THE KETENE ACETALS

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Received January 3, 1949

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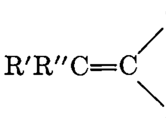
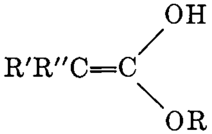
I. Introduction and Historical

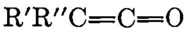
Ketene acetals have the general structure I, which represents an ether of the enolic form (II) of an ester. The name of this class of compounds, however, is derived from the fact that they bear the same structural relationship to the ketenes (III) that acetals bear to aldehydes and ketones.



I



II



III

The first compound of structure I to appear in the literature was reported by Biginelli (6) in 1891 as the diphenyl ether of vinylidene glycol. This structure was assigned to the product obtained from the reaction of an alkaline solution of phenol with methylchloroform and its formation was postulated as shown in reaction 1:

$$CH_3CCl_3 + 2C_6H_5OK + KOH \rightarrow CH_2{=}C(OC_6H_5)_2 + 3KCl + H_2O \qquad (1)$$

Biginelli's compound melted at 95–96°C. At about the same time Heiber (11) reported the product of this reaction to be triphenyl orthoacetate, $CH_3C(OC_6H_5)_3$, m.p. 97–97.5°C. This contradiction remained in the literature, although later workers (45, 50) accepted Biginelli's structure, until Cope (8) presented convincing evidence that neither Biginelli nor Heiber had the compound he reported, but that both had isolated the diphenyl ether of ethylene glycol, m.p. 95–97°C. This product was presumed by Cope to have been formed from ethylene chloride, a contaminant of the methylchloroform used by the earlier workers. The preparation (reaction 8) and properties of ketene diphenylacetal, which are described subsequently, substantiate Cope's conclusion regarding the products reported by Biginelli and Heiber.

The first authentic ketene acetal was described by Reitter and Weindell (39) in 1907 as β-diethoxyacrylic ester (VI). They obtained this compound rather than the expected malonic ester orthoester (V) as the alcoholysis product of the iminoester (IV) derived from cyanoacetic ester (reaction 2). There is no doubt now that the orthoester V was the precursor of the carbethoxyketene diethylacetal obtained in this work. Reitter and Weindell noted the acetal structure of VI and the similarity of its reactions to those of the previously described ketene (48).

$$C_2H_5OOCCH_2CN \xrightarrow[HCl]{C_2H_5OH} \underset{IV}{C_2H_5OOCCH_2C(OC_2H_5){=}NH\cdot HCl} \xrightarrow{C_2H_5OH}$$

$$NH_4Cl + \underset{V}{C_2H_5OOCCH_2(OC_2H_5)_3} \rightarrow C_2H_5OH +$$

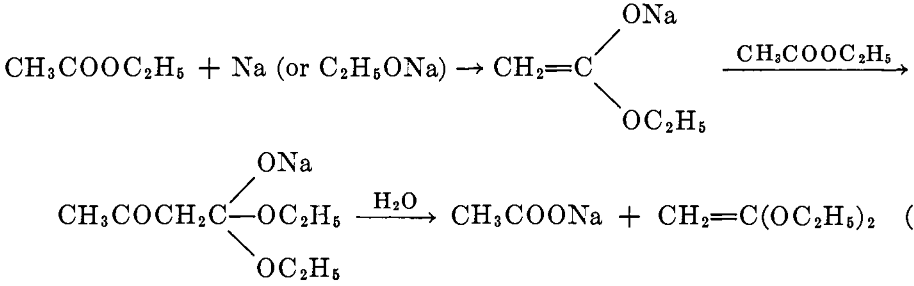
$$\underset{VI}{C_2H_5OOCCH{=}C(OC_2H_5)_2} \quad (2)$$

In 1922 Staudinger and Rathsam (50) attached the name "ketene acetals" to this class of compounds when they described the preparation and properties of phenylketene diethylacetal (VII). This compound was obtained by the pyrolysis of ethyl orthophenylacetate:

$$C_6H_5CH_2C(OC_2H_5)_3 \rightarrow C_2H_5OH + \underset{VII}{C_6H_5CH{=}C(OC_2H_5)_2} \quad (3)$$

Attempts to extend this method to the preparation of ketene acetals from orthoacetic and orthopropionic esters were unsuccessful. These esters when heated alone or with phosphorus pentoxide were reported to pyrolyze to the normal esters, ethyl acetate and ethyl propionate, and ether. It was concluded, therefore, that an orthoester must contain an activated α-hydrogen to undergo the type of pyrolysis shown in reaction 3 (50).

At about the same time as Staudinger and Rathsam described the preparation of VII, Scheibler and Ziegner (45) reported the isolation of the parent compound, ketene diethylacetal, as a minor reaction product from certain acetoacetic ester condensations involving ethyl acetate. Later Scheibler and coworkers (44) described detailed procedures for the preparation of this and other homologous ketene acetals. Essentially, Scheibler's method consisted in decomposition by water of a "primary reaction product," represented in reaction 4 as the addition compound of ethyl acetate to the sodium enolate of this ester, to form sodium acetate and ketene diethylacetal:



$$CH_3COOC_2H_5 + Na\ (\text{or } C_2H_5ONa) \rightarrow CH_2{=}C\begin{matrix} \diagup ONa \\ \diagdown OC_2H_5 \end{matrix} \xrightarrow{CH_3COOC_2H_5}$$

$$CH_3COCH_2C\begin{matrix} \diagup ONa \\ -OC_2H_5 \\ \diagdown OC_2H_5 \end{matrix} \xrightarrow{H_2O} CH_3COONa + CH_2{=}C(OC_2H_5)_2 \quad (4)$$

It was the failure of other investigators (47) to repeat the work reported from Scheibler's laboratory that led to the expansion of the field of the ketene acetals that is discussed in the subsequent sections of this review.

In one instance a ketene acetal has been prepared directly from an ester (1). The action of diazomethane on tricarbomethoxymethane yielded dicarbomethoxyketene dimethylacetal (VIII) in 47 per cent yield; a 17 per cent yield of the *C*-methylated product, tricarbomethoxyethane, which results from the rearrangement of VIII, also was obtained (reaction 5). The success of this reaction is due to the strong enolic character of tricarbomethoxymethane. Staudinger and Meyer (49) had investigated the alkylation of the potassium enolate of methyl diphenylacetate and found that only *C*-alkylation occurred; a similar result was obtained with the sodium enolate of ethyl diphenylacetate resulting from the decarbethoxylation of diphenylmalonic ester (9).

$$(CH_3OOC)_2C{=}C(OH)OCH_3 + CH_2N_2 \rightarrow$$

$$N_2 + \underset{\text{VIII}}{(CH_3OOC)_2C{=}C(OCH_3)_2} \rightarrow (CH_3OOC)_2C(CH_3)COOCH_3 \quad (5)$$

Staudinger and Rathsam (50) attempted the preparation of diphenylketene diethylacetal by the reaction of diphenylketene with orthoformic ester, but found that the ester added to the ketene to produce diphenylcarbethoxyacetaldehyde diethylacetal in the following manner:

$$(C_6H_5)_2C{=}C{=}O + HC(OC_2H_5)_3 \rightarrow (C_6H_5)_2C(COOC_2H_5)CH(OC_2H_5)_2 \quad (6)$$

II. THE PREPARATION OF KETENE ACETALS

A. DEHYDROHALOGENATION OF α-BROMOACETALS

When it became obvious that the procedures described by Scheibler and coworkers (44, 45) could not be duplicated (47), the preparation of ketene diethylacetal by other procedures was undertaken. An obvious approach to this ketene acetal was the dehydrohalogenation of a haloacetal (IX). When this reaction was applied to iodoacetal (IX: X is iodine) with potassium *t*-butoxide in *t*-butyl alcohol as the dehydrohalogenating agent, ketene diethylacetal (X) was obtained in 52 per cent yield (3).

$$\underset{\text{IX}}{XCH_2CH(OC_2H_5)_2} + t\text{-}C_4H_9OK \rightarrow \underset{\text{X}}{CH_2{=}C(OC_2H_5)_2} + KI + t\text{-}C_4H_9OH \quad (7)$$

The use of a tertiary alcohol as a medium for this dehydrohalogenation is essential because of the tendency of primary and secondary alcohols to add to the ketene acetal to produce orthoesters (reaction 28). In this connection it is of interest to note that potassium hydroxide in ethyl alcohol gives 95 per cent of the replacement reaction product, the acetal of glycolic aldehyde ($HOCH_2CH(OC_2H_5)_2$), when the halogen of IX is chlorine; the corresponding bromo- and iodo-acetals give, respectively, 70 per cent and 30 per cent yields of the replacement product with this reagent. The remainder of the iodoacetal in the latter case is converted to ethyl acetate and ethyl orthoacetate, further reaction products of the initially formed ketene acetal X (3). Later it was found (12, 25) that ketene diethylacetal could be prepared in equally good yields using the bromoacetal instead of the iodoacetal in reaction 7.

Ketene diethylacetal, as obtained from reaction 7, is a colorless liquid that boils at 124–126°C. It reacts rapidly and exothermically with water and alcohol at room temperature to form, respectively, ethyl acetate and ethyl orthoacetate (reactions 26 and 28), and it is hydrogenated over Raney nickel to acetaldehyde diethylacetal (reaction 40) (3). In contrast to these properties the product described by Scheibler (44, 45) boiled at 77–78°C. and was isolated from an aqueous reaction mixture.

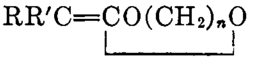
The extension of reaction 7 to other haloacetals has led to the preparation of the chloro- and bromo-ketene acetals (XI) (5, 35); the dichloro- and dibromo-ketene acetals (XII) (35); ketene di-*n*-propyl-, diisobutyl-, and diisoamyl-acetals (XIII) (33); phenylketene dimethylacetal (XIV) (19); and a variety of methylenedioxolanes and methylenedioxanes (XV) (19). Related to these latter groups of cyclic acetals is the ketene acetal of *cis*-1,2-cyclohexanediol (XVI), which has been prepared by Winstein (53) by the procedure of reaction 7. In the case of XIV the product prepared from the bromoacetal by reaction 7 is of considerably higher purity than that resulting from the pyrolysis of the cor-

$XCH{=}C(OC_2H_5)_2$
XI

$X_2C{=}C(OC_2H_5)_2$
XII

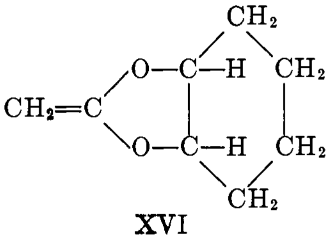
$CH_2{=}C(OR)_2$
XIII

$C_6H_5CH{=}C(OCH_3)_2$
XIV



$RR'C{=}CO(CH_2)_nO$

XV
(R is H, Cl, Br, or C_6H_5;
R′ is H or Cl; *n* is 2 or 3)



XVI

responding orthoester (reactions 3 and 13). The yields of the ketene acetals XI–XV from reaction 7 are 50–85 per cent of the theoretical.

The application of reaction 7 to bromoacetaldehyde diallyl- and dibenzylacetals yields the esters allyl allylacetate, $CH_2{=}CHCH_2CH_2COOCH_2CH{=}CH_2$, and benzyl *o*-tolylacetate, $o\text{-}CH_3C_6H_4CH_2COOCH_2C_6H_5$, in 43 per cent and 46 per cent yields, respectively (14). These products result from the rearrangement of one of the R groups of these ketene acetals (XIII: R is allyl or benzyl) as they are formed from the dehydrohalogenation of the bromoacetals (*cf.* the rearrangement of XXXVI in reaction 16).

The dehydrohalogenation of bromoacetaldehyde diphenylacetal (reaction 8) has been used to prepare ketene diphenylacetal (XVII), which Biginelli (6) reported to have been produced in reaction 1; triphenyl orthoacetate, which Heiber (11) reported to result from reaction 1, was prepared from this ketene acetal by the addition of phenol as shown in reaction 30 (21).

$$BrCH_2CH(OC_6H_5)_2 \xrightarrow{t\text{-}C_4H_9OK} \underset{\text{XVII}}{CH_2{=}C(OC_6H_5)_2} \qquad (8)$$

As the properties of XVII, a liquid boiling at 115–116°C. (1 mm.), and triphenyl orthoacetate, m.p. 61–62°C., do not agree with those reported by Biginelli and Heiber for the compounds they obtained from reaction 1, Cope's conclusion that each of these investigators had isolated the diphenyl ether of ethylene glycol, m.p. 95–97°C., is substantiated.

It is possible to prepare chloro- and bromo-ketene diethylacetals (XI) from the corresponding dihaloacetals using sodium ethoxide in ethyl alcohol solution instead of potassium *t*-butoxide in *t*-butyl alcohol, the dehydrohalogenating agent of reaction 7. This is because the haloketene acetals (XI) react sufficiently slowly with ethyl alcohol in the presence of alkali to permit their isolation (34). However, these ketene acetals may not be allowed to remain too long in this medium as they are slowly transformed to the ethyl orthohaloacetates, $XCH_2C(OC_2H_5)_3$ (reaction 28). This type of reaction product was erroneously described as the isomeric ethoxybromoacetal, $C_2H_5OCHBrCH(OC_2H_5)_2$, in an earlier investigation of the reaction of dibromoacetal with sodium ethoxide (5).

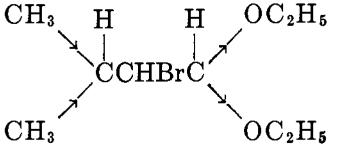
Reaction 7 is not applicable to the preparation of alkylketene acetals. When such bromoacetals as XVIII, XIX, and XX are dehydrohalogenated with potassium *t*-butoxide, the acetals of the corresponding α,β-unsaturated aldehydes (XXI), rather than the ketene acetals, are produced as shown in reaction 9. The kinetics of this reaction show it to be second order and this, together with the fact that the isopropylketene acetal (obtained from reaction 10) which would result from the alternative dehydrohalogenation of XX is stable to the conditions of the reaction, indicates that the mechanism of reaction 9 involves the initial removal of the β-proton by the base followed by expulsion of the bromide anion (17).

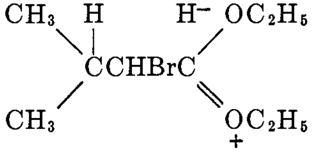
The exclusive removal of the β-proton of XX in this dehydrohalogenation shows that the inductive effects of the methyl and ethoxyl groups do not control

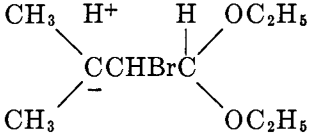
$$\underset{\text{XVIII}}{(CH_3)_2CBrCH(OC_2H_5)_2} \qquad \underset{\text{XIX}}{CH_3CH_2CHBrCH(OC_2H_5)_2}$$

$$\underset{\text{XX}}{(CH_3)_2CHCHBrCH(OC_2H_5)_2} \xrightarrow{t\text{-}C_4H_9OK} \underset{\text{XXI}}{(CH_3)_2C{=}CHCH(OC_2H_5)_2} \qquad (9)$$

the course of the reaction, because the greater effect of the latter groups should facilitate the removal of the proton of the acetal group—obviously the more acidic hydrogen of the two available for dehydrohalogenation in XXa—with the resultant formation of the ketene acetal. It must be concluded, therefore, that the ethoxyl groups function in resonance structures such as XXb, which promote the separation of the hydrogen of the acetal group as a hydride anion rather than as a proton, and thereby permit a structure such as XXc to react with the base to produce XXI.


XXa


XXb


XXc

If oxygen could expand its valence shell as sulfur appears to do in CVIIIa of reaction 60 and permit the hydrogen of the acetal group to resonate as a proton, it might be possible to prepare an alkylketene acetal from such a bromoacetal as XX.

B. REACTION OF SODIUM WITH α-BROMOÖRTHOESTERS

Alkylketene acetals (XXIII) may be prepared by the removal of the elements of an alkyl hypobromite from an α-bromoörthoester (XXII) with metallic sodium as shown in reaction 10.

$$\underset{\text{XXII}}{RCHBrC(OC_2H_5)_3} + 2Na \rightarrow \underset{\text{XXIII}}{RCH{=}C(OC_2H_5)_2} + NaBr + C_2H_5ONa \qquad (10)$$

(R is H or alkyl)

In this manner ketene, methylketene (52), *n*-propylketene, and isopropylketene diethylacetals (17) as well as ketene dimethylacetal (14) have been prepared in 60–80 per cent yields. This is the most general method of preparing ketene acetals, as there is no alternative position in which the double bond may form as there is in the bromoacetal of reaction 9. Ketene acetals prepared by reaction 10 have been found to be quite stable under the conditions of reaction

9 and thereby are shown not to be intermediates in the dehydrohalogenation of the acetals of α-bromoaldehydes to the acetals of α,β-unsaturated aldehydes (17, 42).

The application of reaction 10 to the preparation of dialkylketene acetals, ($R_2C{=}C(OR')_2$), has not been made because it has not been possible as yet to prepare the requisite haloörthoesters, $R_2CXC(OR')_3$ (13). Surprisingly, reaction 10 cannot be used to prepare phenylketene dimethylacetal (XIV); a complex sodium salt of the ester moiety and sodium bromide are the products obtained from the reaction of sodium with trimethyl orthophenylbromoacetate (31).

When α-haloörthoacetic esters are treated with zinc or magnesium, polymeric reaction products instead of ketene acetals are obtained (4). Such products indicate that these metals remove the elements of the alkyl hypohalite intermolecularly from the haloörthoester rather than in the intramolecular manner of reaction 10. This behavior of α-haloörthoesters is in marked contrast to the facile intramolecular removal of the elements of an alkyl hypohalite from a β-haloether by zinc in the Boord method of preparation of olefins (7).

C. PYROLYSIS OF ORTHOESTERS

It was by this procedure that the ketene acetals (VI and VII) described in the earlier literature were prepared (reactions 2 and 3). Although Reitter and Weindell (39) did not isolate the intermediate orthoester (V), they assumed it to be an intermediate in the formation of VI. A study of the preparation of methyl orthocyanoacetate (XXIV) has shown that such negatively substituted orthoesters may be isolated if all traces of acid are removed prior to their distillation (29). Acids catalyze the pyrolysis of the orthoester to the ketene acetal (XXV) as they do the reverse reaction, the addition of the alcohol to the acetal to produce the orthoester (30):

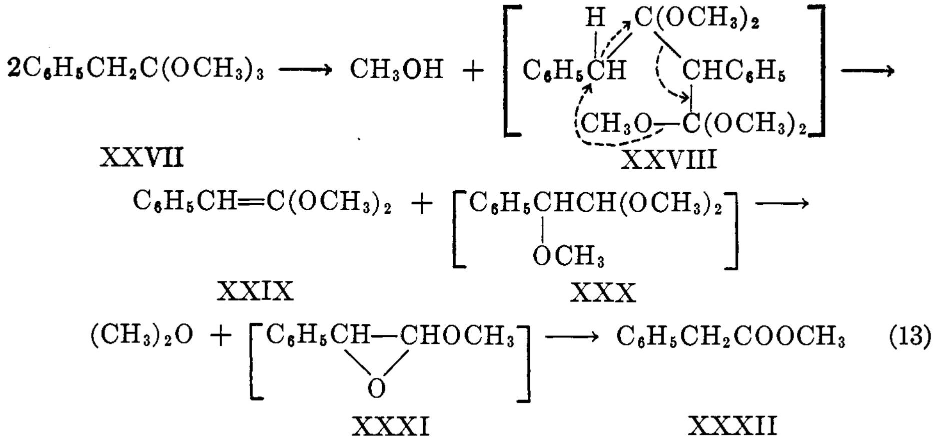
$$\underset{\text{XXIV}}{CNCH_2C(OCH_3)_3} \overset{H^+}{\rightleftarrows} \underset{\text{XXV}}{CNCH{=}C(OCH_3)_2} + CH_3OH \qquad (11)$$

Reaction 11 proceeds to the right when the orthoester is heated and the alcohol removed by distillation; the orthoester is formed from its components at room temperature, but can be isolated by distillation only after the removal of the last traces of the acid catalyst with alkali (30). By following this procedure such orthoesters as V and XXIV may be isolated in the pure state in 62–82 per cent yields (29) and then smoothly pyrolyzed to the ketene acetals (30).

The pyrolysis of ethyl orthophenylacetate (reaction 3) gives the corresponding ketene acetal (VII) in approximately 70 per cent yield when the orthoester is slowly distilled as in a fractional distillation (31). Accompanying this product, however, is a 20 per cent yield of ethyl phenylacetate (XXVI), together with ethylene and a small amount of *meso*-diethyl α,α′-diphenylsuccinate, which Staudinger and Rathsam (50) isolated but did not identify (see reaction 53 for the formation of the homologous methyl ester). The formation of ethyl phenylacetate (XXVI) during this pyrolysis doubtless is the result of further decomposition of the ketene acetal (reaction 12), as the evolution of ethylene is not brisk until the evolution of ethyl alcohol (reaction 3) is nearly complete. Also, each redistillation of the ketene acetal VII usually produces a small amount of XXVI.

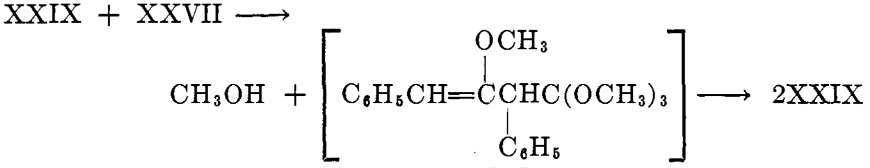
$$\underset{\text{VII}}{C_6H_5CH{=}C(OC_2H_5)_2} \longrightarrow \underset{\text{XXVI}}{C_6H_5CH_2COOC_2H_5} + CH_2{=}CH_2 \qquad (12)$$

As phenylketene *dimethyl*acetal (XXIX) cannot follow reaction 12, it would be expected that the pyrolysis of methyl orthophenylacetate (XXVII) would produce XXIX and none of the normal ester (XXXII). However, this is not the case; the methyl orthoester (XXVII) gives higher yields (33 per cent) of the normal ester (XXXII) and lower yields (59 per cent) of the ketene acetal (XXIX) than does ethyl orthophenylacetate. The methyl orthoester is much more stable than the ethyl ester to pyrolysis, but when heated to 250–260°C. a vigorous evolution of methyl alcohol occurs. However, only 40–50 per cent of the amount of alcohol expected on the basis of reaction 3 distils from the orthoester during this initial rapid pyrolysis, which subsides within 15 min. Thereafter the evolution of the alcohol is quite slow and incomplete. The amount of alcohol obtained, together with the distillation behavior of the product, led to the postulation of the reaction course shown in reaction 13 for this pyrolysis.


XXVII XXVIII XXIX XXX XXXI XXXII (13)

The formation of the intermediate XXVIII from two equivalents of XXVII seems necessary to account for the following observations on this pyrolysis: (*a*) no more than one-half of the expected alcohol is obtained readily from the orthoester, (*b*) rapid distillation of the pyrolysis product gives a mixture (XXIX and XXX) boiling in the range of the original orthoester and having a methoxyl content intermediate between that of the orthoester and that of the ketene acetal, and (*c*) fractional distillation of the mixture from (*b*) is accompanied by marked fluctuations in the boiling point (transformation of XXX *via* XXXI to XXXII) before the final separation of the major reaction products, XXIX and XXXII (31).

This unusual pyrolysis behavior of the orthoester XXVII is in marked contrast to its behavior when pyrolyzed in the presence of one equivalent of the ketene acetal XXIX. In this case *all* the alcohol required for the conversion of the orthoester to the ketene acetal is evolved rapidly; 88 per cent of the ketene acetal, but *no methyl phenylacetate,* is obtained as the pyrolysis product. This behavior leads to the conclusion that the ketene acetal (XXIX) reacts with the orthoester (XXVII) with the elimination of alcohol to produce an intermediate, e.g., XXXIII, which then pyrolyzes to two moles of XXIX, as indicated in reaction 14 (31).

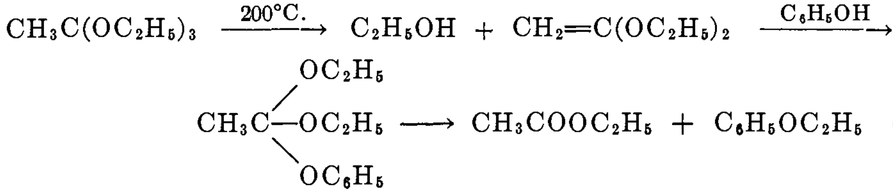


$$\text{XXIX} + \text{XXVII} \longrightarrow \text{CH}_3\text{OH} + \left[\text{C}_6\text{H}_5\text{CH}{=}\underset{\text{C}_6\text{H}_5}{\overset{\text{OCH}_3}{\text{C}}}\text{CHC(OCH}_3)_3 \right] \longrightarrow 2\text{XXIX} \qquad (14)$$

XXXIII

Phenylketene dimethylacetal prepared by reaction 13 is a yellow liquid, which has a decidedly lower refractive index (see No. 14, table 1) than that of the colorless product obtained from the dehydrohalogenation of phenylbromoacetaldehyde dimethylacetal by reaction 7.

Although Staudinger and Rathsam (50) reported that such orthoesters as ethyl orthoacetate and ethyl orthopropionate pyrolyze to the normal ester and diethyl ether, a later study indicates that ethyl orthoacetate is converted to ethyl acetate, ethyl alcohol, and ethylene when heated at 200°C. for 24 hr. (14). Inasmuch as ketene diethylacetal undergoes pyrolysis to ethyl acetate and ethylene (reaction 15a) under the same conditions, it seemed that the ketene acetal might be an intermediate in the pyrolysis of the orthoester. This was shown to be the case when ethyl orthoacetate was pyrolyzed in the presence of phenol, which reacts with the ketene acetal as rapidly as it is formed, and before it can pyrolyze, to convert it *via* the intermediate XXXIV to ethyl acetate and phenetole (reaction 15).

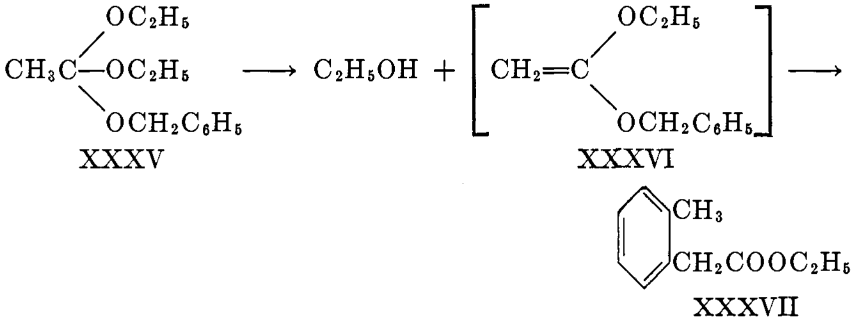


$$\text{CH}_3\text{C(OC}_2\text{H}_5)_3 \xrightarrow{200^\circ\text{C.}} \text{C}_2\text{H}_5\text{OH} + \text{CH}_2{=}\text{C(OC}_2\text{H}_5)_2 \xrightarrow{\text{C}_6\text{H}_5\text{OH}} \text{CH}_3\text{C}(\text{OC}_2\text{H}_5)(\text{OC}_2\text{H}_5)(\text{OC}_6\text{H}_5) \longrightarrow \text{CH}_3\text{COOC}_2\text{H}_5 + \text{C}_6\text{H}_5\text{OC}_2\text{H}_5 \qquad (15)$$

XXXIV

$$\text{CH}_2{=}\text{C(OC}_2\text{H}_5)_2 \longrightarrow \text{CH}_3\text{COOC}_2\text{H}_5 + \text{C}_2\text{H}_4 \qquad (15a)$$

When this pyrolysis procedure was extended to a variety of simple and mixed orthoacetic esters, all appeared to follow the reaction course illustrated in reaction 15. It is possible to rationalize the products of this reaction without the intermediate formation of the ketene acetal, i.e., by the phenol reacting directly with the orthoester to give alcohol and XXXIV, which then would pyrolyze to the products that are isolated. Such a reaction course, however, seems unlikely for the following reasons: (*a*) no phenyl acetate, which could result from an ester interchange between phenol and the reaction product ethyl acetate, is present after the pyrolysis and (*b*) the product of the pyrolysis of diethyl benzyl orthoacetate (XXXV) in the absence of phenol is ethyl *o*-tolylacetate (XXXVII), which can be formed only as shown in reaction 16 by the rearrangement of the intermediate ketene acetal (XXXVI) (14):



(16)

The orthoesters of bromo- and dibromo-acetic acids undergo two types of pyrolysis (14). One of these follows the course of reaction 15 to produce the alcohol, the normal ester, and ethylene. The other type of pyrolysis involves the loss of the elements of ethyl hypobromite to produce an ester containing one less bromine than the original orthoester (reaction 17). Further reaction of the ethyl hypobromite yields the secondary products, acetaldehyde and ethyl bromide, that are obtained from this pyrolysis.

$$Br_2CHC(OC_2H_5)_3 \rightarrow C_2H_5OBr + BrCH{=}C(OC_2H_5)_2 \rightarrow BrCH_2COOC_2H_5 + C_2H_4 \quad (17)$$

$$CH_3CH_2OBr \longrightarrow CH_3CHO + HBr \xrightarrow{C_2H_5OH} C_2H_5Br + H_2O$$

From the behavior of the orthoesters illustrated in reactions 2, 3, 11, 13, 15, 16, and 17 it is evident that pyrolysis to ketene acetals is a quite general reaction. If the orthoester does not have a negative α-substituent such as the phenyl, carbethoxy, or cyano group, the temperature necessary for its pyrolysis also causes the pyrolysis of the resulting ketene diethylacetal to ethylene and the normal ester. To date, neither the pyrolysis of methyl orthoesters without a negative α-substituent nor the pyrolysis of simple aliphatic orthoesters with secondary and tertiary α-carbons have been studied. However, it has been shown that ethyl orthobenzoate, which has no α-hydrogen, pyrolyzes to the normal ester and diethyl ether (14):

$$C_6H_5C(OC_2H_5)_3 \rightarrow C_6H_5COOC_2H_5 + (C_2H_5)_2O \quad (18)$$

D. REACTION OF STRONG BASES WITH ORTHOESTERS

The scope and generality of this method of preparation of ketene acetals are now under investigation in the Wisconsin Laboratory. To date only one report of its use appears in the literature (16). This involves the preparation of tetraethoxyethylene, diethoxyketene diethylacetal (XL), by the action of sodium ethyl on pentaethoxyethane (XXXVIII) as illustrated in reaction 19.

$$\underset{\text{XXXVIII}}{(C_2H_5O)_2CHC(OC_2H_5)_3} + \overset{+}{\mathrm{Na}}\overset{-}{\mathrm{C}}_2\mathrm{H}_5 \longrightarrow$$

$$C_2H_6 + \underset{\text{XXXIX}}{(C_2H_5O)_2\overset{-}{C}C(OC_2H_5)_3\overset{+}{\mathrm{Na}}} \longrightarrow$$

$$\underset{\text{XL}}{(C_2H_5O)_2C{=}C(OC_2H_5)_2} + C_2H_5ONa \qquad (19)$$

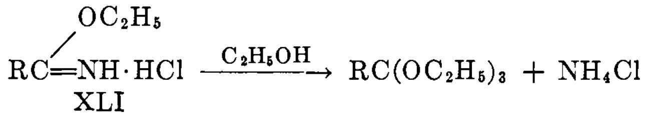
As shown, reaction 19 is a simple acid–base reaction in which a strong base, the ethyl anion, extracts a proton from the ortho ester to form ethane and the carbanion XXXIX, which then by elimination of an ethoxyl anion passes into the ketene acetal XL. The reaction, however, is much more complex than shown, as yields of 39 per cent of XL, 160 per cent of ethane, and 235 per cent of sodium ethoxide, based on the amount of the orthoester XXXVIII used in the reaction, are obtained. Nevertheless, this reaction appears to be the only one feasible for the preparation of the ketene acetal XL, as the orthoester is quite stable to heat; in fact it may be refluxed (b.p. 205–207°C.) for several hours without evidence of decomposition. Diethoxyketene diethylacetal (XL) is of particular interest because it previously has been reported (43) to dissociate spontaneously into the divalent carbon compound, carbon monoxide diethylacetal, $C(OC_2H_5)_2$, b.p. 78°C. The ketene acetal obtained from reaction 19 is a stable, colorless liquid, which boils at 195–196°C. with no evidence of decomposition or dissociation.

E. PREPARATION OF ORTHOESTERS

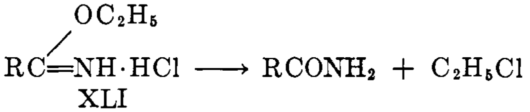
As orthoesters are required for three of the four methods by which ketene acetals are obtained, a few remarks on the preparation of certain members of this class of compounds seem appropriate. An excellent monograph covering the literature on the orthoesters to 1943 has been prepared by Post (38). The following discussion is limited to the observations made on the preparations of those orthoesters that have been studied in connection with the ketene acetals.

The most general and widely used method of preparation of orthoesters is that originated by Pinner (37), which involves the alcoholysis of an iminoester hydrochloride (XLI) obtained from the reaction of alcoholic hydrogen chloride with a nitrile (reaction 20). A study of the optimum conditions for this alcoholysis showed that 60–78 per cent yields of the ethyl esters of the normal-chain aliphatic orthoacids may be obtained; however, the alcoholysis of branched-chain iminoester hydrochlorides (XLI: R is isopropyl or isobutyl) gives only 20–30 per cent yields of the corresponding orthoesters (28). Accompanying the alcoholysis reaction is a competitive decomposition of the iminoester hydrochloride to the amide (reaction 21). In certain alcoholyses a substantial yield of the normal ester also is obtained. The origin of this latter product is not too clear; in certain cases (16) it appears to result from the decomposition of the orthoester into the normal ester and ether (reaction 22) under the catalytic influence of the iminoester hydrochloride (XLI); in other cases it appears that this salt is sufficiently acidic to cleave the orthoester formed in reaction 20 according to reaction 23 (29, 51).

$$\mathrm{RCN + C_2H_5OH + HCl \longrightarrow}$$



$$\underset{\mathrm{XLI}}{\mathrm{RC(OC_2H_5){=}NH\cdot HCl}} \xrightarrow{\mathrm{C_2H_5OH}} \mathrm{RC(OC_2H_5)_3 + NH_4Cl} \qquad (20)$$



$$\underset{\mathrm{XLI}}{\mathrm{RC(OC_2H_5){=}NH\cdot HCl}} \longrightarrow \mathrm{RCONH_2 + C_2H_5Cl} \qquad (21)$$

$$\mathrm{RC(OC_2H_5)_3 \xrightarrow{XLI} RCOOC_2H_5 + (C_2H_5)_2O} \qquad (22)$$

$$\mathrm{RC(OC_2H_5)_3 + XLI \longrightarrow}$$
$$\mathrm{RCOOC_2H_5 + RC(OC_2H_5){=}NH + C_2H_5Cl + C_2H_5OH} \qquad (23)$$

Some of reaction 21 always occurs even under the most favorable conditions that have been found for reaction 20 (28). When the R of XLI has a disubstituted α-carbon and particularly if this carbon has a halogen substituent, the amide of reaction 21 is the major if not the sole reaction product (22). For this reason the α-bromoörthoesters used for the preparation of ketene acetals by procedure B are prepared by the bromination of the orthoesters. This bromination proceeds satisfactorily in the presence of pyridine with esters of orthoacetic acid and its higher homologs, in which the α-carbon is secondary (4, 17, 28, 52). However, if the α-carbon is tertiary as in esters of orthoisobutyric acid, $(CH_3)_2CHC(OR)_3$, it has not been possible to effect such an α-bromination with a wide variety of brominating agents (13).

A case in which reaction 22 appears together with reaction 21 as a competing reaction is in the preparation of pentaethoxyethane, the orthoester (XXXVIII) used in reaction 19, from the alcoholysis of XLI (R is $(C_2H_5O)_2CH$). Under the optimum conditions found only a 12 per cent yield of this orthoester could be obtained from reaction 20; the major reaction products were the amide from reaction 21 and the ester together with some diethyl ether from reaction 22; a small (8 per cent) yield of the nitrile, $(C_2H_5O)_2CHCN$, possibly formed from the decomposition of the iminoester of reaction 23, also is obtained (16).

It is probable that reaction 23 is responsible for some of the normal ester that is often found among the products of the alcoholysis of iminoester salts. Orthoesters are very susceptible to cleavage by acids and it is likely that the iminoester hydrochlorides are sufficiently acidic to effect such a cleavage, particularly if the rate of alcoholysis in reaction 20 is low. In this connection it should be noted that the alcoholysis of XLI (R is isobutyl) is sufficiently slow so that a 21 per cent yield of the normal ester, ethyl isovalerate, is found among the reaction products

(28). Cleavage of the orthoesters is even more likely with diiminoester salts, such as those derived from malono- and succino-nitriles, in which one of the hydrochloride functions is quite acidic. Indeed the alcoholysis of XLII (reaction 24) gives the mono- and di-orthoesters of succinic acid in approximately equal yields (29); and the diiminomalonic ester dihydrochloride (XLIII) converts ethyl orthophenylacetate to the normal ester (reaction 25) quite readily and completely (52).

$$\underset{\text{XLII}}{\mathrm{ClNH_2{=}(CH_3O)C(CH_2)_2C(OCH_3){=}NH_2Cl}} \longrightarrow$$

$$\mathrm{CH_3OOC(CH_2)_2C(OCH_3)_3 + (CH_3O)_3C(CH_2)_2C(OCH_3)_3} \quad (24)$$

$$\underset{\text{XLIII}}{\mathrm{ClNH_2{=}(C_2H_5O)CCH_2C(OC_2H_5){=}NH_2Cl}} + \mathrm{C_6H_5CH_2C(OC_2H_5)_3} \longrightarrow$$

$$\mathrm{NH{=}(C_2H_5O)CCH_2C(OC_2H_5){=}NH_2Cl} +$$

$$\mathrm{C_6H_5CH_2COOC_2H_5 + C_2H_5Cl + C_2H_5OH} \quad (25)$$

When the ketene acetals are available, they are an excellent source of either simple or mixed orthoesters, as the addition of an alcohol to a ketene acetal (reaction 28) is practically quantitative. This procedure has been used to prepare a wide variety of mixed orthoesters of the type $R_2CHC(OR')_2OR''$ (14, 19, 22).

III. Properties and Reactions of Ketene Acetals

A. PHYSICAL PROPERTIES

The boiling points, refractive indices, and densities of the authenticated ketene acetals that have been reported in the literature, together with the boiling points and refractive indices of the corresponding normal esters and orthoesters in which R″ is a monovalent radical, are listed in table 1. With but one exception (No. 22), the ketene acetal structure is associated with a relatively high boiling point compared to that of the corresponding normal ester. For example, ketene diethylacetal (No. 2) boils 48°C. above the normal ester, ethyl acetate, of which it is the *O*-ethyl ether, and only 20°C. below the corresponding orthoester, triethyl orthoacetate. Indeed, this ketene acetal boils at about the same temperature as the *C*-ethyl derivatives of ethyl acetate, ethyl butyrate (b.p. 121°C.), and *n*-butyl acetate (b.p. 126°C.), each of which contains a highly polarized carbalkoxy group (—COOR). The boiling point of the ketene acetal reflects the high polarization that is associated with this structure. This characteristic is even more strikingly illustrated by the difference between the boiling point of ketene diethylacetal and that of its non-polarized hydrogenation product, acetaldehyde diethylacetal ($CH_3CH(OC_2H_5)_2$). The latter compound, which has approximately the same molecular weight as the ketene acetal, boils 25°C. lower and may be assumed to reflect the contribution of the molecular weight to the boiling point of ketene diethylacetal.

The differences between the boiling points of the ketene dialkylacetals and methylketene diethylacetal (Nos. 2, 3, 4, 5, and 9 of table 1) and the correspond-

TABLE 1

Ketene acetals, $RR'C{=}C(OR'')_2$, *the corresponding esters*, $RR'CHCOOR''$ *and orthoesters*, $RR'CHC(OR'')_3$

NO.	R IS	R' IS	R'' IS	KETENE ACETALS					ESTERS		ORTHOESTERS	
				Boiling point	$n_D^{25°}$	$d_{4°}^{25°}$	Preparative procedure	Reference	Boiling point	n_D^t	Boiling point	n_D^t
				°C. (*mm.*)$^{(a)}$					°C. (*mm.*)$^{(a)}$		°C. (*mm*).$^{(a)}$	
1....	H	H	CH_3	89–91	1.3962	0.9274	B	(14)	57	1.3617 (20°)	109	1.3859 (25°)
2....	H	H	C_2H_5	124–126	1.4101	0.8776	A, B	(3, 52)	78	1.3805 (25°)	146	1.3941 (25°)
3....	H	H	n-C_3H_7	153–154	1.4200	0.879$^{(g)}$	A	(33)	101	1.3847 (20°)		
4....	H	H	i-C_4H_9	180–181	1.4212	0.875$^{(g)}$	A	(33)	116	1.3901 (20°)		
5....	H	H	i-C_5H_{11}	210–211	1.4300	0.856$^{(g)}$	A	(33)	142	1.4003 (20°)		
6....	H	H	C_6H_5	115–116 (1)	1.5583$^{(h)}$	1.1544	A	(21)	44 (1)	1.503 (20°)	153 (0.5)	$^{(i)}$
7....	H	H	$>(CH_2)_2$	120–124	1.4465		A	(19)				
8....	H	H	$>(CH_2)_3$	147–155	1.4304		A	(19)				
9....	CH_3	H	C_2H_5	133–134	1.4083	0.8654$^{(h)}$	B	(52)	100	1.3810 (25°)	158	1.4000 (25°)
10....	n-C_3H_7	H	CH_3	142–144	1.4235	0.8834	B	(24)	127	1.3993 (15°)	166	1.4090 (24°)
11....	n-C_3H_7	H	C_2H_5	167–168	1.4204	0.850	B	(17)	144	1.3989 (25°)	50 (3)	1.4086 (25°)
12....	i-C_3H_7	H	C_2H_5	156–157	1.4158	0.8385	B	(17)	134	1.4009 (20°)	59 (7)	1.4056 (25°)
13....	n-C_7H_{15}	H	CH_3	100–105 (10)	1.4370$^{(b)}$	0.8655	B	(24)	95 (10)		140 (45)	1.4255 (21°)
14....	C_6H_5	H	CH_3	85–87 (0.5) 235–238	1.5390 1.5620	1.0575 1.0592	C A	(31) (19)	60 (0.5) 220	1.5050 (20°) 1.5091 (16°)	76 (0.4)	1.5065 (20°)
15....	C_6H_5	H	C_2H_5	86–88 (0.2) 136 (12)	1.5385$^{(b)}$	1.005	C C	(31) (50)	69 (0.1) 109 (12)	1.4992 (18°)	91 (0.1)	1.5050 (20°)
16....	C_6H_5	H	$>(CH_2)_2$	108–112 (0.8)	1.6075		A	(19)				
17....	C_6H_5	H	$>(CH_2)_3$	124–126 (0.6)	1.5840		A	(19)				
18....	CN	H	CH_3	127–128 (11)	1.4630$^{(c)}$	1.055$^{(c)}$	C	(30)	92 (11)	1.4177 (25°)	102 (13)	1.4215 (25°)

19....	CN	H	C_2H_5	145–146 (20)	1.4536[d]		C	(30)	101 (19)	1.4179 (20°)	118 (19)	1.4189 (25°)
20....	$COOC_2H_5$	H	C_2H_5	139–140 (17)	1.4609	1.023	C	(46)	96 (18)	1.4162 (20°)	121 (18)	1.4220 (25°)
21....	$COOCH_3$	$COOCH_3$	CH_3	142–145 (13)				(1)	130 (16)			
22....	C_2H_5O	C_2H_5O	C_2H_5	195–196	1.4213	0.949	D	(16)	199	1.4090 (25°)	207	1.4072 (25°)
23....	Cl	H	CH_3	141	1.4460		A	(19)	131	1.4221 (20°)		
24....	Cl	H	C_2H_5	166	1.4375	1.0534[h]	A	(35)	145	1.4227 (20°)	182	1.4199 (25°)
25....	Cl	Cl	C_2H_5	177	1.4350	1.1672[h]	A	(35)	154	1.4386 (20°)		
26....	Br	H	CH_3	172	1.4880		A	(19)	144	1.4552 (25°)	75 (17)	1.4501 (25°)
27....	Br	H	C_2H_5	182	1.4610	1.3233[h]	A	(5)	158	1.4542 (13°)	194	1.4393 (25°)
28....	Br	Br	C_2H_5	208	1.4895	1.5790[h]	A	(35)	188	1.5017 (13°)	104 (8)	1.4691 (25°)
29....	Cl	H	$>(CH_2)_2$	89–93 (23)	1.4874		A	(19)				
30....	Cl	H	$>(CH_2)_3$	132–135 (23)	1.4780		A	(19)				
31....	Br	H	$>(CH_2)_2$	118–119 (24)			A	(19)				
32....	Br	H	$>(CH_2)_3$	73–75 (2)	1.5007		A	(19)				
33....	Cl	Cl	$>(CH_2)_2$	118–121 (21)	[e]		A	(19)				
34....	Cl	Cl	$>(CH_2)_3$	105–106 (8)	[f]		A	(19)				

[a] Pressures not indicated are atmospheric; the boiling points of esters and orthoesters are generally the upper limits of a 2–3°C. range.

[b] $n_D^{20°}$.

[c] $n_D^{50°}$; $d_4^{50°}$; the melting point of this ketene acetal is 41–42°C.

[d] $n_D^{40°}$; the melting point of this ketene acetal is 37–38°C.

[e] Melting point 55–57°C.

[f] Melting point 67–69°C.

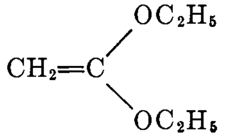
[g] $d_{20°}^{20°}$.

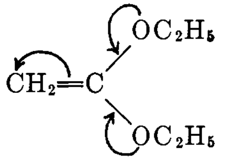
[h] $d_{25°}^{25°}$.

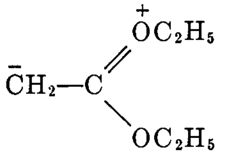
[i] Melting point 61–62°C.

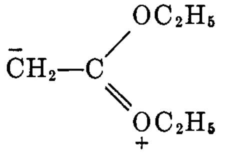
ing alkyl acetates and ethyl propionate have been offered as evidence that the products obtained by Scheibler and coworkers from these esters in reaction 4 do not have the structures assigned to them (33). In each case the boiling points of the products reported by the German investigators were practically the same as, or even lower than, those of the corresponding esters.

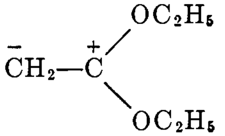
The polarization of the ketene acetals, which is responsible for both their abnormally high boiling points and their extraordinary reactivity, is the result of the unusual hetero-enoid system present in their structures. The *two* alkoxy groups in conjugation with the carbon-to-carbon double bond permit the existence of polarized forms, e.g., Xb, Xc, and Xd, of ketene diethylacetal (X), all of which may be combined in the abbreviated form Xa. Each of these forms contributes to the negative (anionoid or nucleophilic) center on the methylene carbon, which is the seat of the remarkable reactivity of the molecule, and which together with the counterbalancing, though less localized, positive charge produces the permanent polarization that is associated with this structure.


X


Xa

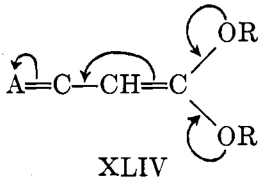

Xb

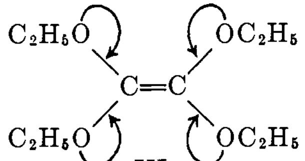

Xc


Xd

If the methylene group of a ketene acetal carries a substituent, such as phenyl, carbethoxy, or cyano, which through a multiple bond may be involved in further conjugation with the alkoxy groups as in XLIV, the polarization of the molecule is enhanced and the boiling point of the ketene acetal is not only above that of the normal ester, but approaches (No. 15, table 1) or even exceeds (Nos. 14, 18, 19, and 20) that of the orthoester, which has a substantially higher molecular weight.

An interesting relationship of boiling points exists between diethoxyketene diethylacetal (No. 22, table 1) and the corresponding normal ester, ethyl diethoxyacetate. This ketene acetal boils lower than both the ester and the ortho-


XLIV


XLa

ester, doubtless owing to the fact that its polarization is diminished if not eliminated by its symmetrical structure (XLa).

Although there are no esters or orthoesters to which the dioxolanes (Nos. 7, 16, 29, 31, 33) and dioxanes (Nos. 8, 17, 30, 32, 34) of table 1 may be appropriately compared, their boiling points are of interest in relationship to those of the ketene dialkylacetals of comparable molecular weight. For example, 2-methylene-1,3-dioxolane (No. 7) boils considerably above ketene dimethylacetal (No. 1) to which it is comparable in molecular weight; in fact it boils nearly as high as ketene diethylacetal (No. 2), which contains two additional carbons with their complement of hydrogen. A similar relationship exists between the other ketene cyclic acetals and the ketene dialkylacetals that they approximate in molecular weight. Doubtless the higher boiling points of these cyclic acetals are related in part to their cyclic structures *per se*—cyclic compounds generally boil above the related open-chain compounds; *cf.* cyclohexane, b.p. 81°C., and hexane, b.p. 68°C. This structural difference, however, is probably not the sole factor involved; the higher boiling points of the cyclic acetals must be due to a considerable extent to their higher polarizations, because these compounds, as will be seen subsequently, are definitely the most reactive of all the ketene acetals.

The refractive index has proved to be a useful and significant property of the ketene acetals. With the exception of the dichloro- and dibromo-ketene acetals (Nos. 25 and 28), the refractive indices of each of the ketene acetals are substantially higher than either of those of the corresponding ester or orthoester. This value indicates the higher purity of phenylketene dimethylacetal (No. 14) prepared by procedure A than that of the product obtained from procedure C. The refractive indices are useful as a means of distinguishing those ketene acetals (e.g., Nos. 14 and 15) that boil at approximately the same temperatures as the corresponding orthoesters. The change in the refractive index affords a convenient means of following the deterioration of samples of the more reactive ketene acetals.

B. REACTIONS WITH COMPOUNDS CONTAINING ACTIVE HYDROGEN

1. Water

All ketene acetals react with water to form an ester and an alcohol (reaction 26) or in the case of dioxolane or dioxane, an ω-hydroxyalkyl ester (reaction 27).

$$\mathrm{RR'C{=}C(OR'')_2 + HOH \rightarrow \underset{XLV}{[RR'CHC(OR'')_2OH]} \rightarrow RR'CHCOOR'' + R''OH} \qquad (26)$$

$$\mathrm{RR'C{=}\underline{CO(CH_2)_nO} + HOH \rightarrow \underset{XLVI}{[RR'CH\underline{C(OH)O(CH_2)_nO}]} \rightarrow RR'COO(CH_2)_nOH} \qquad (27)$$

The rates of reactions 26 and 27 vary over a wide range, depending upon the nature of the substituents R, R′, and R″. The dimethyl and the cyclic acetals (Nos. 7, 8, 14, 16, 17, 23, 26, 29, 30, 31, and 32 of table 1) have an extraordinary affinity for moisture as shown by a rapid drop in their refractive indices when exposed to the air; for example, phenylketene dimethylacetal is completely converted to a mixture of the corresponding ester and orthoester after exposure to moist air for a few hours (19). The other ketene acetals are more stable in water even to the point where the cyanoketene acetals (Nos. 18 and 19) may be recrystallized from their solutions in hot water (30). However, all of these less reactive ketene acetals react rapidly with water containing a trace of acid.

Whether the orthoacid-esters (XLV and XLVI) are intermediates in the hydrolysis of ketene acetals cannot be determined definitely. The fact that reactions 26 and 27 are strongly catalyzed by hydrogen ions and that other active hydrogen compounds are known to add across the double bonds of ketene acetals make these intermediates appear to be likely possibilities.

2. *Alcohols*

Primary and secondary alcohols, in the presence of a trace of acid, add rapidly to ketene acetals to yield orthoesters (2, 3, 14) according to reaction 28. In the absence of the acid catalyst the rate of addition varies widely, depending on the substituents on the methylene carbon of the acetal. Tertiary alcohols do not show this reaction and it is for this reason that *t*-butyl alcohol is the medium generally employed for the dehydrohalogenation of haloacetals in procedure A. In the presence of base the rate of alcohol addition to the haloketene diethylacetals is sufficiently low to permit the isolation of these ketene acetals after the dehydrohalogenation of the dihaloacetaldehyde acetals in ethyl alcohol solution (34).

$$\mathrm{RR'C{=}C(OR'')_2 + R'''OH \xrightarrow{H^+} RR'CHC(OR'')_2OR'''} \qquad (28)$$

While reaction 28 may be used to prepare mixed alkyl orthoesters (14), it does not yield an alkyl diphenyl orthoester when ketene diphenylacetal is treated with an alcohol; instead, the initially formed mixed orthoester (XLVIII) undergoes alcoholysis to yield phenol (reaction 29), which then reacts with the remaining ketene acetal to form triphenyl orthoacetate (reaction 30), which is the principal product isolated (21).

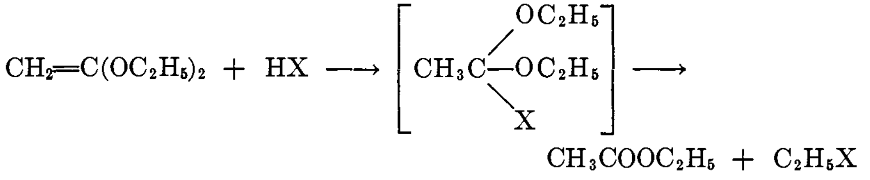
$$\mathrm{CH_2{=}C(OC_6H_5)_2 + ROH \xrightarrow{H^+} \underset{XLVIII}{[CH_3C(OC_6H_5)_2OR]} \xrightarrow{ROH} CH_3C(OR)_3 + 2C_6H_5OH} \qquad (29)$$

$$\mathrm{CH_2{=}C(OC_6H_5)_2 + C_6H_5OH \rightarrow CH_3C(OC_6H_5)_3} \qquad (30)$$

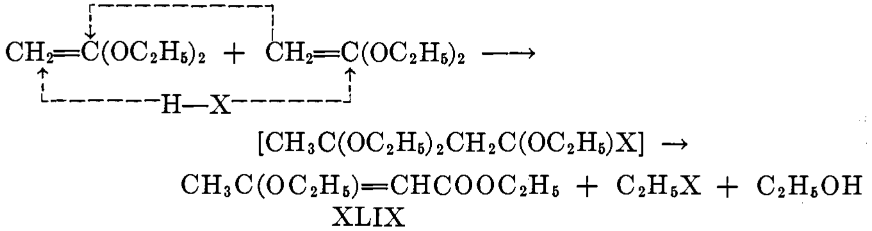
Although phenyl dialkyl orthoacetates undergo pyrolysis to the alkyl acetates and phenetole (reaction 15) when distilled, triphenyl orthoacetate from reaction 30 is quite stable and may be distilled without any evidence of pyrolysis (21).

3. *Acids*

When ketene diethylacetal is added to an ethereal solution of an acid, it is quantitatively converted to ethyl acetate and the ethyl ester of the acid (or the ethyl ether of a phenol) according to reaction 31. If, however, the order of addition is reversed and the acid added to the ketene acetal there is a secondary reaction, which involves the addition of the acid across two molecules of the ketene acetal (reaction 32) to yield ethyl *O*-ethylacetoacetate (XLIX).



$$CH_2{=}C(OC_2H_5)_2 + HX \longrightarrow \left[CH_3C(OC_2H_5)_2X \right] \longrightarrow CH_3COOC_2H_5 + C_2H_5X \quad (31)$$



$$CH_2{=}C(OC_2H_5)_2 + CH_2{=}C(OC_2H_5)_2 \xrightarrow{H-X} [CH_3C(OC_2H_5)_2CH_2C(OC_2H_5)X] \rightarrow CH_3C(OC_2H_5){=}CHCOOC_2H_5 + C_2H_5X + C_2H_5OH \quad (32)$$

XLIX

The extent of reaction 32 with a variety of acids is shown in table 2. It is of interest to note that the yield of XLIX is unrelated to the strength of the acid used, the weaker acids giving as high (or higher) yields of this product as the stronger acids. In each of the cases in which a substantial amount of XLIX is formed, an approximately 20 per cent yield of ethyl orthoacetate is also obtained from the addition of the alcohol produced in reaction 32 to a portion of the ketene acetal (reaction 28); the remainder of the acetal follows reaction 31 (26). Hydrogen fluoride occupies a singular position among the acids of table 2; it does not add to the ketene acetal but instead causes it to polymerize (see Section III F).

Ketene diphenylacetal does not follow either reaction 31 or 32 when treated with hydrogen bromide but instead gives polymeric material (21). This is doubtless due to the inability of the strong oxygen–phenyl bond to undergo the rupture required in reaction 31.

With the exception of 2-methylene-1,3-dioxolane, which undergoes a rapid exothermic polymerization when treated with hydrogen chloride, the methylenedioxolanes and methylenedioxanes of table 1 react with this acid to yield the ω-chloroethyl and propyl esters in a manner similar to their addition of water in reaction 27 to form hydroxy esters (19).

The addition of one molecule of an acid across two molecules of ketene acetal to form the dimeric product XLIX is reminiscent of 1,4-addition to diolefins. Bromine adds to bromoketene diethylacetal (reaction 57) and maleic anhydride and diazonium salts add to ketene diethylacetal (reactions 47 and 58) in a similar manner.

4. Reactive methylene compounds

The highly enolic dibenzoylmethane reacts with ketene acetal (X) in the same manner as phenols and alcohols to yield the mixed orthoester, L (reaction 33). This reaction is reversible and L reverts to its components—slowly (three months) in a vacuum desiccator or rapidly at 140°C. (2). The reversal of this reaction is analogous to the formation of ketene acetals from orthoesters by procedure C of Section II; also it is of interest to note that this orthoester (L) does not undergo the characteristic decomposition of aryl dialkyl orthoesters shown in reactions 15 and 31.

TABLE 2

Conversion of ketene diethylacetal to ethyl O-ethylacetoacetate (XLIX) *by acids*

ACID	YIELD OF XLIX	ACID	YIELD OF XLIX
	per cent		*per cent*
Hydrofluoric	0*	Benzoic	38
Hydrochloric	23	Acetic	37
Hydrobromic	10	Phenol	0†
Trichloroacetic	37	*p*-Bromophenol	0†
Chloroacetic	42	Tribromophenol	26
Formic	35	Trichlorophenol	21

* None of either reaction 31 or 32; only polymerization of the ketene acetal.

† Reaction 31 quantitatively.

$$CH_2{=}C(OC_2H_5)_2 + C_6H_5C(OH){=}CHCOC_6H_5 \rightleftarrows$$

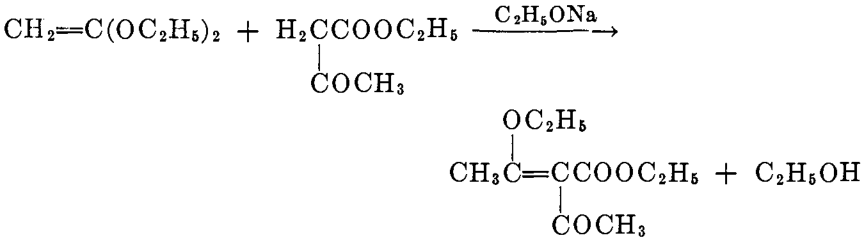
X

$$CH_3C(OC_2H_5)_2OC(C_6H_5){=}CHCOC_6H_5 \qquad (33)$$

L

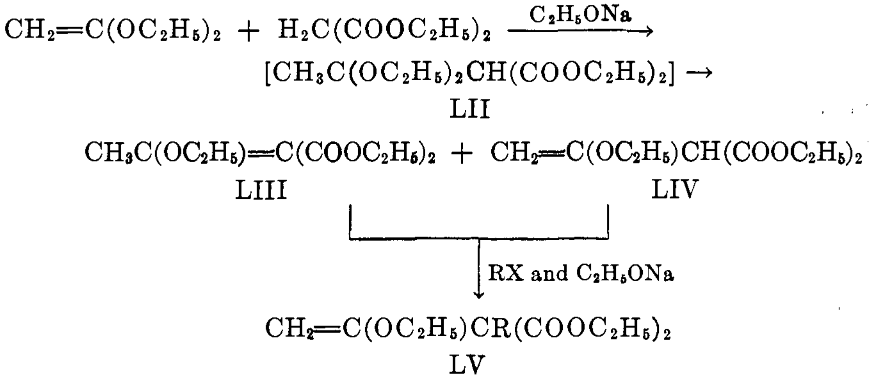
In contrast to the behavior of dibenzoylmethane, the weaker enolic compounds, acetoacetic ester and malonic ester, add to ketene acetal as H— and —CHR_2 to form a carbon-to-carbon linkage (reactions 34 and 35). A remarkable feature of this addition is that it is base-catalyzed. In the absence of base acetoacetic ester gives a 12 per cent yield of LI at 85°C., but malonic ester does not react even at temperatures as high as 200°C. However, in the presence of 1 mole per cent of sodium ethoxide the yield of LI is raised to 55–60 per cent (2) and malonic ester reacts with the ketene acetal at 125°C. to give two products, LIII (in 66 per cent yield) and LIV (in 11 per cent yield), which result from the two modes of alcohol elimination from the intermediate addition product LII in reaction 35 (15). Each of the reaction products, LIII and LIV, may be alkylated to the α-ethoxyvinylmalonic ester, LV (15).

The base-catalyzed reactions 34 and 35 are of particular interest because they are the only ones (which have been observed to date) that do not appear to involve primarily the anionoid methylene carbon of the ketene acetal. Instead, it seems likely that the carbanion of the methylene compound, $:\overset{-}{C}HR_2$, which



$$CH_2{=}C(OC_2H_5)_2 + \underset{COCH_3}{H_2CCOOC_2H_5} \xrightarrow{C_2H_5ONa} CH_3\overset{OC_2H_5}{C}{=}\underset{COCH_3}{C}COOC_2H_5 + C_2H_5OH \quad (34)$$

LI



$$CH_2{=}C(OC_2H_5)_2 + H_2C(COOC_2H_5)_2 \xrightarrow{C_2H_5ONa} \underset{\text{LII}}{[CH_3C(OC_2H_5)_2CH(COOC_2H_5)_2]} \rightarrow$$

$$\underset{\text{LIII}}{CH_3C(OC_2H_5){=}C(COOC_2H_5)_2} + \underset{\text{LIV}}{CH_2{=}C(OC_2H_5)CH(COOC_2H_5)_2} \quad (35)$$

$$\xrightarrow{\text{RX and } C_2H_5ONa} \underset{\text{LV}}{CH_2{=}C(OC_2H_5)CR(COOC_2H_5)_2}$$

is formed by the base, attacks the carbonium center of the polarized form Xd (Section IIIA) of the acetal, $\overset{-}{C}H_2\overset{+}{C}(OC_2H_5)_2$, in a manner similar to the reaction of a carbanion with the positive center of a polarized α,β-unsaturated carbonyl compound ($H_2\overset{+}{C}{—}C{=}C{—}\overset{-}{O}$) in the base-catalyzed Michael reaction.

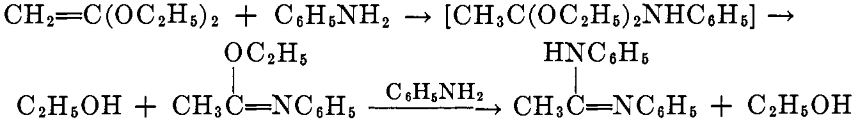
Methylmalonic ester, $CH_3CH(COOC_2H_5)_2$, which has only a single active hydrogen, cannot be caused to react with ketene acetal even in the presence of 1–50 mole per cent of sodium ethoxide and at temperatures up to 200°C. (2). Bis(phenylsulfonyl)methane, $(C_6H_5SO_2)CH_2$, which is sufficiently acidic to dissolve in aqueous alkali, does not add to ketene acetal either alone or in the presence of alkali; instead it produces polymerization of the acetal (2).

5. *Amines*

The reaction of ammonia and certain amines with ketene acetal strikingly illustrates the anionoid character of the acetal (2). The reactivities of these bases are inversely proportional to their base strength, or proportional to their ability to release a proton (i.e., their acidities) to the methylene group of the ketene acetal. Aniline reacts readily with ketene acetal at 25°C. to give as the main reaction product ethyl *N*-phenyliminoacetate in 81 per cent yield; a portion of this product reacts further with aniline to form *N*,*N'*-diphenylacetamidine (reaction 36). The absence of ethyl orthoacetate from the products of this reaction indicates that the amine reacts sufficiently rapidly to consume all of the ketene acetal before the alcohol which is produced in the reaction can be eliminated from the intermediate and react with the ketene acetal to form the orthoester.

Ethylaniline reacts slowly with ketene acetal at 25°C., but quite rapidly at 100°C., to yield *N*-ethyl-*N*-(α-ethoxyvinyl)aniline (LVI). An equivalent amount of ethyl orthoacetate also is formed, regardless of the ratio of the original reactants, indicating that this reaction requires the quantities and follows the course shown in reaction 37.

The stronger base ammonia shows no reaction with ketene acetal at 25°C., but when these compounds are heated together for 3 hr. at 100°C., the main reaction products are acetonitrile (55 per cent) and acetamidine (22 per cent). Reaction 38 illustrates the course of this reaction. Piperidine, like ammonia, does not react readily with ketene acetal, but when the latter is heated with a fivefold excess of the refluxing amine for 2 hr., 1,1,1-tripiperidinoethane (LVII) and an equivalent amount of ethyl orthoacetate are produced according to reaction 39.

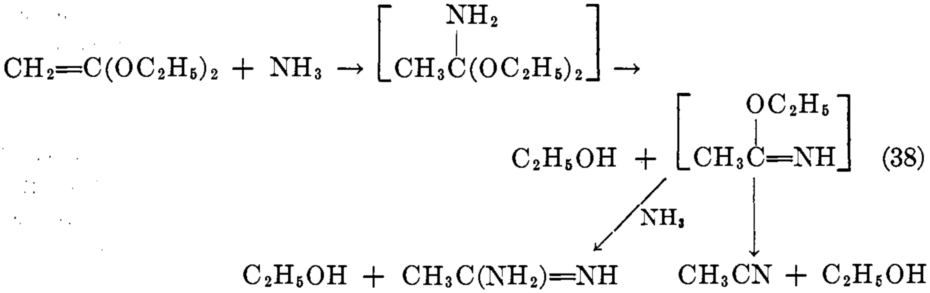


$$CH_2{=}C(OC_2H_5)_2 + C_6H_5NH_2 \rightarrow [CH_3C(OC_2H_5)_2NHC_6H_5] \rightarrow$$

$$C_2H_5OH + CH_3\overset{\overset{\displaystyle OC_2H_5}{|}}{C}{=}NC_6H_5 \xrightarrow{C_6H_5NH_2} CH_3\overset{\overset{\displaystyle HNC_6H_5}{|}}{C}{=}NC_6H_5 + C_2H_5OH \quad (36)$$

$$2CH_2{=}C(OC_2H_5)_2 + C_6H_5NHC_2H_5 \rightarrow$$

$$\underset{\text{LVI}}{CH_2{=}C(OC_2H_5)N(C_2H_5)C_6H_5} + CH_3C(OC_2H_5)_3 \quad (37)$$



$$CH_2{=}C(OC_2H_5)_2 + NH_3 \rightarrow \left[CH_3\overset{\overset{\displaystyle NH_2}{|}}{C}(OC_2H_5)_2\right] \rightarrow$$

$$C_2H_5OH + \left[CH_3\overset{\overset{\displaystyle OC_2H_5}{|}}{C}{=}NH\right] \quad (38)$$

$$\xrightarrow{NH_3} C_2H_5OH + CH_3C(NH_2){=}NH \qquad \downarrow\; CH_3CN + C_2H_5OH$$

$$2CH_2{=}C(OC_2H_5)_2 + 3HNC_5H_{10} \rightarrow$$

$$\underset{\text{LVII}}{CH_3C(NC_5H_{10})_3} + CH_3C(OC_2H_5)_3 + C_2H_5OH \quad (39)$$

6. Hydrogen

One of the first reactions used to characterize ketene diethylacetal was hydrogenation over Raney nickel (3). Only half of the theoretical quantity of hydrogen was absorbed for complete hydrogenation (reaction 40) because the polymer of the acetal, which formed as the hydrogenation proceeded, deactivated the catalyst. From the products of this hydrogenation a 35 per cent yield of acetaldehyde diethylacetal was separated.

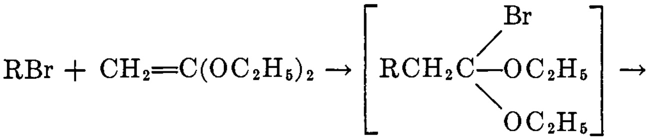
$$CH_2{=}C(OC_2H_5)_2 + H_2 \xrightarrow{Ni} CH_3CH(OC_2H_5)_2 \quad (40)$$

C. ALKYLATION AND ACYLATION OF KETENE ACETALS

1. With alkyl halides

The high anionoid reactivity of ketene acetals indicates that they should undergo a similar type of *C*-alkylation of the methylene carbon with alkyl halides as do ethyl β-diethylaminocrotonate, $CH_3C(N(C_2H_5)_2){=}CHCOOC_2H_5$ (40), and α-methoxystyrene, $C_6H_5C(OCH_3){=}CH_2$ (36). Such an alkylation of ketene acetal does indeed occur with *n*-butyl bromide (reaction 41, R is *n*-C_4H_9), but the yield of the alkylation product, ethyl caproate, amounts to only 13 per cent of the theoretical because the necessary reaction conditions (72 hr. at 250°C.) are so severe that most of the ketene acetal is pyrolyzed to ethyl acetate and ethylene (reaction 15a). However, with more reactive halides the alkylation occurs under less strenuous conditions and the pyrolysis of the ketene acetal is avoided (26). For example, allyl bromide reacts with the ketene acetal to the extent of 46 per cent at 190°C. for 5 hr., while benzyl bromide reacts in 3 hr. at 125°C. to the extent of 71 per cent.

Both mono- and di-alkylated acetic esters are obtained from these alkylations. It appears that the primary reaction product (LVIII), which results from the addition of the halide across the double bond of the ketene acetal, undergoes pyrolysis in two ways: (*a*) to eliminate ethyl bromide and yield the monoalkylated acetic ester (LIX) *via* reaction 41, and (*b*) to lose hydrogen bromide and yield the monoalkylated ketene acetal (LX), which then is further alkylated *via* the intermediate LXI to the dialkylacetic ester (LXII) and ethyl bromide (reaction 42).



$$RBr + CH_2{=}C(OC_2H_5)_2 \rightarrow \left[\begin{array}{l} \qquad\quad Br \\ RCH_2C{-}OC_2H_5 \\ \qquad\quad OC_2H_5 \end{array}\right] \rightarrow$$

LVIII

$$\underset{\text{LIX}}{RCH_2COOC_2H_5} + C_2H_5Br \qquad (41)$$

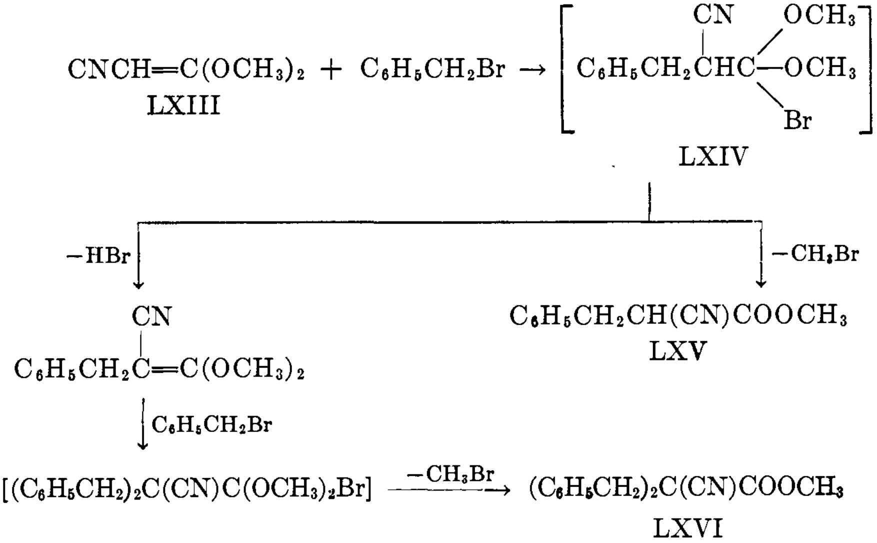
$$\text{LVIII} \rightarrow HBr + \underset{\text{LX}}{RCH{=}C(OC_2H_5)_2} \xrightarrow{RBr}$$

$$\underset{\text{LXI}}{[R_2CHC(OC_2H_5)_2Br]} \rightarrow \underset{\text{LXII}}{R_2CHCOOC_2H_5} + C_2H_5Br \qquad (42)$$

The hydrogen bromide produced in reaction 42 converts an equivalent amount of the ketene acetal to ethyl acetate and ethyl bromide (reaction 31). When allyl bromide is the alkylating agent, the yields of allylacetic ester (LIX: R is allyl) and diallylacetic ester (LXII: R is allyl) are 9 per cent and 31 per cent, respectively; with benzyl bromide the yields of hydrocinnamic ester (LIX: R is benzyl) and dibenzylacetic ester (LXII: R is benzyl) are 14 per cent and 46 per cent, respectively (26).

There is no indication from the study of reactions 41 and 42 that the intermediate LXI undergoes any dehydrohalogenation to yield a dialkylketene acetal in the manner in which the monoalkylated ketene acetal (LX) appears to be formed from LVIII. If such a reaction occurred and the resulting dialkylketene acetal were alkylated, a novel method of preparation of trialkylacetic esters would be available. However, an investigation (24) of the benzylation of monoalkylated ketene acetals further demonstrates the stability to dehydrohalogenation of dialkylated intermediates of the type of LXI. Although the temperature necessary to effect the benzylation of *n*-propylketene diethylacetal causes extensive pyrolysis to ethylene and ethyl valerate (reaction 15a), phenylketene diethylacetal (LX: R is C_6H_5) gives a 59 per cent yield of the monoalkylated product, ethyl α,β-diphenylpropionate, together with a 39 per cent yield of ethyl phenylacetate from the pyrolysis of the ketene acetal. When the more stable *dimethyl* acetals are used, the *n*-propyl-, *n*-heptyl-, and phenyl-ketene acetals yield, respectively, 83 per cent, 87 per cent, and 68 per cent of the monobenzylated products as in the conversion of LX to LXII in reaction 42; there is no evidence of dibenzylation even with the negative phenyl substituent, which might be expected to activate for dehydrohalogenation the α-hydrogen of such an intermediate as LXI.

Cyanoketene dimethylacetal (LXIII), in contrast to the alkyl- and phenylketene acetals, has in the cyano substituent a group of sufficient negativity to activate for dehydrohalogenation the α-hydrogen of the initial benzylation product (LXIV). Consequently, this ketene acetal undergoes the complete benzylation illustrated in reaction 43 to give the following yields of reaction products: 21 per cent of methyl benzylcyanoacetate (LXV), 26 per cent of methyl dibenzylcyanoacetate (LXVI), and 31 per cent of methyl cyanoacetate (30); the latter product results from the reaction of the ketene acetal (LXIII) with the hydrogen bromide eliminated from the intermediate (LXIV).

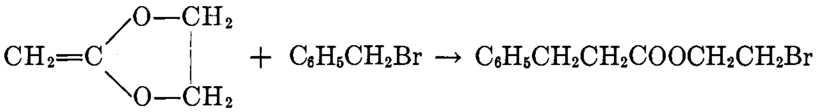


$$\underset{\text{LXIII}}{CNCH{=}C(OCH_3)_2} + C_6H_5CH_2Br \rightarrow \underset{\text{LXIV}}{\left[C_6H_5CH_2CH(CN)C(OCH_3)_2Br\right]}$$

$$\text{LXIV} \xrightarrow{-CH_3Br} \underset{\text{LXV}}{C_6H_5CH_2CH(CN)COOCH_3}$$

$$\text{LXIV} \xrightarrow{-HBr} C_6H_5CH_2C(CN){=}C(OCH_3)_2 \xrightarrow{C_6H_5CH_2Br} [(C_6H_5CH_2)_2C(CN)C(OCH_3)_2Br] \xrightarrow{-CH_3Br} \underset{\text{LXVI}}{(C_6H_5CH_2)_2C(CN)COOCH_3} \qquad (43)$$

In contrast to the extensive dialkylation of ketene diethylacetal in reactions 41 and 42, 2-methylene-1,3-dioxolane (LXVII) reacts with benzyl bromide at 150°C. to yield only the monoalkylation product, β-bromoethyl hydrocinnamate (LXVIII), as shown in reaction 44. The yield amounts to only 43 per cent because of the rapid concurrent polymerization of this cyclic ketene acetal (19).


(44)

LXVII LXVIII

2. *With alkyl sulfates*

The alkylation of *n*-propylketene dimethylacetal (LXIX: R is *n*-propyl) with diethyl sulfate at 145°C. for 15 hr. gives, surprisingly, a 65 per cent yield of methyl α-*methyl*valerate (LXXIII) together with a 20 per cent recovery of the unchanged ketene acetal (24). This unexpected alkylation behavior is explained by the sequence of transformations shown in reaction 45. The conversion of the ketene acetal (LXIX) to LXXIII instead of LXXI is due to the greater reactivity of methyl ethyl sulfate (LXXII), which is eliminated from the intermediate LXX, as a methylating agent than as an ethylating agent. The rate of methylation appears to be sufficiently high to exclude an appreciable amount of ethylation after some of the mixed sulfate (LXXII) is formed, as none of the α-ethylated ester (LXXI) is found among the reaction products even though a large excess of diethyl sulfate is present in the reaction mixture.

$$\underset{\text{LXIX}}{RCH{=}C(OCH_3)_2} + (C_2H_5)_2SO_4 \rightarrow \underset{\text{LXX}}{[RCH(C_2H_5)C(OCH_3)_2SO_4C_2H_5]} \rightarrow \underset{\text{LXXI}}{RCH(C_2H_5)COOCH_3} + \underset{\text{LXXII}}{CH_3SO_4C_2H_5}$$

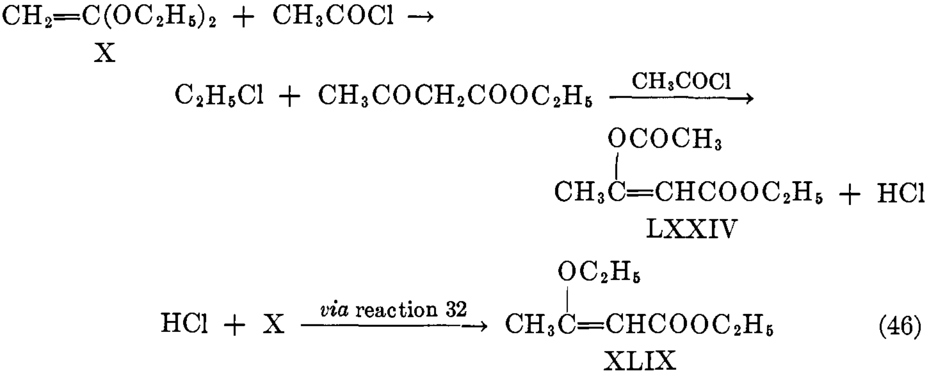
$$RCH{=}C(OCH_3)_2 + CH_3SO_4C_2H_5 \rightarrow [RCH(CH_3)C(OCH_3)_2SO_4C_2H_5] \rightarrow \underset{\text{LXXIII}}{RCH(CH_3)COOCH_3} + \underset{\text{LXXII}}{CH_3SO_4C_2H_5} \quad (45)$$

R is $n\text{-}C_3H_7$.

The continual regeneration of the methylating agent (LXXII) in reaction 45 indicates that the alkyl sulfate merely serves as a carrier of one of the methyl groups from the oxygen to the methylene carbon of the ketene acetal. Consequently, it would be expected that catalytic amounts of dimethyl sulfate would serve to convert the acetal (LXIX) to the α-methylated ester (LXXIII). This is indeed the case; when one equivalent of the ketene acetal is heated with 0.05 equivalent of dimethyl sulfate, 0.3 equivalent of LXXIII is produced (24).

3. *With acyl halides*

Ketene diethylacetal (X) reacts exothermically with *one* equivalent of acetyl chloride at room temperature to give a 30 per cent yield of *O*-acetylacetoacetic ester (LXXIV), as shown in reaction 46. The hydrogen chloride produced in this reaction converts a portion of the ketene acetal to *O*-ethylacetoacetic ester (XLIX) (reaction 32). When the molar ratio of acetyl chloride to the ketene acetal is increased to 3:1, the yield of LXXIV is increased to 52 per cent. Acetoacetic ester is shown to be an intermediate in reaction 46 by (*a*) the separation of a small amount (3 per cent) from the reaction products and (*b*) the acetylation of acetoacetic ester with acetyl chloride (the final step of reaction 46) in the presence of ketene acetal, which absorbs the hydrogen chloride, to a mixture of the isomeric *O*- and *C*-acetal derivatives in 79 per cent yield (26). The *C*-acetyl derivative is formed by the rearrangement of LXXIV.



$$\underset{\mathrm{X}}{\mathrm{CH_2{=}C(OC_2H_5)_2}} + \mathrm{CH_3COCl} \rightarrow \mathrm{C_2H_5Cl} + \mathrm{CH_3COCH_2COOC_2H_5} \xrightarrow{\mathrm{CH_3COCl}} \underset{\mathrm{LXXIV}}{\mathrm{CH_3}\overset{\mathrm{OCOCH_3}}{\overset{|}{\mathrm{C}}}\mathrm{{=}CHCOOC_2H_5}} + \mathrm{HCl}$$

$$\mathrm{HCl} + \mathrm{X} \xrightarrow{\textit{via}\ \text{reaction 32}} \underset{\mathrm{XLIX}}{\mathrm{CH_3}\overset{\mathrm{OC_2H_5}}{\overset{|}{\mathrm{C}}}\mathrm{{=}CHCOOC_2H_5}} \qquad (46)$$

Benzoyl chloride does not react as readily with ketene acetal (X) as does acetyl chloride, but after 2 hr. at 100°C. a 59 per cent yield of ethyl *O*-benzoylbenzoylacetate, $C_6H_5C(OCOC_6H_5){=}CHCOOC_2H_5$, which corresponds to LXXIV of reaction 46, is obtained (26). Similarly, *n*-propylketene dimethylacetal (LXIX: R is *n*-C_3H_7) reacts with benzoyl chloride to give a 60 per cent yield of methyl *O*-benzoyl-α-benzoylvalerate, $C_6H_5C(OCOC_6H_5){=}C(CH_2CH_2CH_3)COOCH_3$ (24). In contrast to ketene and *n*-propylketene acetals, chloroketene diethylacetal fails to show any significant amount of reaction with benzoyl chloride (24).

Benzenesulfonyl chloride does not acylate ketene acetal, but instead causes it to polymerize. A considerable portion of the sulfonyl chloride is recovered unchanged after being heated with the acetal for 2 hr. at 125°C. The remainder of the sulfonyl chloride is recovered as ethyl benzenesulfonate, which is formed from the alcohol eliminated from the polymer; the use of a higher ratio of the ketene acetal to the sulfonyl chloride only serves to increase the yield of this ester (26). It seems likely that there is some significance, as yet undetermined, to the fact that such structurally different sulfur compounds as benzenesulfonyl chloride and bis(phenylsulfonyl)methane (Section III B) produce a polymerization of ketene diethylacetal rather than react in the manner of their carbon analogs.

D. REACTIONS WITH α,β-UNSATURATED CARBONYL COMPOUNDS

1. Maleic anhydride

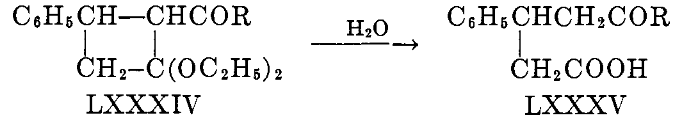
This dieneophile in ether solution readily adds across two molecules of ketene diethylacetal in the 1,4 manner, previously noted with acids in reaction 32, to give 3,5-diethoxy-1,6-dihydrophthalic anhydride (LXXVI) in 70 per cent yield, as shown in reaction 47. The intermediate LXXV is doubtless the precursor of LXXVI, and the alcohol lost from this intermediate converts two equivalents of the ketene acetal to ethyl orthoacetate. Consequently a 4:1 ratio of the ketene acetal to the maleic anhydride is required for the maximum yield of LXXVI, which precipitates quite completely from the ether solution. However, with benzene as the solvent for these reactants, LXXVI is not formed but instead the anhydride of the tetracarboxylic acid, LXXVII. As this latter compound also is formed quite readily when LXXVI is allowed to react with maleic anhydride in benzene solution, the formation of LXXVI exclusively in ether solution appears to be due to its insolubility in this solvent and its consequent precipitation as rapidly as it is formed and before it can react further with the maleic anhydride to produce LXXVII (18).

The anhydride LXXVI is characterized by its hydrolysis *via* the intermediate LXXVIII to the ketodibasic acid LXXIX, which is readily decarboxylated to the monobasic acid LXXX. Dehydrogenation of LXXVI by palladium yields 3,5-diethoxyphthalic anhydride LXXXI, the acid (LXXXII) of which also may be obtained from the reaction of ketene acetal with diethyl acetylenedicarboxylate as shown in reaction 48 (18).

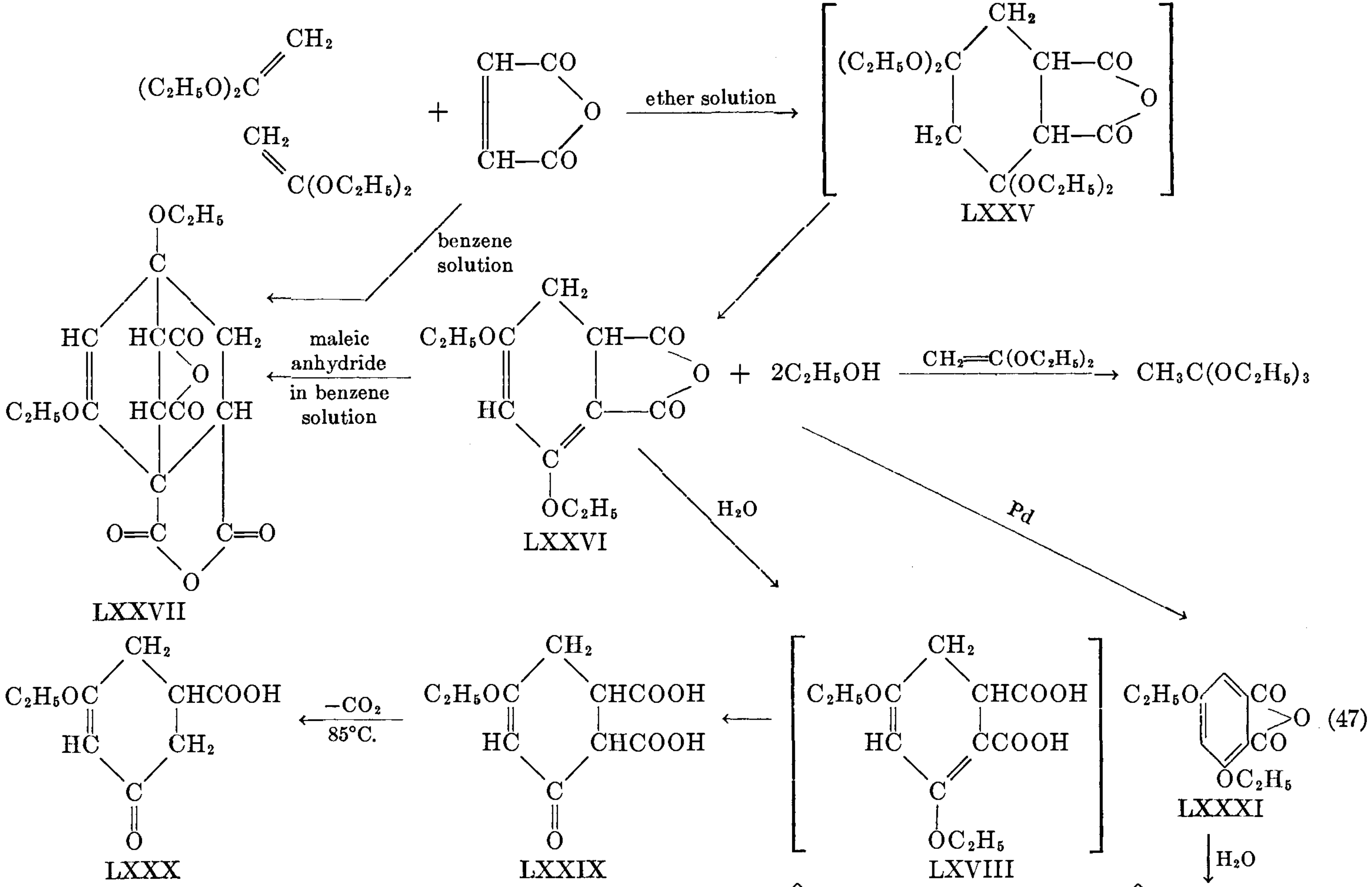
Although maleic anhydride condenses with ketene acetal as shown in reaction 47 at room temperature, dimethylmaleic anhydride does not react with the acetal even after 12 hr. in refluxing benzene. At 175–180°C. a reaction does occur, as none of the original reactants are recovered, but it has not been possible to isolate any definite product from the reaction mixture (18).

2. α,β-Unsaturated ketones

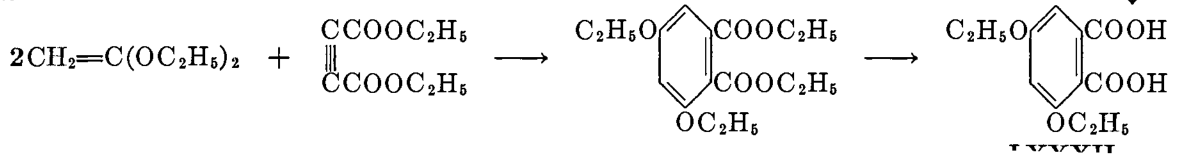
Benzalacetophenone (LXXXIII: R is C_6H_5) and dibenzalacetone (LXXXIII: R is $HC{=}CHC_6H_5$) when heated at 125°C. with an excess of ketene acetal add to only one equivalent of the acetal (reaction 49) to yield the cyclobutane derivatives (LXXXIV), which are characterized by hydrolysis to the corresponding β-phenyl-γ-acylbutyric acids (LXXXV). The yields of the cyclobutane derivatives (LXXXIV) are 87–91 per cent. There is no elimination of alcohol from either of these products, as shown by their analyses and the absence of ethyl orthoacetate in the reaction mixture (18).



$$\underset{\text{LXXXIII}}{C_6H_5CH{=}CHCOR} + CH_2{=}C(OC_2H_5)_2 \rightarrow \underset{\text{LXXXIV}}{\begin{array}{l} C_6H_5CH{-}CHCOR \\ \quad\ | \qquad\ | \\ \quad CH_2{-}C(OC_2H_5)_2 \end{array}} \xrightarrow{H_2O} \underset{\text{LXXXV}}{\begin{array}{l} C_6H_5CHCH_2COR \\ \qquad | \\ \quad CH_2COOH \end{array}} \qquad (49)$$


ether solution
benzene solution
maleic anhydride in benzene solution
LXXV
LXXVI
LXXVII
$CH_2{=}C(OC_2H_5)_2$
$CH_3C(OC_2H_5)_3$
H_2O
Pd
$-CO_2$
85°C.
LXVIII
LXXIX
LXXX
LXXXI
H_2O

(47)

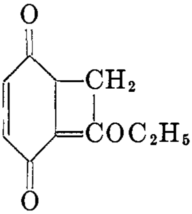

$2CH_2{=}C(OC_2H_5)_2$
$CCOOC_2H_5$
$CCOOC_2H_5$

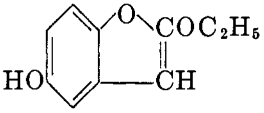
(48)

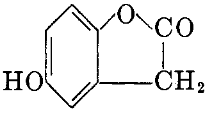
With benzalacetone (LXXXIII: R is CH_3) in reaction 49 ethyl acetate and ethyl orthoacetate are the only reaction products isolated; the major portion of the reaction mixture is a non-distillable tar, which indicates the formation of self-condensation products from the benzalacetone and polymerization of the ketene acetal. Phorone, $(CH_3)_2C{=}CHCOCH{=}CH(CH_3)_2$, does not react with ketene acetal even after 12 hr. at 125°C.; in this case practically all of the ketene acetal is recovered unchanged. The inertness of this di-α,β-unsaturated ketone is attributed to the deactivating influence of the *gem*-dimethyl substituents (18).

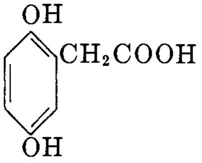
3. Quinones

The reaction between benzoquinone and ketene diethylacetal starts at about 80°C. and, without a solvent, becomes so violent that it cannot be controlled; in benzene solution, however, the reaction proceeds smoothly. The product of this reaction, which involves the condensation of one molecule of the quinone with one of the acetal followed by the loss of alcohol, is isolated in 61 per cent yield. Originally it was thought to be the bicycloöctadiene LXXXVI (18), but later work with other quinones (20) shows it to have the ethoxycoumarone structure (LXXXVII). Hydrogen bromide converts LXXXVII to 5-hydroxy-2-coumaranone (LXXXVIII) and hydrolysis converts it to hydroquinoneacetic (homogentisic) acid (LXXXIX).


LXXXVI

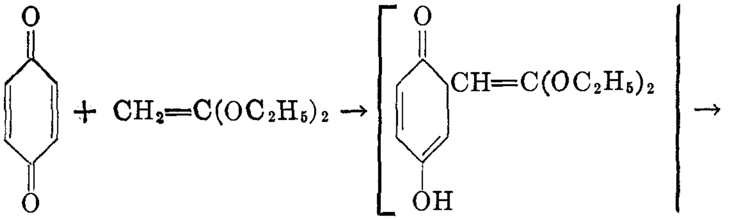

LXXXVII


LXXXVIII

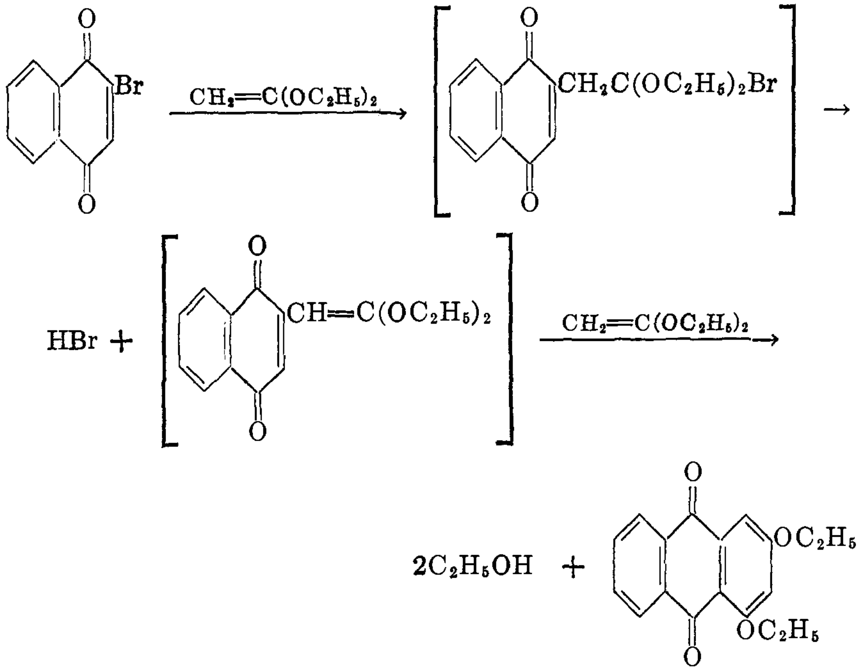

LXXXIX

m-Xyloquinone, bromobenzoquinone, 2,5-dibromobenzoquinone, and 1,4-naphthoquinone react with ketene acetal in a manner similar to benzoquinone to give coumarones corresponding to LXXXVII. These reactions appear to involve a 1,4-addition of the acetal as H and $CH{=}C(OC_2H_5)_2$ to the quinone, followed by the enolization and lactonization of the resulting intermediate, as the formation of LXXXVII is illustrated in reaction 50. *p*-Xyloquinone and 2,6-dibromobenzoquinone react with the ketene acetal, but it has not been possible to isolate any definite condensation product from the tarry products resulting from either of these reactions. Duroquinone does not react with the ketene acetal and is recovered unchanged after a reaction period of 12 hr. at 150°C. (20).

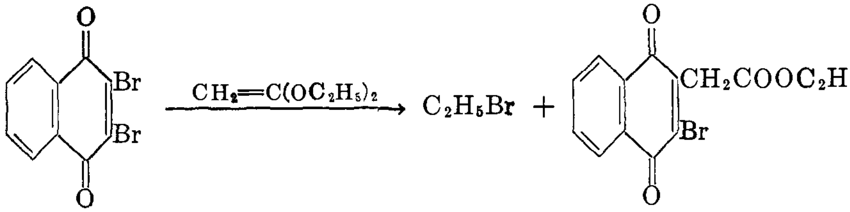
In contrast to the bromobenzoquinones, bromo-1,4-naphthoquinones react with ketene acetal to eliminate ethyl bromide and attach the quinone residue to the methylene carbon in the manner of the alkylation and acylation reactions of Section III C. With 2-bromo-1,4-naphthoquinone the reaction continues with a second molecule of the ketene acetal to give xanthopurpurin diethyl ether (XC) in 21 per cent yield (reaction 51). The hydrogen bromide which is postulated as an elimination product of the first intermediate does not appear as such but as ethyl bromide (obtained in 40 per cent yield) from the reaction of the acid with ketene acetal. The formation of XC with the evolution of ethyl bromide also may be rationalized by assuming the addition of the bromoquinone across two molecules of the ketene acetal in the 1,4 manner of reaction 32 instead of the



LXXXVII (50)



XC (51)



XCI (52)

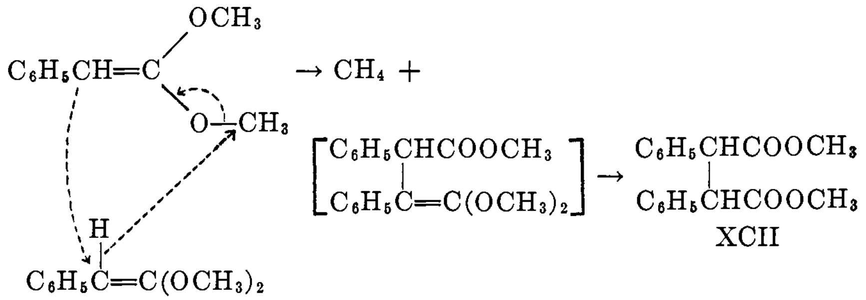
two-step process shown in reaction 51. However, none of the alkylations or acylations of Section III C show any of this type of addition, and for this reason it is believed that reaction 51 initially follows the pattern of reaction 42. With 2,3-dibromo-1,4-naphthoquinone only one equivalent of the ketene acetal appears in the reaction product, ethyl 3-bromo-1,4-naphthoquinon-2-ylacetate (XCI), which is produced in 58 per cent yield according to reaction 52 (20).

The addition of ketene acetal to quinones is greatly influenced by the substituents on the quinone nucleus. While benzoquinone gives a 61 per cent yield of LXXXVII in reaction 50, the more drastic conditions required to produce a reaction with the xyloquinones permit the isolation of only 7 per cent of the coumarone corresponding to LXXXVII in the case of *m*-xyloquinone; the remainder of the reaction mixture is a tar, as is the entire product from the reaction with *p*-xyloquinone. This behavior indicates extensive polymerization of the intermediate products of the type shown in reaction 50. Even though 1,4-naphthoquinone reacts more readily with ketene acetal than do the xyloquinones, tar formation is extensive in this case also and the pure benzocoumarone is obtained in low (2 per cent) yield. Bromo substituents in the benzoquinone nucleus activate it for reaction with the ketene acetal and distinctly higher yields (27–40 per cent) of the coumarones or their degradation products are obtained from the bromobenzoquinones. In reactions 51 and 52 the bromonaphthoquinones behave as acyl halides (*cf.* reaction 46), of which they are indeed vinylogs, and add to the double bond of the ketene acetal.

E. PYROLYSIS

The pyrolysis of various ketene diethylacetals to ethylene and the normal esters (see reactions 12 and 15a) has been discussed above in connection with the pyrolysis of orthoesters (Section II C). Also, mention has been made of the facile rearrangement of ketene diallyl- and dibenzyl-acetals to the corresponding allyl- and benzyl-acetic esters when an attempt is made to prepare these ketene acetals from the bromoacetals by reaction 7.

Under conditions (6 hr. at 200°C.) that cause the complete pyrolysis of ketene



XCII (53)

$$C_6H_5CH{=}C(OCH_3)_2 \longrightarrow C_6H_5CH(CH_3)COOCH_3 \qquad (54)$$

XCIII

diethylacetal (shown in reaction 15a), ketene dimethylacetal is unaffected. In fact, 95 per cent of the dimethylacetal is recovered after heating at 200°C. for 24 hr. (14).

When phenylketene dimethylacetal is heated at 250–260°C. methane is evolved and *meso*-α,α'-diphenylsuccinate (XCII) is formed in 21–29 per cent yields. This pyrolysis appears to involve the elimination of a hydride ion from one molecule of the ketene acetal with a methyl cation from another molecule, as shown in reaction 53. In addition to the succinic ester (XCII) a 22 per cent yield of methyl α-phenylpropionate (XCIII) is produced by the rearrangement of the ketene acetal (reaction 54) (31).

A small amount of the ethyl ester corresponding to XCII is formed during the pyrolysis of ethyl orthophenylacetate to phenylketene diethylacetal (reaction 3). It seems likely that the ketene acetal is the precursor of this product as it is of XCII in reaction 53 (31).

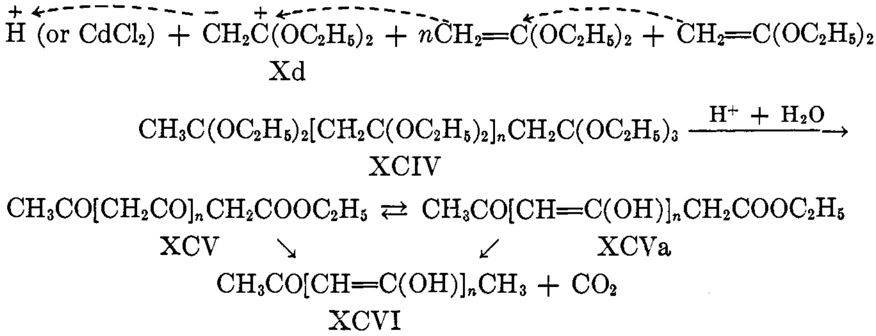
F. POLYMERIZATION

One of the first chemical properties of ketene diethylacetal to be noticed was its tendency to polymerize (3). The polymer appeared as a thin white deposit on the interior of flasks and condensers in which the compound had been distilled and also as a semisolid gum that separated from distilled samples after standing a few days. The cause of this type of polymerization was traced to the acidic glass surfaces of the apparatus; it was generally excessive in apparatus that had been cleaned with ordinary chromic acid–sulfuric acid mixture, and it could be practically eliminated by treatment of such acid-washed apparatus with aqueous alkali solution, followed by rinsing and drying. Similarly, dusting the interior of alkali-washed containers with potassium or sodium *t*-butoxide prevented polymerization of the acetal during storage (12).

The polymerization of ketene acetal by acidified glass surfaces is, presumably, the result of the coördination of a proton with the anionoid methylene group of the acetal, which is shown in reaction 55 as the polarized form Xd (see Section III A), to produce a highly reactive carbonium ion. Since there is no anion available from the glass surface to add to this carbonium ion, as there is with the simpler acids employed in reactions 31 and 32, a chain reaction is initiated and propagated by the successive coördination of the anionoid centers of other ketene acetal molecules with this and similar subsequently formed positive centers (reaction 55).

Other compounds capable of coördinating with the anionoid center of the ketene acetal are more efficient catalysts for this polymerization than are acidified glass surfaces (12). A wide variety of metal chlorides and such non-ionic acids as boron fluoride and aluminum chloride are powerful catalysts for the polymerization. Benzoyl peroxide, which catalyzes the polymerization of many vinyl compounds, has no appreciable effect on ketene acetal, indicating that the polymerization of the acetal does not follow a free-radical mechanism but rather the ionic course shown in reaction 55.

The most satisfactory polymer is obtained with cadmium chloride as the catalyst. This polymer, which is a white powder with approximately the same carbon, hydrogen, and ethoxyl content as the monomer, has the "head-to-tail" structure (XCIV). It is remarkably stable to alkali and heat, but is quite sensitive to acids. It gradually changes to a brownish-red powder on exposure to the laboratory air for 24 hr.; dilute acids at room temperature convert it immediately to a water-insoluble, red oil; refluxing dilute acid converts it to a reddish-black oil which solidifies to a brittle glass on cooling. Both of these red polymers are soluble in aqueous sodium hydroxide solution but are quite insoluble in other solvents; the difference between them appears to be in the extent to which the ethoxyl groups have been removed by hydrolysis. The color and alkali-solubility of this red hydrolysis product indicate it to be a poly-1,3-diketone (XCV), which in the enolic form (XCVa) is highly conjugated.



$$\overset{+}{H}\ (\text{or } CdCl_2) + \overset{+}{C}H_2C(OC_2H_5)_2 + nCH_2{=}C(OC_2H_5)_2 + CH_2{=}C(OC_2H_5)_2 \longrightarrow$$

$$\text{Xd}$$

$$CH_3C(OC_2H_5)_2[CH_2C(OC_2H_5)_2]_nCH_2C(OC_2H_5)_3 \xrightarrow{H^+ + H_2O}$$

$$\text{XCIV}$$

$$\underset{\text{XCV}}{CH_3CO[CH_2CO]_nCH_2COOC_2H_5} \rightleftarrows \underset{\text{XCVa}}{CH_3CO[CH{=}C(OH)]_nCH_2COOC_2H_5} \qquad (55)$$

$$\searrow \qquad \swarrow$$

$$\underset{\text{XCVI}}{CH_3CO[CH{=}C(OH)]_nCH_3 + CO_2}$$

The amount of carbon dioxide evolved during the hydrolysis of XCIV to XCVI indicates the molecular weight of the polymer (XCIV) to be 2600–2700, i.e., n is 20–21. This value for the molecular weight is indicated also by the amount of acetic acid produced by the vigorous oxidation of the polyketoester (XCV). Both of these methods of molecular weight determination, however, serve only to measure the average length of the unit chains (XCIV), which may undergo cross-linking through inter-unit loss of alcohol. The insolubility of the polymer in organic solvents indicates that some of this cross-linking has occurred, but it is not extensive as the ethoxyl content of the polymer is very little lower than that of ketene acetal (12).

Along with the polymer XCIV, small amounts of the dimer (XCVII), of the open-chain trimer (XCVIII), and of 1,3,5-triethoxybenzene (C), the last of which results from the loss of alcohol from the cyclic trimer (XCIX), are formed in the cadmium chloride-catalyzed polymerization of ketene acetal (12).

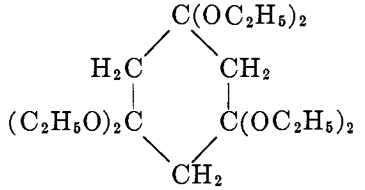
As previously noted in table 2 of Section III B, hydrogen fluoride causes polymerization of ketene diethylacetal. Depending on the concentration of the acetal in an ether solution, various types of polymers may be obtained with catalytic amounts of hydrogen fluoride (27). This catalyst is particularly useful for the production of the trimers, XCVIII and XCIX. For example, a 1 per cent solution of ketene diethylacetal in ether is converted by 5 mole per cent of hydrogen fluoride to the dimer and the trimers in 12–14 per cent and 40–45 per cent yields, respectively. From the latter fraction the cyclic trimer, 1,1,3,3,5,5-hexaethoxycyclohexane (XCIX), m.p. 72–74°C., may be isolated in yields amounting to 22 per cent of the weight of the polymerized ketene acetal. This cyclic trimer is characterized by its ready conversion to C (in 85 per cent yield) and by its hydrolysis to phloroglucinol with carbonic acid (27).

$CH_3C(OC_2H_5)_2CH{=}C(OC_2H_5)_2$

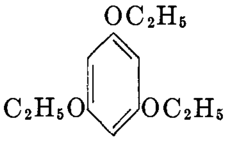
XCVII

$CH_3C(OC_2H_5)_2CH_2C(OC_2H_5)_2CH{=}C(OC_2H_5)_2$

XCVIII



XCIX



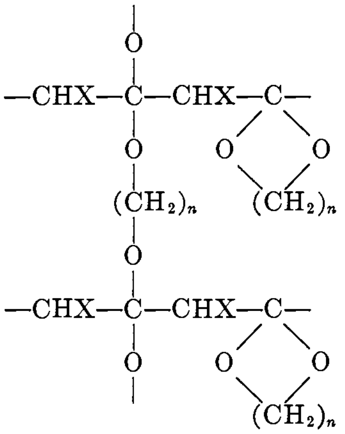
C

In contrast to the unsubstituted ketene acetal shown in reaction 55, the halogenated ketene diethylacetals (12) and methylketene diethylacetal (27) do not polymerize. For example, chloroketene diethylacetal is recovered unchanged after heating with cadmium chloride at 110°C. for 70 hr.; and methylketene diethylacetal reacts with hydrogen fluoride, as it does with other acids, to give ethyl propionate and ethyl fluoride.

The 2-methylene-1,3-dioxolanes and -1,3-dioxanes, the ketene cyclic acetals of table 1, in contrast to the diethylacetals, are characterized by their marked tendency to undergo *spontaneous* polymerization. Only those having a phenyl or two chlorine substituents on the methylene carbon (Nos. 16, 17, 33, and 34) are relatively resistant to polymerization. The other cyclic acetals (Nos. 7, 8, 29, 30, 31, and 32) are obtained pure only with the greatest difficulty because of the polymerization that occurs during their isolation. The use of alkali-washed glassware lowers the rate but does not prevent this polymerization; varying amounts of a voluminous white precipitate generally are present in all freshly distilled samples. The rate of polymerization appears to be related to the purity of the ketene cyclic acetal, i.e., the more pure the acetal the more rapidly it polymerizes. When the polymerization is slight, the ketene acetal usually is found to be contaminated with the ester resulting from the reaction of water with the acetal (reaction 27) (19).

Two types of polymers result from the spontaneous polymerizations of these cyclic acetals. Those from the unsubstituted methylenedioxolane and methylenedioxane (Nos. 7 and 8 of table 1) are solids, which melt over a relatively narrow range and which are hydrolyzed by dilute hydrochloric acid to red, alkali-soluble oils similar to those obtained from the cadmium chloride-polymerized ketene diethylacetal in reaction 55. The polymers obtained from the monohalogenated acetals (Nos. 29–32 of table 1) are talc-like powders that do not melt, but sinter in the range of 290–350°C. They are insoluble in all solvents except concentrated sulfuric acid (from which they cannot be recovered by dilution with water) and remain unaffected after heating for several hours with concentrated hydrochloric acid (19).

Both types of these polymers give the same analytical data as the values calculated for the monomers. Their properties lead to the conclusion that the polymers formed from the methylenedioxolane and methylenedioxane (Nos. 7 and 8) are relatively simple straight chains of the type of XCIV of reaction 55 with a minimum of cross-linking. The more refractory character of the polymers of the monohalogenated ketene cyclic acetals suggests that the chains of these polymers are extensively cross-linked through the bifunctional glycol moieties to form the more complex structure illustrated in part in formula CI (19).



CI

Qualitatively, the dioxalanes of table 1 appear to polymerize more readily than the dioxanes, and the chloro compounds more readily than the bromo compounds. In fact, there is no noticeable difference in the ease with which the chloromethylenedioxolane (No. 29) and the unsubstituted methylenedioxolane (No. 7) undergo spontaneous polymerization. This is in marked contrast to the great difference in the polymerization behavior of ketene and chloroketene diethylacetals noted previously. The dimethylacetals of table 1 show approximately the same tendency to polymerization as the diethylacetals. The unsubstituted dimethylacetals may be induced to polymerize by acidified glass surfaces, cadmium chloride, and other catalysts that are able to coördinate with the anionoid center of the acetal. Chloroketene dimethylacetal shows the same resistance to polymerization (19) that was observed for the corresponding diethylacetal (12).

It is of interest to note that hydrogen chloride, which adds to the other cyclic acetals to yield ω-chloroalkyl esters (*cf.* addition of water in reaction 27), causes an anomalous polymerization of 2-methylene-1,3-dioxolane (19) similar to that which hydrogen fluoride causes with ketene diethylacetal (26, 27).

G. MISCELLANEOUS REACTIONS

1. With bromine

Although all of the ketene acetals readily absorb bromine, the exact course of this reaction has been determined only in the case of bromoketene diethylacetal (35). This ketene acetal absorbs bromine rapidly at 0–5°C. but the absorption stops abruptly after 0.7 of an equivalent of bromine has reacted. The products isolated from this reaction indicate that approximately one-half of the bromine reacts with a single molecule of the acetal, as shown in reaction 56, to yield ethyl dibromoacetate (CII), while the other half adds across two molecules of the acetal (reaction 57), in the 1,4 manner of reaction 32, to yield initially the α,γ,γ-tribromoacetoacetic ester diethylketal (CIII), which then rearranges to ethyl γ,γ,γ-tribromoacetoacetate diethylketal (CIV), the product actually isolated from reaction 57.

$$\mathrm{BrCH{=}C(OC_2H_5)_2} + \mathrm{Br_2} \longrightarrow [\mathrm{Br_2CHC(OC_2H_5)_2Br}] \longrightarrow \mathrm{C_2H_5Br} + \underset{\text{CII}}{\mathrm{Br_2CHCOOC_2H_5}} \tag{56}$$

$$\begin{aligned} 2\mathrm{BrCH{=}C(OC_2H_5)_2} + \mathrm{Br_2} &\rightarrow [\mathrm{Br_2CHC(OC_2H_5)_2CHBrC(OC_2H_5)_2Br}] \\ &\rightarrow \mathrm{C_2H_5Br} + \underset{\text{CIII}}{[\mathrm{Br_2CHC(OC_2H_5)_2CHBrCOOC_2H_5}]} \\ &\rightarrow \underset{\text{CIV}}{\mathrm{Br_3CC(OC_2H_5)_2CH_2COOC_2H_5}} \end{aligned} \tag{57}$$

In addition to the main reaction products (CII and CIV), small and practically equivalent amounts of ethyl tribromoacetate and ethyl γ,γ-dibromoacetoacetate diethylketal, which result from the bromination of CII by CIII, are obtained from these reactions.

2. With diazonium salts

A study of the reaction of phenyl-, *p*-ethoxyphenyl-, *p*-nitrophenyl-, and *p*-carbethoxyphenyl-diazonium chlorides with ketene acetal has been made. As the acetal reacts with water and other hydroxylic solvents, these reactions were carried out with the dry salt in the presence of an excess of the ketene acetal (23).

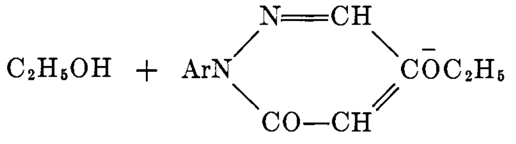
In each case the main reaction product is a 1-aryl-4-ethoxy-6-pyridazone (CVI), the formation of which is rationalized as a cyclization of the hydrazone (CV) resulting from the addition of the diazonium salt across two molecules of the ketene acetal as shown in reaction 58. The yields of the pyridazones (CVI) are 25–35 per cent of the theoretical and it is of interest to note that the yields drop to approximately one-half of these values in each case if the reaction is carried out in pyridine, in which both reactants are soluble.

In addition to CVI, smaller quantities of diarylformazyl formates (CVII), which result from the initial addition of the diazonium salt to a single molecule

$$\mathrm{ArN{=}\overset{+}{N}} + \mathrm{CH_2{=}C(OC_2H_5)_2} + \mathrm{CH_2{=}C(OC_2H_5)_2} + \mathrm{Cl^-} \longrightarrow$$

$$[\mathrm{ArN{=}NCH_2C(OC_2H_5)_2CH_2C(OC_2H_5)_2Cl}] \longrightarrow \mathrm{C_2H_5Cl} + \mathrm{C_2H_5OH}$$

$$+ \underset{\mathrm{CV}}{[\mathrm{ArNHN{=}CHC(OC_2H_5){=}CHCOOC_2H_5}]} \rightarrow$$



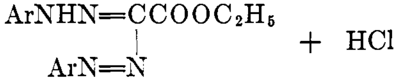
CVI

(58)

of the ketene acetal followed by the subsequent reactions shown in reaction 59, are obtained in certain cases. The yields of CVII vary from zero when Ar is phenyl to 27 per cent when Ar is *p*-ethoxyphenyl.

$$\mathrm{ArN{=}N^+Cl^-} + \mathrm{CH_2{=}C(OC_2H_5)_2} \rightarrow [\mathrm{ArN{=}NCH_2C(OC_2H_5)_2Cl}] \rightarrow$$

$$\mathrm{C_2H_5Cl} + \mathrm{ArNHN{=}CHCOOC_2H_5} \xrightarrow{\mathrm{ArN{=}NCl}}$$



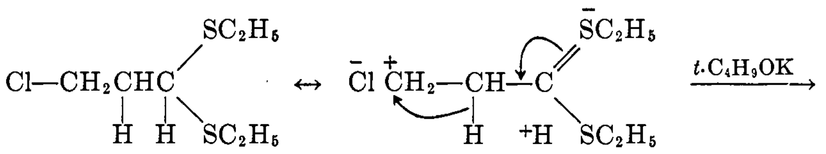
$$\underset{\mathrm{ArN{=}N}}{\mathrm{ArNHN{=}CCOOC_2H_5}} + \mathrm{HCl} \quad (59)$$

CVII

IV. Sulfur and Nitrogen Analogs of the Ketene Acetals

A. KETENE THIOACETALS

One example of a ketene thioacetal appears in the literature and its formation is of exceptional interest. The action of potassium *t*-butoxide on β-chloropropionaldehyde diethylthioacetal (CVIII) yields methylketene diethylthioacetal (CIX) in 77 per cent yield. This unusual dehydrohalogenation is the result of the ability of sulfur to expand its valence shell to permit the existence of the resonance form CVIIIa, which, in the presence of the strongly basic *t*-butoxy anions, undergoes dehydrohalogenation followed by the hydride ion and electron shifts shown in reaction 60. That CIX does not result from the initial formation of the isomeric acrolein diethylthioacetal, $\mathrm{CH_2{=}CHCH(SC_2H_5)_2}$, is shown by the fact that both the latter compound and CIX are stable and not interconvertible under the conditions of reaction 60 (41).



CVIII CVIIIa

$$\mathrm{CH_3CH{=}C(SC_2H_5)_2} \quad (60)$$

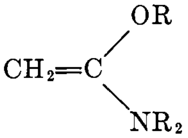
CIX

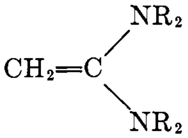
The structure of the ketene thioacetal (CIX) is shown by its conversion to propionic acid with an aqueous solution of mercuric chloride (reaction 61). Methylketene is postulated as an intermediate in this reaction (41).

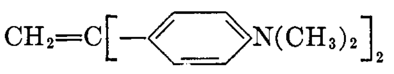
$$\text{CIX} \xrightarrow[\text{HgCl}_2]{\text{H}_2\text{O}} \text{CH}_3\text{CH}{=}\text{C}{=}\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{COOH} \qquad (61)$$

B. NITROGEN ANALOGS OF THE KETENE ACETALS

There are two types of these nitrogen analogs: CX, in which a disubstituted nitrogen replaces one of the alkoxyl groups of a ketene acetal, and CXI, in which both of the alkoxyl groups are so replaced. These compounds are of interest because the presence of the more effective hetero atom, nitrogen, in the heteroenoid system of such compounds would be expected to enhance the reactivity of the methylene carbon. Such a supposition is supported by the observation of Gates (10) that 1,1-bis(*p*-dimethylaminophenyl)ethylene (CXII), which may be considered a vinylog of CXI, is much more reactive with certain quinones than is the analogous 1,1-dianisylethylene, which is a vinylog of ketene dimethylacetal.


CX


CXI


CXII

The preparation of a compound of type CX, *N*-ethyl-*N*-(α-ethoxyvinyl)-aniline (LVI), is described in reaction 37 of Section III B. Hydrolysis converts LVI to ethylaniline, alcohol, and acetic acid; all attempts to stop the hydrolysis at the *N*-ethylacetanilide stage have been unsuccessful. LVI dissolves exothermically in alcohol but distillation of the solution returns LVI unchanged (32).

The preparation of a compound of type CXI was attempted by the pyrolysis of 1,1,1-tripiperidinoethane (LVII), which is obtained from reaction 39. This ethane is remarkably stable to heat—it boils at 255–258°C. without decomposition—but when it is refluxed vigorously over a period of 9 hr., approximately 89 per cent of the theoretical quantity of piperidine slowly distils from it. However, the remaining product is polymeric, indicating either that the loss of piperidine is intermolecular or that the 1,1-dipiperidinoethylene, resulting from the intramolecular loss of piperidine, is polymerized during the long period of pyrolysis (32).

In contrast to the behavior of piperidine in reaction 39, diethylamine and di-*n*-butylamine react with ketene diethylacetal at 120–130°C. to give products of types CX and CXI in 13–16 per cent and 34–41 per cent yields, respectively. The amount of ethyl orthoacetate accompanying these amino compounds indicates that the molecular ratios of reactants shown in reactions 62 and 63 are required (32).

It is apparent from the ratios of reactants required for these reactions that the rate of addition of the amine to the ketene acetal is much lower than that

$$\mathrm{2CH_2{=}C(OC_2H_5)_2 + R_2NH \rightarrow CH_3C(OC_2H_5)_3 + \underset{CX}{CH_2{=}C(OC_2H_5)NR_2}} \qquad (62)$$

$$\mathrm{3CH_2{=}C(OC_2H_5)_2 + 2R_2NH \rightarrow 2CH_3C(OC_2H_5)_3 + \underset{CXI}{CH_2{=}C(NR_2)_2}} \qquad (63)$$

R is C_2H_5 or n-C_4H_9.

at which alcohol adds to form the orthoester. The mechanism of these reactions appears to involve the initial addition of the amine to the acetal followed by a loss of alcohol (which converts an equivalent of the ketene acetal to the orthoester) to form CX; a repetition of this process converts CX to CXI. Evidence for this mechanism is obtained from the aminolysis of ethyl orthoacetate with the amines used in reactions 62 and 63. This aminolysis requires a temperature of 200–220°C., in contrast to the temperature of 120–130°C. used in reactions 62 and 63, and the reaction takes the course shown in reaction 64. The amide (CXV) is obtained in quantitative yields; this, together with the fact that the tertiary amine (CXIV) also is formed, indicates that the intermediate CXIII, at the higher temperature of reaction 64, preferentially pyrolyzes to CXIV and ethyl acetate rather than to alcohol and CX as it does in reaction 62 (32).

$$\mathrm{CH_3C(OC_2H_5)_3 + R_2NH \xrightarrow{220^\circ C.} C_2H_5OH + \underset{CXIII}{CH_3C(OC_2H_5)_2NR_2} \rightarrow \underset{CXIV}{C_2H_5NR_2} + CH_3COOC_2H_5 \xrightarrow{R_2NH} \underset{CXV}{CH_3CONR_2}} \qquad (64)$$

The ethoxyaminoethylenes (CX) and the diaminoethylenes (CXI) show a considerable tendency to polymerize during distillation. Both types are basic and dissolve in dilute (5 per cent) aqueous acids; the CXI type is hydrolyzed to the corresponding amide and the secondary amine. Alcohol converts the diamino compounds (CXI) to the monoamino compounds (CX). Under the mildest conditions of hydrogen absorption (Raney nickel and 2100 p.s.i. of hydrogen at 60°C.) 1,1-bis(diethylamino)ethylene (CXI: R is C_2H_5) undergoes hydrogenolysis and yields a mixture of diethylamine and triethylamine (32).

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