ester was hydrolyzed in a number of sealed tubes by treatment with 0.08 *N* potassium hydroxide in diethylene glycol at 100°. Examined thus, the rate of hydrolysis was about 10% less than that of authentic methyl 1-methylcyclohexanecarboxylate and about $^1/_{20}$ of the rate of hydrolysis of methyl benzoate or authentic methyl cyclohexylacetate. There was no indication of a change in rate of hydrolysis corresponding to the presence of mixed esters.

When bromomethyl cyclohexyl ketone was treated as in A above, 25% of IXb and 17% of Xb were isolated. There was no IVb.

The Reaction by the Method of Mousseron. (B).—A solution of 6.0 g. (0.037 mole) of the chloro ketone in 30 cc. of absolute methanol was added with stirring at 0° to a solution of 2.15 g. (0.091 mole) of sodium in 30 cc. of absolute methanol. The methanol was removed by distillation *in vacuo* at 50–60° and the residue was extracted with 25 cc. of water and 25 cc. of petroleum ether. The aqueous layer yielded cyclohexanecarboxylic acid (identified by its infrared spectra, 0.0079 mole, 21%) and 4.88 g. of silver chloride or 91% of the chloro ketone chloride. The organic extract gave on distillation 0.85 g. of methyl 1-methylcyclohexanecarboxylate (IVa) (identified by infrared spectra and rate of hydrolysis, b.p. 60–62° (20 mm.) 15%), 1.60 g. of the dimethyl ketal IXa (b.p. 120° (20 mm.) 23%) and 0.96 g. of the methyl dimer Xa (b.p. 180° (3.5 mm.), 16%).

Reaction of the Chloroketone under Anhydrous Conditions. (C).—A mixture of 50 cc. of methanol and 5 cc. of benzene was placed in a glass tube and warmed until about one-fourth had distilled out. To this dry methanol was added 2.5 g. of sodium hydride. When solution was complete, a solution of 7.05 g. of the chloro ketone (0.044 mole) in 30 cc. of petroleum ether was added. The tube was sealed and kept at 4° for 45 hours. The tube was opened and the excess base was neutralized by the addition of 10 g. of citric acid in 40 cc. of methanol. The solution was concentrated at the water pump and partitioned between water and ether. The water layer gave a precipitate of 5.11 g. of silver chloride or 81% of the theoretical. Extraction of the ether with sodium carbonate solution gave 0.00042 mole of ether soluble acid which could not be further identified. Distillation of the ether solution gave 2.61 g. of ester IVa (38%, b.p. 58° (15 mm.)), 0.34 g. ketal IXa (b.p. 95–100° (15 mm.), 4%) and 1.53 g. of dimer Xa (b.p. 170° (2 mm.), 20%).

When hydroxymethyl cyclohexyl ketone was treated as in B above, 0.65 g. of a white substance precipitated from solution. From this precipitate, there was isolated 0.28 g. of pure cyclohexanecarboxylic acid, m.p. 29–31°, amide m.p. and mixed m.p. with authentic XI amide 185–187° (reported for cyclohexanecarboxamide, 186°,[9] reported for cyclohexylacetamide 171–172°[10]).

When the hydroxy ketone was treated with sodium methoxide under anhydrous conditions as in C above (but at 100° for 45 hours) there was obtained only a 7% yield of ether soluble acid which was not pure enough to identify with certainty.

The infrared absorption maxima of authentic cyclohexanecarboxylic acid and of the XI isolated in B above are 1256, 1212, 1295, 1307, 935, 892, 1181, 1134, 1143, 1105 and 1017 cm.$^{-1}$ in order of decreasing prominence. The maxima for authentic cyclohexylacetic acid are 1292, 939, 1191, 1232, 1250, 1262, 903, 1330, 1169, 1117, 1069, 1080, 1142, 1032 and 1052 cm.$^{-1}$. The maxima for methyl 1-methylcyclohexanecarboxylate are 1207, 1155, 1132, 1108, 1237, 1308, 1187, 1273, 993, 1263, 1045, 1022, 977, 824, 762, 962 and 771 cm.$^{-1}$. The maxima for methyl cyclohexylacetate are 1162, 1284, 1233, 1220, 1187, 1114, 1256, 1005, 1015, 1311, 1079, 897, 937, 840, 828 and 960 cm.$^{-1}$.

(9) W. Markownikoff, *Ber.*, **25**, 3355 (1892).

(10) J. Gutt, *ibid.*, **40**, 2067 (1907).

BOSTON, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF ENTOMOLOGY, UNIVERSITY OF CALIFORNIA CITRUS EXPERIMENT STATION]

Insecticidal Action of Heterocyclic Analogs of 2,2,2-Trichloro-1-(*p*-chlorophenyl)-ethanol[1]

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Compounds of the type R–CH_2OH·CCl_3, when R is phenyl, *p*-chlorophenyl, *p*-tolyl, thienyl, 5-chlorothienyl, furyl, pyrryl, or N-methyl pyrryl, were prepared and tested as insecticides against four species of insects. From the toxicity data against mosquito larvae and greenhouse thrips it would appear that the pseudo-aromatic heterocyclic rings function as spacers with polarizable characteristics.

The over-all mechanism of insecticidal action of DDT, 2,2,2-trichloro-1,1-bis-(*p*-chlorophenyl)-ethane (I) has not yet been ascertained even for a single species of insect, and the effect on insect toxicity of changing the ring substituents is still under study. Few investigations have been concerned with the effect of interchanging heterocyclic and aromatic rings. Several reports have appeared on the insecticidal properties of thiophene analogs of DDT.[2–5] These revealed that thiophene substitution for the benzene ring was accompanied by a decrease in toxicity upon most of the test insects. However, the mode of action of 2,2,2-trichloro-1,1-bis-(5-chlorothiophene-2)-ethane was shown to resemble qualitatively that for DDT and appeared to affect the same locus in the insect nervous system.[5] Compounds of the 2,2,2-trichloro-1-aryl-ethanol type are synthetic precursors of the DDT-type molecule, yet they exhibit narrow-spectrum insecticidal properties; they are thus ideally suited for activity–structure studies with certain insects.

The compounds in Table I were synthesized. These compounds and their acetates were assayed against mosquito larvae (*Culex quinquefasciatus* Say), greenhouse thrips (*Heliothrips haemorrhoidalis* Bouché), the house fly (*Musca domestica* L.), and citrus red mite (*Paratetranychus citri* McG.).

The preparation of the 2,2,2-trichloro-1-aryl type ethanols using chloral and aromatic Grignard reagents has been reported.[6] Recently the synthesis

(1) Paper No. 771, University of California Citrus Experiment Station, Riverside, California. Presented before the Division of Agricultural and Food Chemistry, 123rd Meeting, Am. Chem. Soc., Los Angeles, 1953.

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TABLE I

PHYSICAL PROPERTIES OF 2,2,2-TRICHLORO-1-R-ETHANOLS

No.	R	M.p., °C.	B.p. °C.	Mm.	Acetate M.p., °C.
II	4-ClC_6H_4	47–48	128–132	1	124–125
III	C_6H_5	36–37	110–114	5	87–88
IV	4-$CH_3C_6H_4$	62–63	128–131	5	107–108
V	C_4H_3S	28.5–29.5	128–129	4	61.0–61.6
VI	5-ClC_4H_2S	46.5–47.5	142–143	1	90.5–91.5
VII	C_4H_3O	33–34	.....	...	B.p. 135 (23 mm.)
VIII	C_4H_4N	*ca.* 5 dec.	.....	...	69.8–70.8 dec.
IX	N-$CH_3C_4H_3N$	66.5–67.2 dec.	.....	...	63.0–64.0 dec.

of VII was accomplished by condensation of chloral with furan in the presence of glacial acetic acid and molecular quantities of anhydrous zinc chloride.[7] The thienyl derivatives reported in this work (V and VI) were prepared from 2-thiophenemagnesium bromide or 5-chlorothiophene-2-magnesium bromide and freshly distilled chloral. These reactions proceeded normally and provided 56 and 50.5% yields, respectively, of the carbinols that were purified by distillation at reduced pressure and crystallization from petroleum ether. The purified compounds were stable and crystallized as colorless fine needles. The acetates were prepared by refluxing with acetic anhydride-catalyzed by trifluoroacetic acid.[8]

VIII and IX were prepared as with furan analogs, but because of the instability of these pyrroles, modifications were necessary: molecular quantities of anhydrous zinc chloride were dissolved in anhydrous ether before addition to the reaction mixture of the parent pyrrole and chloral, with reaction temperature below 10°; solutions of the carbinols were stored at 0° and solvents removed at reduced pressures and temperatures to avoid extensive decomposition. The acetates were prepared by the Schotten–Baumann procedure, with a pyridine solution of the carbinol reacting with acetic anhydride at room temperature for several days.[6] VIII was unstable at temperatures above its melting point (approximately 5°), but its acetate was crystallized from petroleum ether as colorless prisms. When VIII acetate was isolated it decomposed slowly and spontaneously to hydrogen chloride and a deep purple polymer. Both IX and its acetate crystallized from petroleum ether and decomposed in a manner analogous to VIII acetate.

The insect assays were made by standard methods as previously described.[9,10] Results are given in Table II. None of the compounds were toxic to adult female house flies when applied topically at 500 micrograms per gram of body weight. Compound II was quite effective against the citrus red mite. It appears from the toxicity data for the greenhouse thrips and the mosquito larvae that heterocyclic and aromatic rings can be interchanged in this series of compounds without appreciable change in effectiveness. The unsaturated ring function in such compounds may therefore be essentially that of a spacer with polarizable characteristics.

(7) J. R. Willard and C. S. Hamilton, THIS JOURNAL, **73**, 4806 (1951).
(8) P. W. Morgan, *Ind. Eng. Chem.*, **43**, 2575 (1951).
(9) R. L. Metcalf, *J. Econ. Ent.*, **41**, 875 (1948).
(10) R. B. March and R. L. Metcalf, *Bull. Calif. State Dept. Agr.*, **38**, 93 (1949).

TABLE II, $R_1—\underset{H}{\overset{R_2}{\overset{|}{C}}}(O)—CCl_3$

	R_1	R_2	Thrips LD_{50}	Mosquito larvae LD_{50}	Mites % mortality at 0.25% concn.
II	4-ClC_6H_4	H	9×10^{-1}	8×10^{-3}	64
	4-ClC_6H_4	Acetate	1	9×10^{-4}	0
III	C_6H_5	H	.....	7×10^{-3}	..
	C_6H_5	Acetate	3×10^{-1}	3×10^{-2}	3
IV	4-$CH_3C_6H_4$	H	6×10^{-1}	8×10^{-3}	0
	4-$CH_3C_6H_4$	Acetate	.....	8×10^{-4}	..
V	C_4H_3S	H	>1	9×10^{-3}	0
	C_4H_3S	Acetate	6×10^{-1}	8×10^{-3}	0
VI	5-ClC_4H_2S	H	>1	7×10^{-3}	0
	5-ClC_4H_2S	Acetate	>1	6×10^{-2}	0
VII	C_4H_3O	H	1	9×10^{-3}	0
	C_4H_3O	Acetate	1	8×10^{-3}	0
VIII	C_4H_4N	H	.....	8×10^{-3}	..
	C_4H_4N	Acetate	.....	8×10^{-2}	..
IX	N-$CH_3C_4H_3N$	H	9×10^{-1}	6×10^{-2}	0
	N-$CH_3C_4H_3N$	Acetate	7×10^{-1}	8×10^{-3}	12

Experimental[11]

2,2,2-Trichloro-1-(2-thiophene)-ethanol (V).—To the Grignard reagent from 50.5 g. (0.31 mole) of 2-bromothiophene in 250 ml. of anhydrous ether and 7.9 g. (0.325 mole) of magnesium was added 45 g. (0.305 mole) of freshly distilled chloral. Immediately after the chloral addition, the complex was decomposed with 30 g. (0.57 mole) of ammonium chloride in 1 l. of ice and water. The resulting red ether solution was separated, washed once with 10% sulfuric acid solution and three times with water, and dried over sodium sulfate. After removal of the ether, the residue was distilled to give 55 g. of an oil, b.p. 128–129° (4 mm.), which slowly crystallized. Recrystallization from petroleum ether (b.p. 60–80°) yielded 40 g. (56%) of colorless fibrous needles, m.p. 28.5–29.5°.

Anal. Calcd. for $C_6H_5OSCl_3$: C, 31.12; H, 2.18. Found: C, 31.47; H, 2.40.

2,2,2-Trichloro-1-(2-thiophene)-ethyl Acetate.—A solution of 5 g. of V, 10 g. of acetic anhydride and 0.5 ml. of trifluoroacetic acid was refluxed for 3.5 hours, then poured into 500 ml. of ice and water. The resulting solid was separated and crystallized from petroleum ether (b.p. 60–80°) to give 5.5 g. (93%) of colorless platelets, m.p. 61.0–61.6°.

Anal. Calcd. for $C_8H_7O_2SCl_3$: C, 35.12; H, 2.58. Found: C, 35.34; H, 2.73.

2,2,2-Trichloro-1-(5-chlorothiophene-2)-ethanol (VI).—Using the procedure for V, 50 g. (0.253 mole) of 5-chloro-2-bromothiophene yielded 47 g. of an oil, b.p. 142–143° (1 mm.), which crystallized on standing. Recrystallization from petroleum ether (b.p. 30–60°) gave 34 g. (50.5%) of colorless needles, m.p. 46.5–47.5°.

Anal. Calcd. for $C_6H_4OSCl_4$: C, 27.09; H, 1.52. Found: C, 27.33; H, 1.79.

2,2,2-Trichloro-1-(5-chlorothiophene-2)-ethyl Acetate.—Using the procedure for the acetate of V, 5 g. of VI gave 5.6 g. (95%) of colorless prisms, m.p. 90.5–91.5°.

Anal. Calcd. for $C_8H_6O_2SCl_4$: C, 31.19; H, 1.96. Found: C, 31.43; H, 1.88.

2,2,2-Trichloro-1-(2-pyrryl)-ethanol (VIII).—To a solution of 26.8 g. (0.4 mole) of pyrrole in 300 ml. of anhydrous ether at 0° was added 29.5 g. (0.2 mole) of freshly distilled chloral. To this was added with cooling a solution of 27.2 g. (0.2 mole) of anhydrous zinc chloride in 700 ml. of anhydrous ether at a rate to maintain the temperature below 0°. Immediately after the addition of the zinc chloride solution, the resulting dark amber solution was poured into an equal volume of ice water; then the ether solution was separated and washed twice with water, once with 5% sodium bicarbonate solution, and twice more with water. It

(11) All melting points corrected. Analyses performed by G. Swinehart, Kerckhoff Laboratories of Biology, California Institute of Technology, Pasadena, California.

was then treated with decolorizing carbon and with attapulgus clay. Ether was removed at reduced pressure, keeping the temperature below 20°. The 34.5 g. (40%) of resulting oil VIII was rapidly colored by decomposition and could not be recrystallized.

2,2,2-Trichloro-1-(2-pyrryl)-ethyl Acetate.—Five grams of VIII was dissolved in 50 ml. of pyridine and 50 ml. of acetic anhydride. After three days the solution was poured into 1 l. of ice-water and the solid separated. Recrystallization from petroleum ether (b.p. 60–80°) yielded 4.5 g. (75%) of colorless needles, m.p. 69.8–70.8° dec.

Anal. Calcd. for $C_8H_8O_2NCl_3$: C, 37.46; H, 3.14. Found: C, 36.96; H, 3.07.

2,2,2-Trichloro-1-(N-methylpyrryl-2)-ethanol (IX).—As in the procedure used for VIII, 32.4 g. (0.4 mole) of N-methylpyrrole gave 40 g. of dark purple oil. This was dissolved in excess hot petroleum ether (b.p. 60–80°), treated with decolorizing carbon and attapulgus clay, then cooled by dry ice for 24 hours, then at 0° for 24 hours to yield 24 g. (26.5%) of colorless prisms, m.p. 58–60° dec. Two crystallizations from petroleum ether (b.p. 60–80°) raised the m.p. to 66.5–67.2° dec.

Anal. Calcd. for $C_7H_8ONCl_3$: C, 36.79; H, 3.53. Found: C, 36.99; H, 3.16.

2,2,2-Trichloro-1-(N-methylpyrryl-2)-ethyl Acetate.—By the procedure used for the acetate of VIII, 10 g. of the above carbinol yielded 8.5 g. (72%) of colorless prisms from petroleum ether (b.p. 30–60°), m.p. 63.0–64.0° dec.

Anal. Calcd. for $C_9H_{10}O_2NCl_3$: C, 39.95; H, 3.73. Found: C, 39.58; H, 4.01.

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[CONTRIBUTION FROM HICKRILL CHEMICAL RESEARCH LABORATORY]

On the Reported Rearrangement of 2,4,7-Tribromotropone to 3,5-Dibromobenzamide

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The interesting report of Nozoe, *et al.*, that 2,4,7-tribromotropone is rearranged by ammonia to a mixture of 2,5- and 3,5-dibromobenzamide is incorrect. It is shown by infrared analysis that the mixture contains no appreciable amount of 3,5-dibromobenzamide and consists of the expected 2,4- and 2,5-dibromobenzamide in the approximate ratio of 1:2.

The aromatizing rearrangements of tropolone methyl ethers with methoxide ion and of 2-halotropones with hydroxide ion have been used by many workers in the field as the key reactions for determining the position of substituents in the tropolone ring system. It is therefore a matter for concern, particularly to us who have relied extensively on the rearrangement of halotropones,[2] when Nozoe, *et al.*,[3] asserts that 2,4,7-tribromotropone rearranges in methanolic ammonia to **3,5-dibromobenzamide**, that is, with simultaneous rearrangement of a bromine atom. That "this is a remarkable phenomenon that should be well-remembered[3]" seemed worthy of independent experimental investigation.

Dauben and Ringold[4] have communicated the preparation of 2,4,7-tribromotropone (I) by the reaction of bromine and 2-cyclohepten-1-one and have assigned its structure by isolation of 2,5-dibromobenzoic acid on treatment of I with ethanolic hydroxide ion. Nozoe, *et al.*,[5] have prepared I by the direct bromination of cycloheptanone and have confirmed its structure by rearrangement with hydroxide ion to 2,4- and 2,5-dibromobenzoic acids.[3] Unable to reproduce this latter preparation, presumably because of the inadequacy of the published experimental details, we have found that cycloheptanone can be converted quantitatively to a tribromo derivative[6] which when treated with bromine under more drastic conditions gives I in 41% yield.

The rearrangement of I was effected both in methanolic ammonia and liquid ammonia according to Nozoe, *et al.*[3] We likewise found the task of separation by crystallization difficult, although 2,5-dibromobenzamide could be isolated in pure form. The unpurified amides were hydrolyzed both with sulfuric acid according to Nozoe, *et al.*,[3] and with alkali, the product in both cases having identical infrared spectra. The unpurified mixture of dibromo acids was converted to the mixture of methyl esters with diazomethane. Comparison of the infrared spectrum of this mixture with the spectra of the pure methyl esters of 2,4- (II), 2,5- (III) and 3,5- (IV) dibromobenzoic acids (Table I) shows that both II and III are present and that IV is not detectable, even though the differences between the spectra are very favorable for the detection of IV. A small amount of unidentified material can be observed however. Either by calculation using the six wave numbers in bold-face type in Table I or by comparison with the infrared spectra of synthetic mixtures of II and III (40/60, 34/66 and 30/70), it appears that the mixture consists of about 1 part II and 2 parts III.

Contrary to the report of Nozoe, *et al.*,[3] the rearrangement of 2,4,7-tribromotropone with ammonia does not give 3,5-dibromobenzamide but

(1) Sterling Chemistry Laboratory, Yale University, New Haven, Conn.

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(6) According to O. Wallach, *Ann.*, **418**, 36 (1919), cycloheptanone is converted to a dibromo derivative, m.p. 70–72°, in hot glacial acetic acid, whereas according to Nozoe, *et al.*,[5] in ice-cooled acetic acid it is converted to a tetrabromo derivative, m.p. 78°. It is under conditions identical with Nozoe's within the limits of the published description, that we obtain a tribromocycloheptanone, m.p. 71–72°.