-Methyl-2-*n*-butylaminopropyl furoate hydrochloride was obtained in 23% yield by washing with isopropyl ether and recrystallization from ethanol-isopropyl ether solution.



$\text{COOCH}_2\text{C}(\text{CH}_3)_2\text{NHC}_5\text{H}_{11}\cdot 2\text{H}_2\text{SO}_4$, 2-Methyl-2-*n*-amylaminopropyl Nicotinate Disulfate.^a—Tenth molar quantities of 2-methyl-2-*n*-amylaminopropyl hydrochloride and nicotiny chloride were refluxed in 50 ml. of chloroform for approximately 18 hours. The reaction mixture was poured into hot water, the chloroform evaporated off and the 2-methyl-2-*n*-amylaminopropyl nicotinate set free as a dark oil by the addition of sodium hydroxide solution. The oil was dissolved in isopropyl ether and treated dropwise with concentrated sulfuric acid. The oil which precipitated was converted into a crystalline hygroscopic solid in a yield of 78% by trituration with anhydrous ether, suction

filtration and drying in a vacuum desiccator. On stirring the product with anhydrous acetone and suction filtration the product became less hygroscopic. Without further purification the product had a melting point of 135-142° and gave a sulfate analysis only 0.1% low in sulfur, the latter likely due to a balancing of errors. On three recrystallizations from absolute alcohol and anhydrous ether, the melting point was 153-153.5°. *Anal.* Calcd. for C₁₅H₂₄O₂N₂·2H₂SO₄: S, 13.93. Found: S, 14.05.

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Alkyl Half Esters of *cis*-3,6-Endomethylene- Δ^4 -tetrahydrophthalic Acid

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Due to the continuing interest in alkyl chain length as a function of melting point, it was desirable to prepare the half esters of *cis*-3,6-endomethylene- Δ^4 -tetrahydrophthalic acid and compare the melting points of these compounds with those of phthalic³ and *cis*- Δ^4 -tetrahydrophthalic acids⁴ previously prepared.

This series of half esters melted with a more regular pattern in the compounds of alkyl chain length from methyl to octyl than the corresponding half esters of phthalic or tetrahydrophthalic acids. The series has a minimum at 34° for the octyl ester and then rises in a general pattern by small increments to 70° at the octadecyl half ester. In general it can be said that the melting points of these compounds are intermediate between the analogous compounds derived from phthalic or tetrahydrophthalic acids. The compounds prepared are listed in Table I.

Experimental

The Half Esters of Methyl through Amyl.—A mixture of an excess of the appropriate water-free alcohol and the anhydride was refluxed three hours. After cooling the excess alcohol was removed from a steam-bath under reduced pressure. The oily residue generally solidified to a crystalline mass on cooling. Recrystallization was effected by alternately using petroleum ether and "heptane" until a constant melting product was obtained after vacuum drying.

The Half Esters of Hexyl through Dodecyl.—A mixture of 0.5 mole of the appropriate alcohol and 0.5 mole of the anhydride was slowly heated with stirring until the temperature rose to around 135°. At this point heating was

(1) Abstracted in part from the thesis submitted to Georgetown University in 1951, by Leonard M. Rice, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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(3) J. F. Goggins, Jr., and J. F. Copenhaver, *THIS JOURNAL*, **61**, 2909 (1939).

(4) White, Trigg, Sankins and E. E. Reid, private communication.

(6) Acknowledgment is made to Socony Vacuum Company for the 2-thiophene carboxylic acid used in the preparation of the acid chloride.

TABLE I
 ALKYL HALF ESTER OF *cis*-3,6-ENDOMETHYLENE- Δ^4 -TETRAHYDROPHthalic ACID

R	M.p., °C.	Formula	Carbon, %		Hydrogen, %		Acid no.	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
CH ₃ ^a	101-102	C ₁₀ H ₁₂ O ₄	61.21	61.35	6.17	6.08	196	195
C ₂ H ₅	74-75	C ₁₁ H ₁₄ O ₄	62.68	63.12	6.72	6.63	210	212
<i>n</i> -C ₃ H ₇	71-72	C ₁₂ H ₁₆ O ₄	64.31	64.44	7.19	7.10	224	226
<i>n</i> -C ₄ H ₉	65-66	C ₁₃ H ₁₈ O ₄	65.56	65.63	7.62	7.22	238	240
<i>n</i> -C ₅ H ₁₁	51-52	C ₁₄ H ₂₀ O ₄	66.64	66.95	7.99	7.73	252	254
<i>n</i> -C ₆ H ₁₃	52-53	C ₁₅ H ₂₂ O ₄	67.68	68.00	8.33	7.98	266	270
<i>n</i> -C ₇ H ₁₅	43-44	C ₁₆ H ₂₄ O ₄	68.59	68.88	8.63	8.28	280	279
<i>n</i> -C ₈ H ₁₇	32-33	C ₁₇ H ₂₆ O ₄	69.32	69.24	8.99	9.05	294	290
<i>n</i> -C ₉ H ₁₉	45-46	C ₁₈ H ₂₈ O ₄	70.10	70.01	9.15	9.13	308	310
<i>n</i> -C ₁₀ H ₂₁	50-51	C ₁₉ H ₃₀ O ₄	70.77	71.10	9.38	9.38	322	321
<i>n</i> -C ₁₁ H ₂₃	53-54	C ₂₀ H ₃₂ O ₄	71.39	71.60	9.62	9.46	336	333
<i>n</i> -C ₁₂ H ₂₅	52-53	C ₂₁ H ₃₄ O ₄	71.96	72.13	9.78	9.61	350	356
<i>n</i> -C ₁₃ H ₂₇	53-54	C ₂₂ H ₃₆ O ₄	72.46	72.08	9.95	9.98	364	365
<i>n</i> -C ₁₄ H ₂₉	59-60	C ₂₃ H ₃₈ O ₄	73.24	73.17	10.12	10.44	378	373
<i>n</i> -C ₁₅ H ₃₁	59-60	C ₂₄ H ₄₀ O ₄	73.42	73.26	10.27	10.18	392	389
<i>n</i> -C ₁₆ H ₃₃	63-64	C ₂₅ H ₄₂ O ₄	73.84	73.70	10.41	10.44	406	402
<i>n</i> -C ₁₇ H ₃₅	63-64	C ₂₆ H ₄₄ O ₄	74.24	73.98	10.54	10.48	420	414
<i>n</i> -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(CH₃)₄

By W. F. SHEEHAN, JR., AND VERNER SCHOMAKER

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A reinvestigation of tetramethylsilane by electron diffraction¹ has led to the result Si-C = 1.888 ± 0.02 Å. (previous report²: 1.93 ± 0.03 Å.), in agreement with the values found for carborundum³

(1) See K. Hedberg and A. J. Stosick, *THIS JOURNAL*, **74**, 951 (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).

(1.88-1.90 Å.), the three other methylsilanes⁴ (1.87 Å.), and Si₂(CH₃)₆⁵ (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 \angle Si-C-H = 110°; the average of the deviations $|(s_{\text{calcd}}/s_{\text{obsd}}) - (s_{\text{calcd}}/s_{\text{obsd}})|$ 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: \angle Si-C-H, 110 ± 3°; C-H, 1.10 ± 0.05 Å.⁷; and Si-C, 1.888 ± 0.02 Å.⁷

(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.

CONTRIBUTION No. 1671

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Antitubercular Studies. III. Hydroxylamines and Thiosemicarbazones

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

RECEIVED APRIL 25, 1952

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