Anal.[11] Calcd. for C_4H_8O: C, 66.63; H, 11.18. Found: C, 66.71; H, 11.22.

Continued distillation of the residue from the original preparation gave a 92% recovery of excess methyl alcohol and a 57% yield of ethyl alcohol.

To an identical mixture of allyl ethyl ether and methyl alcohol, only the mercuric acetate was added and reflux carried out for 1 hr. The boiling point remained at 56.8°. When 1.0 g. sulfuric acid was added, reaction occurred, as in the above example. Another such mixture of allyl ethyl ether and methyl alcohol was refluxed for 2 hr. with 1.0 g. sulfuric acid alone, but no reaction occurred. Reflux for an additional 3 hr. after the addition of 1.0 g. boron trifluoride etherate similarly gave no reaction. Upon addition of 1.9 g. mercuric acetate, reaction occurred, giving allyl methyl ether (n_D^{25} 1.3730) with less than 1 hr. reflux. Reflux of another such mixture of allyl ethyl ether and methanol with 4 g. of 0.72*M* sodium methoxide in methanol for 1.2 hr. gave no reaction.

Examples of reaction (2). Preparation of allyl cyclohexyl ether. A mixture of 99 g. (1 mole) cyclohexanol, 70 g. (1.2 moles) allyl alcohol, 57 g. benzene, 1.5 g. of 45% solution of boron trifluoride in ether, and 4.6 g. (0.04 mole) mercuric acetate was heated under reflux, and the reflux condensate collected in a Dean-Stark water separator. After reflux for 1 hr., 1.6 g. of the boron trifluoride solution and 4 g. mercuric acetate were added and reflux continued for an additional 2 hr. The reaction mixture was then flash-distilled at 0.1 mm. into a receiver cooled with Dry Ice-acetone, and the distillate washed four times with 50 ml. portions of water, dried, and fractionated. An 86.2 g. yield of material, b.p. 81–89°/36–37 mm., found by bromine number analysis to be 84% pure, was obtained. The yield was thus 42% based on cyclohexanol. The crude product was dissolved in an equal volume of benzene, 5 g. boric acid added, and azeotropic distillation carried out until no further water separated out. The pure allyl cyclohexyl ether was then obtained by fractional distillation: b.p. 81–83.5°/38–39 mm., n_D^{25} 1.4483, d_4^{25} 0.8830.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.51; H, 11.49.

By essentially identical procedures *allyl ether* was prepared in 46% yield: b.p. 94–94.8°, n_D^{25} 1.4134, d_4^{25} 0.8027.

Anal. Calcd. for $C_6H_{10}O$: C, 73.43; H, 10.27. Found: C, 73.43; H, 10.13.

The same method gave *allyl n-butyl ether*, b.p. 64–65°/120 mm., n_D^{25} 1.4029, d_4^{25} 0.7794 (lit.[12] b.p. 117.8–118°/763 mm., n_D^{20} 1.4057, d_4^{20} 0.7829), in 55% yield.

The same method gave *allyl octadecyl ether* in 47% yield: b.p. 146–153°/0.15–0.20 mm., m.p. 26–27°.

Anal. Calcd. for $C_{21}H_{42}O$: C, 81.21; H, 13.63. Found: C, 81.10; H, 13.62.

Allyl benzyl ether was also prepared in 51% yield by this method: b.p. 71–71.5°/5 mm., n_D^{25} 1.5052, d_4^{25} 0.9548.

Anal. Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.43; H, 8.60.

Example of reaction (3). The preparation of allyl octadecyl ether. A solution of 135 g. (0.5 mole) *n*-octadecyl alcohol in 85 g. benzene was prepared and in this solution there were dissolved, in order, 46.6 g. (0.4 mole) allyl ether, 2.0 g. mercuric acetate, and 1.0 g. of a 45% solution of boron trifluoride in ether. The solution was heated under reflux, and the condensate led through a continuous water separator. After 3 hr., 3 g. of an aqueous layer had separated and the solution had turned quite dark. An additional 2.0 g. mercuric acetate and 1.0 g. boron trifluoride solution were added and reflux continued until another 1.5 g. of an aqueous layer had separated.

In order to remove unreacted alcohol, 5 g. boric acid was next added and reflux resumed until no further water appeared. The reaction mixture was then stripped by heating to 97° under 0.35 mm. pressure, and the residue then fractionally distilled to give 110.2 g. allyl octadecyl ether, b.p. 146–152°/0.30 mm., a yield of 71% based on octadecyl alcohol.

Acknowledgment—We wish to acknowledge the technical assistance of Mr. Charles D. Stills in a portion of this work.

PHILADELPHIA, PA.

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(11) Microanalyses by Mr. C. W. Nash and associates.

(12) E. A. Talley, A. S. Hunter, and E. Yanovsky, *J. Am. Chem. Soc.*, **73**, 3528 (1951).

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

Reactions of Succinyl Dichloride with Organometallic Reagents[1]

JAMES CASON AND ELMER J. REIST

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The reaction of diethylcadmium with succinyl dichloride gives no 3,6-octanedione but yields instead γ-ethyl-γ-caprolactone, succinic anhydride, and both pseudo and normal ethyl esters of γ-ketocaproic acid. These products are shown to be consistent with the view that succinyl dichloride is a normal open-chain structure, but γ-ketocaproyl chloride is a cyclic structure (γ-chloro-γ-caprolactone). The reaction of ethylmagnesium bromide with succinyl dichloride also yields products consistent with the above-cited structures. Although the cadmium reaction with succinyl dichloride appears of no value for practical preparative purposes, the Grignard reaction with this dichloride furnishes a useful synthesis of γ-keto acids. The mechanism of the Grignard reaction with acid chlorides in presence of ferric chloride is discussed, and it is suggested that the key step involved, which leads to high yields of ketones, is extraction of halogen from the acid chloride by ferric chloride.

In view of recent evidence[2] that succinyl dichloride exists as the normal open-chain diacid dichloride and that γ-keto acid chlorides exist at room temperature as cyclic structures (γ-chloro-γ-lactones), it is of interest to determine whether the reactions of succinyl dichloride with Grignard and cadmium reagents yield products consistent with such structures. These reagents are selected

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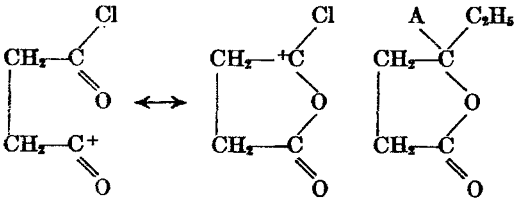
(1) This investigation was supported in part by a research grant (E-86) from the National Institutes of Health, U. S. Public Health Service. A part of these data was presented at the 127th meeting of the American Chemical Society, Cincinnati, Ohio, March 30, 1955.

(2) J. Cason and E. J. Reist, *J. Org. Chem.*, **23**, 1492 (1958).

because the Grignard reagent is believed to react with an acid chloride by addition to carbonyl,[3] whereas the cadmium reagent is believed[4] to react by initial extraction of chlorine from the acid chloride. Of further interest is the reaction of succinyl dichloride with the Grignard reagent in the presence of anhydrous ferric chloride. This reaction has been recently demonstrated[5,6] to constitute an effective preparation of ketones, and certain proposals concerning the mechanism of the reaction have been presented. Examination of these reactions of succinyl dichloride is the subject of the present report.

Reactions with diethylcadmium. According to the mechanism which has been described[4] for reaction of a cadmium reagent with an acid chloride, the initial reaction product from succinyl dichloride would be the cyclic acylonium ion represented in two resonance forms in I. Attack by the carbanion from the cadmium reagent (or by some other species equivalent to the carbanion) at the position of the charge in form Ib would yield the cyclic form (II) of γ-ketocaproyl chloride. Attack at the position of charge in form Ia would yield the open-chain form of γ-ketocarproyl chloride; however, this has been shown[2] to cyclize rapidly at room temperature to the cyclic form, II. Since the cadmium reagent reacts relatively slowly with acid chlorides at room temperature,[7] it follows that the ultimate product of the reaction with diethylcadmium should be γ-ethyl-γ-caprolactone (III), arising from reaction of II with diethylcadmium. Examination of this reaction has indeed shown that none of the product expected (3,6-octanedione) from the normal diacid dichloride structure could be isolated, while γ-ethyl-γ-caprolactone was obtained, although in yields of only 13-15%.



Ia Ib II, A = Cl
III, A = C_2H_5
IV, A = OC_2H_5

The product obtained in largest amount (20-45% yields) from reaction of diethylcadmium with succinyl dichloride was ethyl γ-ketocaproate, isolated as a mixture of the normal open-chain ester and cyclic pseudo ester, IV. Ester formation in the cadmium reaction has been demonstrated[8] to result from reaction of the acid chloride with ether in presence of the Lewis acids in the reaction mixture; however, when as much ether as possible is distilled after formation of the cadmium reagent and the reaction with the acid chloride is carried out after addition of benzene (as was the case in the present work), ester formation is ordinarily of the order of magnitude of 5%. The large amount of ester in the present instance could arise from an unexpectedly high order of reactivity of the cyclic acid chloride, II, with ether; however, this was found to be not the case. A cadmium reaction with γ-ketocaproyl chloride yielded only 6% or less of ethyl γ-ketocaproate and about 17% of lactone III. Since about 20% recovery of γ-ketocaproic acid was realized from the reaction, it would appear that acid chloride II is relatively inert towards reaction with either ether or the cadmium reagent, in line with expectations arising from steric considerations and the structure II.

In the hope that the bulkier di-*n*-butyl ether would reduce the yield of ester, one reaction between succinyl dichloride and diethylcadmium was carried out in that ether as solvent. In this instance, the yield of *n*-butyl γ-ketocaproate proved to be about 40%, and the yield of lactone III dropped to about 5%. The higher yield of butyl ester may be ascribed to the fact that the ether was sole solvent for the reaction, whereas benzene was the principal solvent in reactions utilizing diethyl ether.

Since acid chloride II is unreactive towards ether in presence of the cadmium reagent, no high order of reactivity would be expected for the cyclic ion, I. The only rationale which appears able to account for the high ratio of ester is a cyclic transition state involving succinyl dichloride. The driving force behind a reaction involving such a transition state would be the lower energy of cyclic products with five-atom rings and distribution of steric interferences between two centers of reaction. A form such as V would yield the product, VI, which is a cyclic structure for an ester acid chloride, a form not encountered in a rather careful investigation of such compounds.[9] An intermediate such as VI would be expected to either lose ethyl chloride to yield succinic anhydride or react with the cadmium reagent to give the pseudo ester, IV. Succinic anhydride was isolated from the reaction in 15% yield, and the ethyl γ-ketocaproate was somewhat less than one-half pseudo ester, recognized by its infrared absorption at 5.64 μ and by the high index of refraction of the ester from the cadmium reaction. Since pseudo ester is rearranged to normal ester with acid catalysis,[10]

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[3] C. E. Entemann and J. R. Johnson, *J. Am. Chem. Soc.*, **55**, 2900 (1933).

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

[5] W. C. Percival, R. B. Wagner, and N. C. Cook, *J. Am. Chem. Soc.*, **75**, 3731 (1953).

[6] R. T. Morrison and M. Wishman, *J. Am. Chem. Soc.*, **76**, 1059 (1954).

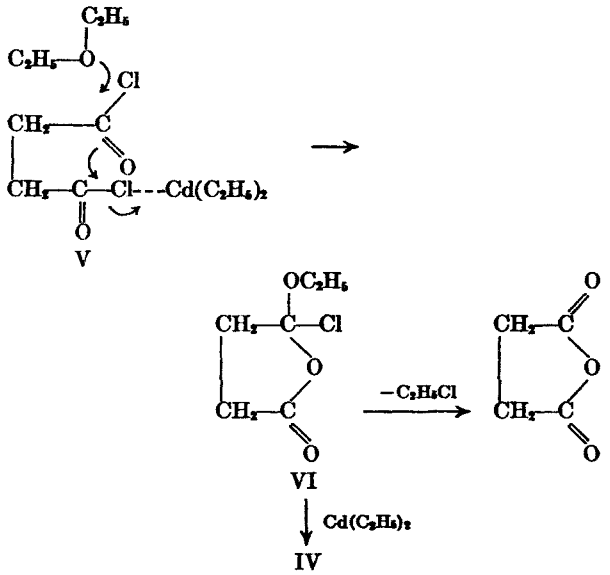
[7] J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946).

[8] J. Cason, *Chem. Revs.*, **40**, 15 (1947).

[9] J. Cason and R. D. Smith, *J. Org. Chem.*, **18**, 1201 (1953).

[10] D. P. Langlois and H. Wolff, *J. Am. Chem. Soc.*, **70**, 2624 (1948).

isolation of normal ester would be expected on account of Lewis acids in the reaction mixture; however, presence of any psuedo ester must be interpreted as evidence of its formation in the initial reaction. For comparison purposes, a modification of the procedures of Langlois and Wolff[10] was used to prepare the pseudo esters of both levulinic and γ-ketocaproic acids.



Thus, the available information concerning the high ratio of ester formation from succinyl dichloride may be correlated on the basis of a cyclic transition state such as V, in which there may be involved other Lewis acids than the organocadmium reagent (both cadmium chloride and magnesium halides are present in the reaction mixtures). Such a transition state would be expected to be less favored in the case of glutaryl dichloride, where the ring would contain six atoms, and this behavior has been observed in investigations of glutaryl dichloride (see following paper).

Reactions with ethylmagnesium bromide. The Grignard reaction with succinyl dichloride gave significantly different ratios of products under three different conditions investigated. The products isolated are summarized in Table I, in which are also included for comparison the products obtained from the cadmium reaction. The striking difference in products attests the different mechanisms of these two reactions.

Although there were used nearly two moles of Grignard reagent per mole of succinyl dichloride, it may be noted that the principal reaction product at 0° is γ-ketocaproyl chloride, isolated as γ-ketocaproic acid after hydrolysis. Isolation of this product is ascribed to the low reactivity[11] of the halogen in the cyclic form (II) towards the Grignard reagent, hence slow conversion at 0° to γ-ethyl-γ-caprolactone (III). A low order of reactivity of the carbonyl group in II is also expected on account of the high yields of lactones obtained[12] in reaction of a Grignard reagent with ethyl levulinate. The insignificant yield of ethyl γ-ketocaproate is consistent with the high reactivity of the Grignard reagent (in comparison with the cadmium reagent), which renders diethyl ether unable to compete effectively for reaction with acid chloride. This is observed in all Grignard reactions except those with highly hindered acid chlorides where extraction of halogen by a Lewis acid becomes a significant reaction path.

TABLE I

YIELDS[a] IN REACTIONS OF SUCCINYL DICHLORIDE WITH ORGANOMETALLIC REAGENTS

Compounds Isolated	Yield[b] from Diethylcadmium	Yield from Ethylmagnesium Bromide		
		0°	−40°	−40°, $FeCl_3$
Ethyl γ-ketocaproate	20–45%	4%	—	—
γ-Ethyl-γ-caprolactone (III)	13–15%	6%	4–10%	12%
γ-Ketocaproyl chloride[c] (II)	—	54%	8%	14%
3,6-Octanedione[d]	—	3–7%	2–7%	23%
3-Ethyloctane-3-ol-6-one[e]	—	—	13–19%	—

[a] Yield figures are approximate since they were determined by isolation, and some of the isolations were troublesome. A range is indicated where significant variations were observed in different runs. In some reactions, other unidentified fractions were isolated; *cf.* Experimental. [b] In one run, after solvent had been distilled from the product the residue was allowed to stand overnight before fractional distillation. There crystallized a 15% yield of succinic anhydride; after recrystallization, m.p. 119–120°, no depression on admixture with an authentic sample of succinic anhydride. In the other runs, this substance was probably hydrolyzed during the work-up. [c] Isolated as γ-ketocaproic acid, after hydrolysis. [d] Isolated as 2-methyl-3-ethyl-2-cyclopentenone, after cyclization by alkali. [e] Isolated largely as the dihydrofuran resulting from dehydration of the hemiacetal. The yield of this material in the −40° run was probably considerably higher than indicated, for considerable quantities of higher-boiling material were obtained, and the properties of this material indicated that it is a dimer of the dehydration product of the hydroxy ketone (*cf.* Experimental).

The small yield of 3,6-octanedione (or its further reaction products) can be rationalized only on the basis that the initial product of the Grignard re-

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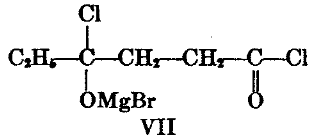
(11) Recovery of γ-ketocaproyl chloride from the Grignard reaction with succinyl dichloride, and failure to recover this acid chloride from the cadmium reaction, as reported in Table I, should not be interpreted as demonstrating a higher order of reactivity of the cadmium reagent towards an acid chloride. A recent investigation [J. Cason and R. J. Fessenden, *J. Org. Chem.*, 22, 1326 (1957)] has shown that the cadmium reagent is far less reactive than the Grignard reagent. The cadmium reaction reported in Table I was continued for 3 hours at 40° and for an additiona 2 hours under reflux in benzene solvent. Even under these conditions, when γ-ketocaproyl chloride was used as starting material in the reaction with diethylcadmium, 20% of it failed to react.

(12) J. Cason, P. B. Brewer, and E. L. Pippen, *J. Org. Chem.*, 13, 239 (1948).

action, VII, loses magnesium halide more rapidly than it reacts with another mole of Grignard reagent, and also the resultant γ-keto acid chloride



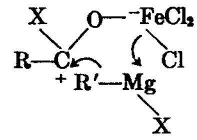
$C_2H_5-\underset{\text{OMgBr}}{\overset{\text{Cl}}{C}}-CH_2-CH_2-\underset{O}{\underset{\|}{C}}-Cl$

VII

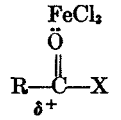
closes to the γ-chloro-γ-lactone (II) more rapidly than it reacts with Grignard reagent. An alternate explanation that structure II is formed directly *via* a cyclic transition state such as V, wherein Grignard reagent takes the place of ether and magnesium halide takes the place of cadmium reagent, seems invalidated by the large drop in yield of acid chloride II when the temperature is lowered to −40°. This observation also renders unlikely the direct conversion of VII to II by displacement of halogen from the carbonyl group in VII. Such an intramolecular reaction involving a five-atom ring would hardly be expected to have a higher energy of activation than reaction of the acid chloride with Grignard reagent.

The drop in yield of acid chloride II when the temperature is lowered to −40° can only be ascribed to this substance not being formed at the lower temperature, for it would certainly survive if formed. Acid chloride II may fail to form either because intermediate VII becomes stabilized at this temperature or because the open-chain γ-ketocaproyl chloride reacts with Grignard reagent at −40° more rapidly than it cyclizes. Since the latter seems unlikely on grounds cited in the preceding paragraph, intermediate VII probably survives for a sufficient time to allow reaction with additional Grignard reagent to give the dimagnesium derivative. The dimagnesium derivative must lose magnesium halide at a significant rate at −40° to give 3,6-octanedione, for the major product of the low temperature reaction (in addition to a higher-boiling, unidentified fraction) is the keto alcohol resulting from further reaction of 3,6-octanedione.

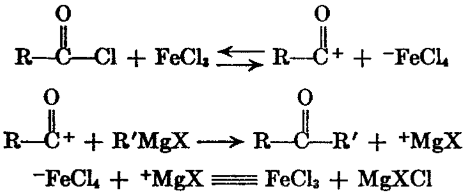
Mechanism of the Grignard reaction in presence of ferric chloride. The only reaction reported in Table I which gives 3,6-octanedione as the major product is the low temperature Grignard reaction in presence of ferric chloride. The yield of dione is more than three times that obtained in absence of ferric chloride. Since none of the keto alcohol, from further reaction of the dione, could be isolated, it must be concluded that ferric chloride does not simply promote the Grignard reaction with a carbonyl group, but rather that it has a specific effect in favoring reaction with an acid chloride. Previous investigators have suggested[6] that the effect of ferric chloride arises from its participation in a cyclic transition state (VIII) of the type suggested by Swain and Boyles[13] for reaction of a ketone with a Grignard reagent. An alternate suggestion[5] differed somewhat, in that there was visualized an intermolecular reaction between the ferric chloride complex, IX, and a carbanion (or equivalent) from the Grignard reagent. These explanations have in common a failure to differentiate between carbonyl in an acid chloride and in other structures such as a ketone. Since our data show that ferric chloride promotes discrimination in favor of an acid chloride, a satisfactory mechanism must include this factor, and must also involve regeneration of ferric chloride which is used in catalytic amounts. A mechanism which seems consistent with the experimental observations is that presented in the following equations:



VIII



IX



$$R-\overset{O}{\overset{\|}{C}}-Cl + FeCl_3 \rightleftarrows R-\overset{O}{\overset{\|}{C}}{}^+ + {}^-FeCl_4$$

$$R-\overset{O}{\overset{\|}{C}}{}^+ + R'MgX \longrightarrow R-\overset{O}{\overset{\|}{C}}-R' + {}^+MgX$$

$${}^-FeCl_4 + {}^+MgX \equiv FeCl_3 + MgXCl$$

This mechanism embodies the essential features of the mechanism proposed[4] for reaction of the cadmium reagents, except that ferric chloride functions as a stronger Lewis acid which will extract halogen at lower temperatures than those at which cadmium reagents are effective. The reality of this mechanism may be checked by investigation of a compound which gives rise to rearrangement if the acylonium ion is formed.[9] It has already been demonstrated[9] that ferric chloride at room temperature does promote rearrangement attributed to extraction of halogen from an acid chloride to give the acylonium ion. The only facts not established are reactivity of ferric chloride in this regard at −40°, and ability of ferric chloride to compete with the Grignard reagent in reaction with an acid chloride. Such an investigation is presently under way in these laboratories.

EXPERIMENTAL[14]

The pseudo methyl ester of levulinic acid was prepared for determination of its infrared spectrum. The procedure of Langlois and Wolff[10] was used; however, the semicarbazone

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[13] C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, 73, 870 (1951).

[14] Melting points are corrected and boiling points are uncorrected. Distillations, unless otherwise specified, were through a half-meter column of the simple Podbielniak type which has been described in detail (J. Cason and H. Rapoport, *Laboratory Text in Organic Chemistry*, Prentice-Hall, Inc., New York, 1950, pp. 237–243). Infrared spectra were recorded on a Baird double beam spectrophotometer. Microanalyses are by the Microanalytical Division, Department of Chemistry, University of California.

of the normal ester could not be completely precipitated, even on addition of a large volume of diethyl ether. Distillation yielded a sample of pure pseudo ester, however, b.p. 93–95°/15 mm., n_D^{25} 1.4330, single carbonyl band in the infrared spectrum at 5.64 μ. From the distillation residue could be isolated semicarbazone of the normal ester, m.p. 175° (dec.).

Pseudo ethyl ester of γ-ketocaproic acid. This ester was obtained in very poor yield when pyridine was used as base in the reaction; however, a satisfactory procedure using sodium carbonate was developed.

The acid chloride of γ-ketocaproic acid was prepared from 26 g. of acid by the procedure previously described.[2] To a mixture of 60 ml. of absolute ethanol and 25 g. of anhydrous sodium carbonate, the acid chloride was added dropwise with vigorous shaking as the *p*H was held above 6 and the temperature was held below 30°. After the addition had been completed during a 5-hr. period, shaking was continued for an additional hour, after which 100 ml. of ether was added. After removal of salt by filtration and of solvent by distillation, there was obtained a residue of 24.9 g. of crude ester. To this ester were added 40 ml. of absolute ethanol, 14.4 g. of semicarbazide hydrochloride and 12 g. of sodium acetate, then the mixture was shaken for 25 hr. After addition of a large volume of dry ether the precipitated material was removed by filtration. Removal of solvent at reduced pressure from the filtrate left 16 g. of residue which was distilled to yield a product, b.p. 91–94°/9 mm., cloudy with a trace of inorganic material. After standing overnight, the clear supernatant liquid was decanted to give a colorless product, n_D^{18} 1.4400.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.67; H, 8.76.

The infrared spectrum exhibited a single carbonyl band at 5.64 μ.

The normal ethyl ester of γ-ketocaproic acid was obtained either by reaction of diethylcadmium with γ-carbethoxybutyryl chloride[2] or by esterification of the keto acid with ethanol in presence of sulfuric acid; b.p. 92°/9 mm., n_D^{25} 1.4233. The infrared spectrum exhibited a single carbonyl band at 5.80 μ.

Reaction of diethylcadmium with succinyl dichloride.[15] (*A*). In 425 ml. of anhydrous diethyl ether, there was prepared in the usual manner, under an atmosphere of nitrogen, a Grignard reagent from 98 g. (0.90 mole) of redistilled ethyl bromide and 21.6 g. (0.90 g.-atom) of magnesium. The solution of Grignard reagent was cooled to 0°, 90 g. (0.50 mole) of powdered anhydrous cadmium chloride was added in several portions during about 2 min., then the cooling bath was removed and the solution stirred 10 min. before it was stirred under reflux until a negative Gilman test for Grignard reagent was obtained (usually about 30 min.). After a negative test for Grignard reagent had been obtained ether was distilled until rate of distillation became slow, then 300 ml. of anhydrous thiophene-free benzene was added, and an additional 100 ml. of solvent was distilled. Finally, 350 ml. of additional dry benzene was added and the solution was cooled with stirring to 5–14° with an ice bath. A solution of 50 g. (0.325 mole) of succinyl dichloride in 150 ml. of benzene was added during about 2 min. The stirred mixture was allowed to warm to 38–40° and held at this temperature for 3 hr., after which it was heated under reflux for an additional 2 hr. After addition of ice and 12*N* sulfuric acid and extraction of the aqueous phase with benzene, the total benzene solution was washed with sodium carbonate solution twice and with water three times. Distillation from a Claisen flask of the material recovered from the benzene solution yielded 30.3 g. of colorless liquid, b.p. about 60°/1 mm. Fractionation of this product through the column at 9 mm. pressure yielded the fractions tabulated below:

Fraction	Weight, g.	Boiling Point	n_D^{25}
1	1.62	72–82°	1.4562
2	2.41	82–90°	1.4467
3	13.31	90–93°	1.4296
4	4.00	93–103°	1.4356
5	5.07	103.5–104°	1.4476
6	0.47	103.5°	1.4469

Fraction 3 gave an analysis in agreement with that of an ethyl ester of γ-ketocaproic acid (center cut used for analysis).

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.52; H, 8.93.

The infrared spectrum of frac. 3 exhibited two carbonyl bands, at 5.64 μ and at 5.80 μ. The index of refraction indicates somewhat less than 50% pseudo ester in the mixture. A semicarbazone, prepared by a common method[16] from frac. 3, had m.p. 106.0–106.5°; the semicarbazone of ethyl γ-ketocaproate has been reported[17] as melting at 106°.

Fraction 6 (center cut of frac. 5) gave an analysis in agreement with that of γ-ethyl-γ-caprolactone.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.32; H, 9.80.

The infrared spectrum of this fraction showed a single carbonyl band at 5.68 μ, the expected position[18] for a γ-lactone. Frac. 5 was insoluble in water but dissolved in 10% aqueous sodium hydroxide; acidification of the alkaline solution yielded starting material. A *hydroxy hydrazide* of the lactone was prepared from hydrazine by the procedure of Blaise[19] and recrystallized from ethyl acetate to yield a white product of m.p. 75–76°.

Anal. Calcd. for $C_8H_{18}N_2O_2$: C, 55.14; H, 10.41; N, 16.08. Found: C, 55.68; H, 10.11; N, 16.05.

The infrared spectrum of the hydroxy hydrazide, taken in a Nujol mull on account of insolubility in the common spectral solvents, exhibited a single carbonyl band at 6.10 μ. Thus, the structure must be that of a hydroxy hydrazide, as has been reported by others,[20] not the cyclic structure assumed by Blaise.[19]

In one run similar to that described above, solvent was removed from the benzene extracts and the residue was allowed to stand overnight. A crystallizate weighing 5 g. separated, and after recrystallization had m.p. 120°, no depression on admixture with an authentic sample of succinic anhydride.

(*B*). To 4.32 g. (0.18 g.-atom) of magnesium and 50 ml. of anhydrous di-*n*-butyl ether, stirred under an atmosphere of nitrogen, there was added a solution of 19.6 g. (0.18 mole) of freshly distilled ethyl bromide in 50 ml. of di-*n*-butyl ether at such a rate (about 1-hour addition time) that the temperature was held at about 40°. After the mixture had been stirred for an additional hour, there was added 10.0 g. (0.10 mole) of anhydrous cadmium chloride, then stirring was continued for another hour at about 80°. Since the Gilman test for Grignard reagent was still positive after this period, an additional 10 g. of cadmium chloride was added. After 15 min. additional stirring at 80°, the test for Grignard reagent had become negative. The reaction mixture was cooled to about 55°, and there was added during about one min. a solution of 10 g. (0.065 mole) of succinyl dichloride

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(15) Succinyl dichloride used in reactions described in this paper was prepared by the method reported in ref. (2).

(16) R. L. Shriner and R. C. Fuson, *Identification of Organic Compounds*, John Wiley and Sons, Inc., New York, 1948, pp. 170, 171.

(17) M. Maire, *Bull. soc. chim. France*, [4], **3,** 285 (1908).

(18) R. S. Rasmussen and R. R. Brattain, *J. Am. Chem. Soc.*, **71,** 1073 (1949).

(19) E. E. Blaise, *Compt. rend.*, **140,** 790 (1905).

(20) R. M. Joyce, W. E. Hanford, and J. Harmon, *J. Am. Chem. Soc.*, **70,** 2529 (1948); J. B. Umland and S. A. Witkowski, *J. Org. Chem.*, **22,** 346 (1957).

dissolved in 50 ml. of di-*n*-butyl ether. The temperature of the reaction mixture rose to about 90° during 3 min., while becoming rather viscous and dark. Heating with stirring was continued for an additional 3 hr. at 75–80°, then the mixture was cooled and worked up as described for the reaction in diethyl ether. Fractional distillation at 9 mm. pressure yielded the following fractions:

Fraction	Weight, g.	Boiling Point	n_D^{25}
1	0.29	69–106°	1.4507
2	0.52	106–108°	1.4445
3	0.59	108–115°	1.4382
4	2.81	115–117°	1.4296
5	1.93	117°	1.4303

The boiling point and index of refraction of frac. 2 indicate that it consists largely of γ-ethyl-γ-caprolactone.

Fraction 4 has an analysis in agreement with that of a butyl ester of γ-ketocaproic acid.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.60; H, 9.68. Found: C, 64.38; H, 9.53.

The *semicarbazone*, prepared by a common method,[16] had m.p. 97.5–98.5°.

Anal. Calcd. for $C_{11}H_{21}N_3O_3$: C, 54.33; H, 8.69; N, 17.28. Found: C, 54.61; H, 8.40; N, 17.28.

Reaction of ethylmagnesium bromide with succinyl dichloride. There is described a representative run under each of the three conditions investigated.

(*A*) *At 0°*. To 120 g. (0.78 mole) of succinyl dichloride dissolved in 300 ml. of dry benzene, arranged for stirring under an atmosphere of nitrogen and cooled to 0°, there was added dropwise a solution in 600 ml. of ether of Grignard reagent prepared from 36 g. (1.5 g.-atoms) of magnesium and 180 g. (1.65 moles) of freshly distilled ethyl bromide. It had been found in earlier runs that use of ether alone as solvent was unsatisfactory on account of rapid precipitation of a complex which stopped the stirrer. The rate of addition of Grignard reagent was adjusted so that the temperature of the reaction mixture could be maintained in the range −5° to +5°. Soon after addition began, the reaction mixture turned brick red; as addition proceeded, the color gradually changed to orange. After addition had been completed the reaction mixture was stirred at 0° for 2 hr., then decomposed with ice and 12*N* sulfuric acid. The aqueous and organic phases were separated, the organic phase was washed once with water, then this phase was placed on a mechanical shaker for 10 hr.[21] with a saturated aqueous sodium carbonate solution. After the shaking period, the aqueous alkaline layer was separated and the organic phase was washed with water.

The sodium carbonate extract was acidified to Congo Red with 12*N* sulfuric acid, then continuously extracted with ether for 24 hr. Removal of ether from the extract left a residue of 60.6 g., which yielded on distillation 50 g. of γ-ketocaproic acid, b.p. 140°/10 mm., which solidified slowly on cooling. The semicarbazone of this acid had m.p. 164.0–164.2° and gave no melting point depression on admixture with the semicarbazone of an authentic sample of γ-ketocaproic acid.

The original aqueous phase obtained after decomposition of the Grignard complex was also continuously extracted with ether for 24 hr. This extract yielded an additional 2 g. of γ-ketocaproic acid, b.p. 120°/4 mm., and 3 g. of ethyl-γ-ketocaproate, b.p. 90°/10 mm., infrared spectrum identical with that of the normal ethyl ester of γ-ketocaproic acid.

The organic phase from which the keto acid was extracted with carbonate contained neutral material which was not readily separated by direct distillation; however, the products obtained after alkali treatment could be partially separated. The residue remaining after removal of solvent was heated under reflux for 4 hr. with excess 10% aqueous sodium hydroxide. The cooled basic solution was extracted five times with ether, and each extract was washed once with water. Removal of solvent from the dried extract and distillation yielded 2.65 g. of impure 2-methyl-3-ethyl-2-cyclopentenone, b.p. 81–83°/10 mm., n_D^{25} 1.4600 (lit.,[22] b.p. 90°/15 mm.). The infrared spectrum showed bands at 5.93 and 6.01 μ, indicative of an α,β-unsaturated ketone, while the ultraviolet spectrum gave similar indication with a band of λ_{max} 235.5 mμ, ε 5400. As shown in the characterization of this compound in section (*C*) below, the extinction coefficient and index of refraction of this sample indicate that it is only about 40% cyclic ketone.

The basic solution remaining after extraction of the saponification mixture was acidified to Congo Red with 12*N* sulfuric acid, then extracted five times with ether. Distillation of the material recovered from this extract yielded 6 g. of γ-ethyl-γ-caprolactone, b.p. 107°/10 mm., n_D^{25} 1.4466. The infrared spectrum contained one carbonyl band at 5.69 μ.

When a reaction was carried out as described above except that there were used only 1.5 moles of ethyl bromide per mole of succinyl dichloride, the yield of γ-ketocaproic acid was reduced to 44%. Further reduction of ethyl bromide to 1.2 moles resulted in only 39% yield of γ-ketocaproic acid.

(*B*) *Grignard reaction at −40°*. The Grignard reaction was carried out in the general manner described under (*A*), except at lower temperature; and there were used as reactants 1 mole of magnesium and of ethyl bromide, 0.5 mole of succinyl dichloride. Addition of the Grignard solution to the dichloride, dissolved in 200 ml. of ether, was begun at −70°, but it was soon found necessary to allow the reaction mixture to warm up to the range −35° to −40° in order to prevent the precipitated complex from stopping the stirrer. After completion of the addition, which required about 3 hr., the mixture was decomposed with ice (the mixture was acidic without addition of acid).

After separation of the aqueous and organic phases from the reaction, the aqueous phase was extracted four times with ether. The ether extracts were washed once with water, then stirred under reflux for 1 hr. with 400 ml. of saturated aqueous sodium carbonate solution. The cooled ether phase was separated and extracted once more with saturated sodium carbonate solution and once with water. The aqueous phases were combined and acidified to Congo Red with 12*N* sulfuric acid, then extracted four times with ether. Distillation of the product recovered from the dried ether extracts yielded 5 g. of γ-ketocaproic acid, b.p. 115°/2 mm. The semicarbazone of this acid had m.p. 165–166° and gave no depression on mixing with an authentic sample.

Content of the *neutral fraction* remaining after carbonate extraction was evaluated by work-up in two ways. *Method* (*a*), *direct distillation*. The organic phase remaining after extraction with sodium carbonate was dried over magnesium sulfate, the solvent was removed by distillation, and the residue was distilled to yield the following fractions:

Fraction	Weight, g.	B.P./pressure	n_D^{25}
1	1.42	30–64°/20 mm.	—
2	11.24	64–68°/20 mm.	1.4422
3	2.41	69–109°/20–9 mm.	1.4527
4	1.80	109–111°/9 mm.	1.4589
5	1.85	111–148°/9–4 mm.	1.4705
6	1.35	*ca.* 148°/9–0.5 mm.	1.4823

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(21) Simple extraction in a separatory funnel with carbonate yields a small amount of keto acid, and subsequent extractions continue to yield small amounts of acid. This behavior is ascribed to the fact that the material actually in the ether solution is γ-chloro-γ-caprolactone, which is hydrolyzed to the keto acid. This is supported by the observation that attempted distillation of the residue from the unextracted ether solution leads to evolution of hydrogen chloride and tar formation.

(22) E. E. Blaise, *Compt. rend.*, **158**, 709 (1914); H. Pringsheim and J. Leibowitz, *Ber.*, **56**, 2037 (1923).

Fraction 2 has a boiling point consistent with that expected for 2,2,5-triethyl-2,3-dihydrofuran (dehydration product of hemiacetal of 3-ethyl-3-hydroxy-6-octanone); however, elementary analysis was not in agreement with this formula, and it seems probable that this fraction is an azeotrope of the dihydrofuran with a small amount of the keto alcohol and/or the hemiacetal. Redistillation of frac. 2 gave material boiling sharply at 72°/28 mm., n_D^{25} 1.4390, infrared spectrum unchanged. The infrared spectrum exhibited weak carbonyl bands at about 5.9 and 6.0 μ, and the ultraviolet spectrum showed no significant absorption except for a rapid rise in absorption as the wavelength was decreased to 210 mμ (characteristic of a carbon-carbon double bond not conjugated). A usual method[16] for preparing semicarbazones gave a reasonable yield from frac. 2 of a derivative whose analysis was in agreement with that calculated for the *semicarbazone of 3-ethyl-3-hydroxy-6-octanone.*

Anal. Calcd. for $C_{11}H_{23}N_3O_2$: C, 57.61; H, 10.11; N, 18.32. Found: C, 57.55; H, 10.05; N, 18.12.

Shortly after recrystallization from water, this semicarbazone had m.p. 90–92° (literature,[23] m.p. 95°), but on standing the m.p. dropped to 79–82° (one recrystallized sample, which had been dried for several days, had m.p. 79.5–80.5°). The low-melting form was converted to the high-melting form by heating at 85–90° for 3–4 hr., and on standing at room temperature changed back to the low-melting form. This behavior suggests polymorphism in the semicarbazone; however, there is also the possibility of a change in structure related to keto alcohol and hemiacetal.

Fracs. 3 and 4 should contain any lactone or dione formed in the reaction; however, no pure components could be isolated until after the alkali treatment described below. The high-boiling material is also described below.

Method (b), alkali treatment prior to distillation. In a run carried out as described above, solvent was removed from the organic phase remaining after carbonate extraction to leave a residue of 35.2 g., which was heated under reflux with 10% aqueous sodium hydroxide for 4 hr. The cooled alkaline solution was extracted four times with ether, and the extracts were washed with water.

The total aqueous phases were acidified to Congo Red with 12*N* sulfuric acid and extracted four times with ether. There was recovered from this extract 3.0 g. of γ-ethyl-γ-caprolactone, b.p. 108–109°/12 mm., n_D^{25} 1.4470.

Material recovered from the extracts of neutral material was distilled to yield the following fractions:

Fraction	Weight, g.	B.P./pressure	n_D^{25}
1	1.95	<65°/20 mm.	1.4470
2	14.45	65°/20 mm.	1.4393
3	4.42	65–151°/20–4 mm.	1.4620
4	7.30	151–153°/4 mm.	1.4716

The characteristics of *frac. 2* were the same as described for this fraction in Method (a); these included analysis, infrared spectrum, and semicarbazone formation.

Fraction 3 contained very little material boiling in the range of 3-ethyl-2-methyl-2-cyclopentenone (93–97°/20 mm.); however, in another run there was isolated 3.8 g. (7% yield) of this product (for characterization, refer to run with ferric chloride). As indicated in Table I, the ratio of the several products obtained in this reaction was rather variable; this is ascribed partly to the uncertain reaction conditions resulting from the barely stirrable mixtures arising from complex precipitation, partly to the uncertainty introduced from the azeotropic material in frac. 2, and partly to the significant amount of high-boiling uncharacterized material described in the next paragraph.

Fraction 4 appears to be some type of dimer of the primary reaction products. No reaction with 2,4-dinitrophenylhydrazine or semicarbazide was observed. The infrared spectrum showed a broad, weak band in the carbonyl region near 6 μ, and a strong band in the ether region (8.9 μ). Redistillation yielded a component boiling sharply at 152–153°/4 mm., with unchanged infrared spectrum. The ultraviolet spectrum showed no absorption except the end absorption characteristic of a carbon-carbon double bond. Elementary analysis (C, 76.99; H, 11.57) is in fair agreement with $C_{20}H_{36}O_2$, the formula for a dimer of 2,2,5-triethyl-2,3-dihydrofuran.

(*C*) *Grignard reaction at −40° in presence of ferric chloride.* A reaction was carried out as described under section (*B*) using the same quantities of reagents, except that 1.5 g. (0.009 mole) of anhydrous ferric chloride was added to the succinyl dichloride solution before addition of Grignard reagent was begun. Addition was started at −65°, but during the course of the 2 hr. required for addition, the temperature was allowed to rise as high as −45° in order to prevent stopping of the stirrer by precipitated complex. After addition was complete, stirring was continued for an additional 5 min., then the reaction mixture was decomposed by pouring onto ice (mixture acid to Congo Red).

The aqueous and organic phases of the reaction mixture were separated, and the organic phase was washed first with water then three times with saturated aqueous sodium carbonate solution (shaking 5–10 min. with each wash), finally with water. The total aqueous carbonate extracts were acidified to Congo Red with 12*N* sulfuric acid and extracted four times with ether. The ether extracts were washed once with water and dried over anhydrous magnesium sulfate. From this extract was recovered 9.5 g. of γ-ketocaproic acid, b.p. 140–160°/10 mm., slowly solidifying on cooling. The semicarbazone, after crystallization from water, had m.p. 167–168° and showed no depression on mixing with an authentic sample of the semicarbazone of γ-ketocaproic acid.

From the extract of neutral material, remaining after carbonate extraction, there was recovered 26.5 g. Since no constant-boiling fractions could be separated by direct distillation, the distilled fractions (weight 22.5 g.) were combined and heated under reflux for 4 hr. with 450 ml. of 10% aqueous sodium hydroxide solution. The cooled basic solution was extracted four times with ether, and the ether extracts were washed once with water. The neutral material recovered from the ether extracts was distilled to yield 14.0 g. of 2-methyl-3-ethyl-2-cyclopentenone, b.p. 85°/10 mm., n_D^{25} 1.4810.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 76.52; H, 10.09.

The infrared spectrum of the cyclopentenone showed strong bands at 5.9 and 6.05 μ, as expected for an α,β-unsaturated ketone. This was confirmed by the ultraviolet spectrum: λ_{max} 235 mμ, ϵ 13,500.

The *semicarbazone*, prepared as usual,[16] had m.p. 217–218° (dec.).

Anal. Calcd. for $C_9H_{15}N_3O$: C, 59.64; H, 8.34; N, 23.18. Found: C, 60.16; H, 8.61; N, 23.28.

The combined aqueous alkaline phases, remaining after saponification and extraction of neutral material, were acidified to Congo Red with 12*N* sulfuric acid and extracted three times with ether. Distillation of the material recovered from the ether extracts yielded 8.65 g. of γ-ethyl-γ-caprolactone, b.p. 108–110°/10 mm., n_D^{25} 1.4460.

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(23) Huan, *Compt. rend.*, **188**, 1175 (1929).