Attempted Hydrolysis of 1. A solution of 1 (3 mg) in dioxane (2.5 ml) was heated with 2.5 ml of 1 *N* HCl and the reaction was monitored by GLC on a SE-30 column periodically for 1 hr. No change in the intensity of the peak associated with 1 was observed during this time period.

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Registry No.—1, 56051-00-4; 2, 56051-01-5.

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α-Chlorination of Aliphatic Acids by Molecular Chlorine

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We have previously reported that enolizing catalysts such as H_2SO_4, HCl, or $FeCl_3$ together with *m*-dinitrobenzene as a radical trapper increase the ratio of α- vs. β-chlorination of propionic acid by molecular chlorine.[1]

As an extension of this study concerning the effect of catalyst, the authors discovered that aliphatic acids can be effectively α-chlorinated in the presence of molecular oxygen as a radical trapper, which was pointed out in the Cl_2 addition to double bond[2] and in the phosphorus chloride catalyzed chlorination of alkanes.[3] The significant effect of molecular oxygen on the α-chlorination in the presence of 95% H_2SO_4 is listed in Table I.

Table I
Effect of Radical Trappers on the Chlorination Product of Butyric Acid[a]

Radical trapper	(mol %)	Registry no.	Yield, % α-Chloro acid	Yield, % β-Chloro acid
m-$C_6H_4(NO_2)_2$	(7.0)	99-65-0	6.7	1.4
O_2[b]		7782-44-7	22.3	0

[a] Chlorine gas was continuously introduced into the substrate at the flow rate of 200 ml/min at 120° for 3 hr in the dark with initial amounts of butyric acid (0.2 mol) and H_2SO_4 (0.02 mol). [b] The flow rate of O_2 was 200 ml/min.

The authors discovered also that the yield of α-chlorinated product further increases by the use of chlorosulfonic acid instead of concentrated H_2SO_4 as an enolizing catalyst. The remarkable effect of chlorosulfonic acid is probably due to the ability of formation of a more homogenous mixture and to the stronger acidity compared with that of H_2SO_4. Moreover, the authors examined the ability of some radical trappers and found that chloranil has an apparent effect on the α-chlorination.[4] These results are summarized in Table II for the chlorination of isovaleric acid as a substrate.

Table II
Effect of Chlorosulfonic Acid and Chloranil on Chlorination of Isovaleric Acid[a]

O_2:Cl_2 mol ratio[b]	Chloranil, mmol	Enolizing catalyst (mmol)	Yield, % α-Chloro acid	Yield, % β-Chloro acid
1:2	0.04	95% H_2SO_4 (171)	23.0	1.2
1:2	0.04	$ClSO_3H$ (60)	70.6	0.0
1:2	0	$ClSO_3H$ (60)	72.8	0.0
No O_2	0	$ClSO_3H$ (60)	41.6	2.7
No O_2	3	$ClSO_3H$ (60)	65.6	7.3

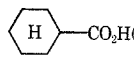
[a] Dark reaction at 140° for 3 hr with an initial amount of isovaleric acid of 600 mmol. [b] The flow rates of Cl_2 and O_2 gas were 100 and 50 ml/min, respectively.

Table II shows that the most effective α-chlorination of isovaleric acid by molecular chlorine in the dark is possible in the presence of chlorosulfonic acid, molecular oxygen, and chloranil at 140°. The chlorination in the absence of these three addenda gave a mixture of several chloro acids.

Various aliphatic acids can be similarly α-chlorinated in the presence of the above catalysts ($ClSO_3H$, O_2, and chloranil) to give its corresponding α-chloro acids alone in excellent yields (Table III). No β-chloro acid is detected except with isobutyric, *n*-butyric, and isocaproic acid, which produce only a trace of the corresponding β-chloro acid. It is of interest to note that the α-chlorination is predominant even in the presence of tertiary hydrogen, e.g., isovaleric acid. These products were characterized on the basis of boiling point, ir, and NMR spectra of the corresponding methyl ester which is prepared by H_2SO_4-catalyzed esterification with a mixture of methyl alcohol and ethylene dichloride[5] (Table IV).

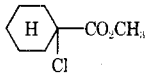
The authors already proposed that the acid-catalyzed chlorination of aliphatic acid by molecular chlorine in the dark may proceed via the ionic chlorination of enolized aliphatic acid, $RCH{=}C(OH)_2$, where the radical trappers minimize the radical chlorination.[1,6] The above results

Table III
Yields of α- and β-Chloro Acids with Various Substrates

Registry no.	Substrate (mol)	Reaction time, hr[b]	Reaction temp, °C	Yield, % α-Chloro acid	Yield, % β-Chloro acid	α-Chloro acid registry no.
79-31-2	$(CH_3)_2CHCO_2H$ (0.45)	2.5	120	74.6	0.3	594-58-1
107-92-6	$CH_3(CH_2)_2CO_2H$ (0.45)	2.5	120	82.0	1.6	4170-24-5
97-61-0	$CH_3(CH_2)_2\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCO_2H$ (0.35)	2.0	120	81.1	0.0	55905-12-9
105-43-1	$CH_3CH_2\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2CO_2H$ (0.18)	1.0	120	78.1	0.0	921-48-2
646-07-1	$CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}H(CH_2)_2CO_2H$ (0.16)	1.0	120	78.6	6.4	29671-29-2
98-89-5	 (0.23)	2.0	110[c]	73.4	0.0	25882-61-5

[a] Reactions were carried out with a 4:1:0.04 mole ratio of aliphatic acid:$ClSO_3H$:chloranil. A mixture of Cl_2 and O_2 gas (2:1 mole ratio) was introduced into the substrate in the dark at 120°. [b] Although the reaction was continued for 3 hr, the maximum yield of α-chloro acid was obtained at this reaction time. [c] The reaction temperature was lowered to 110° for the comparison with the literature. According to the literature,[7] the yield of α-chlorocyclohexanecarboxylic acid at 110° was less than 10% in PCl_3-catalyzed chlorination by molecular chlorine.

Table IV
Physical Properties and Identification of Methyl Esters of Produced Chloro Acids

Registry no.	Compd	Bp, °C (mm)	Ir, $\nu_{C=O}$, cm^{-1}[a]	NMR chemical shift[b]
26464-32-4	$CH_3CH_2\underset{\displaystyle Cl}{\underset{\vert}{C}}HCO_2CH_3$	87–88 (82)[c]	1750[d]	3.68 (s, 3 H, OCH_3), 4.20 (t, 1 H, J = 7.0, α-H), 1.92 (quintet, 2 H, J = 7.0, β-H), 1.00 (t, 3 H, J = 7.0, γ-H)
55905-13-0	$(CH_3)_2CH\underset{\displaystyle Cl}{\underset{\vert}{C}}HCO_2CH_3$	152–153	1740	3.72 (s, 3 H, OCH_3), 4.00 (d, 1 H, J = 6.8, α-H), 2.20 (octet, 1 H, J = 6.8, β-H), 0.94 (d, 6 H, J = 6.8, γ-H)
22421-97-2	$(CH_3)_2\underset{\displaystyle Cl}{\underset{\vert}{C}}CO_2CH_3$	29–31 (50–52)[e]	1734[f]	3.62 (s, 3 H, OCH_3), 1.63 (s, 6 H, β-H)
55905-14-1	$CH_3(CH_2)_2\underset{\displaystyle CH_3}{\underset{\vert}{\overset{\displaystyle Cl}{\overset{\vert}{C}}}}CO_2CH_3$	66–67 (11)	1747	3.73 (s, 3 H, OCH_3), 1.80–2.20 (m, 2 H, β-H), 1.68 (s, 3 H, α-Me), 1.10–1.60 (m, 2 H, γ-H), 0.97 (t, 3 H, J = 6.0, γ-Me)
55905-15-2	$CH_3CH_2\underset{\displaystyle CH_3}{\underset{\vert}{\overset{\displaystyle Cl}{\overset{\vert}{C}}}}HCO_2CH_3$	71–72 (10)	1750	3.70 (s, 3 H, OCH_3), 3.98–4.32 (two doublets,[g] 1 H, J = 5.7 and 8.4, α-H), 1.72–2.30 (m, 1 H, β-H), 1.20–1.72 (c, 2 H, γ-H), 0.85–1.20 (c, 6 H, β- and γ-Me)
55905-16-3	$CH_3\underset{\displaystyle CH_3}{\underset{\vert}{\overset{\displaystyle Cl}{\overset{\vert}{C}}}}HCH_2CO_2CH_3$	71–72 (11)	1750	3.74 (s, 3 H, OCH_3), 4.20 (t, 1 H, J = 8.0, α-H), 1.60–2.10 (c, 3 H, β- and γ-H), 0.96 (d, 6 H, J = 6.0, γ-Me)
25882-62-6		64 (2)	1750[h]	3.82[i] (s, 3 H, OCH_3), 1.81–2.34 (br, 4 H, β-H), 1.17–1.81 (br, 6 H, γ- and δ-H)

[a] Neat. [b] The NMR spectra were measured by a 60-MHz Jeol C-60 HL NMR spectrometer at 25° as ca. 30% solutions in CCl_4. Chemical shifts are given in parts per million relative to internal Me_4Si on the δ scale and coupling constants are reported in hertz. The following abbreviations are used: s, singlet; d, doublet; t, triplet; m, unresolved multiplet; c, complex; br, broad. [c] Lit.[8] bp 146–150°. [d] Lit.[8] 1750 cm^{-1}. [e] Lit.[8] bp 150°. [f] Lit.[8] 1735 cm^{-1}. [g] Two doublets are probably due to the asymmetric C_α and C_β carbons. [h] Lit.[7] 1748 cm^{-1}. [i] Lit.[7] 3.78 (s) as ca. 20% solutions in CCl_4.

seem to give further support to this mechanism, i.e., the chlorination of aliphatic acids by molecular chlorine in the presence of molecular oxygen, chlorosulfonic acid, and chloranil in the dark may proceed via this enol form or ketene, RCH=C=O, to give α-chloro acid selectively.

Experimental Section

General. All aliphatic acids and chlorosulfonic acid were the best commercial grade available and distilled before use. Commercial chloranil and *m*-dinitrobenzene were purified by recrystallization. Ir spectra were measured by a Perkin-Elmer Model 337 spec-

Table V
Elemental Analyses of New Compounds

Compd	% calcd C	% calcd H	Mol formula	% found C	% found H
$(CH_3)_2CHCHCO_2CH_3$ (Cl)	47.85	7.36	$C_6H_{11}O_2Cl$	46.55	7.52
$CH_3(CH_2)_2CCO_2CH_3$ (Cl, CH_3)	51.07	7.96	$C_7H_{13}O_2Cl$	50.80	8.22
$CH_3CH_2CHCHCO_2CH_3$ (CH_3, Cl)	51.07	7.96	$C_7H_{13}O_2Cl$	50.97	8.06
$CH_3CHCH_2CHCO_2CH_3$ (CH_3, Cl)	51.07	7.96	$C_7H_{13}O_2Cl$	51.17	7.86

trophotometer and NMR spectra were measured on a 60-MHz Jeol C-60 HL NMR spectrometer at 25° using Me_4Si as an internal standard. Reaction products analyses were done on a Yanagimoto Model GCG 550 gas chromatograph employing a flame ionization detector and a 1.5 m × 3 mm copper column packed with Apiezon grease L 15% on Celite 545 of 80–100 mesh. The column was operated at 50–200°, with nitrogen as a carrier (30 ml/min) and hydrogen of flow rate 30 ml/min. The yields shown in Tables I–III were determined by the internal standard method.

Typical Procedure for the Chlorination in Table I. Butyric acid (17.62 g, 0.2 mol), concentrated H_2SO_4 (1.96 g, 0.02 mol), and *m*-dinitrobenzene (2.78 g, 0.017 mol) were placed in a 100-ml four-necked flask fitted with a Dimroth condenser, a thermometer, and a gas inlet tube with sponge glass end. After gaseous N_2 was passed through the reaction mixture for ca. 30 min to expel oxygen, the butyric acid was chlorinated at 120° for 3 hr by bubbling a mixture of gaseous chlorine (flow rate ca. 100 ml/min) and oxygen (200 ml/min) dried with concentrated H_2SO_4 with magnetic stirring in the dark. After completion of the reaction, chlorine remaining in the solution was expelled out by bubbling N_2 gas into it for ca. 30 min. In general, a fraction of the reaction mixture (0.5–1.5 g) was added with water (10 ml) and extracted three times with chloroform (each 10–20 ml). The dried chloroform extract, after being dried with anhydrous Na_2SO_4 and vacuum distilled, was esterified with diazomethane in ether and the ether solution was analyzed by GLC.

Typical Procedure for the Chlorination in Tables II and III. In a 300-ml four-necked flask fitted with a Dimroth condenser, a thermometer, and a gas inlet tube were placed isovaleric acid (61.2 g, 0.6 mol), chlorosulfonic acid (6.20 g, 0.06 mol) as an acid catalyst, and chloranil (0.743 g, 0.003 mol). After being passed with N_2 gas for ca. 30 min to expel oxygen, a mixture of Cl_2 and O_2 gas (in a mole ratio of 2:1) were introduced into the substrate in the dark at 140°. Aliquots (2 ml) of the reaction mixture were taken out at given intervals of time and esterified by refluxing with a mixture of concentrated H_2SO_4 (0.05 ml), methyl alcohol (3 ml), and ethylene dichloride (8 ml) for 10 hr. The cooled mixture was separated and the organic layer was washed successively with water, aqueous $NaHCO_3$, and again with water. The organic solution was dried over anhydrous Na_2SO_4 and then analyzed by GLC.

The analogous work-up was applied to other acids. The elemental analysis data for new compounds among obtained α-chloro acids are shown in Table V.

Registry No.—Chlorosulfonic acid, 7790-94-5; chloranil, 118-75-2; isovaleric acid, 503-74-2; α-chloroisovaleric acid, 921-08-4.

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An Acid Protecting Group

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In some related work we were interested in utilizing an acid protecting[2] group that could be readily cleaved under mild acidic conditions as well as under catalytic-reductive conditions. The model studies reported herein indicate that an acid protected as its benzyloxymethyl ester can fulfill these two requirements.

The benzyloxymethyl esters can be synthesized in good yields by reaction of the sodium salt of the acid with benzyl chloromethyl ether in hexamethylphosphoramide[3,4] at room temperature. Employing these reaction conditions,

$$\underset{\text{I or II}}{R{-}\overset{O}{\overset{\|}{C}}ONa} + PhCH_2OCH_2Cl \xrightarrow[\text{room temp}]{HMPA} \underset{\text{III or IV}}{R{-}\overset{O}{\overset{\|}{C}}OCH_2OCH_2Ph}$$

I, R = n-C_5H_{11}; II, R = Ph; III, R = n-C_5H_{11}; IV, R = Ph

benzyloxymethyl hexanoate (III) and benzyloxymethyl benzoate (IV) were prepared in 73 and 68% yields, respectively.

Hydrolysis of the benzyloxymethyl esters III and IV with an aqueous HCl–THF solution at room temperature for 2 hr afforded the corresponding acids hexanoic V and benzoic VI in good yields.

$$\underset{\text{III or IV}}{R{-}\overset{O}{\overset{\|}{C}}OCH_2OCH_2Ph} \xrightarrow[\text{room temp, 2 hr}]{\text{aq HCl-THF}} \underset{\text{V or VI}}{R{-}\overset{O}{\overset{\|}{C}}OH}$$

V, R = n-C_5H_{11}; VI, R = Ph

$$\text{III or IV} \xrightarrow[\substack{\text{ETOH, 1 atm,}\\ \text{room temp}}]{5\%\ Pd/C\text{-}H_2} \text{V or VI}$$

Reductive removal of the benzyloxymethyl group in esters III and IV was readily achieved by reduction of III and IV, respectively, with 5% Pd/C in ethanol in the presence of hydrogen at 1 atm at room temperature. These results are summarized in Table I.

Experimental Section

Benzyloxymethyl Hexanoate (III). Sodium hexanoate (13.8 g, 0.1 mol), benzyl chloromethyl ether (15.7 g, 0.1 mol), and hexamethylphosphoramide (80 ml) were placed in a 250-ml flask fitted with a stopper and the resulting mixture was allowed to stir at room temperature for 2 days. The reaction mixture was poured into 700 ml of water and extracted with 2 × 500 ml of hexanes. The hexane extracts were combined and washed consecutively with a