3. Reduction of ethyl α-acetamidoacetoacetate with either Raney nickel or Adams catalyst afforded, after hydrolysis, *dl-allo*-threonine in 55–58% yield. No *dl*-threonine could be isolated directly.

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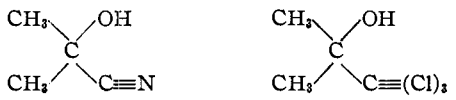
[CONTRIBUTION FROM THE GROSVENOR LABORATORY]

The Synthesis of α-Alkoxyisobutyric Acids and Alkyl Methacrylates from Acetonechloroform

BY CH. WEIZMANN, M. SULZBACHER AND E. BERGMANN

From the similarity of acetonecyanohydrin and acetonechloroform the latter appears a possible



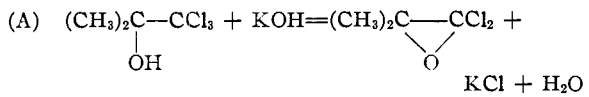
starting material for the preparation of α-hydroxy-isobutyric and methacrylic acid. Equally, its analogs and homologs could be used for the synthesis of the analogs and homologs of these acids.

Literature data regarding the hydrolysis of acetonechloroform and similar compounds are scanty and contradictory: the formation of α-hydroxy-,[1] α-chloro-isobutyric acid and methacrylic acid,[2] *e. g.*, has been observed from acetonechloroform,[3,4] but most of the latter suffers undefined decomposition to acetone, carbon monoxide, phosgene and formic acid.[5]

When acetonechloroform is treated with a solution of four moles of potassium hydroxide or sodium butoxide in *butyl alcohol* at 0°, a vigorous reaction takes place; the alkaline reaction disappears, potassium (or sodium) chloride precipitates in the expected quantity, and the salt of a monobasic acid $C_8H_{16}O_3$ is formed which was identified as *α-butoxy-isobutyric acid.* Every alcohol investigated has given the same reaction which can be formulated as

$$(CH_3)_2C(OH)CCl_3 + 4KOH + ROH = (CH_3)_2C(OR)COOK + 3KCl + 3H_2O$$

As it is surprising that under these conditions a tertiary alcoholic hydroxyl group should be alkylated, the following mechanism is suggested



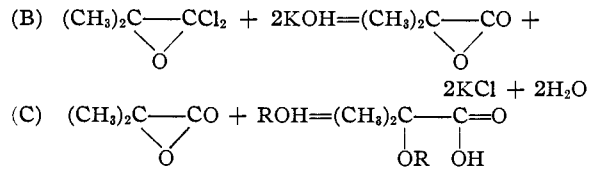
(1) Willgerodt and Schiff, *J. prakt. Chem.*, [2] **41**, 519 (1890).

(2) Ostropjatow, *Ber.*, **29**, Ref. 908 (1896).

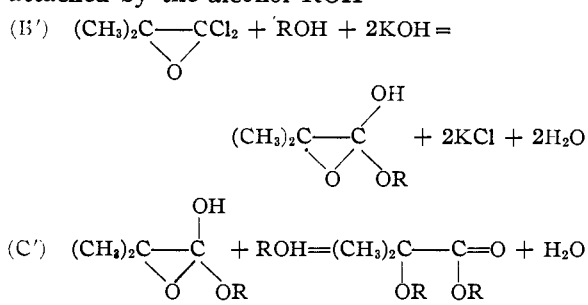
(3) The observations of Thomas and Oxley (British Patent 505,103 (1937) *C. A.* **33**, 7821 (1939)) could not be confirmed; they are theoretically most unlikely.

(4) Trichloromethyl-phenylcarbinol: Jozicz, *Chem. Zentrl.*, **68**, I, 1013 (1897). Rapson, Saunder and Stewart, *J. Chem. Soc.*, **74** (1944). It is doubtful whether the trichloromethylisopropylcarbinol studied by Jozicz actually had that structure; see Howard, THIS JOURNAL, **49**, 1068 (1927).

(5) Compare Bressanin and Segre, *Gazz. chim. ital.*, **41**, I, 671 (1911). See also Peser, *C. A.*, **42**, 514 (1948).



Analogously, the product of step (A) can be attacked by the alcohol ROH



Such esters, indeed, in which the alkyl radicals of the ester and of the ether group are identical, have been observed as by-products.[6]

The intermediary formation of an ethylene oxide from such trichlorinated alcohols and alkaline reagents has already been assumed by Jozicz[4] in order to explain the formation of α-chloroacids in the hydrolysis; this would be due to a pinacolonic re-arrangement, *e. g.*

One might be tempted to assume that the α-alkoxy acids in the above synthesis are formed through the intermediate of these α-chloroacids; however, the high yields obtained would imply that the rearrangement proceeds almost quantitatively, which is unlikely. Moreover, one would rather expect α-chloroacids of such structure to give the corresponding unsaturated acids, upon treatment with alcoholic potassium hydroxide. Methyl methacrylate does not add alcohols under the experimental conditions employed here.

That the acids obtained are actually the α- and not the isomeric β-alkoxy-compounds, can be

(6) The opening of lactone rings by alcohols to form alkoxy acids is not without analogies. See F. E. Küng, U. S. Patent 2,352,641 (*C. A.*, **38**, 5500 (1944)). We owe this observation to one of the Referees. Compare also Aston and Greesburg, THIS JOURNAL, **62**, 2590 (1940).

concluded from the observation that trichloromethylphenylcarbinol gives α-alkoxyphenylacetic acids. In this case, no β-alkoxylation is possible.

Primary alcohols give higher yields in alkoxyacids than secondary, secondary higher ones than tertiary alcohols in the reaction with acetonechloroform. The reaction is, also, not specific for acetonechloroform, but is applicable to its homologs and analogs. A number of examples are given in the Experimental Part.

"De-alkoxylation" of the α-alkoxyisobutyric acids to methacrylic acid is best carried out by heating the esters with the equivalent amount of phosphorus pentoxide. Oxalic acid and zinc chloride cause the same transformation with a lower rate of conversion and somewhat lower yield. Heating with anilinium hydrobromide is without effect on the alkoxyesters. Heating with alcoholic sulfuric acid also causes de-alkoxylation; therefore, frequently in the esterification of the alkoxyacids, some alkyl methacrylate is formed, and its quantity increases with increasing stringency of the conditions of esterification. The alkoxyacids containing secondary alkyl radicals are more easily converted into unsaturated compounds, and in the case of *t*-alkyl compounds, no alkoxy ester has been isolated from the esterification with alcoholic sulfuric acid.

The alkoxyacids are fairly stable; they are viscous liquids which can be characterized by crystalline derivatives, *e. g.*, the phenylhydrazides. Amides are best prepared from the esters; thus α-methoxyisobutyr-(β-hydroxyethyl)-amide was synthetized. An attempt to prepare the acid chlorides in pure state failed; however, the crude chlorides, obtained by means of thionyl chloride, can be used for the preparation of such substances as *phenyl α-butyoxyisobutyrate;* in this reaction, however, and still more in the preparation of phenyl α-isobutyoxyisobutyrate, substantial quantities of phenyl methacrylate were formed. This is somewhat surprising as the α-acyloxyisobutyric acids can easily be converted into the corresponding acid chlorides.[7]

An interesting parallel to our reaction is to be seen in the observation by Banti[8] that in presence of alcoholic potassium hydroxide solution, acetonechloroform and aniline give an anilinoisobutyric acid, m. p. 185°, or its anilide, m. p. 155–157°. The anilino-anilide (m. p. 122°) which is formed from methacrylic acid or methacrylanilide and aniline at 190°[9] is undoubtedly the β-anilino-compound, Banti's anilide, therefore, the α-anilino-anilide, also formed from α-bromoisobutyrylanilide and aniline at low temperature.[10,11]

(7) Blaise, *Compt. rend.*, **154**, 1087 (1912); **155**, 47 (1913); **175**, 1216 (1922); **176**, 1148 (1923); *Bull. soc. chim.*, [4] **15**, 666 (1914); Blaise and Herzog, *Compt. rend.*, **184**, 1332 (1927), and further publications.

(8) Banti, *Gazz. chim. ital.*, **59**, I, 819 (1929).

(9) Autenrieth and Pretzel, *Ber.*, **36**, 1262 (1903); Autenrieth, *ibid.*, **38**, 2534 (1905).

(10) Compare the formation of α-anilinoisobutyronitrile (reduction to isopropylaniline) from acetonecyanohydrin and aniline: Bucherer and Grolée, *Ber.*, **39**, 990 (1906). See Mulder, *Rec. trav. chim.*, **26**, 181 (1907); Bucherer, German Patent 157,710 (*Chem. Zentr.*, **76**, I, 415 (1905); v. Walther and Huebner, *J. prakt. Chem.*, [2] **93**, 126 (1916).

(11) Ethyl α-bromoisobutyrate and aniline give at 160° the esters of both the isomeric anilinoisobutyric acids: Bischoff and Mintz, *Ber.*, **25**, 2326 (1892).

(12) The acid had been prepared before by Barker and Skinner, THIS JOURNAL, **46**, 407 (1924); b. p. 81.5–83° (8–9 mm.).

(13) Compare Madsen, *Z. physik. Chem.*, **92**, 107 (1918).

Experimental

The experiments in the **α-methoxyisobutyric acid** series are described in detail; the analogous ones with its homologs are summarized in the tables.

To a cold and vigorously stirred solution of 448 g. of potassium hydroxide in 250 cc. of water and 1000 cc. of methyl alcohol, which was contained in a three-necked flask, fitted with mercury-sealed stirrer, reflux condenser and dropping funnel, a solution of 355 g. of acetonechloroform in 700 cc. of methyl alcohol was slowly added. The violent reaction, which was accompanied by the precipitation of potassium chloride, was checked by energetic cooling. The mixture was stirred for one hour at room temperature and then for two hours at boiling temperature. The inorganic salt was filtered off and washed with methyl alcohol (441 g., calcd. 447.1 g.).

The clear filtrate was freed from methyl alcohol at ordinary pressure and from most of the water *in vacuo*, and the residue was treated with a slight excess of dilute sulfuric acid (congo red). The inorganic precipitate was filtered, thoroughly washed with ether and the aqueous solution extracted with the same solvent. The residue of the combined and dried extracts distilled at 98–99° (20 mm.); yield, 167 g. (70.8%).[12,13] The same result is obtained when instead of aqueous-methanolic potassium hydroxide solution, methyl alcoholic sodium methoxide is used.

Anal. Calcd. for $C_5H_{10}O_3$: C, 50.8; H, 8.5; OCH_3, 26.3; mol. wt., 118. Found: C, 50.5; H, 8.6; OCH_3, 25.9; mol. wt., 117 (by titration).

Phenylhydrazide from 3 g. of the acid and 3.5 g. of phenylhydrazine at 120° (two hours): the melt solidified upon cooling. The product crystallized from boiling water in needles of m. p. 103°.

Anal. Calcd. for $C_{11}H_{16}O_2N_2$: C, 63.5; H, 7.7; N, 13.5; OCH_3, 14.9. Found: C, 63.2; H, 7.9; N, 13.2; OCH_3, 14.6.

Methyl Ester.—The solution of 118 g. of α-methoxyisobutyric acid in 125 cc. of methyl alcohol, containing 25 cc. of concentrated sulfuric acid, was refluxed for twelve hours. The excess of methyl alcohol was distilled off and the cold residue poured into the double volume of concentrated brine. The ester layer, which separated, was washed again with an equal volume of brine and dried over calcium chloride; b. p. 134–135° (lit. 144.8–145° (767 mm)); yield, 105 g. (79.6%). The use of larger quantities of sulfuric acid produced a dark resinous by-product.

Anal. Calcd. for $C_6H_{12}O_3$: C, 54.5; H, 9.1; OCH_3, 47.0. Found: C, 54.1; H, 9.2; OCH_3, 46.9.

Methacrylates from α-Methoxyisobutyric Acid.—(a) A mixture of 39.6 g. of methyl α-methoxyisobutyrate and 30 g. of phosphorus pentoxide was heated in the presence of some hydroquinone for two hours. The liquid was directly distilled off from the brown resinous mass and redistilled. The methyl methacrylate boiled at 99–100°; yield, 28.4 g. (95%).

(b) A mixture of 39.6 g. of methyl α-methoxyisobutyrate and 20 g. of freshly fused zinc chloride was heated in presence of some hydroquinone for two hours. Fractional distillation in a Widmer column gave: b. p. 98–102°, methyl methacrylate, 18.0 g. (60%); b. p. 130–135°, methyl α-methoxyisobutyrate, 8.0 g. (20.4% of initial amount).

(c) A mixture of 39.6 g. of methyl α-methoxyisobutyrate and 30 g. of anhydrous oxalic acid was heated in the

TABLE I

α-ALKOXYISOBUTYRIC ACIDS

Acetone chloroform, g.	ROH, R	Cc.	Alkali[a]	G.	Acid formed, -butyric	Formula	B. p., °C.	Mm.	Yield, g.	%	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Mol. wt. Calcd.	Mol. wt. Found[b]
35.5	Ethyl	350	$NaOC_2H_5$	54.4	α-Ethoxyiso-[14,15,16]	$C_6H_{12}O_3$	97	19	18.5	70.1[c]	54.5	53.9	9.1	9.0	132	131
35.5	Ethyl	200	KOH	45	α-Ethoxyiso-	$C_6H_{12}O_3$	99	20	18.0	68.2					132	131
35.5	Butyl	350	$NaOC_4H_9$	76.8	α-Butoxyiso-	$C_8H_{16}O_3$	121	20	23.0	71.9	60.0	59.8	10.0	9.8	160	158
35.5	Butyl	400	KOH	45	α-Butoxyiso-	$C_8H_{16}O_3$	111	8	25.0	78.1					160	159
177.5	Isobutyl	1220	KOH	224	α-Isobutoxyiso-[17]	$C_8H_{16}O_3$	116	20	98.0	61.2	60.0	59.7	10.0	10.0	160	160
177.5	Isobutyl	1250	KOH	250	α-Isobutoxyiso-	$C_8H_{16}O_3$	116	20	120.0	75.0					160	159
71.0	2-Ethylhexyl	600	KOH	90	α-(2-Ethylhexoxy)-iso-	$C_{12}H_{24}O_3$	133	4	61.0	70.5[d]	66.6	67.0	11.1	11.2	216	214
88.7	Dodecyl[e]	700	KOH	112	α-Dodecoxyiso-	$C_{16}H_{32}O_3$	200	16	32.0	23.5[f]	70.5	70.4	11.8	11.3	272	278
88.7	Allyl[g]	430	KOH	112	α-Allyloxyiso-	$C_7H_{12}O_3$	115	22	50.0	69.4	58.3	58.5	8.3	8.6	144	145
35.5	2-Ethoxyethyl	250	KOH	45	α-(2-Ethoxyethoxy)-iso-	$C_8H_{16}O_4$	136	12	17.0	48.3	54.6	55.0	9.1	9.6	176	170
71.0	2-Butoxyethyl	540	KOH	90	α-(2-Butoxyethoxy)-iso-	$C_{10}H_{20}O_4$	140	5	44.0	50.0	58.8	58.6	9.8	10.3	204	200
44.5	2-Ethoxyethoxyethyl	230	KOH	56	α-(2-Ethoxyethoxyethoxy)-iso-	$C_{10}H_{20}O_5$	178	12	9.0	16.3	54.5	54.5	9.1	8.9	220	216
88.7	Isopropyl	1000	KOH	112	α-Isopropoxyiso-	$C_7H_{14}O_3$	106	15	32.0	43.8	57.5	57.8	9.6	9.9	146	145
88.7	*t*-Amyl	650	KOH	112	α-*t*-Pentoxyiso-	$C_9H_{18}O_3$	115	20	17.5	20.1	62.1	62.5	10.4	10.6	174	172

[a] The quantities of potassium hydroxide are "pure KOH." The technical product, containing about 13% of water, was used. [b] By titration. [c] The crude product contained a small amount of ethyl ester, which was removed by treatment with soda solution and extraction with ether. Re-acidification gave the pure acid. Calcd.: OC_2H_5 34.1. Found: 33.9. [d] Small quantities of 2-ethylhexyl α-2-ethylhexoxyisobutyrate of b. p. 168° (4 mm.) were isolated. When the reaction was brought to completion at 130° (instead of 100°) and the crude product extracted with ether, before acidification, one third of the total reaction product consisted of that ester. [e] The reaction was begun at 35° and completed at 70°. [f] Besides the acid, 38 g. (17.3%) of dodecyl α-dodecoxyisobutyrate of b. p. 276° (15 mm.) were isolated. [g] The reaction was started at 0° and completed at room temperature.

TABLE II

α-ALKOXY ACIDS

Chlorinated alcohol	G.	ROH, R	Cc.	Alkali	G.	Acid formed	Formula	B. p. °C.	Mm.	Yield, G.	%	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Mol. wt., Calcd.	Mol. wt., Found
Methyl ethyl ketone chloroform	96	Isobutyl	800	KOH	112	α-Isobutoxymethyl ethyl acetic	$C_9H_{18}O_3$	123	20	54.0	62.1	62.1	62.5	10.4	10.6	174	177
Cyclohexanone-chloroform	109	Isobutyl	800	KOH	112	1-Isobutoxycylcohexanecarboxylic	$C_{11}H_{20}O_3$	165	30	61.0	61.0	66.0	66.4	10.0	10.2	200	211
2-Ethylhexanal-chloroform	111	Isobutyl	800	KOH	101	2-Isobutoxy-2-ethylheptoic	$C_{12}H_{24}O_3$	172	20	59.5	57.4	67.8	68.0	11.3	11.7	230	232

presence of some hydroquinone for two hours. The liquid product was directly fractionated: b. p. 98–102°, methyl methacrylate, 10.0 g. (33.3%); b. p. 130–135°, methyl α-methoxyisobutyrate, 24.0 g. (60.6% of initial amount).

(d) When the amount of oxalic acid was doubled, the yield in methyl methacrylate rose to 13.0 g. (43.4%).

(e) **(β-Butoxyethyl) Methacrylate.**—A mixture of 32 g. of α-methoxyisobutyric acid with 120 cc. of butyl cellosolve and 10 cc. of concd. sulfuric acid was heated at 130° in presence of tannic acid for twelve hours. The reaction product was poured into water (in which butyl cellosolve and the methoxyacid are soluble) and the supernatant ester layer extracted with ether. (β-Butoxyethyl) methacrylate boiled at 122° under 12 mm. pressure; yield, 48 g. (80%). A small head fraction, b. p. 69–70° (13 mm.), was identified as butyl methacrylate. No ester of α-methoxyisobutyric acid was observed.

(14) See Bischoff, *Ber.*, **32**, 1758 (1899); Schreiner, *ibid.*, **12**, 179 (1879).

(15) Hell and Waldbauer, *ibid.*, **10**, 448 (1877).

(16) Blaise and Picard, *Bull. soc. chim.*, [4], **11**, 587 (1922).

(17) Prepared before from iodoform and sodium isobutoxide (b. p. 141–144° (34 mm.)); Gorbow and Kessler, *Ber.*, **20**, ref. 776 (1887).

Table I lists the homolog α-alkoxyisobutyric acids, prepared from acetonechloroform.

The **phenylhydrazide of α-ethoxyisobutyric acid** was prepared, as described for the methoxy compound. It boiled at 195–200° (24 mm.) and solidified upon cooling. From dilute alcohol or isooctane it crystallized in prisms, m. p. 84°.

Anal. Calcd. for $C_{12}H_{18}O_2N_2$: C, 64.1; H, 8.9; N, 12.6; OC_2H_5, 20.3. Found: C, 64.9; H, 7.9; N, 12.7; OC_2H_5, 19.9.

The **phenylhydrazide of α-butoxyisobutyric acid** boiled at 210° (24 mm.) and crystallized from petroleum ether in form of needles, m. p. 108–109°.

Anal. Calcd. for $C_{14}H_{22}O_2N_2$: C, 67.2; H, 8.8; N, 11.2. Found: C, 67.0; H, 8.7; N, 11.0.

Table II summarizes the preparation of analogous α-alkoxy acids from chlorinated alcohols.

The experiment, leading from trichloromethylphenylcarbinol (benzaldehydechloroform) to **α-methoxyphenylacetic acid**, is described in detail.

A solution of 56.4 g. of benzaldehydechloroform[18] in

(18) Prepared from chloral and benzene in the presence of aluminum chloride (b. p. 145° (15 mm.); m. p. 37°); Dinesmann, *Compt. rend.*, **141**, 201 (1905).

TABLE III

ESTERS OF α-ALKOXYISOBUTYRIC ACIDS

$(CH_3)_2C(OR)COOH$ R	G.	R'OH R'	Cc.	H_2SO_4 conc., cc.	Temp. °C.	Time, hr.	Product, -isobutyrate	Formula	B. p. °C.	Mm.	Yield, G.	%	Carbon, % Calcd.	Carbon, % Found	Hydrogen % Calcd.	Hydrogen % Found
Ethyl	79.2	Ethyl	90	15	Reflux	13	Ethyl α-ethoxy-	$C_8H_{16}O_3$	55	13	84.0	87.5[a]	60.0	59.8	10.0	9.9
Butyl	160.0	Methyl	200	2	Reflux	20	Methyl α-butoxy-	$C_9H_{18}O_3$	60	6	130.5	75.0	62.1	62.1	10.4	10.8
Butyl	32.0	Butyl	50	6	Reflux	12	Butyl α-butoxy-	$C_{12}H_{24}O_3$	218	760	33.6	77.7[b]	66.6	66.2	11.2	11.0
Butyl	40.0	2-Ethoxy-ethyl	120	0.5	110	5	2-Ethoxyethyl α-butoxy-	$C_{12}H_{24}O_4$	122	13	46.0	80.0[c]	62.1	62.2	10.3	10.6
Butyl	40.0	2-Ethoxy-ethoxy-ethyl	180	0.5	110	5	2-Ethoxyeth-oxyethyl α-butoxy-	$C_{14}H_{28}O_5$	152	12	42.0	62.0[d]	60.9	61.2	10.1	10.4
Butyl	30.0	2-Butoxy-ethoxy-ethyl	130	0.4	110	5	2-Butoxyeth-oxyethyl α-butoxy-	$C_{16}H_{32}O_5$	176	11	48.0	90.0	63.2	63.5	10.5	10.8
Isobutyl	64.0	Butyl	200	2	Reflux	12	Butyl α-isobut-oxy-	$C_{12}H_{24}O_3$	103	12	65.0	75.2	66.6	66.6	11.2	11.0
Isobutyl	80.0	Isobutyl	125	20	Reflux	13	Isobutyl α-iso-butoxy-	$C_{12}H_{24}O_3$	204	760	77.0	71.2[e]	66.6	66.4	11.2	11.1
Isobutyl	128.0	2-Ethyl-hexyl	360	40	130	10	2-Ethylhexyl α-isobutoxy-	$C_{16}H_{32}O_3$	115	13	44.0	20.0[f]	70.6	70.4	11.8	11.7
2-Ethyl-hexyl	100.0	Butyl	230	2	Reflux	20	Butyl α-2-ethyl-hexoxy-	$C_{16}H_{32}O_3$	155	10	110.0	87.3	70.6	70.8	11.8	11.7
2-Ethyl-hexyl	...	See Table I Note *d*			....	..	2-Ethylhexyl α-2-ethylhexoxy-	$C_{20}H_{40}O_3$	168	4	...	...	73.0	72.5	12.2	11.4
2-Ethyl-hexyl	40.0	*n*-Dodecyl	120	1	120	24	Dodecyl α-2-ethyl-hexoxy-	$C_{24}H_{48}O_3$	232	10	61.1	86.0[g]	75.0	74.7	12.5	13.1
n-Dodecyl	...	See Table I Note *f*			....	..	Dodecyl α-dodecoxy	$C_{28}H_{56}O_3$	276	15	...	...	76.4	76.8	12.8	12.6
Allyl	28.8	Allyl	50	3	Reflux	6	Allyl α-allyloxy-	$C_{10}H_{18}O_3$	190	760	25.5	69.3[h]	65.2	65.4	8.9	8.7
2-Ethoxy-ethyl	22.0	2-Ethoxy-ethyl	60	0.3	110	5	2-Ethoxyethyl α-2-ethoxyethoxy-	$C_{12}H_{24}O_4$	138	12	24.0	77.5	58.1	58.5	9.7	10.1
2-Ethoxy-ethyl	23.0	2-Ethoxy-ethoxy-ethyl	90	0.3	120	5	2-Ethoxyeth-oxyethyl α-2-ethoxyethoxy-	$C_{14}H_{28}O_6$	163	12	25.0	65.5	57.5	57.1	9.6	9.8
Isopropyl	29.2	Butyl	50	10	Reflux	10	Butyl α-iso-propoxy-	$C_{11}H_{22}O_3$	181	760	7.0	17.3[i]	65.3	65.5	10.9	10.9

[a] 6.9 g. (10.0%) of ethyl methacrylate was formed. [b] 6.0 g. (21.1%) of butyl methacrylate was formed. With 10 cc. of sulfuric acid, the quantity of butyl methacrylate rose to 18.0 g. (63.3%) while that of the butoxy ester decreased to 15.2 g. (35.2%). [c] The same result was obtained by ester interchange reaction when methyl α-butoxyisobutyrate was heated with ethyl cellosolve in a column until no more methanol distilled over. [d] The same result was obtained by ester interchange reaction between methyl α-butoxyisobutyrate and ethyl carbitol. [e] 8.5 g. (12.0%) of isobutyl methacrylate was formed. [f] 112.0 g. (70.0%) of 2-ethylhexyl methacrylate was formed. [g] The ester solidified slightly below room temperature and could be recrystallized by precipitation of its acetonic solution with alcohol. [h] 5.1 g. (20.2%) of allyl methacrylate was formed. This was resinified when the heating time and the amount of sulfuric acid were doubled; under these conditions, only 18.4 g. (50.0%) of allyl α-allyloxyisobutyrate was obtained. [i] 21.0 g. (73.9%) of butyl methacrylate was formed. This tendency of de-alkoxylation is still more outspoken for α-*t*-pentoxyisobutyric acid which (17.4 g.) with butyl alcohol (30 cc.) in presence of concentrated sulfuric acid (6 cc.) gave only butyl methacrylate (90.1%).

100 cc. of methanol was slowly added to a solution of 56 g. of potassium hydroxide in 200 cc. of methanol, the temperature being maintained at about 45°. The mixture was stirred for one hour at boiling temperature, allowed to cool and filtered from potassium chloride (56 g.). The clear solution was evaporated *in vacuo*, and the residue was treated with a slight excess of dilute sulfuric acid. The oily layer was separated and combined with the ether extract of the aqueous solution. α-Methoxyphenylacetic acid of b. p. 165° (18 mm.) and m. p. 72° (from ligroin) was obtained in a yield of 30 g. (72.2%).

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.1; H, 6.0; OCH_3, 18.7. Found: C, 65.3; H, 6.2; OCH_3, 18.6.

The esters of the α-alkoxyisobutyric acids are listed in Table III. They were prepared by direct esterification of the acids with an excess of the alcohols in the presence of a small quantity of concentrated sulfuric acid as catalyst and of about 0.5% of tannic acid as polymerization inhibitor. It is, however, not necessary to isolate the α-alkoxyacids for the preparation of these esters. The following example shows that the same ultimate yields can be obtained without such isolation.

The solution obtained from 156.8 g. of potassium hydroxide in 750 cc. of butyl alcohol and 124.2 g. of acetone-chloroform in 250 cc. of butyl alcohol (0°, two hours), and filtered from the potassium chloride (154.0 g.) formed, was acidified with concentrated sulfuric acid at 0° (congo red) and filtered again. The filtrate, containing the free α-butoxyisobutyric acid, was boiled with 50 cc. of concentrated sulfuric acid, 5 g. of tannic acid and 300 cc. of carbon tetrachloride (azeotropic distillation). After nine hours, the amount of water liberated became negligible. The greater part of the organic solvents was distilled off and the residue washed with water, 20% sodium carbonate solution and water, and dried. Fractional distillation gave three fractions: butyl alcohol, butyl methacrylate (20.0 g., 20.1%) and butyl α-butoxyisobutyrate (70.0 g., 46.3%).

The esterification of 52.2 g. of α-isobutoxymethylethylacetic acid with 80 cc. of isobutanol in the presence of 14 cc. of concentrated sulfuric acid gave 54.0 g. (78.2%) of isobutyl-α-isobutoxy methylethylacetate of b. p. 220° and 5.7 g. (12.2%) of isobutyl tiglate.

The esterification of 50.0 g. of 1-isobutoxycyclohexane-

TABLE IV

UNSATURATED ESTERS

Starting material	Conditions	Unsaturated ester	Yield, %	B. p. °C.	Mm.	Remarks
Ethyl α-ethoxyisobutyrate	P_2O_5, 80°, 2 hr.	Ethyl methacrylate	90.0	120	760	See Table III, note *a*
Butyl α-butoxyisobutyrate	P_2O_5, 60°, 1 hr.	Butyl methacrylate	100.0	160	760	See Table III, notes *b*, *i*
Butyl α-isopropoxyisobutyrate	P_2O_5, 60°, 1 hr.	Butyl methacrylate	95.0	160	760	
Isobutyl α-isobutoxyisobutyrate	P_2O_5, 60°, 1 hr.	Isobutyl methacrylate[19]	91.0	56	18	See Table III, note *e*
2-Ethylhexyl α-isobutoxyisobutyrate	P_2O_5, 100°, 2 hr.	2-Ethylhexyl methacrylate[20]	90.0	120	18	See Table III, note *f*
Methyl methacrylate	2-Ethylhexanol, 1% H_2SO_4, column	2-Ethylhexyl methacrylate	75.0	120	18	Alkyl exchange
Methyl methacrylate	Ethylcellosolve, 1% H_2SO_4, column	2-Ethoxyethyl methacrylate[19]	75.0	70	22	Alkyl exchange
Methyl methacrylate	Butylcellosolve, 1% H_2SO_4, column	2-Butoxyethyl methacrylate	76.0	112	15	Alkyl exchange
Allyl α-allyloxyisobutyrate	P_2O_5, 60°, 1 hr.	Allyl methacrylate[21]	90.0	82	17	See Table III, note *h*
Methyl methacrylate	Diethylamino ethanol, 1% Na, column	β-Diethlaminoethyl methacrylate[22]	40.0	112	25	Alkyl exchange
Isobutyl α-isobutoxy-methylethylacetate	P_2O_5, 70°, 1 hr.	Isobutyl tiglate	95.0	180	760	
Isobutyl 1-isobutoxycyclohexanecarboxylate	P_2O, 100°, 2 hr.	Isobutyl 1-cyclohexenecarboxylate	85.0	140	28	See also esterification of acids
Isobutyl 2-isobutoxy-3-ethylheptoate	P_2O_5, 100°, 2 hr.	Isobutyl 3-ethyl-2-heptenoate	85.0	135	20	

carboxylic acid with 100 cc. of isobutanol and 15 cc. of concentrated sulfuric acid gave 18.5 g. (28.9%) of isobutyl 1-isobutoxycyclohexanecarboxylate of b. p. 154° (28 mm.) and 32 g. (70.3%) of isobutyl 1-cyclohexenecarboxylate.

The esterification of 46.0 g. of 2-isobutoxy-3-ethylheptoic acid with 100 cc. of isobutanol and 15 cc. of concentrated sulfuric acid gave 42.0 g. (73.4%) of isobutyl 2-isobutoxy-3-ethylheptoate of b. p. 155° (23 mm.) and 8.5 g. (20.0%) of isobutyl-3-ethyl-2-heptenoate.

The unsaturated esters, mainly methacrylates, encountered in this investigation, are listed in Table IV. It includes some esters of methacrylic acid which have not been prepared through the intermediary of α-alkoxyisobutyric esters but through alkyl exchange with methyl methacrylate.

In order to identify the unsaturated ester from isobutyl α-isobutoxymethylethylacetate, a sample was saponified with methyl alcoholic potassium hydroxide solution. The free acid obtained distilled at 197–203°, solidified and had m. p. 60°. These constants point to **tiglic acid** for which the literature records m. p. 65° and b. p. 199°.

When a carbon disulfide solution of the acid was kept for three days in the sunlight with a slight excess of bromine, an oily dibromide was formed which was brought to crystallization by the following treatment: dissolution in sodium carbonate solution, extraction with ether, acidification, re-extraction with carbon disulfide and evaporation, m. p. 85°.[23]

Of course, under these experimental conditions, angelic acid would also give the dibromide of its *trans*-isomer tiglic acid. The m. p. of the dibromide, however, excludes the possibility that the unsaturated ester formed was isobutyl α-ethyl-acrylate. The m. p. of the dibromide of α-ethylacrylic acid is 75°.[24]

α-Butoxy-isobutyryl Chloride and its Esterification with Phenol.—To a solution of 32 g. of freshly distilled α-butoxyisobutyric acid in 25 cc. of dry chloroform, 25 g. of thionyl chloride was slowly added, and the solution was kept at 18° during sixteen hours. After this time, the gas development had practically ceased. The weight increase of a trap showed that hydrogen chloride and sulfur dioxide had been liberated in a quantity of about 97%. The reaction mixture was a clear, brown liquid.

At 0°, a solution of 19.7 g. of phenol in 40 cc. of pyridine was added gradually. After twenty-four hours at room temperature, the product was diluted with 50 cc. of benzene, washed with water, dilute sulfuric acid and cold sodium hydroxide solution, and dried. The solvent was removed and the residue distilled under 20 mm. pressure in presence of hydroquinone. The liquid boiled, practically without residue, between 90 and 145°. It consisted of (a) b. p. 95–100° (16 mm.), phenyl methacrylate,[19] 10 g. (30.9%); (b) b. p. 138–140° (14 mm.), **phenyl α-butoxyisobutyrate**, 20 g. (42.4%).

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.2; H, 8.5. Found: C, 71.4; H, 8.7.

When the same reaction was carried out with 32 g. of α-isobutoxyisobutyric acid, 26 g. (80.2%) of phenyl methacrylate was the only product.

Aminolysis of Methyl α-Methoxyisobutyrate with Ethanolamine.—A mixture of 27.7 g. of methyl α-methoxyisobutyrate and 12.2 g. of monoethanolamine was heated on the steam-bath. After about fifteen minutes, it homogenized, and gentle refluxing (methyl alcohol) started. After three hours, the reaction was not yet quite complete, and fractional distillation gave: at 30–35° (10 mm.), methyl α-methoxyisobutyrate, 8.0 g. (28.7% of the initial quantity); at 63–70° (10 mm.), ethanolamine, 3.0 g. (24.5% of the initial quantity) and at 150–152° (16 mm.), **α-methoxyisobutyr-(β-hydroxyethyl)-amide**, 24.0 g. (74.5%).

The amide is a colorless, highly viscous oil which solidifies to a white crystalline mass at 0°.

Anal. Calcd. for $C_7H_{15}O_3N$: C, 52.1; H, 9.3; N, 8.7. Found: C, 51.8; H, 9.2; N, 8.7.

Summary

Acetonechloroform, when treated at 0°, with an alkali alkoxide or a solution of alkali hydroxide in an alcohol, gives the salt of an α-alkoxyisobutyric acid in good yield. Ten such α-alkoxyisobutyric acids have been prepared and their reac-

(19) Du Pont de Nemours & Co., *Ind. Eng. Chem.*, **28**, 1160 (1936).

(20) Roehm and Haas, French Patent 801,658; *Chem. Zentr.*, **108**, I, 429 (1937).

(21) Rehberg, Fisher and Smith, THIS JOURNAL, **65**, 1003 (1943); Rutovski and Zabrodina, *C. A.*, **35**, 4121 (1941).

(22) du Pont, British Patent 475,131; *Chem. Zentr.*, **109**, I, 2963 (1938).

(23) The dibromides of tiglic and angelic acid have the same m. p.: Wislicenus, *Ann.*, **272**, 12 (1893). Tiglic acid dibromide does not coalesce with water.

(24) Faworski, *J. prakt. Chem.*, [2] **51**, 541 (1895).

tions investigated. The reaction appears to be general for all analogs and homologs of acetonechloroform; three new α-alkoxyacids have thus been synthesized. A reaction mechanism has been suggested for this somewhat surprising reaction, and the analogous reaction of acetonechloroform and aniline has been discussed.

The dealkoxylation of the esters of the α-alkoxyacids to α,β-unsaturated esters has been investigated and a number of known and new esters of this series have been prepared.[25]

(25) (Note added February 19, 1948): In the November, 1947, issue of THIS JOURNAL (p. 2667), McElvain and Stevens describe the formation of ethyl α-ethoxyisobutyrate from acetonechloroform and 3 moles of sodium ethoxide in absolute alcohol. They also quote the British Patent 578,082 corresponding to the present paper (*C. A.*, **41**, 2075 (1947); applied in 1943; compare Weizmann, British Patent 587,545, applied in 1944).

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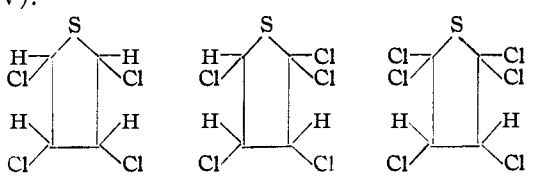
[CONTRIBUTION FROM RESEARCH AND DEVELOPMENT DEPARTMENT OF SOCONY-VACUUM LABORATORIES, A DIVISION OF SOCONY-VACUUM OIL CO., INC.]

The Chlorination of Thiophene. I. Addition Products

BY HARRY L. COONRADT AND HOWARD D. HARTOUGH

A study of the reaction of thiophene with chlorine was undertaken in these Laboratories when it became evident that the reaction was much more complex than had been indicated in the literature. Prior investigators reported[1] that when the reaction products were distilled, hydrogen chloride was evolved throughout the distillation and the presence of addition products was indicated since the substitution products distilled without decomposition. A study of addition products formed in the reaction was made by the present authors in order to determine, in part, their chemical potentialities since these compounds had been destroyed in the past by the methods used in processing the chlorinated mixtures.

The addition compounds isolated from the reaction mixture were α-2,3,4,5-tetrachlorothiolane,[2] m.p. 111.5–113.5°, (I), β-2,3,4,5-tetrachlorothiolane, m.p. 44.5–46°, (II), 2,2,3,4,5-pentachlorothiolane (III), and 2,2,3,4,5,5-hexachlorothiolane (IV).



I, m. p. 111.5–113.5° III IV
II, m. p. 44.5–46°

The addition products were described previously by Steinkopf and Köhler[3] as "hydrogen chloride addition products." The assumption of addition products was based on the separation of a liquid material from exhaustively chlorinated thiophene, 2-thiophenecarboxylic acid or 4,5-dibromo-2-thiophenecarboxylic acid to which was assigned the structure of 2,3,4,5,5-pentachloro-2-thiolene or 2,3,4,4,5-pentachloro-2-thiolene. We isolated no such addition product from exhaustively chlorinated thiophene, and it seems probable that the material of Steinkopf and Köhler was not a single compound. The present work indicates that the addition compounds are chlorine addition products. Hydrogen chloride did not form addition products with 2,5-dichlorothiophene at 0° or −40° nor with 2,3,4,5-tetrachlorothiophene at 0°.

There are six possible geometrical isomers of 2,3,4,5-tetrachlorothiolane. Two were isolated and identified. These compounds may be viewed as the products of the addition of chlorine to thiophene. The *alpha* isomer, I, was obtained as a white crystalline product when partially chlorinated thiophene was cooled and filtered. The *beta* isomer, II, was obtained when partially chlorinated thiophene was distilled to remove the more volatile components, the residue cooled to crystallize and separate I, and the filtrate fractionated under reduced pressure. The higher boiling fractions contained II.

The structures of I and II were indicated by the method of synthesis and analysis. Further evidence for the structure assigned to I was obtained by dehydrohalogenation. Pyrolysis yielded hydrogen chloride and dichlorothiophenes composed of about 50% 2,3-dichlorothiophene, and 50% 2,4-dichlorothiophene with a trace of 2,5-dichlorothiophene. However, when I reacted with ethanolic potassium hydroxide, dichlorothiophenes composed of approximately 54% 3,4-dichlorothiophene, 44% 2,4-dichlorothiophene, 2% 2,5-dichlorothiophene, and no 2,3-dichlorothiophene were obtained. This conversion of I to all four possible dichlorothiophenes is evidence for the structure assigned. II upon treatment with ethanolic potassium hydroxide yielded a mixture of dichlorothiophenes.

The 2,2,3,4,5-pentachlorothiolane (III) was separated in low yield by the fractionation under reduced pressure of chlorinated thiophene. A superior method of preparation was found to be

(1) W. Steinkopf, "Die Chemie des Thiophens," Theodor Steinkopff, Dresden, 1941, p. 35.

(2) This terminology is in accord with that in Patterson, "The Ring Index," Reinhold Publishing Corp., New York, N. Y., 1940, p. 44. Other terminology, except that derived from thiacyclopentane, is cumbersome and occasionally misleading. The *alpha* and *beta* isomers of tetrachlorothiolane have been so designated by the present authors.

(3) Steinkopf and Köhler, *Ann.*, **532**, 250 (1937).