TABLE I

DIALKYLAMINOETHYL ARYLOXYACETATE HYDROCHLORIDES

$ROCH_2COOCH_2CH_2NR'_2 \cdot HCl$

R	R'	Yield, % Crude	Yield, % Purified	M.p., °C. (uncor.)	Formula	Chlorine, % Calcd.[a]	Chlorine, % Found[b]
$2,4\text{-}Cl_2C_6H_3$	CH_3	66	43[c]	169–170	$C_{12}H_{16}O_3NCl_3$	10.78	10.59
$2,4\text{-}Cl_2C_6H_3$	C_2H_5	81	26[c]	140–141	$C_{14}H_{20}O_3NCl_3$	9.94	9.68
$2,4,5\text{-}Cl_3C_6H_2$	CH_3	64	53[d]	175–176.5	$C_{12}H_{15}O_3NCl_4$	9.76	9.76
$2,4,5\text{-}Cl_3C_6H_2$	C_2H_5	73	43[d,e]	157–159	$C_{14}H_{19}O_3NCl_4$	9.07	8.92

[a] Ionizable chlorine. [b] Analysis by R. L. Kersey, Jr. [c] Recrystallized from acetone. [d] Recrystallized from acetone and ether. [e] Prepared as the free base by M. S. Newman, William Fones and Mary Renoll.[8]

TABLE II

2-METHYL-2-ALKYLAMINOPROPYL ARYLOXYACETATE HYDROCHLORIDES

$ROCH_2COOCH_2C(CH_3)_2NHR' \cdot HCl$

R	R'	Yield, % Purified	M.p., °C. (uncor.)	Formula	Chlorine, % Calcd.	Chlorine, % Found[a]
C_6H_5	$n\text{-}C_3H_7$	27	130–131	$C_{15}H_{24}O_3NCl$	11.75	11.52
C_6H_5	$n\text{-}C_4H_9$	30	130.5–131.5	$C_{16}H_{26}O_3NCl$	11.23	10.81
C_6H_5	$n\text{-}C_5H_{11}$	26	146–147	$C_{17}H_{28}O_3NCl$	10.75	10.55
$\beta\text{-}C_{10}H_7$	$n\text{-}C_4H_9$	22	160–162	$C_{20}H_{28}O_3NCl$	9.69	9.49
$\beta\text{-}C_{10}H_7$	$n\text{-}C_5H_{11}$	19	155–157	$C_{21}H_{30}O_3NCl$	9.33	9.17
$2,4\text{-}Cl_2C_6H_3$	$n\text{-}C_5H_{11}$		129–130	$C_{17}H_{26}O_3NCl_3$	8.90[b]	8.94
$2,4,5\text{-}Cl_3C_6H_2$	$n\text{-}C_5H_{11}$[c]	25	153–154	$C_{17}H_{25}O_3NCl_4$	8.18[b]	8.17
$2,4,5\text{-}Cl_3C_6H_2$	$n\text{-}C_6H_{13}$[c]		148–149	$C_{18}H_{27}O_3NCl_4$	7.93[b]	7.49

[a] Analyses by R. L. Kersey, Jr., and W. E. Reid, Jr. [b] Ionizable chlorine. [c] Acknowledgment is made to Gildo Suffredini for his assistance in the preparation of this compound.

and some of the oils will be tested[8] as plant growth-regulating substances.

The acids used in this work were purchased from Eastman Kodak Co. or were made from the corresponding potassium phenolate and potassium chloroacetate.[9,10] Potassium β-naphthoxyacetate and potassium 2,4,5-trichlorophenoxyacetate were recrystallized from water and the free acids from glacial acetic acid.

Phenoxyacetyl chloride was purchased from Eastman Kodak Co. The other acid chlorides were prepared by the reaction of the acid with excess thionyl chloride.[11] In the preparation of β-naphthoxyacetyl chloride and 2,4-dichlorophenoxyacetyl chloride, three molar quantities of thionyl chloride were used and in the preparation of 2,4,5-trichlorophenoxyacetyl chloride, six molar quantities were used. In each case the reaction mixture was refluxed gently until it became liquid. This usually required 1 to 1.5 hours. In all cases the thionyl chloride was distilled off on a water-bath, at atmospheric pressure and under a vacuum and after the addition of toluene, under a vacuum. The acid chlorides thus prepared were used without further purification.

β-Dimethylaminoethyl 2,4-Dichlorophenoxyacetate Hydrochloride.—A mixture of 0.1 mole each of 2,4-dichlorophenoxyacetyl chloride and β-dimethylaminoethanol, in 30 ml. of chloroform, was refluxed gently for 5 hours. The reaction mixture was poured slowly into 800 ml. of hot 0.25 *N* sodium hydroxide solution and the chloroform was evaporated off. An oil separated. This oil was dissolved in isopropyl ether and the solution was saturated with dry hydrogen chloride. The crystalline precipitate of crude dimethylaminoethyl 2,4-dichlorophenoxyacetate hydrochloride was filtered with suction; yield 21.8 g. On recrystallization from anhydrous acetone the yield was 14.2 g., 43%, m.p. 169–170°.

2-Methyl-2-*n*-amylaminopropyl 2,4,5-Trichlorophenoxyacetate Hydrochloride. $2,4,5\text{-}Cl_3C_6H_2OCH_2COOCH_2C(CH_3)_2NHC_5H_{11} \cdot HCl$.—To 0.1 mole of 2-methyl-2-*n*-amylamino-1-propanol hydrochloride, in 25 ml. of chloroform, was added slowly a solution of 0.1 mole of 2,4,5-trichlorophenoxyacetyl chloride, in 25 ml. of chloroform. The reaction mixture was refluxed gently for 5 hours and was poured into 500 ml. of boiling water. The chloroform was evaporated off and excess alkali was added. The aqueous solution was decanted from the oily lower layer. The oily product was dissolved in 100 ml. of ether. The ethereal solution was filtered and stirred with 50 ml. of *N* hydrochloric acid. A heavy white crystalline precipitate of 2-methyl-2-*n*-amylaminopropyl 2,4,5-trichlorophenoxyacetate hydrochloride was formed. The product was filtered with suction, washed with ether and air-dried; yield 10.7 g. (24%), m.p. 152–154°. On recrystallization from absolute ethanol and isopropyl ether the m.p. was 153–154°.

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(8) Tests will be carried out by Dr. R. F. Smart, of the Department of Biology, University of Richmond.

(9) F. Spitzer, *Ber.*, **34**, 3192 (1901).

(10) R. Pokorny, THIS JOURNAL, **63**, 1768 (1941).

(11) V. H. Freed, *ibid.*, **68**, 2112 (1946).

Cyclopropanes. VIII.[1] Cyclopropanecarboxaldehyde

BY LEE IRVIN SMITH AND EDGAR R. ROGIER

In connection with the work described in a previous paper[2] considerable amounts of cyclopropanecarboxaldehyde were required. Catalytic conversion of tetrahydrofurfuryl alcohol to dihydrofuran, and thermal rearrangement of the latter to cyclopropanecarboxaldehyde, as described by Wilson,[3] proved impractical in our hands for preparation of large amounts of the aldehyde. Application of the Oppenauer oxidation to cyclopropylcarbinol, with

(1) Paper VII, L. I. Smith and E. R. Rogier, THIS JOURNAL, **73**, 3840 (1951).

(2) Cyclopropanes. V, L. I. Smith and E. R. Rogier, *ibid.*, **73**, 3831 (1951).

(3) C. L. Wilson, (a) *J. Chem. Soc.*, 53, 58 (1945); (b) THIS JOURNAL, **69**, 3002 (1947).

benzil as the acceptor, failed to yield any aldehyde. Cyclopropylglyoxal, prepared by action of selenium dioxide upon methyl cyclopropyl ketone, was rearranged by action of alkali to cyclopropylglycolic acid which it was hoped could be cleaved to the aldehyde by action of lead tetraacetate. However, the yields in the first two steps were too low to make useful this synthetic route to the aldehyde. The problem was finally solved by application of the new aldehyde synthesis announced by Friedman.[4] Reduction of cyclopropanecarboxpiperidide or of cyclopropyl cyanide, by action of one-quarter mole of lithium aluminum hydride, produced cyclopropanecarboxaldehyde in 19 and 48% yields, respectively. The identity of the aldehyde was established by its conversion, by action of alkaline permanganate, into cyclopropanecarboxylic acid. A number of derivatives of the aldehyde were prepared for comparison of the melting points with the values in the literature.

TABLE I

MELTING POINTS OF DERIVATIVES OF CYCLOPROPANECARBOXALDEHYDE

Derivatives	M.p., °C. Literature	This work
Dimedon	160-162,[a] 168[a]	166–166.5
2,4-Dinitrophenylhydrazone	186–187.5[b]	185.5–186.5
p-Nitrophenylhydrazone	129–132[a]	142.5–143
Oxime	86[c,d]	
Phenylhydrazone	67[d]	
Semicarbazone	125–126,[c] 127–128[e]	139–139.5

[a] Ref. 3a. [b] Ref. 3b. [c] E. D. Venus-Danilowa and V. F. Kazimirova, *J. Gen. Chem.* (*U. S. S. R.*), **8**, 1438 (1938) [*C. A.*, **33**, 4204 (1939)]. [d] Z. I. Shuikina, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 983 (1937) [*C. A.* **31**, 5332 (1937)]. [e] N. J. Demjanow and M. Dojarenko, *Ber.*, **41**, 43 (1908).

Experimental Part[5]

γ-Chlorobutyronitrile (49–51%) was prepared from trimethylene chlorobromide according to the procedure of Allen.[6]

Cyclopropyl cyanide (60%), b.p. 58–59° (54 mm.), was prepared from γ-chlorobutyronitrile by the method of Schlatter.[7]

Cyclopropanecarboxylic acid (79%) was prepared from γ-chlorobutyronitrile by the method of McClosky and Coleman.[8]

Cyclopropanecarboxylic Acid Chloride.—The acid (51 g.) was added slowly (one hour) and with stirring to purified thionyl chloride[9] (84 g.). The solution was warmed (60–70°) and stirred for one hour and the product was distilled through a column (15 × 1.5 cm.) packed with glass helices. The chloride (59.5 g., 95%) boiled at 114–119°.

Cyclopropanecarboxpiperidide.—The acid chloride (30 g.) was added slowly (one hour) and with stirring to a solution of piperidine (55 g., dried over sodium hydroxide and distilled) in ether (750 cc.) in which anhydrous sodium carbonate (15 g.) was suspended. Stirring was continued for three hours, and the mixture was set aside overnight. Water and sulfuric acid were added, the ether layer was removed, dried (magnesium sulfate) and the solvent was removed. The residue (34 g., 78%), distilled through a column (8 × 1.5 cm.) packed with glass helices, boiled at 105–108° (1.5–2.5 mm.).

Anal. Calcd. for $C_9H_{15}ON$: C, 70.54; H, 9.87. Found: C, 69.11, 69.36; H, 9.87, 9.60.

Cyclopropanecarboxaldehyde. A. From Cyclopropanecarboxpiperidide.—A solution of lithium aluminum hydride (0.061 mole) in dry ether (90 cc.) was added rapidly (five to ten minutes) and with stirring to a cooled (−15°) solution of the piperidide (28.7 g., 0.189 mole) in dry ether (120 cc.). The mixture was stirred for 30 minutes at −15° and then for three to four hours at room temperature. Water was slowly added, followed by dilute sulfuric acid until the mixture was slightly acidic. The ether layer was removed and the aqueous layer was extracted twice with ether. The combined ether solutions were dried (magnesium sulfate), the solvent was removed by distillation through a column (20 × 1.8 cm.) packed with glass helices. The residue was distilled through a column (15 × 1.5 cm.) packed with glass helices. The product (2.6 g., 20%) boiled at 97–99° and gave the orange-red 2,4-dinitrophenylhydrazone melting at 185.5–186.5° and the reddish-brown *p*-nitrophenylhydrazone melting at 142.5–143°.

B. From Cyclopropyl Cyanide.—A solution of lithium aluminum hydride (0.197 mole) in dry ether (250 cc.) was added slowly (30 minutes) and with stirring to the nitrile (50 g., 0.75 mole) in dry ether (220 cc.) in an apparatus cooled in a bath of Dry Ice and provided with a calcium chloride guard tube. Stirring was continued for 15 minutes; the cooling bath was removed and shortly (20 to 30 minutes) a vigorous reaction began. The cooling bath was immediately replaced; after the reaction subsided, the bath was removed and the mixture was stirred for 30 minutes. A small amount of hydroquinone was added, followed by cautious addition of dilute (10%) sulfuric acid, with cooling, until the mixture was faintly acidic. The ether layer was removed, the aqueous layer was extracted twice with ether. The combined ether solutions were dried (magnesium sulfate) and the product (25.3 g., 48%) boiling at 97–101°, was isolated as described under A above. The yield of aldehyde was not affected when the reaction mixture was allowed to come to room temperature and then refluxed for 30 minutes after completion of the exothermic reaction. However, in a larger run, using four times the quantities given above, the yield dropped to 38%. The dimedon derivative of this product crystallized from methanol in white prisms melting at 166–166.5°; the semicarbazone, crystallized several times from petroleum ether (B), melted at 139–139.5°. The aldehyde (1 g.) was oxidized by action of alkaline permanganate[10] and the resulting acid was converted into the *p*-bromophenacyl ester, which melted at 72–72.5° alone or when mixed with an authentic specimen of the ester prepared from cyclopropanecarboxylic acid.[11]

Cyclopropylcarbinol.—Ethyl cyclopropanecarboxylate (22.4 g., 0.2 mole) was reduced by action of lithium aluminum hydride (2.2 g., 0.06 mole) according to the procedure of Nystrom and Brown.[12]

The carbinol (8.3 g., 58%) boiled at 122–123° and had $n^{25.2}D$ 1.426.[13] It did not react with permanganate at room temperature, nor with bromine in chloroform. The phenylurethan[14] crystallized from benzene–petroleum ether in white needles, or from aqueous ethanol in white platelets, melted at 75.5–76°. Demjanow and Fortunatow[13] report this phenylurethan to melt at 100–104°.

Cyclopropylcarbinol (2 g.), benzil (17.4 g.) and aluminum *t*-butoxide (6.8 g.) were heated at 50–60° in benzene (60 cc.) for six hours.[15] Water (0.5 cc.) was added and the benzene solution was extracted twice with saturated aqueous sodium bisulfite. Sodium carbonate was added to the aqueous extract, which was then thoroughly extracted with ether. The ether extract was dried (magnesium sulfate) and the solvent was removed. The residual oil (0.5–1 cc.)

(4) L. Friedman, Abstracts of the 116th Meeting of the A. C. S., Organic Division, Atlantic City, New Jersey, September, 1949.

(5) Microanalyses by R. Amidon, J. Buckley, W. Cummings, W. Hunter, R. Kelly and H. Turner.

(6) C. F. H. Allen, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 150.

(7) M. J. Schlatter, *Org. Syntheses*, **23**, 20 (1943).

(8) C. M. McClosky and G. H. Coleman, *ibid.*, **24**, 36 (1944).

(9) L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed. D. C. Heath and Company, Boston, Mass., 1941, p. 381.

(10) R. L. Shriner and R. C. Fuson, "Systematic Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 170.

(11) L. I. Smith and E. R. Rogier, THIS JOURNAL, **73**, 3831 (1951).

(12) R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197 (1947).

(13) N. J. Demjanow and K. Fortunatow, *Ber.*, **40**, 4397 (1907), report the b.p. as 123.2–123.4° and $n^{16.1}D$ (1.4313).

(14) For procedure, ref. 9, p. 163.

(15) Procedure of H. Adkins and R. C. Franklin, THIS JOURNAL, **63** 2381 (1941).

did not reduce Tollens reagent, nor did it yield a derivative with 2,4-dinitrophenylhydrazine.

Cyclopropylglyoxal.—Acetic acid (17 cc.), water (15 cc.), dioxane (375 cc.) and selenium dioxide (66 g.) were mixed and heated on a steam-bath until solution was complete. Methyl cyclopropyl ketone (50 g.) was then added; the solution was heated for five hours and then allowed to stand overnight. The solution was decanted from the gray deposit of selenium, dioxane was removed under reduced pressure, and the residue was distilled through a column (15 × 1.5 cm.) packed with glass helices. The product (24.7 g.), a light yellow-green liquid with a sharp odor, boiled at 40–41° (10 mm.), and had $n^{20}D$ 1.481. A center cut was taken for analysis.

Anal. Calcd. for C_5H_6O: C, 61.21; H, 6.16. Calcd. for $C_5H_6O \cdot H_2O$: C, 51.7; H, 6.9. Found: C, 57.45; H, 6.52.

A sample, prepared as above but with omission of acetic acid, was analyzed. Found: C, 55.67; H, 6.47. The substance was therefore a mixture of cyclopropylglyoxal and its hydrate. On standing overnight, the product polymerized, but the monomer could be recovered by distillation of the polymer with a trace of phosphorus pentoxide. The glyoxal reduced Tollens solution, and formed a 2,4-dinitrophenylhydrazone which crystallized from ethanol in orange-red needles melting at 173–173.5°.

Anal. Calcd. for $C_{11}H_{10}O_5N_4$: C, 47.48; H, 3.62. Found: C, 47.47; H, 3.76.

Cyclopropylglycolic Acid.—Crude cyclopropylglyoxal (9.3 g.) was dissolved in water (50 cc.), the solution was cooled (0°), and aqueous sodium hydroxide (4 g. in 50 cc.) was added with stirring. The mixture was kept at 0° for three hours, then allowed to stand at room temperature for 18 hours. The light yellow solution was concentrated to 20 cc. under reduced pressure and thoroughly extracted with ether. The aqueous layer was acidified with dilute sulfuric acid and continuously extracted with ether for 48 hours. The extract was dried (magnesium sulfate), the solvent was removed, and the residue was crystallized from chloroform–petroleum ether. The white needles melted at 77.5–78.5° and weighed 3.1 g.

Anal. Calcd. for $C_5H_8O_3$: C, 51.72; H, 6.94; neut. equiv., 116.1. Found: C, 51.75; H, 7.16; neut. equiv., 117.3, 117.7.

The *p*-bromophenacyl ester crystallized from aqueous ethanol, formed white needles which melted at 93–93.5°.

Anal. Calcd. for $C_{13}H_{13}O_4Br$: C, 49.86; H, 4.18. Found: C, 49.90; H, 4.21.

The acid (1 g.) and potassium permanganate (2.5 g.) were dissolved in water (50 cc.) and the solution was allowed to stand at room temperature for three days. Excess permanganate and manganese dioxide were reduced with sodium bisulfite and the clear solution was concentrated under reduced pressure to a small volume. The solution was acidified and extracted with ether; solvent was removed from the extract and the residual liquid acid was converted into the *p*-bromophenacyl ester melting at 71–72° alone or when mixed with the *p*-bromophenacyl ester of cyclopropanecarboxylic acid.

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Cyclopropanes. IX.[1] Methyl Cyclopropyl Ketone

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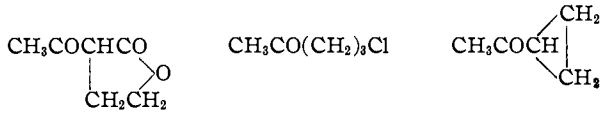
Preparation of methyl cyclopropyl ketone (III) in fairly large amounts *via* the published procedures is difficult and time-consuming. Preliminary to the researches reported in this series of papers, an investigation of the methods for preparation of the ketone was carried out. The best route to the ketone involves conversion of α-acetobutyrolactone (I) to 5-chloro-2-pentanone (II) (61–67%) by action of constant boiling hydrochloric acid[2] and conversion of II to the ketone (III) (74–78%) by action of dry, powdered potassium hydroxide.[3]



I II III

Experimental Part

5-Chloro-2-pentanone (II).—A solution of hydrochloric acid (38%, 450 cc.) in water (500 cc.) was added to α-acetobutyrolactone (512 g., 4 moles).[4] The mixture was shaken for a short time until homogeneous, and then allowed to stand at room temperature until evolution of carbon dioxide almost ceased (two to three hours). The flask was then equipped with a separator and an efficient reflux condenser and the mixture was brought to the boiling point (open flame). The constant boiling hydrochloric acid in the distillate (lower layer) was continuously returned to the flask; the product (upper layer) was removed. Distillation was continued until the distillate did not contain appreciable amounts of II (four to five hours). The product was dried (magnesium sulfate) and distilled under reduced pressure. The distillate, a colorless liquid (293–320 g., 61–67%), boiled at 50–51° (8 mm.). Only a few drops of fore-run and a very small amount of residue were obtained.

Methyl Cyclopropyl Ketone (III).—Powdered potassium hydroxide (400 g., 90%, technical, flakes ground in a mortar) was placed in a 5-l. 3-necked round-bottomed flask equipped with a Hershberg stirrer, dropping funnel and reflux condenser. A thermometer was suspended through the condenser and fixed so that the bulb was just above the stirrer. Stirring was begun, and 5-chloro-2-pentanone (II) (595 g., 4.93 moles) was added as follows: 200 cc. of the chloroketone at such a rate that the temperature was maintained at 65–75°, then 50 cc. of water all at once, followed by another 200 cc. of the chloroketone at 65–75°, then 50 cc. of water, and finally the remainder of the chloroketone at 65–75°. Stirring was continued while the temperature was maintained at about 65° for two hours and then allowed to fall to 30°. The mixture was cooled (ice-bath), water (400–500 cc.) was added, and then dilute sulfuric acid until the mixture was neutral. The ketone layer was extracted with two 400-cc. portions of ether, the combined ether extracts were dried (magnesium sulfate), the solvent was removed, and the residual liquid was added to the bulk of the ketone. The product was distilled through a column (45 × 1.8 cm.) packed with small bent pieces of wire screening. The distillate (306–326 g., 74–78%) boiled at 110–111°.

All of the procedures reported in the literature for this re-

TABLE I

REACTION CONDITIONS AND REAGENTS FOR PREPARATION OF III

Reactant	Reagent and conditions	Yield, %
II	KOH, dry, powdered	74–78
II	$LiNH_2$ in boiling ether	Trace
II	$LiNH_2$ in boiling benzene	None
II	KOH, 50% aqueous, warm	44
II	Collidine at 140°	None
5-Bromo-2-pentanone	KOH, water[a]	46
5-Bromo-2-pentanone	KOH in dry methanol	None
5-Bromo-2-pentanone	$NaOCH_3$ in dry methanol	None

[a] M. Idzkowska and E. Wagner, *J. Russ. Phys. Chem. Soc.*, **30**, 259 (1897); *Chem. Centr.*, **69**, II, 474 (1898).

(1) Paper VIII, L. I. Smith and E. R. Rogier, THIS JOURNAL, **73**, 4047 (1951).

(2) Modification of the procedure of S. E. Forman, British Patent 601,803; *C. A.*, **42**, 7787 (1948).

(3) Modification of the procedures of N. D. Zelinski and E. F. Dengin, *Ber.*, **55**, 3354 (1922).

(4) We wish to thank Dr. Max Tishler and Dr. Earl Pierson, of Merck and Company, Inc., for their generous gifts of this compound.