

steam distillation device of the type described by Fieser,¹⁴ with a small condenser sealed on, was used. The condenser arm (length, 4.5 cm.) was cooled by ice-water during the experiment. The brominated mixture (see above) was transferred with some ether into the inner tube of this apparatus and the ether was blown off with nitrogen. The boiler flask, half-filled with dist. water, was then heated to allow the collection of about 1 ml. of distillate per min. When practically all of the acetylene tetrabromide had gone over, crystals of diacetylene hexabromide began to appear in the condenser arm. At this point the steam-distillation was stopped and the crystals were freed from water by draining as completely as possible. The flask was then kept in a vacuum desiccator for half a day and weighed.

The collected crude acetylene tetrabromide was extracted from the distillate with ether, and the solution was dried and evaporated *in vacuo*. The oily residue showed n_D^{20}

(14) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 161.

1.6343, while a redistilled commercial sample, after having gone through the described operations, gave the value 1.6340.

Anal. Calcd. for $C_2H_2Br_4$: Br, 91.95. Found: Br, 92.18 (Carius).

The extent of the reliability of the procedure may be illustrated by the following results obtained by steam distilling two artificial mixtures: (a) applied, 20 mg. of diacetylene hexabromide mixed with about 14 parts of acetylene tetrabromide; recovered, 19.8 mg. (99%); (b) applied, 75.6 mg. of hexabromide and 2.5 parts of tetrabromide; recovered, 78 mg. (103%).

Acknowledgment.—We wish to thank Mr. M. Gumpel and Dr. S. C. Crane of these laboratories for advice in handling the ultrasonic equipment; likewise, Dr. A. J. Haagen-Smit, Mr. G. A. Swinehart and Dr. A. Elek for microanalyses.

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[CONTRIBUTION FROM THE WARNER-CHILCOTT RESEARCH LABORATORIES]

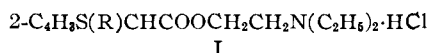
Antispasmodics. III. Basic Alkyl Ester Acid Addition and Quaternary Ammonium Salts of α -(2-Cycloalken-1-yl)-2-thienylacetic Acids

BY FREDERICK LEONARD¹ AND LEON SIMET

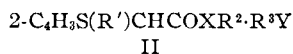
RECEIVED DECEMBER 7, 1954

A large number of basic alkyl esters of α -(2-cycloalken-1-yl)-2-thienylacetic acids of the general formula II have been prepared for pharmacological evaluation in the form of their acid addition and quaternary ammonium salts. Several have been found to possess anticholinergic activity of a high order.

The synthesis, antispasmodic activity and toxicity of a number of 2-diethylaminoethyl ester hydrochlorides of α -substituted 2-thienylacetic acids were reported in the first paper² of this series. Two of the compounds described therein, namely, 2-diethylaminoethyl α -(2-cyclopenten-1-yl)-2-thienylacetate hydrochloride [I, R = 1-(2-C₅H₇)]³ and its 2-cyclohexen-1-yl homolog [I, R = 1-(2-C₆H₉)] were found to possess *in vitro* and *in vivo* antispasmodic activity in the clinically useful range. The preparation was therefore undertaken, with these substances as model compounds, of a



variety of basic alkyl ester, thiol ester and N-basic alkyl amide acid addition and quaternary ammonium salts of the general formula II. These substances may be regarded as having been derived from the esters I, by expansion of the alcoholic ethylene group with or without branching and/or



replacement of the diethylamino residue by other dialkylamino radicals, by incorporation of the diethylaminoethyl chain into a nitrogenous ring system, by replacement of the alcoholic carboxyl oxygen atom by sulfur or nitrogen.

The parent basic alkyl esters of the acid addition and quaternary ammonium salts II were obtained by (1) condensation of α -(2-cycloalken-1-yl)-2-thienylacetic acids (III) with tertiary amino alkyl

halides in the presence of anhydrous potassium carbonate, (2) reaction of α -(2-cycloalken-1-yl)-2-thienylacetyl chlorides (IV) with basic alcohols, or (3) amination of ω -bromoalkyl α -(2-cycloalken-1-yl)-2-thienylacetates (V). The ω -bromoalkyl esters (V) were prepared either by interaction of the acids (III) with alkylene dibromides in the presence of potassium carbonate or by treatment of the acid chlorides (IV) with alkylenebromohydrins. Interaction of 2-diethylaminoethylmercaptan with the acid chlorides IV gave thiol esters. Two N-diethylaminoethyl amides were obtained when the substituted acetyl chlorides (IV) were treated with N,N-diethylethylenediamine.

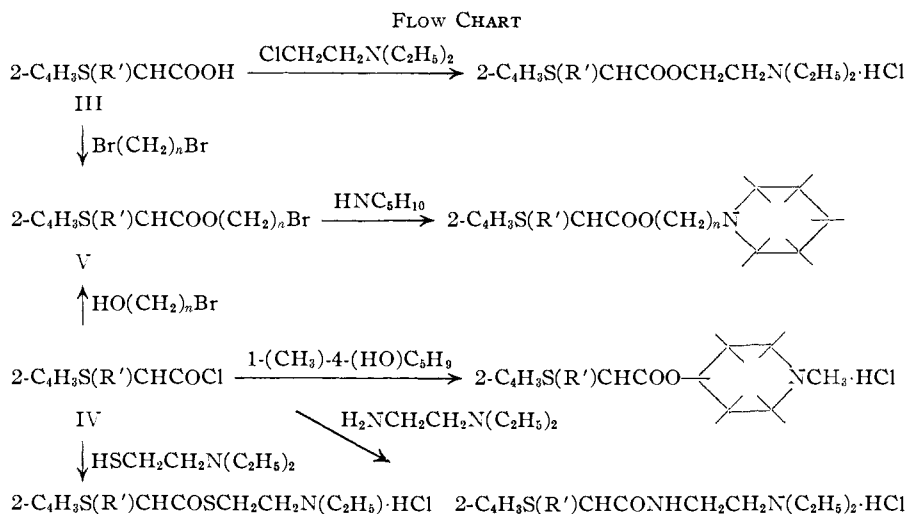
These reactions are illustrated in the flow chart. Crude hydrochlorides were converted to the free bases for purification. With very few exceptions the bases were fractionated *in vacuo* prior to conversion to acid addition and quaternary ammonium salts. In a number of instances particularly "clean" bases were isolated. These were, therefore, converted without distillation to the desired final products.

Quaternization of the free bases of the ester hydrochlorides I was attempted with several different types of halides. Methyl iodide, benzyl bromide, ethyl bromoacetate and *n*-butyl γ -bromocrotonate reacted rapidly when refluxed in acetone or benzene with I base. Addition of ethyl iodide to I base [R = 1-(2-C₅H₇)] was only about 30% complete after 72 hours of reflux in benzene solution, but addition of ethyl bromide to I base [R = 1-(2-C₆H₉)] was practically quantitative when the reagents dissolved in acetone were heated in a pressure bottle at 100° for 24 hours. *p*-Xylene dibromide quaternized rapidly with two molecules of the basic

(1) Nepera Chemical Co., Yonkers, New York.

(2) F. Leonard, *THIS JOURNAL*, **74**, 2915 (1952).

(3) "Neotropine Hydrochloride Warner," U. S. Patent 2,561,385, July 24, 1951.



esters (I) but neither bis- nor monoquaternary salts could be obtained from *o*- or *m*-xylene dibromide, a result which, on the basis of steric considerations, was not unexpected. When alkylene dihalides (methylene diiodide, ethylene dibromide, trimethylene dibromide, hexamethylene dibromide) were refluxed with the ester bases I for periods up to 48 hours in low boiling solvents (acetone, benzene, ethanol) no signs of quaternization were observed. Attempts to quaternize the bases (I) with the same dihalides (a) in acetone under pressure at 100° yielded small amounts of sirups which could not be purified or (b) in methyl isobutyl ketone at 145° under pressure gave unworkable tars. Attempted quaternization of the basic esters (I) with a few homologous ethyl α -bromo-alkanoates (C₃ to C₆) and ethyl α -bromophenylacetate likewise failed when the reaction was attempted in refluxing ethanol or benzene acetone under pressure at 100° and methyl isobutyl ketone under pressure at 145°. Several of the free basic esters gave nicely crystalline methiodides but others yielded sirupy products with methyl bromide, methyl iodide, ethyl iodide, dimethyl sulfate, only one of which (compound 12, Table IV) could be worked up to analytical purity.

Preliminary *in vitro* activity data, obtained from isolated rabbit ileum studies, have shown that several of the basic ester acid addition and quaternary ammonium salts described herein (no. 34, Table III; 2, 3, 12, 27, Table IV) possess anticholinergic activities which are equal to or greater than that of the most effective compounds described previously.²

Experimental⁴

Basic Alcohols.—2-Dimethylaminoethanol was purchased from Eastman Kodak Co., 1,2,2,6-tetramethyl-4-piperidinol and 3-pyridol were generously supplied by Mr. E. Kastning, of the W. R. Warner Manufacturing Division. The other basic alcohols utilized in this investigation were prepared by one of the procedures described below. Physical data which are not yet in the literature are given in Table I.

2-Di-*n*-butylaminoethanol, 2-(1-piperidyl)-ethanol and 2-(4'-morpholinyl)-ethanol were prepared by dropwise addition (with cooling if necessary to keep temperature of reaction mixture below 50°) of 37.5 g. (0.3 mole) of ethylene bromohydrin to a stirred solution of 0.6 mole of the appropriate amine in 100 ml. of dry benzene. The resulting mix-

tures were refluxed for five hours, cooled and treated with 0.7 mole of 40% sodium hydroxide. The organic layers were removed, the aqueous layers extracted with ether and the extracts combined with the original benzene layers. The combined solutions were washed with water and fractionated. 2-(1-Pyrrolidyl)-ethanol was synthesized by the same general reaction utilizing, however, chloroform as the reaction solvent and modified conditions of work-up as follows. The reaction mixture was evaporated to a sirup, the minimum volume of water added to dissolve the residue and the resulting solution treated with 0.7 mole of 40% sodium hydroxide. The organic layer was separated, treated with four successive portions of sodium hydroxide pellets and fractionated. 2-Ethylmethylaminoethanol was obtained when 2-ethylaminoethanol was refluxed with a mixture of formic acid and formaldehyde using the conditions

TABLE I
BASIC ALCOHOLS

	Yield, %	°C. B.P.,	Mm.	<i>n</i> _D ²⁰
1 2-Ethylmethylaminoethanol	55	62-63	25 ^a	1.4372
2 2-Di- <i>n</i> -butylaminoethanol	78	116-119	17 ^b	1.4439
3 2-(1-Pyrrolidyl)-ethanol	56	88-89	17 ^c	1.4736
4 2-(1-Piperidyl)-ethanol	80	^d	
5 2-(4-Morpholinyl)-ethanol	81	119-120	25 ^e	1.4765
6 1-Diethylamino-2-propanol	81	64-65	30 ^f
7 1-(1'-Piperidyl)-2-propanol	85	91-92 ^g	24	1.4615
8 1,3-Bis-diethylamino-2-propanol	68	134-137	33 ^h	1.4467
9 1,3-Bis-di- <i>n</i> -propylamino-2-propanol	66	108-111	23 ⁱ	1.4491
10 3-Diethylamino-2,2-dimethylpropanol	86	95-98	18 ^j	1.4414
11 2,2-Dimethyl-3-(1-piperidyl)-propanol	92	119-120	19 ^k	1.4653
12 2-Diethylaminocyclohexanol	16	109-110	18 ^l	1.4649
13 1-Methyl-4-piperidinol	74	106-107	22 ^m	1.4763
14 1-Methyl-3-piperidinol	82	93-94	26 ⁿ	1.4733
15 2-Dibenzylaminoethanol	80	114-118	0.001 ^o	1.5676

^a French Patent 795,597 [*C.A.*, 30, 591 (1936)] gave b.p. 146-148° (734 mm.). ^b W. B. Burnett, R. L. Jenkins, C. H. Peet, E. E. Dreger and R. Adams, *THIS JOURNAL*, 59, 2248 (1937), gave b.p. 226-228° and *n*_D²⁰ 1.4444. ^c J. v. Braun, O. Braunsdorf and K. R ath, *Ber.*, 55, 1673 (1922), found b.p. 187-189°. ^d F. F. Blicke and C. E. Maxwell, *THIS JOURNAL*, 64, 428 (1942) reported b.p. 196-199°. ^e F. F. Blicke and C. E. Maxwell, *ibid.*, gave b.p. 220-222°. ^f A. R. Goldfarb, *THIS JOURNAL*, 63, 2280 (1941), found b.p. 62.5-63.5° (22 mm.). ^g F. F. Blicke and C. E. Maxwell (ref. *d*) reported b.p. 191-194°. ^h C. K. Ingold and E. Rothstein, *J. Chem. Soc.*, 1666 (1931), gave b.p. 114° (9 mm.). ⁱ G. B. Bachman and R. L. Mayhew, *J. Org. Chem.*, 10, 243 (1945), found b.p. 99-101° (3 mm.) and *n*_D²⁰ 1.4483. ^j C. Mannich, B. Lesser and F. Silten, ref. 8, reported b.p. 90-91° (12 mm.). ^k C. Mannich, B. Lesser and F. Silten, *ibid.*, gave b.p. 140° (39 mm.). ^l H. Heckel and R. Adams, *THIS JOURNAL*, 49, 1303 (1933), reported b.p. 106-106.5° (17 mm.) and *n*_D²⁴ 1.4659. ^m S. M. McElvain and K. Rorig, ref. 10, reported b.p. 95-98° at 16 mm. ⁿ Benzoate hydrochloride has m.p. 189-192°. R. Paul and S. Tchelitcheff, *Compt. rend.*, ref. 16a, reported b.p. 79° (15 mm.) and *n*_D¹⁶ 1.4695 for the alcohol and m.p. of 194° for the benzoate hydrochloride. J. H. Biel, H. L. Friedman, H. A. Leiser and E. P. Springler, ref. 16b, found b.p. 80-82° (15 mm.). ^o Hydrochloride showed m.p. 182-185°. W. S. Gump and E. J. Nikawitz, *THIS JOURNAL*, 72, 1309 (1950), found b.p. 190-195° (5 mm.) for free base and m.p. 182-184° for the hydrochloride.

(4) All melting and boiling points are uncorrected.

described by Icke, Wisegarner and Alles⁵ for the preparation of dimethyl-2-phenylethylamine. Alkylation of ethanolamine with benzyl chloride afforded 2-dibenzylaminoethanol. 2-Diethylaminocyclohexanol was synthesized in low yield by hypochlorination of cyclohexene⁶ followed by amination in benzene solution of the resulting chlorohydrin with two equivalents of diethylamine at 150° under pressure.

1-Diethylamino-2-propanol and 1-(1'-piperidyl)-2-propanol were prepared in satisfactory yield from propylene oxide and diethylamine and piperidine, respectively.

1,3-Bis-diethylamino-2-propanol and 1,3-bis-di-*n*-propylamino-2-propanol were obtained readily when epichlorohydrin was treated with the appropriate amine.

3-Diethylamino-2,2-dimethylpropionaldehyde⁷ and 2,2-dimethyl-3-(1-piperidyl)-propionaldehyde,⁷ dissolved in one-half their volume of ethanol, were hydrogenated in the presence of Raney nickel to the corresponding alcohols.⁸ Reduction was complete in 4.5 to 5 hours when the initial hydrogen pressure was 1800 lb. p.s.i. and the bomb temperature gradually raised to 70–80°.

Hydrogenation of 1-methyl-4-piperidone in the presence of Raney nickel gave 1-methyl-4-piperidinol.^{9,10}

1-Methyl-3-piperidinol was prepared by catalytic reduction of an aqueous solution (100 ml.) of 38 g. (0.2 mole) of 3-hydroxy-1-methylpyridinium bromide¹¹ in the presence of 6 g. of Raney nickel at an initial hydrogen pressure of 1750 lb. p.s.i. and a temperature of 200–230°. The cooled mixture was filtered and saturated with sodium hydroxide. The liberated amine was separated from the alkaline layer, combined with the ethereal extracts (three) of the aqueous layer, dried over anhydrous potassium carbonate and fractionated *in vacuo*.¹²

Basic Propyl Chlorides.—All but one of the halides used in this study were known compounds and were prepared by interaction of 0.4 mole of an amine with 0.2 mole of trimethylene chlorobromide in 50 ml. of ether following the general procedure developed by Marxer,¹³ and Adams and Whitmore.¹⁴ Data on these compounds are given in Table II.

2-Diethylaminoethyl mercaptan was prepared by alkaline decomposition of 2-diethylaminoethylisothiuronium chloride following the procedure of Albertson and Clinton.¹⁵

(5) R. N. Icke, B. B. Wisegarner and G. A. Alles, *Org. Syntheses*, **25**, 89 (1945).

(6) G. H. Coleman and H. F. Johnstone, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., p. 158.

(7) C. Mannich, B. Lesser and F. Sitlen, *Ber.*, **65**, 378 (1932).

(8) C. Mannich, B. Lesser and F. Sitlen, ref. 7, effected this conversion in poor yield by means of a sodium amalgam reduction. W. Wenner, *J. Org. Chem.*, **15**, 301 (1950), catalytically reduced the aldehydes in aqueous solution at pH 4.0–4.5 at 150 lb. hydrogen pressure and 79–80° in the presence of Raney nickel.

(9) S. M. McElvain and K. Rorig, *THIS JOURNAL*, **70**, 1826 (1948).

(10) This compound also has been prepared from chelidonic acid (for references to this method see ref. 9 and R. J. Toomey and E. R. Riegel, *J. Org. Chem.*, **17**, 1492 (1952)). K. Bowden and P. N. Grien, *J. Chem. Soc.*, 1164 (1952), found that catalytic reduction of 1,3-dicyano-2-propanol gave 4-piperidinol accompanied by some 1,3-diamino-2-propanol. Treatment of 4-piperidinol with a mixture of formic acid and formaldehyde gave 1-methyl-4-piperidinol.

(11) Prepared by Dr. E. H. Sakal in these laboratories during the course of another investigation. A solution of 190 g. (2 moles) of methyl bromide dissolved in 300 ml. of acetone was rapidly added to a solution of 95 g. (0.5 mole) of 3-pyridol dissolved in a mixture of 280 ml. of ethanol and 600 ml. of acetone. The resulting solution became warm, the reaction vessel was stoppered immediately, the stopper wired in place and the mixture let stand overnight at room temperature. The crystalline precipitate was removed by suction filtration, washed with a mixture of ethanol and acetone and dried; yield 145.8 g. (76%), m.p. 149–152°. A sample recrystallized from absolute alcohol melted at 153–154°. *Anal.* Calcd. for C₅H₇BrNO: C, 37.90; H, 4.24; N, 7.37; Br, 42.03. Found: C, 38.11; H, 4.44; N, 7.30; Br, 42.06.

(12) (a) R. Paul and S. Tchelitcheff, *Compt. rend.*, **221**, 560 (1945); (b) J. H. Biel, H. L. Friedman, H. A. Leiser and E. P. Springeler, *THIS JOURNAL*, **74**, 1485 (1952), obtained this alcohol when a glacial acetic acid solution of *N*-ethyltetrahydrofurfurylamine or *N,N*-diethyltetrahydrofurfurylamine was treated with gaseous hydrogen bromide at 100–105°. The amines were prepared by reductive aminolysis of furfural in the presence of Raney nickel catalyst.

(13) A. Marxer, *Helv. Chim. Acta*, **24**, 214E (1941).

(14) R. R. Adams and F. C. Whitmore, *THIS JOURNAL*, **67**, 735 (1945).

(15) N. F. Albertson and F. O. Clinton, *ibid.*, **67**, 1222 (1945).

TABLE II

TERTIARYAMINOPROPYL CHLORIDES, RCH ₂ CH ₂ CH ₂ Cl				
R	Yield, %	°C. B.p.	Mm.	<i>n</i> _D ²⁰
Diethylamino	68	75–76	31 ^{a,b}	1.4402
Di- <i>n</i> -propylamino	45	103–105	25 ^b	1.4426
Di- <i>n</i> -butylamino	57	123–125	18 ^{a,b}	1.4464
1-Pyrrolidyl	68	82–83	17 ^c	1.4763
1-Piperidyl	76	100–101	25 ^{a,b}	1.4722
4-Morpholinyl	66	110–111	20 ^b	1.4736

^a Ref. 13. ^b Ref. 14. ^c *Anal.* Calcd. for C₇H₁₄ClN: C, 56.95; H, 9.56. Found: C, 56.91; H, 9.30.

A sodium-*n*-butanol reduction¹⁶ of *N,N*-diethylaminoacetonitrile afforded *N,N*-diethylethylenediamine.

α -(2-Cyclopenten-1-yl)-2-thienylacetyl Chloride.—Thionyl chloride (50.8 g., 0.428 mole) was added rapidly to a solution of 80.8 g. (0.39 mole) of α -(2-cyclopenten-1-yl)-2-thienylacetic acid^{2,17} in 100 ml. of dry benzene and the mixture warmed at 50° for three hours. Benzene was removed *in vacuo*, the residual oil redissolved in fresh benzene and the solution again concentrated *in vacuo*. The crude residue was fractionated giving 74 g. (84%) of α -(2-cyclopenten-1-yl)-2-thienylacetyl chloride, b.p. 106–111° (1 mm.), *n*_D²⁰ 1.5552. A sample refractionated for analysis distilled at 121° (3 mm.) and had *n*_D²⁰ 1.5547.

Anal. Calcd. for C₁₁H₁₁OSCl: C, 58.29; H, 4.89; Cl, 15.65. Found: C, 58.45; H, 4.70; Cl, 15.60.

α -(2-Cyclohexen-1-yl)-2-thienylacetyl Chloride.—To a solution of 184 g. (0.827 mole) of α -(2-cyclohexen-1-yl)-2-thienylacetic acid^{2,17} in 550 ml. of dry chloroform, 171.5 g. (1.44 moles, 104.5 ml.) of thionyl chloride were added with constant stirring during one hour at room temperature. The reaction mixture gradually darkened; it was stirred for 17 hours at room temperature, refluxed for 1.5 hours and concentrated *in vacuo* to a dark oil. Fractionation gave 104 g. (57%) of the acid chloride, b.p. 130–136° (2 mm.), *n*_D²⁰ 1.5596. Redistillation gave an analytically pure sample, b.p. 111–112° (0.7 mm.), *n*_D²⁰ 1.5602.

Anal. Calcd. for C₁₂H₁₃ClOS: C, 59.88; H, 5.44; Cl, 14.73. Found: C, 59.84; H, 5.56; Cl, 14.66.

2-Bromoethyl α -(2-Cyclopenten-1-yl)-2-thienylacetate.—A solution of 26.3 g. (0.21 mole) of ethylene bromohydrin in 50 ml. of dry benzene was added dropwise with constant stirring to 45.2 g. (0.2 mole) of α -(2-cyclopenten-1-yl)-2-thienylacetyl chloride dissolved in 100 ml. of dry benzene and the mixture refluxed for eight hours. The cooled solution was washed until neutral with 5% sodium carbonate, water and evaporated *in vacuo*. The residual oil was fractionated *in vacuo* and gave 55 g. (88% yield) of 2-bromoethyl α -(2-cyclopenten-1-yl)-2-thienylacetate, b.p. 132–136° (0.003 mm.), *n*_D²⁰ 1.5553. The analytical sample distilled at 135–136° (0.003 mm.) and had *n*_D²⁰ 1.5545.

Anal. Calcd. for C₁₃H₁₅BrO₂S: C, 49.53; H, 4.80. Found: C, 48.88; H, 4.87.

5-Bromopentyl α -(2-Cyclopenten-1-yl)-2-thienylacetate.—1,5-Dibromopentane was obtained by the action of phosphorus tribromide (0.42 mole) on 1,5-dihydropentane (0.6 mole) at 0°. A fraction (66.4 g., 0.29 mole) of the dibromide, which distilled at 110–116° (23–27 mm.) and had *n*_D²⁰ 1.5093,¹⁸ dissolved in 130 ml. of ethyl acetate was stirred and refluxed for nine hours with a mixture of 55 g. (0.26 mole) of α -(2-cyclopenten-1-yl)-2-thienylacetic acid^{2,17} and 40 g. of anhydrous potassium carbonate. The cooled reaction mixture was filtered and the precipitate washed three times with ethyl acetate. The combined filtrate and washings were evaporated *in vacuo* and the residual oil fractionated. The portion of the product which distilled over the range 166–181° (0.001–0.003 mm.), *n*_D²⁰ 1.5383, was collected in 51% yield (48 g.) and redistilled at 0.008 mm. with no change in refractive index; b.p. 148–150°.

(16) M. S. Bloom, D. S. Breslow and C. R. Hauser, *ibid.*, **67**, 539 (1945).

(17) F. Leonard and L. Simet, *ibid.*, **74**, 3218 (1952).

(18) C. L. Wilson, *J. Chem. Soc.*, 48 (1945), prepared 1,5-dibromopentane by the action of a mixture of 50% hydrobromic and 50% sulfuric acids on tetrahydropyran; reported boiling point 106–108° (19 mm.).

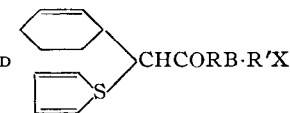
TABLE III: BASIC ALKYL ESTERS ACID ADDITION AND QUATERNARY AMMONIUM SALTS OF α -(2-CYCLOPENTEN-1-YL)-2-THIENYLACETIC ACID

Cmpd.	R	B	R'X	Bases		Recrystn.			Formula	Acid addition and quaternary salts					
				°C.	B.p., Mm.	n _D ²⁰	med. ^a	M.p., °C.		Carbon, %		Hydrogen, %		Halogen, %	
									Calcd.	Found	Calcd.	Found	Calcd.	Found	
1	OCH ₂ CH ₂	NHCH(CH ₃) ₂	HCl	121-125	0.001	1.5235	H	149-151	C ₁₆ H ₂₄ ClNO ₂ S	58.25	58.19	7.33	7.42	10.75	10.72
2	OCH ₂ CH ₂	N(CH ₃) ₂	HCl	<i>b</i>	<i>b</i>	<i>b</i>	O	105.5-106.5	C ₁₅ H ₂₂ ClNO ₂ S	57.02	57.23	7.02	7.20	11.23	11.50
3	OCH ₂ CH ₂	N(CH ₃)(C ₂ H ₅)	HBr	123-131	0.001	1.5312	J	81.5-83.5	C ₁₆ H ₂₄ BrNO ₂ S	51.34	51.08	6.46	6.28	21.35	21.40
4	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	HBr	<i>c</i>	<i>c</i>	<i>c</i>	J	100-101	C ₁₇ H ₂₆ BrNO ₂ S	52.57	52.86	6.75	7.02	20.58	20.46
5	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	(COOH) ₂	<i>c</i>	<i>c</i>	<i>c</i>	B	109.5-110.5	C ₁₉ H ₂₇ NO ₆ S	57.41	57.18	6.85	6.71
6	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	Citric acid	<i>c</i>	<i>c</i>	<i>c</i>	C	126-127	C ₂₃ H ₃₃ NO ₉ S	55.30	55.20	6.66	6.45
7	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	CH ₃ I	<i>c</i>	<i>c</i>	<i>c</i>	M	101-103	C ₁₈ H ₂₃ INO ₂ S	48.11	48.20	6.28	6.25	28.24	28.50
8	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₂ H ₅ I	<i>c</i>	<i>c</i>	<i>c</i>	L	149-141	C ₁₉ H ₃₀ INO ₂ S	49.23	49.35	6.53	6.66	27.38	27.58
9	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₆ H ₅ CH ₂ Br	<i>c</i>	<i>c</i>	<i>c</i>	O	128-130	C ₂₄ H ₃₂ BrNO ₂ S	60.23	60.31	6.74	6.76	16.70	16.33
10	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	<i>p</i> -BrCH ₂ C ₆ H ₄ CH ₂ Br	<i>c</i>	<i>c</i>	<i>c</i>	H	189-191	C ₂₄ H ₃₀ Br ₂ N ₂ O ₄ S ₂	57.38	57.50	6.65	6.89	18.19	18.23
11	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₂ H ₅ OOCCCH ₂ Br	<i>c</i>	<i>c</i>	<i>c</i>	A	134.5-135.5	C ₂₁ H ₃₂ BrNO ₄ S	53.15	53.15	6.80	7.06	16.85	16.67
12	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₄ H ₉ OOCC=CHCH ₂ Br	<i>c</i>	<i>c</i>	<i>c</i>	H	116-117	C ₂₅ H ₃₈ BrNO ₄ S	56.82	56.55	7.25	7.04	15.12	15.16
13	SCH ₂ CH ₂	N(C ₂ H ₅) ₂	HCl	132-141	0.01	1.5472	K	109.5-110.5	C ₁₇ H ₂₆ ClNO ₂ S	56.71	56.44	7.28	7.23	9.85	9.92
14	NHCH ₂ CH ₂	N(C ₂ H ₅) ₂	HCl	150-156	.001	1.5381	Q	123-124	C ₁₇ H ₂₇ ClN ₂ O ₂ S	59.55	59.86	7.94	7.64	10.34	10.32
15	OCH ₂ CH ₂	N(<i>n</i> -C ₃ H ₇)	HCl	115-126	.001	1.5106	N	88-89	C ₁₉ H ₃₀ ClNO ₂ S	61.34	61.16	8.13	7.90	9.53	9.54
16	OCH ₂ CH ₂	NC ₄ H ₉	HCl	125-130	.001	1.5346	K	110.0-110.5	C ₁₇ H ₂₄ ClNO ₂ S	59.70	60.06	7.08	6.94	10.37	10.30
17	OCH ₂ CH ₂	NC ₄ H ₉	HCl	<i>b</i>	<i>b</i>	<i>b</i>	<i>d</i>	<i>e</i>	C ₁₉ H ₂₆ ClNO ₂ S	9.96	10.13
18	OCH ₂ CH ₂	NC ₄ H ₉ O	HCl	133-142	0.001	1.5352	K	113.5-114.0	C ₁₇ H ₂₄ ClNO ₂ S	57.04	56.60	6.76	6.49	9.91	9.83
19	OCH ₂ CH ₂	N(CH ₂ C ₆ H ₅) ₂	HCl	<i>b</i>	<i>b</i>	<i>b</i>	F	114.5-116.5	C ₂₇ H ₃₀ ClNO ₂ S	69.28	69.00	6.46	6.70	7.58	7.49
20	OCH ₂ CH ₂ CH ₂	N(C ₂ H ₅) ₂	HCl	<i>b</i>	<i>b</i>	<i>b</i>	B	117.5-119.5	C ₁₈ H ₂₈ ClNO ₂ S	60.49	60.32	7.89	8.09	9.91	10.16
21	OCH ₂ CH ₂ CH ₂	NC ₄ H ₉	HCl	133-145	0.001	1.5295	K	106-107	C ₁₈ H ₂₆ ClNO ₂ S	60.74	60.66	7.36	7.13	9.96	9.93
22	OCH ₂ CH ₂ CH ₂	NC ₄ H ₉	HCl	<i>b</i>	<i>b</i>	<i>b</i>	P	142.5-145	C ₁₉ H ₂₈ ClNO ₂ S	61.69	61.94	7.63	7.51	9.59	9.56
23	OCH ₂ CH ₂ CH ₂	NC ₄ H ₉ O	HCl	<i>b</i>	<i>b</i>	<i>b</i>	F	136-137	C ₁₈ H ₂₆ ClNO ₂ S	58.13	57.92	7.05	6.80	9.54	9.67
24	OCH(CH ₃)CH ₂	N(C ₂ H ₅) ₂	HCl	113-123	0.001	1.5117	<i>e</i>	<i>e</i>	C ₁₈ H ₂₈ ClNO ₂ S	60.40	60.31	7.89	7.73	9.91	10.02
25	OCH(CH ₃)CH ₂	NC ₄ H ₉	HCl	130-136	.001	...	G	149-150	C ₁₉ H ₂₈ ClNO ₂ S	61.68	61.51	7.63	7.87	9.59	9.58
26	OCH ₂ C(CH ₃) ₂ CH ₂	N(C ₂ H ₅) ₂	HNO ₃	115-122	.005	...	F	85-86	C ₂₀ H ₃₂ N ₂ O ₆ S	58.24	57.96	7.82	7.56
27	OCH ₂ C(CH ₃) ₂ CH ₂	NC ₄ H ₉	HNO ₃	140-152	.001	...	O	107.5-108.5	C ₂₁ H ₃₂ N ₂ O ₆ S	59.40	59.67	7.60	7.53
28	OCH ₂ (CH ₂) ₃ CH ₂	N(C ₂ H ₅) ₂	HCl	146-154	.001	1.5105	P	91.5-92.0	C ₂₀ H ₃₂ ClNO ₂ S	62.22	62.27	8.36	8.56	9.19	9.24
29	OCH ₂ (CH ₂) ₃ CH ₂	NC ₄ H ₉	HCl	148-155	.001	1.5237	K	103.5-104.5	C ₂₁ H ₃₂ ClNO ₂ S	63.37	63.49	8.10	8.02	8.91	8.90
30	OCH(CH ₂) ₂	[N(C ₂ H ₅) ₂] ₂	HCl	140-148	.001	...	J	129.5-130.0	C ₂₂ H ₃₇ ClN ₂ O ₂ S	61.57	61.33	8.69	8.67	8.26	8.45
31	OCH(CH ₂) ₂	[N(<i>n</i> -C ₃ H ₇) ₂] ₂	2.HCl	150-162	.001	...	Q	166.0-166.5	C ₂₆ H ₄₆ Cl ₂ N ₂ O ₂ S	59.87	60.17	8.89	8.66	13.60	13.60
32	2-[(C ₂ H ₅) ₂ N]C ₆ H ₁₀ O- ^f		HBr	127-141	.005	1.5453	J	153-154	C ₂₁ H ₃₂ BrNO ₂ S	57.00	56.75	7.29	7.10	18.06	18.07
33	3-C ₆ H ₄ NO- ^g		HCl	132-145	.001	1.5729	O	121.0-122.5	C ₁₆ H ₁₆ ClNO ₂ S	59.71	59.56	5.02	5.03	11.02	11.05
34	1-CH ₃ -4-C ₆ H ₉ O- ^h		Citric acid	130-134	.001	1.5325	D	139.5-140.0	C ₂₃ H ₃₁ NO ₉ S	55.51	55.14	6.28	6.26
35	1-CH ₃ -4-C ₆ H ₉ O- ^h		CH ₃ I	130-134	.001	1.5325	P	148.5-150.0	C ₁₈ H ₂₆ INO ₂ S	48.32	48.54	5.86	5.88	28.37	28.40
36	1-CH ₃ -3-C ₆ H ₉ O- ⁱ		HBr	124-137	.001	1.5352	O	152-153	C ₁₇ H ₂₄ BrNO ₂ S	52.86	53.09	6.26	6.31	20.69	20.76
37	1,2,6,6-(CH ₃) ₄ -4-C ₅ H ₆ O- ^j		HBr	145-162	.001	1.5263	M	164.5-166.0	C ₂₀ H ₃₀ BrNO ₂ S	56.08	55.88	7.06	7.00	18.66	18.71
38	1,2,6,6-(CH ₃) ₄ -4-C ₅ H ₆ O- ^j		CH ₃ I	145-162	.001	1.5263	H	191-193	C ₂₁ H ₃₂ INO ₂ S	51.54	51.58	6.59	6.73	25.93	26.00

^a Code: A, acetone; B, ethyl acetate; C, ethylene dichloride; D, isopropyl alcohol; E, acetone-ethanol; F, acetone-ether; G, acetone-hexane; H, ethanol-ether; I, ethyl acetate; J, ethyl acetate-ether; K, ethyl acetate-hexane; L, ethyl acetate-methanol; M, ethyl methyl ketone-ether; N, ethylene dichloride-ether; O, isopropyl alcohol-ether; P, ethyl acetate-ethanol-ether; Q, ethyl acetate-ethanol-hexane. ^b Base converted without distillation to salt. ^c For physical data on base see F. Leonard and L. Simet, ref. 17.

^d Purified by repeated (6 times) dissolution in ethanol and precipitation with ether. ^e Extremely hygroscopic compound. Not possible to take melting point. ^f 2-Diethylamino-cyclohexoxy. ^g 3-Pyridoxy. ^h 1-Methyl-4-piperidoxy. ⁱ 1-Methyl-3-piperidoxy. ^j 1,2,6,6-Tetramethyl-4-piperidoxy.

TABLE IV

BASIC ALKYL ESTER ACID ADDITION AND QUATERNARY AMMONIUM SALTS OF α -(2-CYCLOHEXEN-1-YL)-2-THIENYLACETIC ACID

Compd.	R	B	R'	Base		n_D^{20}	Re-crystn. medium ^a	M.p., °C.	Formula	Acid addition and quaternary salts					
				°C.	Mm.					Carbon, % Calcd. Found	Hydrogen, % Calcd. Found	Halogen, % Calcd. Found			
1	-OCH ₂ CH ₂	N(C ₂ H ₅) ₂	(COOH) ₂	^b	^b	^b	H	130.5-132.0	C ₂₀ H ₂₉ NO ₆ S	58.38	58.63	7.10	7.09
2	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	CH ₃ I	^b	^b	^b	M	135.5-136.5	C ₁₉ H ₃₀ INO ₂ S	49.23	49.20	6.53	6.20	27.38	27.10
3	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₂ H ₅ Br	^b	^b	^b	F	149-150	C ₂₀ H ₃₂ BrNO ₂ S	55.80	55.53	7.49	7.56	18.56	18.73
4	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₆ H ₅ CH ₂ Br	^b	^b	^b	P	124-125	C ₂₅ H ₃₄ BrNO ₂ S	60.96	61.14	6.97	7.19	16.21	16.50
5	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	<i>p</i> -BrCH ₂ C ₆ H ₄ CH ₂ Br	^b	^b	^b	H	174.5-176.0	C ₄₄ H ₆₂ Br ₂ N ₂ O ₄ S ₂	58.27	58.13	6.89	7.14	17.62	17.31
6	OCH ₂ CH ₂	N(C ₂ H ₅) ₂	C ₂ H ₅ OCOCH ₂ Br	^b	^b	^b	E	136-137	C ₂₂ H ₃₄ BrNO ₄ S	54.10	53.95	7.02	6.76	16.36	16.58
7	SCH ₂ CH ₂	N(C ₂ H ₅) ₂	HCl	145-160	0.001	1.5522	J	130.5-132.0	C ₁₈ H ₂₈ CINOS ₂	57.80	57.74	7.55	7.73	9.48	9.38
8	NHCH ₂ CH ₂	N(C ₂ H ₅) ₂	HCl	150-165	.001	1.5430	J	135-136	C ₁₈ H ₂₉ CIN ₂ OS	60.57	60.81	8.19	8.06	9.94	9.92
9	OCH ₂ CH ₂	N(<i>n</i> -C ₄ H ₉) ₂	HCl	144-155	.001	1.5100	J	106.5-107.5	C ₂₂ H ₃₆ CIN ₂ OS	63.83	63.62	8.77	8.72	8.56	8.57
10	OCH ₂ CH ₂	NC ₄ H ₈	HBr	133-141	.001	1.5386	J	112-113	C ₁₈ H ₂₆ BrNO ₂ S	53.99	53.96	6.55	6.32	19.96	19.90
11	OCH ₂ CH ₂	NC ₄ H ₈ O	HCl	147-161	.001	1.5424	F	145-146	C ₁₈ H ₂₆ CINO ₂ S	58.13	57.92	7.05	6.91	9.54	9.51
12	OCH ₂ CH ₂ CH ₂	N(C ₂ H ₅) ₂	HCl	138-148	.001	1.5109	I	138-139	C ₁₉ H ₃₀ CINO ₂ S	61.34	61.19	8.13	7.92	9.53	9.60
13	OCH ₂ CH ₂ CH ₂	N(C ₂ H ₅) ₂	(CH ₃) ₂ SO ₄	138-148	.001	1.5109	^e	^d	C ₂₁ H ₃₅ NO ₆ S ₂	54.62	54.57	7.64	7.73
14	OCH ₂ CH ₂ CH ₂	N(<i>n</i> -C ₃ H ₇)	HBr	148-150	.001	1.5100	J	112.5-113.5	C ₂₁ H ₃₄ BrNO ₂ S	56.73	56.38	7.71	7.71	17.97	17.90
15	OCH ₂ CH ₂ CH ₂	NC ₄ H ₈	HCl	135-146	.001	1.5321	I	128-129	C ₁₉ H ₂₈ CINO ₂ S	61.68	61.46	7.63	7.57	9.58	9.60
16	OCH ₂ CH ₂ CH ₂	NC ₅ H ₁₀	HCl	145-159	.001	1.5325	N	168-169	C ₂₀ H ₃₀ CINO ₂ S	62.54	62.51	7.89	7.59	9.24	9.48
17	OCH ₂ CH ₂ CH ₂	NC ₄ H ₈ O	HCl	140-157	.001	1.5355	P	149-150	C ₁₉ H ₂₈ CINO ₂ S	59.13	59.18	7.31	7.55	9.19	9.37
18	OCH(CH ₃)CH ₂	N(C ₂ H ₅) ₂	HBr	134-135	.001	1.5173	F	149-151	C ₁₉ H ₃₀ BrNO ₂ S	54.80	54.86	7.26	7.21	19.20	19.20
19	OCH(CH ₃)CH ₂	NC ₅ H ₁₀	HCl	148-160	.001	1.5307	J	147-148	C ₂₀ H ₃₀ CINO ₂ S	62.56	62.43	7.88	7.75	9.24	9.28
20	OCH ₂ C(CH ₃) ₂ CH ₂	N(C ₂ H ₅) ₂	H ₂ SO ₄	135-150	.001	1.5126	O	129.5-130.5	C ₂₁ H ₃₆ NO ₆ S ₂	54.64	54.47	7.64	7.65
21	OCH ₂ (CH ₂) ₃ CH ₂	N(C ₂ H ₅) ₂	HBr	150-175	.001	1.5146	J	102-103	C ₂₁ H ₃₄ BrNO ₂ S	56.74	56.52	7.71	7.58	17.98	17.92
22	OCH ₂ (CH ₂) ₃ CH ₂	NC ₅ H ₁₀	HCl	^e	^e	^e	J	117.5-119.0	C ₂₃ H ₃₄ CINO ₂ S	64.13	63.95	8.32	8.06	8.61	8.79
23	OCH(CH ₂) ₂	[N(C ₂ H ₅) ₂] ₂	HCl	140-149	0.001	1.5098	J	124.5-125.5	C ₂₃ H ₃₉ CIN ₂ O ₂ S	62.34	62.32	8.87	8.62	8.00	8.18
24	1-CH ₃ -4-C ₆ H ₅ O- ^f		HCl	144-156	.003	1.5437	N	175-176	C ₁₈ H ₂₆ CINO ₂ S	60.74	61.04	7.37	7.28	9.96	9.91
25	1-CH ₃ -4-C ₆ H ₅ O- ^f		CH ₃ I	144-156	.003	1.5437	F	140-141	C ₁₉ H ₂₈ INO ₂ S	49.46	49.37	6.12	6.33	27.51	27.30
26	1-CH ₃ -3-C ₆ H ₅ O- ^g		HBr	141-144	.001	1.5411	H	185.5-186.0	C ₁₈ H ₂₆ BrNO ₂ S	53.99	54.26	6.55	6.25	19.96	19.96
27	1,2,6,6-(CH ₃) ₄ -4-C ₆ H ₅ O- ^h		HBr	155-190	.005	1.5462	J	160-161	C ₂₁ H ₃₂ BrNO ₂ S	57.00	57.12	7.29	7.07	18.07	18.29
28	1,2,6,6-(CH ₃) ₄ -4-C ₆ H ₅ O- ^h		CH ₃ I	155-190	.005	1.5462	H	184.5-186.0	C ₂₂ H ₃₄ INO ₂ S	52.49	52.52	6.81	6.74	25.21	25.32

^a For code see note *a* to Table III. ^b For physical data on base see F. Leonard and L. Simet, ref. 17. ^c Purified by repeated dissolution in ethyl acetate and precipitated with ether (six times). ^d Extremely hygroscopic compound. Not possible to take melting point. ^e Base converted without distillation to salt. ^f 1-Methyl-4-piperidoxy. ^g 1-Methyl-3-piperidoxy. ^h 1,2,6,6-Tetramethyl-4-piperidoxy.

Anal. Calcd. for $C_{16}H_{21}BrO_2S$: C, 53.77; H, 5.91. Found: C, 54.67; H, 5.85.

Since the only "carbon-elevating" impurities which possibly could have been present in the ester were either the starting acid or 1,5-bis-5-[α -(2-cyclopenten-1-yl)-2-thienylacetoxy]-pentane, substances which it was believed could be separated easily from the product of the subsequent amination reaction, it was believed that the analysis was satisfactory and this bromoester therefore was aminated with no further purification.

5-Bromopentyl α -(2-Cyclohexen-1-yl)-2-thienylacetate.—Prepared in the same manner as the homologous 2-cyclopenten-1-yl ester from 44.5 g. (0.20 mole) of α -(2-cyclohexen-1-yl)-2-thienylacetic acid, 69.0 g. (0.30 mole) of 1,5-dibromopentane and 30.4 g. (0.22 mole) of anhydrous potassium carbonate. Fractionation at 0.001 mm. gave 50 g. of ester, b.p. 137–144°, n_D^{20} 1.5430. The entire batch was redistilled with no change in refractive index, b.p. 142–143° (0.001 mm.).

Anal. Calcd. for $C_{17}H_{23}BrO_2S$: C, 54.98; H, 6.24. Found: C, 55.12; H, 6.07.

Esters of the basic propyl chlorides were obtained when the chlorides were stirred with either α -(2-cyclopenten-1-yl)-2-thienylacetic or α -(2-cyclohexen-1-yl)-2-thienylacetic acid in ethyl acetate solution in the presence of anhydrous potassium carbonate in the manner described before.¹⁷ The preparation of 2-(4'-morpholinyl)-ethyl α -(2-cyclohexen-1-yl)-2-thienylacetate hydrochloride is typical of the technique employed for the interaction of the acid chlorides with the various basic alkanols, 2-diethylaminoethyl mercaptan and N,N-diethylethylenediamine.

2-(4'-Morpholinyl)-ethyl α -(2-Cyclohexen-1-yl)-2-thienylacetate Hydrochloride.—A solution of 6.6 g. (0.05 mole) of 2-(4'-morpholinyl)-ethanol in 35 ml. of dry benzene was added rapidly with stirring to a solution of 12 g. (0.05 mole) of α -(2-cyclohexen-1-yl)-2-thienylacetyl chloride in 65 ml. of dry benzene. The mixture was refluxed for 12 hours, let cool and basified with 40% sodium hydroxide. The benzene layer was separated and the aqueous alkaline layer extracted with ether. The benzene layer and the ether extracts were combined and dried over anhydrous potassium carbonate. Removal of the ether and distillation of the residual oil gave 11.5 g. (69%) of basic ester, b.p. 147–161° (0.001 mm.), n_D^{20} 1.5424, which was dissolved in 50 ml. of ethyl acetate and treated with 7.0 ml. of 4.92 N ethanolic hydrochloric acid. Ether (100 ml.) was added to the acidified solution (to first appearance of turbidity) and the solution placed in the refrigerator. The ester hydrochloride was filtered off, washed with an ether-ethyl acetate mixture and ether, dried (yield 10.1 g., m.p. 144–145°) and recrystallized from an acetone-ether mixture; yield 8.1 g., m.p. 145–146°.

The aminolysis of 5-bromopentyl α -(2-cyclopenten-1-yl)-2-thienylacetate with piperidine illustrates the technique employed for conversion of the various ω -bromoesters to basic alkyl esters.

5-(1'-Piperidyl)-pentyl α -(2-Cyclopenten-1-yl)-thienylacetate Hydrochloride.—Piperidine (8.5 g., 0.10 mole) was added dropwise to a stirred solution of 17.9 g. (0.05 mole) of

5-bromopentyl α -(2-cyclopenten-1-yl)-2-thienylacetate in 50 ml. of dry benzene. Precipitation of piperidine hydrobromide started almost at once. The mixture was stirred and refluxed for nine hours, treated with water and the benzene layer separated. The benzene layer was made acidic with 40 ml. of 1:4 concentrated hydrochloric acid, the aqueous layer separated and extracted with ether. The acidic layer was basified, extracted three times with ether, the extracts combined and dried over potassium carbonate. Fractionation of the ethereal solution gave 13.3 g. (74%) of basic ester, b.p. 148–155° (0.001 mm.), n_D^{20} 1.5237, which was dissolved in ethyl acetate and converted to a hydrochloric acid addition salt. The salt was isolated in the manner described above for the morpholinylethyl ester; yield 12.8 g., m.p. 99–102°. Three recrystallizations from an ethyl acetate-hexane mixture gave 11.1 g. of analytically pure 5-(1'-piperidyl)-pentyl α -(2-cyclopenten-1-yl)-2-thienylacetate hydrochloride, m.p. 103.5–104.5°.

Quaternization of the basic esters was effected in the manner described for the preparation of 4-[α -(2-cyclopenten-1-yl)-2-thienylacetoxy]-1,1,2,6-pentamethylpiperidinium iodide and 2-[α -(2-cyclohexen-1-yl)-2-thienylacetoxy]-ethyl-dimethylethylenammonium bromide.

4-[α -(2-Cyclopenten-1-yl)-2-thienylacetoxy]-1,1,2,6-pentamethylpiperidinium Iodide.—A solution of 7.0 g. (0.02 mole) of 1,2,2,6-tetramethyl-4-piperidyl α -(2-cyclopenten-1-yl)-2-thienylacetate and 3.3 g. (0.023 mole) of methyl iodide in 70 ml. of acetone was refluxed for four hours, treated with an additional portion of 0.8 g. of methyl iodide and let stand overnight. The quaternary salt crystallized after dilution with absolute ether (60 ml.) and standing in the refrigerator; yield 5.4 g., m.p. 191–194°. Recrystallized from a mixture of ethanol and ether the salt melted at 191–193°.

2-[α -(2-Cyclohexen-1-yl)-2-thienylacetoxy]-ethyl-dimethylethylenammonium Bromide.—A mixture of 9.7 g. (0.3 mole) of 2-diethylaminoethyl α -(2-cyclohexen-1-yl)-2-thienylacetate,^{2,17} 3.7 g. (0.33 mole) of ethyl bromide and 50 ml. of dry acetone was heated in a pressure bottle on a steam-bath for 24 hours. On cooling, the reaction product crystallized. The precipitate was removed by filtration washed with a 1:1 mixture of acetone and ether and dried. Two recrystallizations from an acetone-ether mixture gave 8.3 g. of 2-[α -(2-cyclohexen-1-yl)-2-thienylacetoxy]-ethyl-dimethylethylenammonium bromide.

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