chloropropene. There was also scatter and there were both positive and negative intercepts in the *kt versus t* plots. Therefore, the rate constants were calculated from the slopes of these plots.

The *cis*- and *trans*-1-chloropropenes were obtained from commercial chloropropene. The foreshot materials boiling under 28° were discarded. The fractions 28–37° were distilled and *cis*- and *trans*- rich cuts were redistilled. The cuts used were *cis*, b.p. 29.5–31.2° at 760 mm. (lit.[17] b.p. 30.8° at 738 mm.) and *trans*, b.p. 36.4° at 761 mm. (lit.[17] 37° at 738 mm.) Infrared spectra indicated intercontamination. For the kinetic runs "infinity" chloride values as well as the initial weights of the 1-chloropropenes were obtained.

Consistent with the presence of an unreactive impurity, the apparent rate constants of the *cis* isomer fell with time. If f is the fraction of *cis*-1-chloropropene actually present, then the following modification of 2 should be used to calculate k.

$$kt(b - fa) = 2.303 \log a(b - x)/b(a - x/f) \qquad (3)$$

For $b \gg fa$ and $f \simeq 1$, the initial points should give fair values of k. These k's can be used at large t's to evaluate f. This was done and it was found that f = 0.86 removed most of the curvature from the kt versus t plots and gave consistent k's independent of initial reactant concentrations (see Fig. 1). One "bad" run not used in the calculation of the final k is given for comparison.

Consistent with the presence of a reactive impurity in the *trans*-1-chloropropene, *kt versus t* plots showed positive intercepts in the *kt* axis. These plots were essentially parallel. It can be shown that if this impurity was the *cis*-isomer and its consumption by methoxide was relatively fast, the slopes of the *kt versus t* plots would give the true rate constant for *trans*-1-chloropropene (see Fig. 2). As different *trans* fractions were used, no single factor could be found to correct the concentrations—fortunately this was unnecessary. One other difficulty should be mentioned. Because the elimination was slow, it would have been desirable to make runs above 150°; however, the vapor pressure of the methanol at 150° was already dangerously high and occasional explosions of the Pyrex ampules did occur.

cis-β-Chlorocrotonic acid, m.p. 59–61° (lit.,[8] m.p. 60.3–60.6°) and sodium methoxide solutions were diluted with methanol (in this isomer the carboxylate and methyl groups are *cis*). The concentration of sodium methoxide is that remaining after the acid has been neutralized. Although the *kt versus t* plots appeared to be adequate, there appeared to be an ionic strength effect on k: log k appeared to increase linearly with $(a + b)$, that is, with the sodium chlorocrotonate plus the sodium methoxide concentrations (plots of k *versus* $(a + b)$ or log k *versus* $(a + b)^{1/2}$ showed somewhat more scatter). From plots of log k *versus* $(a + b)$, extrapolated values, k_0, were calculated which were then corrected for solvent expansion.

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CHICAGO 16, ILL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF CALIFORNIA]

Influence of Steric Hindrance on the Reaction of Acid Chlorides with Alcohols

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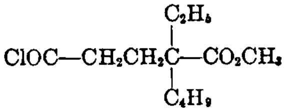
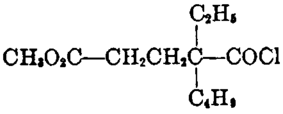
The reaction of α-butyl-α-ethyl-γ-carbomethoxybutyryl chloride (II) with alcohols is highly sensitive to traces of moisture. With carefully dried methanol at 0°, at least one fourth the yield was half ester. The unhindered acid chloride, I, is not subject to facile reaction with traces of water. At high temperature (180°), isomer II is no longer subject to preferential reaction with water. These results are correlated on the basis of dual reaction paths for the acid chloride (ionic and bimolecular displacement). Behavior of the hindered acid chloride under various conditions is consistent with the dual reaction path. There is described a high temperature method involving a continuous reactor for quantitative conversion of ester acid chloride II to dimethyl α-butyl-α-ethylglutarate.

In connection with an investigation[1] which required substantial quantities of the ester acid chloride, I, dimethyl α-butyl-α-ethylglutarate was



$$\mathrm{ClOC{-}CH_2CH_2C(C_2H_5)(C_4H_9){-}CO_2CH_3}$$

I



$$\mathrm{CH_3O_2C{-}CH_2CH_2C(C_2H_5)(C_4H_9){-}COCl}$$

II

required as an intermediate for synthesis of the ester acid chloride. Since direct esterification of the hindered carboxyl proceeds slowly and in poor yield,[2] and large amounts of diazomethane were regarded as undesirable, the diester was prepared by reaction of the ester acid chloride, II, with methanol. About one third the yield in this reaction, carried out at 0°, proved to be the half ester that would result from hydrolysis of II, even when there was used methanol that had been dried with magnesium. Although it was initially assumed that this half ester resulted from anhydride present as an impurity in II, this has proved not to be the case. Furthermore, isomer I or the ester acid chloride of glutaric acid reacts with undried commercial methanol, under the same conditions as used for isomer II, to give a quantitative yield of diester.

When acid chloride II was allowed to react with undried n-butyl alcohol, there was again obtained about 25% yield of half ester; however, butanol dried over magnesium gave only 10% yield of half ester. When the butanol, as well as the apparatus, was dried by azeotropic distillation the yield of half ester could be reduced to 5%, but this small amount persisted. The evidence suggests that the highly hindered acid chloride reacts with water

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[1] J. Cason and K. W. Kraus, *J. Org. Chem.*, **26**, 1772 (1961).

[2] J. Cason, *J. Org. Chem.*, **13**, 227 (1948).

present in very carefully dried reagents; in fact, such a hindered acid chloride may be regarded as a remarkably efficient drying agent.

The effect of hindrance, evidenced in the reactions of the acid chlorides with alcohols, may be rationalized on the basis of the published evidence[3,4] that an acid chloride may react either by way of a unimolecular ionization or a bimolecular substitution. In the case of the bimolecular substitution, hindrance would interfere with reaction of the alcohol and preferentially favor reaction with traces of water to give half ester. In the case of the ionic pathway, hindrance should be of little significance, on account of the high reactivity of the acylonium ion. The ionic pathway should have the higher activation energy and smaller negative entropy of activation, hence be favored by an increase in temperature. This effect was observed for the hindered acid chloride reactions (*cf.* Table I), when acid chloride II was added to boiling methyl or butyl alcohol. Furthermore, when isomer II and undried methanol were injected simultaneously into a gas chromatography column at 185°, the only chromatography band observed was that for the diester, which appeared at the same retention time recorded when the diester was injected.

TABLE I

REACTION OF ESTER ACID CHLORIDE II WITH ALCOHOLS[a]

Alcohol Used[b]	Yield Data, % Diester	Yield Data, % Methyl half ester
M + 10% H_2O	45	55
M + 1% H_2O	61	39
M, undried	66	34[c]
M, dried	71	29[c]
M, undried[d]	73	27[e]
M, dried[d]	80	20[c]
B, undried[f]	75	25
B, dried	90	10
B, superdried[g]	95	5
B, undried[d]	95	5

[a] Reactions carried out as described in Experimental, at 0° unless otherwise specified. [b] M indicates methanol, B indicates 1-butanol. Commercial grades of the alcohols were used; distillation from magnesium was used for drying. [c] Immediate gas chromatography gave the indicated results, which remained unchanged on standing of the reaction mixture. [d] These runs were carried out at the boiling point of the alcohol used. [e] This run was carried out on a larger scale, and the yields were determined by fractional distillation. [f] In reactions utilizing butanol, immediate gas chromatography showed 1-2% of butyl half ester and dibutyl ester. The quantities of these products increased rapidly on standing. [g] Butanol, dried with magnesium, was distilled from the apparatus until about two thirds had been distilled. The residue was used directly for the reaction.

Archer and Hudson[4] also observed that the ionic pathway is more prominent as the ionizing power of the solvent is increased. This effect is probably responsible for the fact (*cf.* Table I) that addition of water to the methanol causes a relatively modest increase in the amount of half ester formed. As the concentration of water is increased, the ionic pathway becomes more prominent, hence reduces the effect of hindrance.

The present investigation also includes data that are consistent with the observation of Ashdown[5] that reaction of an acid chloride with alcohol in dilute solution in ether is second order with respect to alcohol and first order in acid chloride. Such a reaction should be especially subject to hindrance. Although isomer II reacts almost instantaneously with excess alcohol at 0°, in ether solution the rate of reaction at 0° becomes quite slow.

In the extremely dry alcohol solution resulting from reaction of an acid chloride, the hydrogen chloride generated is very effective in catalysis of direct esterification of any acid formed. In some runs with isomer I, gas chromatography immediately after mixing the reagents showed presence of 2-5% of half ester, but after ten to twenty minutes only diester could be detected.[6] This observation suggests that inclusion of weak bases to neutralize the acid formed in reaction of an acid chloride with an alcohol is a poor idea unless acid-sensitive structures are involved. Formation of ester by direct esterification is not helpful for salvage of acid formed in such a hindered structure as that from isomer II.

The very effective catalysis of hydrogen chloride in very dry alcohol solution is also prominent in catalysis of transesterification. In instances where the butyl ester is formed from isomer II by reaction at 0°, immediate gas chromatography gives traces (1-2%) of the half butyl ester and dibutyl ester, and the ratio of these products increases rapidly on standing. In contrast, the methyl butyl ester from isomer I, whose methyl ester is highly hindered, gives no significant rate of transesterification when the reaction mixture is allowed to stand.

For synthesis of hindered esters on a preparative scale, the above-described observations suggest feeding the heated acid chloride into the alcohol or alcohol vapor at a rather high temperature. As described in the Experimental, application of this principle in a continuous reactor easily gives dimethyl α-butyl-α-ethylglutarate in quantitative yield from ester acid chloride II. Such a reactor should prove to be quite convenient for conversion of many acid chlorides to the esters.

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(3) R. F. Hudson and J. E. Wardbill, *J. Chem. Soc.*, 1729 (1950).

(4) B. L. Archer and R. F. Hudson, *J. Chem. Soc.*, 3259 (1950).

(5) A. A. Ashdown, *J. Am. Chem. Soc.*, 52, 268 (1930).

(6) In the moderately hindered ester acid chloride of *sym*-dimethylsuccinic acid, considerable half ester is formed in the initial reaction with undried methanol; however, after a twenty-four-hour period of standing only diester is present (observation of F. J. Schmitz in this laboratory).

EXPERIMENTAL

Ester acid chlorides I and II were prepared as has been described.[2] All samples of isomer II were prepared from half ester which was free of anhydride (analysis[1] by infrared spectroscopy and by gas chromatography).

Analysis of reaction mixtures was usually by gas chromatography at 185°, using a 1.5 m. × 8 mm. o.d. column containing silicone grease partitioning agent.[7] This partitioning agent gives satisfactory bands for the half esters, and all the reaction products are separated. Bands were identified by comparison of retention times with those of authentic samples, and quantitative determinations were by comparison of areas of bands from reaction mixtures with areas given by known amounts of authentic samples of the respective compounds. Knowns and unknowns were always chromatographed sequentially. In instances where infrared spectra were used for confirmatory analysis, the characteristic bands which have been cited previously[1] were utilized.

Reaction of ester acid chlorides with alcohols. In a representative reaction, 10 ml. of the alcohol was placed in a dried 50-ml. three-necked flask equipped with a stopper, a ball joint-sealed stirrer, and a serum cap. After the stirred alcohol had been cooled to 0°, 1 ml. of the ester acid chloride was injected through the serum cap by means of a hypodermic syringe. The mixture was stirred for 1 min., then a sample was withdrawn through the serum cap for injection in gas chromatography. Any additional samples were withdrawn at later appropriate times. In instances where the reaction was run in a boiling alcohol, the stopper was replaced by a reflux condenser.

In some runs in which samples were analyzed by infrared absorption, after the 1-min. period, results were in agreement with those obtained by gas chromatography, although the analysis by infrared absorption was less accurate. Principal use of infrared analysis was to show that reaction of the acid chloride had occurred rapidly at 0°, rather than on injection into gas chromatography at high temperature. As a further check against reaction after injection, one run with isomer I was worked up after the 1-min. reaction time by addition of 50 ml. of ice water. The product was extracted with ether, and this extract was injected for gas chromatography. A quantitative yield of diester was indicated.

In reactions of either isomer I or the ester acid chloride of glutaric acid, the product was 100% diester after a half hour. In some runs, 2–5% of half ester could be detected after the 1-min. reaction time. Results obtained with isomer II under various conditions are summarized in Table I.

In one *run in dry ether*, 9 ml. of ether containing 0.12 ml. of methanol was cooled to 0°, then 0.3 ml. of ester acid chloride II was injected. Injection of a sample of the resultant mixture into gas chromatography showed 100% diester; however, the same result was obtained by simultaneous injection of methanol and an ether solution of isomer II from separate syringes. When solvent was evaporated from the reaction mixture at reduced pressure after an hour at 0°, the residue showed the infrared spectrum of the ester acid chloride.

Synthesis of dimethyl-α-butyl-α-ethylglutarate in continuous reactor. The reactor was of Y-shape, with separate heaters wound on the upper arms which were about 50 cm. long. About 10-cm. below the junction of the arms, a ground joint connected the reactor to a condenser, which was in turn connected to a receiver whose side arm was protected by a drying tube. In the acid chloride arm, a thermometer rested against the glass about midway in the arm on the lower side so that the acid chloride ran over the thermometer bulb. This thermometer was high enough to be unaffected by the vapor temperature of the methanol. At the bottom of the methanol arm, a thermometer was placed in the vapor. Reagents were added from separatory funnels at the tops of the respective arms, as a small pressure was applied so that addition could be made against the pressure generated by vaporization of methanol.

Several exploratory runs were made to determine best conditions, during which it was found that too high a temperature in the acid chloride arm gives some half ester, presumably on account of conversion of ester acid chloride to anhydride prior to reaction with methanol. In a typical run under satisfactory conditions, methanol was added at the rate of 3–4 ml./min. as the heat input was adjusted to give a temperature of 170–180°. Ester acid chloride was added at the rate of about 0.2 g./min., as that arm was heated at 97–100°. A run utilizing 10.4 g. of ester acid chloride was completed in about 55 min., but no determination was made of maximum possible rate of addition.

Immediate gas chromatography of the effluent reaction mixture indicated 100% diester. The reaction mixture was poured into ice water containing one equivalent of sodium carbonate,[8] and the product was extracted with ether. Gas chromatography of the extract also showed only diester, as did infrared analysis of material left (quantitative yield) after removal of solvent. Work-up of the sodium carbonate extract yielded <50 mg. (<0.5%) of half ester.

BERKELEY, CALIF.

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[7] J. Cason and W. T. Miller, *J. Org. Chem.*, 24, 1814 (1959).

[8] Addition of water without neutralization of the hydrochloric acid gives some hydrolysis of ester. Some hydrolysis is also likely if the effluent from the reactor is not protected from moist air.