[Contribution from the Department of Chemistry of the University of Wisconsin]

Ketene Acetals. XXXVI. The Preparation and Properties of Acylketene Acetals

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Benzoyl chloride reacts with one equivalent each of ketene dimethylacetal and triethylamine in ether solution to give 50–55% yields of benzoylketene acetal (VIII), the hydrochloride of the amine and small amounts of methyl β-benzoyloxycinnamate (X) and methyl dibenzoylacetate (XI). With an excess of the amine lesser amounts of VIII are formed, and some of the amine is converted to the methyl-quaternary salt. Acylketene acetals are best prepared from the acyl chloride and an excess of the ketene acetal. Aroyl chlorides and aliphatic acyl chlorides with two or three α-substituents give high yields (67–85%) with four equivalents of the ketene acetal. Straight chain aliphatic acyl chlorides require up to one hundred equivalents of the ketene acetal to give comparable yields of the acylketene acetals. With the latter acyl halides the 3-acyloxy-2-alkenoic esters XIII, which result from the O-acylation of the acylketene acetals, are the main products with lower concentrations of the ketene acetal. Succinyl chloride yields the enol lactone XX, *via* the intramolecular O-acylation of the initially formed monoacylketene acetal XIX.

An earlier paper[2] in this series reported the reaction of ketene diethylacetal (I) with an equivalent amount of acetyl or benzoyl chloride to yield the O-acyl derivative of a β-keto-ester, acetoacetic or benzoylacetic ester, as the principal reaction product. It was suggested that these O-acyl derivatives III resulted from the acylation of the enol form of the β-keto ester II, which was thought to be the initial product of the reaction. This reaction course seemed substantiated when it was shown that the β-keto ester could be O-acylated with the acyl chloride in the presence of the ketene acetal, which removed the hydrogen chloride produced in the reaction as readily as did pyridine, the base commonly used for this purpose.

$$\mathrm{RCOCl} + \underset{\mathrm{I}}{\mathrm{CH_2{=}C(OEt)_2}} \longrightarrow \mathrm{EtCl} + \underset{\mathrm{II}}{\mathrm{RCOCH_2COOEt}}$$

$$\underset{\mathrm{II}}{\mathrm{RCOCH_2COOEt}} \xrightarrow[\mathrm{I}]{\mathrm{RCOCl}} \underset{\mathrm{III}}{\mathrm{RC(OCOR){=}CHCOOEt}} + \mathrm{CH_3COOEt} + \mathrm{EtCl}$$

More recently, it was found that the reaction of ketene dimethylacetal and methylketene diethylacetal with methyl chloroformate[3] gave the corresponding carbomethoxyketene acetals, $\mathrm{RC(COOCH_3){=}C(OR)_2}$, and that the reaction of four equivalents of the ketene acetal I with acetyl chloride produced acetylketene acetal[4] (IV). In each of these acylations of the ketene acetal one equivalent of the acetal was consumed by the hydrogen chloride produced in the initial reaction, *e.g.*

$$\mathrm{CH_3COCl} + \underset{\mathrm{I}}{\mathrm{CH_2{=}C(OEt)_2}} \longrightarrow \mathrm{CH_3COCH_2\overset{+}{C}(OEt)_2Cl^-} \xrightarrow{\mathrm{CH_2{=}C(OEt)_2}} \underset{\mathrm{IV}}{\mathrm{CH_3COCH{=}C(OEt)_2}} + \mathrm{CH_3COOEt} + \mathrm{EtCl}$$

It was suggested that the nucleophilic center of IV could reside on the oxygen to give an active species, $\mathrm{\overset{-}{O}{-}C(CH_3){=}CH{-}C(OEt){=}\overset{+}{O}Et}$, which might well make IV, rather than the β-keto-ester, the precursor of the 3-acyloxyalkenoic esters III that were obtained as the principal reaction product in the earlier work.[2]

Inasmuch as ketene acetals are quantitatively convertible by hydrolysis to the corresponding esters, it seemed desirable to investigate the preparation of a variety of acylketene acetals in the hope of developing a novel method of preparation of β-keto esters and the ketones to which they may be converted by decarbalkoxylation. The first phase of this study involved the acylation of the ketene acetal in the presence of a tertiary amine, which, it was hoped, would serve the dual purpose of (a) increasing the reactivity of the acyl halide by ionization *via* the quaternary compound V, and (b) conserving the ketene acetal by combining with the hydrogen chloride produced in the reaction.

Benzoyl chloride was found to react with one equivalent each of ketene dimethylacetal (VI) and triethylamine in diethyl ether to give 50–55% yields of benzoylketene acetal (VIII), m.p. 55°, 11% of methyl β-benzoyloxycinnamate (X), 5–7% of methyl dibenzoylacetate (XI) and 75–80% of triethylamine hydrochloride. These yields were not materially altered by varying the order of mixing the reactants. The relatively low and fairly constant yields of benzoylketene acetal (VIII) are apparently due to a number of side reactions that either prevented the formation of VIII or converted it to other products after it was formed. The initial reaction of V and VI produces the intermediate

$$\mathrm{C_6H_5COCl} + \mathrm{Et_3N} \longrightarrow \underset{\mathrm{V}}{\mathrm{C_6H_5CO\overset{+}{N}Et_3\overset{-}{C}l}}$$

$$\underset{\mathrm{VI}}{\mathrm{CH_2{=}C(OCH_3)_2}} + \mathrm{V} \longrightarrow \underset{\mathrm{VII}}{\mathrm{C_6H_5COCH_2{-}\overset{+}{C}(OCH_3)_2\overset{-}{C}l}} + \mathrm{Et_3N} \xrightarrow{\text{(a)}} \underset{\mathrm{VIII}}{\mathrm{C_6H_5COCH{=}C(OCH_3)_2}} + \mathrm{Et_3NHCl}$$

$$\underset{\mathrm{VII}}{\mathrm{C_6H_5COCH_2\overset{+}{C}(OCH_3)_2\overset{-}{C}l}} \xrightarrow{\text{(b)}} \underset{\mathrm{IX}}{\mathrm{C_6H_5COCH_2COOCH_3}} + \mathrm{CH_3Cl}$$

$$\mathrm{IX} + \mathrm{C_6H_5COCl} + \mathrm{Et_3N} \longrightarrow \underset{\mathrm{X}}{\mathrm{C_6H_5C(OCOC_6H_5){=}CHCOOCH_3}} + \mathrm{Et_3NHCl}$$

$$\mathrm{VI} + 2\mathrm{V} \longrightarrow \underset{\mathrm{XI}}{\mathrm{(C_6H_5CO)_2CHCOOCH_3}}$$

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[1] Wisconsin Alumni Research Foundation Research Assistant, 1954–1955; Allied Chemical and Dye Corporation Fellow, 1955–1956.

[2] S. M. McElvain and D. G. Kundiger, This Journal, **64**, 254 (1942).

[3] S. M. McElvain and R. D. Mullineaux, *ibid.*, **74**, 1811 (1952).

[4] S. M. McElvain and H. F. McShane, Jr., *ibid.*, **74**, 2662 (1952).

VII, which may (a) be deprotonated by the amine to form VIII and the amine hydrochloride, or (b) lose methyl chloride to form benzoylacetic ester (IX), which then may be O-benzoylated in the presence of the amine to X. It is quite likely that some of the original ketene acetal VI is lost in competing with the tertiary amine for the proton of VII. The diacylated ester XI is doubtless formed along with some of the monoacylated ester IX from V and VI in a manner similar to the mono- and dibenzylation of ketene acetal with the reactive halide, benzyl bromide.[4] Finally, it was found that both X and XI were formed in small amounts from the interaction of the acylketene acetal VIII with benzoyl chloride under the reaction conditions used.

When the benzoylation of VI was carried out with an excess of the amine as solvent instead of ether, a somewhat lower yield of VIII (40%) resulted; the most striking feature of this reaction was the precipitation of the amine as a mixture of the hydrochloride and the methyl-quaternary salt. The latter compound was formed by demethylation of VII to IX.[5]

$$\text{VII} \longleftrightarrow \text{C}_6\text{H}_5\text{COCH}_2\text{C(OCH}_3\text{)}{=}\overset{+}{\text{O}}\text{CH}_3\bar{\text{Cl}} + \text{Et}_3\text{N} \longrightarrow$$
$$\text{IX} + \text{Et}_3\overset{+}{\text{N}}\text{CH}_3\bar{\text{Cl}}$$

The substitution of pyridine for triethylamine in the above reaction gave much less satisfactory results. About 42% of the theoretical amount of methyl chloride was evolved; from the reaction mixture was obtained an impure salt—from which some methylpyridinium chloride was separated—and a viscous, ether-soluble product that failed to crystallize. It appears from these results that the pyridine is much less effective for the deprotonation of the intermediate VII than is triethylamine.

Since 50–55% of the acylketene acetal seemed to be the maximum yield that could be obtained from the reaction of benzoyl chloride with the ketene acetal in the presence of an amine, the acylation reaction in the presence of an excess of the ketene acetal was investigated. When benzoyl chloride was added to 4 equivalents of refluxing VI (b.p. 90°), it reacted readily to evolve 96% of the theoretical amount of methyl chloride and produce an 84% yield of benzoylketene acetal (VIII). Similar yields of the corresponding ketene acetals—or their hydrolysis products—were obtained from *m*- and *p*-methoxybenzoyl chlorides and *o*- and *p*-nitrobenzoyl chlorides. However, the rates at which these acyl chlorides reacted with VI were quite different, *e.g.*, the reaction of *p*-nitrobenzoyl chloride was vigorous at −10° while that of *p*-methoxybenzoyl chloride was only moderate at room temperature.

Benzoyl chloride reacts with the benzoylketene acetal (VIII) to form the benzoyloxycinnamic ester X in about 10% yield in 2 hours at 35°, but at 80° this O-acylation goes to the extent of 67% in this time. None of the dibenzoylacetic ester XI was found in any of the acylations in which a tertiary amine was not present. For this reason it is believed that the reactive species in the amine reactions is the quaternary structure V, which forms the mono- and diacyl esters, IX and XI, in competition to the main product, benzoylketene acetal (VIII).

In the absence of the tertiary amine a keto-ester such as IX does not compete successfully with either the ketene acetal (VI) or the benzoylketene acetal (VIII) for the acyl chloride. For example, the very active acid chloride, *p*-nitrobenzoyl chloride, reacts at −10° with VI in the presence of either methyl benzoylacetate (IX) or methyl valerylacetate to give an 87% yield of *p*-nitrobenzoylketene acetal. In contrast to the relative inertness of these keto esters, benzoylketene acetal (VIII) reacts with *p*-nitrobenzoyl chloride at −10° to give a 59% yield of methyl *β*-*p*-nitrobenzoyloxycinnamate; at 80° this product is formed in 84% yield.

Benzoyl chloride reacts with the homologous methylketene dimethylacetal (4 equivalents) in the same manner as with VI to give an 88% yield of methylbenzoylketene dimethylacetal, $\text{C}_6\text{H}_5\text{COC(CH}_3\text{)}{=}\text{C(OCH}_3\text{)}_2$.

The reactions of the ketene acetal (VI) with two representative aliphatic acyl chlorides, valeryl and lauroyl chlorides, were next investigated. When the ratio of VI to the acyl chloride was 4:1, the yields of the acylketene acetals (XII) amounted to only 24–32%; the major reaction products were the 3-acyloxy-2-alkenoic esters XIII. Increasing the ratio of VI to acyl chloride to 20:1 raised the yields of XII to 55–60%; a ratio of 100:1 for these reactants produced an 86% yield of the acylketene acetals XII. Apparently, these acylketene acetals are O-acylated much more readily than the unsubstituted ketene acetal VI is C-acylated.

$$\underset{\text{VI}}{2\text{CH}_2{=}\text{C(OCH}_3\text{)}_2} + \text{RCOCl} \longrightarrow$$
$$\underset{\text{XII}}{\text{RCOCH}{=}\text{C(OCH}_3\text{)}_2} + \text{CH}_3\text{COOCH}_3 + \text{CH}_3\text{Cl}$$

$$\text{XII} + \text{RCOCl} \longrightarrow$$
$$\underset{\text{XIII}}{\text{RC(OCOR)}{=}\text{CH}{-}\text{COOCH}_3} + \text{CH}_3\text{Cl}$$

In contrast to these straight chain acyl chlorides, acetyl chlorides with two or more *α*-substituents, *e.g.*, trimethyl-, trichloro- and diphenylacetyl chlorides, gave good (67–81%) yields of the corresponding acylketene acetals when treated with only 4 equivalents of the ketene acetal VI. This fact indicates that competition of XII with VI for the acyl halide is markedly reduced or eliminated if the R of XII is of sufficient size to sterically inhibit the reactivity of the adjacent carbonyl group. The higher yields of XII in these cases do not seem related to the reactivity of the acyl chloride as the reaction with trichloroacetyl chloride is extremely vigorous and had to be run at low temperatures to be controlled, while the reaction of trimethylacetyl chloride was noticeably less vigorous than that of valeryl chloride.

The large excesses of the ketene acetal that are required for high yields of the acylketene acetals

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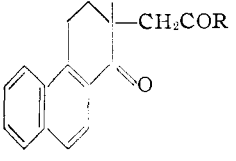
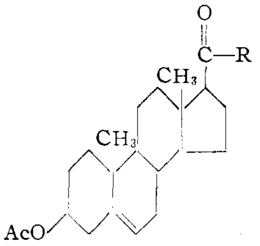
(5) Mr. Philip L. Weyna in this Laboratory has observed a similar reaction between a ketene acetal and dimethylaniline hydrochloride in solution in dimethylaniline

$$\text{C}_6\text{H}_5\text{N(CH}_3\text{)}_2\cdot\text{HCl} + \text{CH}_2{=}\text{C(OCH}_3\text{)}_2 \longrightarrow$$
$$\text{CH}_3\text{C(OCH}_3\text{)}{=}\overset{+}{\text{O}}\text{CH}_3\bar{\text{Cl}} \xrightarrow{\text{C}_6\text{H}_5\text{N(CH}_3\text{)}_2}$$
$$\text{CH}_3\text{COOCH}_3 + \text{C}_6\text{H}_5\text{N(CH}_3\text{)}_3\text{Cl}^-$$

with some of the aliphatic acyl chlorides does not make the use of the reaction prohibitive. The excess may be recovered and used again; also, the products are formed under extremely mild conditions and are generally quite clean. For this reason the procedure may prove to be one of choice when expensive acyl chlorides are to be used. For example, 1-keto-2-methyl-1,2,3,4-phenanthryl-2-acetyl chloride (XIV) gave, after recovery of the excess ketene acetal VI, 75% of the acylketene acetal (XV), m.p. 149–150°, and, after hydrolysis and decarboxylation of the remaining material, 16% of the methyl ketone XVI. If the reaction products were hydrolyzed and decarboxylated directly without isolation of XV, a 97% yield of the methyl ketone XVI was obtained. Similarly, 3-β-acetoxy-etio-5-cholenyl chloride (XVII) gave 78–80% yield of the acylketene acetal (XVIII), m.p. 173–175°.

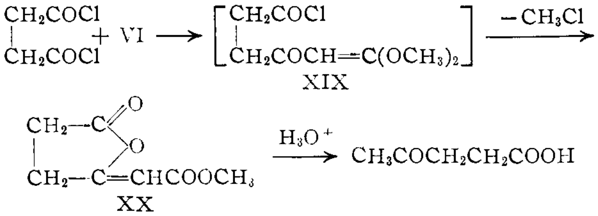


XIV, R is Cl
XV, R is $CH{=}C(OCH_3)_2$
XVI, R is CH_3



XVII, R is Cl
XVIII, R is $CH{=}C(OCH_3)_2$

Dibasic acid chlorides in which the functional groups are well separated react with ketene acetal VI to give the corresponding diacylketene acetals,[6] $(CH_3O)_2C{=}CHCO(CH_2)_nCOCH{=}C(OCH_3)_2$. Succinyl chloride, however, formed a different type of product. When treated with 4 equivalents of ketene acetal, this acyl chloride gave a 65% yield of a product, m.p. 71–72.5°, to which the methylenebutyrolactone structure XX is assigned. This product is the result of an intramolecular O-acylation of the acylketene acetal function of the monoacylketene acetal (XIX) by its acyl chloride function. The product XX has an absorption band at 5.60 μ in the infrared, which is characteristic of a 5-membered enol lactone[7]; it shows no absorption at the hydroxyl frequency indicating the absence of any of the tautomeric hydroxyfuran structure.[8] XX is readily hydrolyzed and decarboxylated to levulinic acid; on standing or on exposure to air it underwent resinification so rapidly that it could not be obtained sufficiently pure for analysis.



A compound analogous to XX, which contains a malonic ester instead of an acetic ester residue as a ring substituent, has been reported by Ruggli and Maeder[9] as one of the products of the reaction of succinyl chloride with sodiomalonic ester.

Experimental

Benzoylation of Ketene Dimethylacetal. (a) In Diethyl Ether in Presence of Triethylamine.—To a solution of 22 g. (0.25 mole) of ketene dimethylacetal (VI) and 25.3 g. (0.25 mole) of triethylamine in 200 ml. of dry ether was added dropwise 35.1 g. (0.25 mole) of benzoyl chloride. The mixture was refluxed for 2 hours and the precipitated triethylamine hydrochloride (m.p. 258–260°, authentic sample, m.p. 260–261°) was collected by filtration in two crops (27.3 g., 79%).

When the ether solution was cooled in a Dry Ice–acetone cold bath, 26.3 g. (55%) of precipitated benzoylketene dimethylacetal (VIII) (see Table I) was separated by filtration. The ether filtrate was extracted with several portions of 5% hydrochloric acid, then with 5% sodium bicarbonate and finally with 5% sodium hydroxide. When the sodium hydroxide extracts were acidified, 1.7 g. (4.8%) of **methyl dibenzoylacetate (XI)** was isolated by extraction with ether. The material gave a deep red coloration with ferric chloride solution and was recrystallized from absolute ethanol to obtain an analytical sample, m.p. 109.5–110°.

Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.31; H, 5.10.

The ether solution which had been extracted with acid, bicarbonate and base was evaporated to an oily residue which was taken up in 5 ml. of ethanol. After several days the residue had partially crystallized. After trituration with 70% alcohol the crystalline material was filtered off; the yield of **methyl β-benzoyloxycinnamate (X)** was 4.1 g. (11%). Recrystallization from aqueous ethanol gave an analytical sample, m.p. 84–85° (see Table II). The product gave no enol test when treated with ferric chloride solution.

After removal of solvent the mother liquors were distilled to give 1.0 g. (3%) of methyl benzoate. A red viscous oil amounting to 3.75 g. remained as an undistillable residue.

The yields of the various products remained essentially unchanged when ketene dimethylacetal was added to a mixture of benzoyl chloride and triethylamine in ether under similar conditions.

(b) In Triethylamine.—To a solution of 8.8 g. (0.1 mole) of ketene dimethylacetal (VI) in 50 ml. of anhydrous triethylamine was added dropwise 14.0 g. (0.1 mole) of benzoyl chloride during a period of 1.5 hours. The temperature of the reaction mixture rose from 24 to 30°. After magnetically stirring the reaction mixture for an additional 1.25 hour, it was heated to reflux. Distillation yielded triethylamine as the first material collected, b.p. 86–89°, n^{25}_{D} 1.3982; it follows, therefore, that no methyl acetate (b.p. 57°, n^{25}_{D} 1.3593) was formed in the reaction. The cold trap contained 0.25 g. (5%) of methyl chloride.

The volatile products were removed at 8 mm. pressure (50°) and the residue was then diluted with 100 ml. of dry ether. The precipitated amine salt (12.4 g.) was separated by filtration; it melted at 220–250°. This melting point could not be improved by washing the salt with ether or upon prolonged drying; triethylamine hydrochloride melts at 260–261°.

The ether filtrate was washed several times with 5% hydrochloric acid to remove any remaining triethylamine and to hydrolyze benzoylketene dimethylacetal to methyl benzoylacetate. The ether layer was dried and distilled. After removal of the ether solvent, 7.4 g. (41.5%) of methyl benzoylacetate, b.p. 95–97° (0.1 mm.), n^{25}_{D} 1.5378, was collected. An undistillable residue remained from which 2.1 g. of methyl β-benzoyloxycinnamate was obtained by crystallization.

When ketene dimethylacetal (0.1 mole) was added to a mixture of benzoyl chloride (0.1 mole) in excess triethyl-

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[6] Professor William S. Johnson, Dr. R. Pappo and collaborators in this Laboratory have found that ketene acetal and certain substituted azelaic acid chlorides give high yields of the diacylketene acetals, which were converted to the corresponding methyl ketones and isolated as such.

[7] R. B. Woodward and E. G. Kovach, This Journal, **72**, 1009 (1950).

[8] H. Hodgson and R. R. Davies, *J. Chem. Soc.*, 806 (1939), reported the preparation of a compound claimed to be 2-hydroxyfuran which spontaneously darkened and resinified. However, doubts have been expressed as to the validity of such a structure (R. H. Thomson, *Quart. Rev.*, **X**, 34 (1956)).

[9] P. Ruggli and A. Maeder, *Helv. Chim. Acta*, **26**, 1476 (1943).

TABLE I

ACYLKETENE ACETALS, $RCOCR'=C(OCH_3)_2$

					Analyses, %			
					Calcd.		Found	
R is	R' is	Yield, %	M.p. or b.p. (mm.), °C.	Formula	C	H	C	H
C_6H_5	H^a	84	55–56	$C_{11}H_{12}O_3$	68.73	6.29	68.73	6.42
p-$CH_3OC_6H_4$	H	81	98–100	$C_{12}H_{14}O_4$	64.85	6.35	64.66	6.25
p-$NO_2C_6H_4$	H^b	88	155–157	$C_{11}H_{11}NO_5$	55.69	4.67	55.80	4.71
o-$NO_2C_6H_4$	H	90	118–119	$C_{11}H_{11}NO_5$	55.69	4.67	55.78	4.70
C_6H_5	CH_3	88	110–111(0.1)^c	$C_{12}H_{14}O_3$	69.88	6.84	70.10	6.71
$(CH_3)_3C$	H^d	75	49–50	$C_9H_{16}O_3$	62.77	9.37	62.68	9.45
Cl_3C	H	81	75–77	$C_6H_7Cl_3O_3$	30.86	3.02	31.23	3.30
$(C_6H_5)_2CH$	H	67	101–102	$C_{18}H_{18}O_3$	76.58	6.43	76.81	6.43
$CH_3(CH_2)_{10}$	H	60	27–29^e	$C_{16}H_{30}O_3$	71.07	11.19	70.94	11.43
XV		75	149–150	$C_{21}H_{27}O_4$	74.54	6.56	74.49	6.46
XVIII^f		80	173–175	$C_{26}H_{36}O_5$	72.52	8.90	72.45	8.80

^{a} λ_{max} 277 mμ, ϵ 14,300 (cyclohexane); the infrared spectrum had strong absorption peaks at 6.11 and 6.40 μ (acylketene acetal) and at 6.32 and 6.75 μ (phenyl group). ^{b} 3 g. of this ketene acetal was hydrolyzed by dilute hydrochloric acid in aqueous methanol to 2.6 g. of methyl p-nitrobenzoylacetate, m.p. 110–111°, which contained 53.96% C and 4.27% H (calcd. 53.80 and 4.06); reported m.p. 106–107° (W. H. Perkin and G. Bellenot, *J. Chem. Soc.*, **49**, 443 (1886). ^{c} $n^{25}D$ 1.5452, d^{25}_4 1.0987. ^{d} λ_{max} 254 mμ, ϵ 10,700 (cyclohexane). ^{e} B.p. 142–143° (0.05 mm.); λ_{max} 245 mμ, ϵ 15,600 (cyclohexane); ^{f} λ_{max} 266 mμ, ϵ 17,500; the infrared spectrum showed strong absorption peaks at 6.04 and 6.45 μ.

amine under conditions identical to those described above, the various products were obtained in comparable yields.

(c) **In Excess Ketene Dimethylacetal.**—To 17.6 g. (0.20 mole) of ketene dimethylacetal heated to reflux and magnetically stirred was added 7.0 g. (0.05 mole) of benzoyl chloride over a period of 30 minutes. After an additional hour of refluxing, 2.4 g. (96%) of methyl chloride had collected in a cold trap. The volatile material in the reaction flask was removed at 60–70° (20 mm.). After the addition of 10 ml. of dry ether the contents of the flask crystallized when cooled; filtration gave 8.1 g. (0.042 mole, 84.5%) of benzoylketene dimethylacetal (VIII), m.p. 52–54°. Recrystallization from dry ether yielded 7.5 g. of product, m.p. 54.5–55.5°.

When 10 drops of 10% hydrochloric acid was added to a water–ether slurry of 13.2 g. of benzoylketene dimethylacetal, hydrolysis occurred with the evolution of considerable heat. The aqueous layer was extracted with ether and after drying, the ether was removed under reduced pressure. The residue was distilled from a modified Claisen flask to yield 11.5 g. (94%) of methyl benzoylacetate, m.p. 90–92° (0.05 mm.), $n^{25}D$ 1.5378. When heated with phenylhydrazine this ester gave 1,3-diphenylpyrazolone-5, which, after recrystallization from aqueous methanol, melted at 137–138° (reported[10] 137°).

Preparation of Other Acylketene Acetals.—Following procedure (c) anisoyl, m-methoxybenzoyl and trimethylacetyl chlorides were substituted for benzoyl chloride. The yields and properties of the anisoyl and trimethylacetylketene acetals are listed in Table I.

The m-methoxybenzoylketene acetal from 32.4 g. of the acid chloride was not isolated, but hydrolyzed to the keto ester by stirring with 50 ml. of water containing 10 ml. of 5% hydrochloric acid. The keto ester was treated with 440 ml. of 4.5% sodium hydroxide solution and the mixture stirred at room temperature overnight. It was then heated on the steam-bath for 1 hour, acidified with 35 g. of sulfuric acid in 100 ml. of water, heated for another hour, then cooled and extracted with ether. The extracts were dried and distilled through a modified Claisen flask to yield: (a) 0.75 g., b.p. 30–76° (25 mm.); (b) 2.1 g., b.p. 76–138° (25 mm.), $n^{25}D$ 1.3980; (c) 11.8 g., b.p. 138–141° (25 mm.), $n^{25}D$ 1.5370; (d) 10.4 g., b.p. 141–144° (25 mm.), $n^{25}D$ 1.5383. Fractions (c) and (d) amounted to 22.2 g. (78%) of m-methoxyacetophenone (reported[11] b.p. 125–126° (12 mm.), $n^{20}D$ 1.5431).

A semicarbazone derivative was prepared, m.p. 192–194° (reported[12] crude m.p. 182–183°; after several recrystallizations the m.p. was 195–197°). The dark brown residue from the distillation was dissolved in ether and extracted with 5% sodium bicarbonate. Upon acidification of the basic extracts, 3.5 g. (12%) of pale yellow m-methoxybenzoic acid, m.p. 106–108°, precipitated. After one recrystallization from water, the melting point was 107–108° and was not depressed when mixed with authentic material.

With o- and p-nitrobenzoyl chlorides (4.64 g. used in each case) the previously cooled (Dry Ice and acetone) ketene acetal was added to the acyl chloride and the mixture allowed to warm with stirring. In the case of the p-compound at −10° a vigorous reaction began to produce an insoluble yellow product, which was separated by dilution with ether and filtration; it was recrystallized from benzene. The acylation of ketene dimethylacetal with p-nitrobenzoyl chloride was carried out equally well in the presence of an equivalent of either methyl benzoylacetate or methyl valerylacetate, showing that the ketene acetal is more reactive toward acylation than is either of these β-keto-esters.

In an attempt with 2,4,6-trinitrobenzoyl chloride, it was added to the ketene acetal cooled to −70° in a Dry Ice–acetone cold bath. An extremely violent reaction occurred; blue smoke was evolved and only carbonized tar remained in the reaction flask.

Trichloroacetyl chloride (17.6 g.) and diphenylacetal chloride (4.0 g.) were added dropwise to 4 equivalents of the ketene acetal cooled in a Dry Ice–acetone bath and the mixture stirred and allowed to warm to room temperature. Reaction with evolution of methyl chloride began in each case between −40 and −10°. Dilution of the reaction mixture with ether, followed by cooling, precipitated the acylketene acetals, which were recrystallized from benzene–petroleum ether mixture.

Benzoyl chloride and methylketene dimethylacetal[13] reacting as in (c) yielded benzoylmethylketene dimethylacetal, which was isolated by distillation of the reaction mixture (see Table I). A sample of this acylketene acetal was hydrolyzed with dilute hydrochloric acid and then treated with hydroxylamine hydrochloride after which the mixture was neutralized with sodium bicarbonate and heated for 1 hour on a steam-bath. Acidification of the resulting solution with dilute hydrochloric acid gave 4-methyl-3-phenylisoöxazolone-5, which after drying overnight melted at 121–122° (reported[14] 123–124°).

Methyl β-Acyloxycinnamates (see Table II).—The methyl benzoyloxycinnamate (X) obtained in (a) above was also obtained (i) in 4.2% yield along with a 4% yield of methyl dibenzoylacetate (XI) from the interaction of benzoyl chloride, benzoylketene acetal (VIII) and triethylamine in ether solution; (ii) in 67% yield by refluxing a benzene solution of VIII and benzoyl chloride for 1 hr.; (iii) in 85% yield by the interaction of methyl benzoylacetate (4.2 g.) and benzoyl chloride (3.37 g.) in 10 ml. of pyridine at reflux temperature for 2 hr. The product was isolated by pouring

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[10] L. Knorr and C. Klotz, *Ber.*, **20**, 2546 (1887).

[11] K. von Auwers, *et al.*, *Ann.*, **408**, 212 (1915).

[12] A. Wahl and C. Silberzweig, *Bull. soc. chim.*, [4] **11**, 69 (1912).

[13] S. M. McElvain and J. T. Venerable, THIS JOURNAL, **72**, 1661 (1950). This ketene acetal was prepared for the present work by dealcoholation of methyl orthopropionate with aluminum t-butoxide (S. M. McElvain and W. R. Davie, *ibid.*, **73**, 1400 (1951)).

[14] A. Haller and E. Bauer, *Compt. rend.*, **152**, 1446 (1911).

the reaction mixture into water; it was recrystallized from absolute ethanol.

Methyl β-*p*-nitrobenzoyloxycinnamate was similarly prepared in 84% yield from (i) benzoylketene acetal (VIII) and *p*-nitrobenzoyl chloride in refluxing benzene; these reactants gave a 59% yield of this acylketene acetal in ether at −10 to 0° for 2 hr. and (ii) in 94% yield from methyl benzoylacetate in anhydrous pyridine.

Acylation of Ketene Dimethylacetal with Aliphatic Acyl Chlorides. (a) **With Valeryl Chloride.**—To 35.2 g. (0.40 mole) of ketene dimethylacetal, heated to reflux (89°) and magnetically stirred, 12.06 g. (0.10 mole) of freshly distilled valeryl chloride was added dropwise. After the addition was completed (30 minutes) the contents of the flask were refluxed for 1 hour. The reaction mixture then was cooled to 50° and the volatile material removed under reduced pressure (22 mm.). The volatile products were collected in a cold trap and refractionated to obtain the unreacted ketene dimethylacetal, b.p. 89–91°. The material remaining in the reaction flask was cooled in an ice-bath while 8 ml. of 1% hydrochloric acid was added. The contents of the flask were stirred for 15 minutes at room temperature and the water-insoluble products were removed by extraction with ether. After the ether extracts were dried over sodium sulfate, the ether was removed under reduced pressure and the residue was distilled through a 25-cm. Podbielniak column at 0.1 mm. to give the following fractions: (a) 0.6 g., b.p. 25–50° (0.1 mm.), n^{25}_{D} 1.4473; (b) 0.05 g., b.p. 50–55° (0.1 mm.), n^{25}_{D} 1.4292; (c) 3.7 g., b.p. 55–56° (0.1 mm.), n^{25}_{D} 1.4295; (d) 0.7 g., b.p. 56–83° (0.1 mm.), n^{25}_{D} 1.4428; (e) 5.55 g., b.p. 83–85° (0.1 mm.); n^{25}_{D} 1.4455; (f) 2.1 g., b.p. 85–87° (0.1 mm.), n^{25}_{D} 1.4475.

Fractions (b) and (c) amounted to 3.75 g. (23.7%) of methyl valerylacetate. Redistillation of (c) from a modified Claisen flask gave a product, b.p. 54–55° (0.1 mm.), n^{25}_{D} 1.4315, d^{25}_{4} 0.9893; it contained 60.57% C and 8.97% H; (calcd. for $C_8H_{14}O_3$: C, 60.72; H, 8.92).

When heated with phenylhydrazine, methyl valerylacetate gave 1-phenyl-3-*n*-butylpyrazolone-5, which was recrystallized from aqueous methanol, m.p. 84–85° (reported[15] 79°).

Fractions (e) and (f) amounted to 7.65 g. (63.2%) of **methyl 3-pentanoyloxy-2-heptenoate**. The analytical sample (see Table II) was obtained by redistillation of the material through a modified Claisen flask, b.p. 106° (0.4 mm.), n^{25}_{D} 1.4460, d^{25}_{4} 0.9853, $\lambda_{\max}$ 215 mμ, ε 6,200 (ethyl alcohol). This product gave no coloration with ferric chloride.

When 6.03 g. (0.05 mole) of valeryl chloride was added to 88 g. (1.0 mole) of ketene dimethylacetal and the reaction products separated in the manner described above, a 56% yield of methyl valerylacetate was obtained along with 28% of the methyl heptenoate. The excess ketene dimethylacetal was recovered by fractionation of the volatile material collected in the cold trap.

In another experiment 88 g. (1.0 mole) of ketene dimethylacetal was added to 1.24 g. (0.0103 mole) of valeryl chloride and after 1 hour of heating at reflux the excess ketene acetal was removed under reduced pressure. The residue was stirred overnight at room temperature with 25 ml. of 3% sodium hydroxide. The reaction mixture was then acidified with concentrated hydrochloric acid, heated for 15 minutes on a steam-bath and then treated with excess 2,4-dinitrophenylhydrazine reagent. The orange precipitate was collected and recrystallized from ethanol to yield, in two crops, 2.51 g. (86.5%) of 2,4-dinitrophenylhydrazone of methyl *n*-butyl ketone, m.p. 106–107° (reported[16] 106°).

(b) **With Lauroyl Chloride.**—To 17.6 g. (0.20 mole) of the ketene acetal was added in one portion 10.9 g. (0.05 mole) of freshly distilled lauroyl chloride. The temperature of the reaction mixture rose at a moderate rate to 65° as the evolution of methyl chloride became vigorous. The contents of the flask were refluxed for 1 hour. At that time 2.45 g. (98%) of methyl chloride had collected in the cold trap.

The contents of the flask were cooled to 50° while the pressure was reduced to 22 mm. in order to remove the low-boiling products. The oily residue was distilled through a modified Claisen flask to give the following fractions: (a) 0.95 g., b.p. 40–50° (0.1 mm.), n^{25}_{D} 1.4493; (b) 4.5 g., b.p. 155–165° (0.1 mm.), n^{25}_{D} 1.4726; (c) 2.45 g., b.p. 200–204° (0.1 mm.), n^{25}_{D} 1.4590; (d) 3.10 g., b.p. 204–210° (0.1 mm.), n^{25}_{D} 1.4579. Fraction (b) represented a 32% yield of lauroylketene dimethylacetal; upon redistillation an analytical sample was obtained (see Table I). Fractions (c) and (d) amounted to 5.5 g. (51%) of methyl 3-dodecanoyloxy-3-tetradecenoate which, when redistilled, had the properties shown in Table II.

When 10.9 g. (0.05 mole) of lauroyl chloride was added to 88 g. (1.0 mole) of ketene dimethylacetal, a 55–60% yield of lauroylketene dimethylacetal was obtained along with a corresponding less amount of the methyl decenoate.

If after removal of the volatile products of the above acylation reaction, the oily residue was treated with dilute acid, as described in the valerylation of ketene dimethylacetal, a 55% yield of methyl lauroylacetate was obtained: b.p. 117–118° (0.1 mm.), m.p. 27.5–28.5° (reported[17] b.p. 137–139° (0.9 mm.), m.p. 28.7°).

(c) **With XIV.**—To 1.00 g. (0.00373 mole) of 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthryl-2-acetic acid,[18] suspended in 10 ml. of dry benzene was added 2 ml. (about a sixfold excess) of oxalyl chloride. The flask was fitted with a reflux condenser and protected by a drying tube. The acid dissolved in 20 minutes as the evolution of gas ceased. The condenser was replaced with a vacuum take-off adapter protected by a drying tube. Excess oxalyl chloride and solvent were removed under reduced pressure (22 mm.) while the flask was swirled in a warm water bath (50°). Two successive 3-ml. portions of benzene were added and removed under reduced pressure.

To the white solid acid chloride XIV was added 32.8 g. (0.373 mole) of ketene dimethylacetal which previously had been cooled in a Dry Ice–acetone cold bath. After replacement of the vacuum take-off adapter with the spiral condenser and drying tube, the contents of the flask were magnetically stirred and rapidly heated to reflux in an oil-bath at 100°. After 1 hour the flask was partially cooled before the volatile products were removed under reduced pressure and caught in a cold trap. Since the volatile material was at least 95% pure ketene dimethylacetal, it was redistilled for use in other acylation reactions.

When the residue in the reaction flask was treated with 2 ml. of dry ether, it crystallized. This material was recrystallized from purified ethyl acetate to yield a total of 0.945 g. (75%) of 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthryl-2-acetylketene dimethylacetal (XV), whose properties are shown in Table I.

The non-crystalline residues and the mother liquors were combined and the solvent removed under reduced pressure. To this was added 5 ml. of a solution containing 10 ml. of acetic acid, 3 ml. each of concentrated hydrochloric acid and water. The mixture was refluxed for 1 hour and then diluted with 25 ml. of cold water. It was now extracted with ether and the ether extracts in turn extracted with bicarbonate solution. Upon evaporation of the ether 0.16 g. (16%) of 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthryl-2 methyl ketone (XVI), m.p. 106–108° (reported[18] 109–109.5°) was obtained. After one recrystallization from aqueous methanol the melting point was 109–110°, and there was no depression of melting point on admixture with an authentic sample of this ketone.

In a similar experiment the entire residue which remained after removal of the excess ketene dimethylacetal under reduced pressure was hydrolyzed to yield 97% of XVI.

(d) **With XVII.**—To a solution containing 500 mg. (1.39 mmoles, m.p. 238.5–240.5°) of 3-β-acetoxyetio-5-cholenic acid and 8 ml. of dry benzene in a 25-ml. round-bottom flask were added 5.8 ml. of oxalyl chloride and one drop of pyridine. After the solution had remained at room temperature for 1.5 hours, the solvent and excess reagent were removed under reduced pressure. The white solid residue which remained was redissolved in 5 ml. of dry benzene and the solvent was once again removed by swirling the flask in a 40° water-bath at reduced pressure; this treatment with benzene was repeated.

To the solid acid chloride XVII was added 12.2 g. (139 mmoles) of ketene dimethylacetal, which had been pre-

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[15] E. E. Blaise and A. Cornillot, *Compt. rend.*, **178**, 1186 (1924).

[16] C. F. H. Allen, This Journal, **52**, 2955 (1930).

[17] S. S. Stenhagen, *Arkiv. Kemi, Mineral. Geol.*, **A20**, No. 19 (1945).

[18] A. L. Wilds and L. W. Beck, This Journal, **66**, 1688 (1944).

TABLE II

METHYL β-ACYLOXYCINNAMATES AND 3-ACYLOXYALKENOATES, RC(OCOR′)=CHCOOCH$_3$

R	R′	M.p. or b.p. (mm.), °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
C_6H_5	C_6H_5	84–85	$C_{17}H_{14}O_4$	72.33	72.21	5.00	5.05
C_6H_5	p-$NO_2C_6H_4$	109–110	$C_{17}H_{13}O_6N$	62.39	62.38	4.00	3.87
n-C_4H_9	n-C_4H_9	106(0.4)[a]	$C_{13}H_{22}O_4$	64.45	64.45	9.16	9.13
n-$C_{11}H_{23}$	n-$C_{11}H_{23}$	210–212(0.1)[b]	$C_{27}H_{50}O_4$	73.92	73.98	11.49	11.69

[a] n^{25}_D 1.4460, d^{25}_4 0.9853, λ_{max} 216 mμ, ε 6200 (ethanol). [b] n^{25}_D 1.4575, d^{25}_4 0.9151, λ_{max} 216 mμ, ε 7850 (ethanol).

viously cooled in a Dry Ice–acetone cold bath. The resulting mixture was treated as in the preceding experiment (c).

The reaction product, a white crystalline solid, was taken up in benzene and after the addition of petroleum ether (b.p. 60–68°) was allowed to crystallize. Upon filtration, 467 mg. of 3β-acetoxyetio-5-cholenylketene dimethylacetal (XVIII) was isolated. Its properties are shown in Table I.

Reaction of Succinyl Chloride with Ketene Acetal.—To 35.2 g. (0.40 mole) of ketene dimethylacetal was added dropwise 7.74 g. (0.05 mole) of freshly distilled succinyl chloride while the reaction mixture was magnetically stirred and heated at reflux. After completion of the addition, the mixture was refluxed for 1 hour and allowed to cool. The volatile material was removed at 50–60° under reduced pressure. The residue, under nitrogen, was placed in a refrigerator overnight. The precipitate (3.2 g.) which formed was filtered and washed with cold (Dry Ice–acetone) ether. After removal of ether, the mother liquors were allowed to cool overnight in a refrigerator. A second crop of crystals was obtained to give a total yield of 5.05 g. (65%) of **γ-carbomethoxymethylene-γ-butyrolactone (XX)**, m.p. 71–72.5°.

The material became an intractable tar when exposed to air for several minutes and could not be isolated sufficiently pure for analysis. The infrared spectrum displayed an absorption peak at 5.60 μ, characteristic of a five-membered enol–lactone carbonyl.[7]

Heat was evolved when 4.65 g. of this product was dissolved in 10 ml. of 20% hydrochloric acid. As the solution was heated to reflux for 1 hour a rather moderate evolution of gas occurred. The solution was then made just basic by addition of 10% sodium hydroxide and steam distilled. No volatile material other than water was detected in the distillate. The solution was then acidified with 10% hydrochloric acid and evaporated to dryness. The oily residue of sodium chloride was extracted with ether and after evaporation of the extracts, 2.0 g. of viscous oil remained. It had an infrared spectrum essentially identical with that of levulinic acid. Some of the oil was treated with 2,4-dinitrophenylhydrazine reagent to yield the 2,4-dinitrophenylhydrazone of levulinic acid, m.p. 204.5–206° (reported[19] 206°), which showed no depression of melting point when mixed-melted with authentic material.

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(19) H. H. Strain, THIS JOURNAL, **57**, 760 (1935).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

Vinylation. II.[1] Stereochemistry and Synthesis of β-Methoxystyrenes[2]

BY SIDNEY I. MILLER

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A rule of *trans* nucleophilic addition to acetylenes is suggested. The methoxide-catalyzed addition of methanol to phenylacetylene to give a high-boiling β-methoxystyrene is stereospecific and probably *trans*. Small quantities of the unexpected α-methoxystyrene also were found. Different routes to β-methoxystyrene from phenylacetaldehyde dimethylacetal led to a mixture of isomeric β-methoxystyrenes from which the low-boiling isomer was obtained. Certain features of the infrared spectra of the α- and β-methoxystyrenes are discussed. An infrared study of the system methanol–phenylacetylene indicated that gross interactions such as H-bonding or complexing between these molecules were absent.

As a model for the stereochemical course of reactions involved in the preparation of alkoxyalkenes, the formation of the β-methoxystyrenes (I) from phenylacetaldehyde dimethylacetal (II) and from phenylacetylene (III) was investigated. The most serious attempt to solve this general problem was that of Dufraisse and Chaux.[3] They prepared mixtures of the β-ethoxystyrenes by various methods but could isolate only one of the isomers. Their work, as well as Sigmund and Uchann's studies on the pyrolytic decomposition of acetals,[4] are background to this work.

In order to obtain the reference compounds (I), several synthetic approaches were tried; reaction sequences are given in Chart I. Ihb (hb = high boiling) was isolated pure while Ilb (lb = low boiling) was obtained almost free from Ihb. The higher boiling point and refractive index,[5] and especially the characteristic infrared bands, strongly suggest that Ihb is the *cis* isomer formed from III by *trans* addition.

β-Methoxystyrene (Ihb).—β-Alkoxystyrenes often have been prepared by the base-catalyzed addition of alcohols to III.[3,6–8] The sealed tube reactions of III with sodium methoxide in methanol gave excellent yields of Ihb. None of Ilb could be detected in the above product. In contrast to its facile isomerization at room temperature or lower on exposure to air, neither thermal nor base-catalyzed isomerization of Ihb had occurred even after one week at 149°. Taking into account the facts that Ihb was the major product and that the equilibrium mixture of I contained

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(1) For paper I see S. I. Miller and G. Shkapenko, THIS JOURNAL, **77**, 5038 (1955).

(2) Work supported by the Office of Ordnance Research, U. S. Army.

(3) C. Dufraisse and R. Chaux, *Bull. soc. chim.*, [4] **39**, 905 (1926).

(4) F. Sigmund and R. Uchann, *Monatsh.*, **51**, 234 (1929).

(5) A. Wasserman, "Stereochemie," K. Freudenberg, editor, Leipzig, 1933, p. 721.

(6) T. L. Jacobs and W. R. Scott, Jr., THIS JOURNAL, **75**, 5500 (1953).

(7) (a) J. U. Nef, *Ann.*, **308**, 264 (1899); (b) C. Moureu, *Bull. soc. chim.*, [3] **31**, 526 (1904).

(8) K. Auwers, *Ber.*, **44**, 3514 (1911).