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Ketens *in situ* and Cycloaddition to Them

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The review deals with the methods of generation of ketens *in situ*, particularly their reaction behaviour, mainly in cycloaddition to compounds containing multiple bonds. The ways in which ketens are polymerised *in situ*, associated both with the structure of the ketens themselves and the methods of their preparation, are also discussed. The bibliography incorporates 102 references.

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1. INTRODUCTION

More than 60 years have elapsed since the first mention of ketens in papers by Wilsmore[1] and Staudinger and co-workers[2], and yet at present only a few stable representatives of this class of compound have been isolated in a pure state: keten itself, dimethyl-, diphenyl-, and perfluoro-dimethyl-ketens, and certain others. Monosubstituted ketens are particularly difficult to prepare.

At the same time the number of ketens which have not been characterised in a free state but are used as intermediates (*in situ*) is much greater. Because of their high reactivity, ketens are of considerable interest for organic synthesis both in the laboratory and in industry. For this reason, several reviews have been devoted to the chemistry of ketens (mainly to the simplest of them)—the reviews of Lacey[3], Kagan[4], and somewhat earlier Hanford and Sauer[5] and Quadbeck[6]. A recent review by Dashkevich and Beilin was devoted to the chemistry of carbon suboxide.

However, none of the authors enumerated above dealt with the problem of the reactivity (and also a systematic account of the data concerning the methods of generation) of ketens *in situ*, which sometimes differs from the reactivity of ketens isolated in a pure state even in the same reactions.

The aim of the present review is to give a general account of the literature information (up to 1967 inclusive) on the methods of generation of ketens *in situ* and their participation in cycloaddition reactions†. The review is restricted to only this type of reaction because it is precisely in these reactions that the specific reactivity of keten *in situ* is shown most markedly. In this connection di- and tri-merisation are also discussed, but the reactivity of the dimers themselves, which has been described fairly completely in the available reviews on the chemistry of diketen, is consistently disregarded.

An exception to this principle is made in the present review only under discussion of the mechanism of addition to ketens (including ketens *in situ*) where it is possible for a better understanding of the problem to give a more general account also of certain other addition reactions of ketens apart from cycloaddition.

† The term "cycloaddition" is employed by the present authors in view of its wide use in the chemical literature, instead of the term "cycloformation" which they believe to be more correct.

We also believe it to be desirable to restrict the discussion of ketens formed as intermediates as a result of the Wolff rearrangement[8] in the photolysis and thermolysis of diazo-carbonyl compounds exclusively to reactions involving cycloaddition to these ketens *in situ*, particularly since, when the Wolff rearrangement is carried out in an aprotic medium, certain ketens can be isolated and characterised in a pure form[9,10].

The review also does not deal with the structural analogues of ketens, for example sulphenes *in situ*, the chemistry of which was dealt with in a recent review by Opitz[11].

2. METHODS OF GENERATION OF KETENS IN SITU

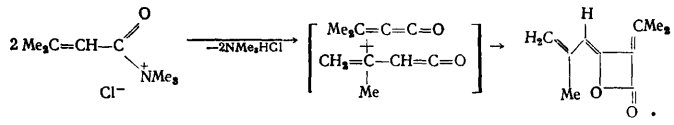
One of the early and most widespread methods for the generation of ketens *in situ* is the elimination of hydrogen halides from acid halides with a hydrogen atom in the α-position under the action of strongly basic tertiary amines[12,13]:

$$\text{>CH—C(=O)—Cl} + \text{Alk}_3\text{N} \rightarrow [\text{>C=C=O}] + \text{Alk}_3\text{NHCl}.$$

However, this method has not been used for a long time, since initially only diphenylketen could be isolated in monomeric form and used further for preparative purposes. Other ketens formed by this method underwent di- and tri-merisation before isolation. Only in recent years have attempts been resumed to find preparative applications of ketens *in situ* using various "intercepting" components. By dehalogenating the halides of mono- and di-substituted acetic acid, it proved possible to generate and introduce into further reactions many ketens which have not been described in a pure state. For example, after unsuccessful attempts by Staudinger[14] to isolate dichloroketen by the thermolysis of dichloromalonic anhydride, there was no further information in the literature about the participation of this keten in any reactions until in 1965 Stevens et al.[15] obtained dichloroketen as an intermediate from dichloroacetyl chloride and a trialkylamine in the presence of cyclopentadiene as an "interceptor" of keten *in situ*. Hull obtained difluoroketen by a similar procedure[16]. Since this method of generation of ketens *in situ* has been extended to reactions of tertiary amines with acid dichlorides of the type $ClCO-(CH_2)_n-COCl$, the intermediate bisketens also became available[17-21].

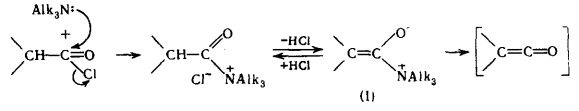
The intermediate formation of ketens in the interaction of tertiary amines with the chlorides of $\alpha\beta$-unsaturated

acids is unlikely, since in this case the α-hydrogen atom is by no means as labile as in substituted acetylchloride. Nevertheless the formation of a β-lactone in the solvolysis of a quaternary salt obtained from the chloride of dimethylacrylic acid and trimethylamine is evidence, according to Payne[22], of the intermediate formation of ketens, which are then further dimerised:



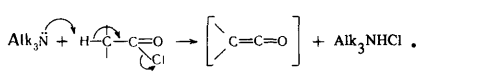
The mechanism of the interaction of acid chlorides with tertiary amines has not been the subject of a special investigation. However, since it proved possible to isolate the adducts of acid halides with weakly basic tertiary amines (pyridine, *NN*-dialkylanilines, etc.), it was suggested[13], by analogy, that the reaction of acid halides with strongly basic amines also involves the formation of a quaternary salt of the type $Alk_3\overset{+}{N}COR\,Cl^-$.

According to Pracejus[23], keten is formed from this quaternary salt via an intermediate dipolar compound (I) of keten with trialkylamine:



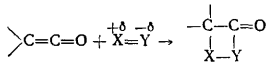
(I)

This mechanism of the formation of intermediate ketens from quaternary ammonium salts, analogous to the Hofmann degradation, is one of several which are possible. On the other hand, intermediate ketens can be obtained also without the preliminary formation of quaternary salts from acid chlorides and amines—by an E_2 bimolecular elimination mechanism:

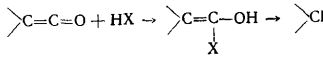


The problem of which of these two mechanisms actually occurs in the interaction is important for the elucidation of the mode of the secondary process—the addition of the "interceptor" reagent to the C=O or C=C bond of the intermediate keten, provided a stabilised keten is not formed in the reaction.

Nevertheless this aspect too remained fairly obscure for a long time, i.e. as regards the mode of reactions involving additions to stable ketens. Most investigators regarded the addition to the C=C bond of ketens and the addition to the C=O bond with subsequent isomerisation to the product of addition to the C=C bond as equally probable[24-26]. Mueller[27], who summarised the various views, suggested that reagents containing multiple bonds (C=C, C=O, C=N, N=N,) etc., add to ketens at their C=C bond with formation of cycloadducts:

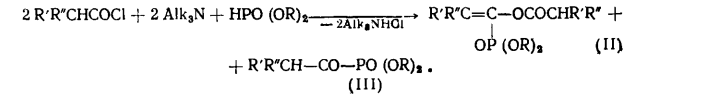


Reagents without multiple bonds, mainly substances with a mobile hydrogen atom (water, amines, alcohols, acids) add to ketens at their carbonyl group with possible (but not obligatory) subsequent isomerisation of the vinyl alcohol to a carbonyl derivative:



In some cases it is possible to acylate the intermediate vinyl alcohol by a second keten molecule, whereupon of course isomerisation does not occur. Hydrocyanic acid[28], Gringard reagents[29], lithium tetrahydroaluminate[30], and dialkyl phosphites[31,32] add to the carbonyl group of keten in this way.

The intermediate ketens from acid chlorides and tertiary amines probably also enter into addition reactions both at the C=C and C=O bonds. For example, addition to the C=O bond is observed in the interaction of dialkyl phosphites with mono- and di-substituted acetyl chlorides in the presence of triethylamine[33]:



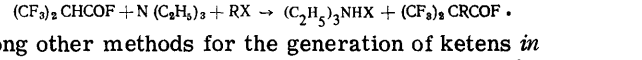
(II)

(III)

When R′ = R″ = H and R = CH_3, the yields of compounds (II) and (III) are 70 and 16% respectively. The formation in this case of α-oxophosphonic esters (III) together with the acyloxyvinyl adduct (II) can be explained both by addition to the C=C bond of the intermediate keten *in situ* and by the isomerisation of the vinyl alcohol derivative, which may occur at the same time as the acylation of the hydroxy-group of a second keten molecule *in situ*; finally, the formation of compounds (II) and (III) may be caused by the difference in the rates of addition of the vinyl alcohol derivative and dialkyl phosphite to the C=C bond of a keten *in situ*.

Although the method of generation of ketens *in situ* discussed has found wide application, it is not universal. Unsuccessful attempts to intercept many potential ketens without their preliminary isolation from the reaction mixture can probably be explained by the short lifetime of the intermediate ketens in monomeric form or by the low rate of interception of ketens *in situ*, as a result of which the principal reaction products are often resinous oligomers or at best keten dimers and trimers.

The fluoride of hexafluoroisobutyric acid reacts with triethylamine in quite a different way[34]. Neither the hydrofluoride of triethylamine, nor perfluorodimethylketen (known in a pure state), nor the product of its oligomerisation are formed, fluorophosgene and a complex adduct with the amine being isolated. In the presence of an alkyl halide RX, the corresponding triethylammonium halide is obtained, but not the fluoride, the formation of which might confirm indirectly the intermediate generation of the keten:

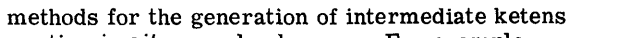


Among other methods for the generation of ketens *in situ*, the dehalogenation of α-halogeno-acid halides, for example with the aid of zinc activated with copper[35-37], is of practical interest. The bromides of trihalogenoacetic acids in a solvent inert with respect to ketens (ether, ethyl acetate) enter into this reaction most readily:

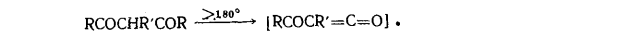


where X = Cl[35], or Br[36].

Difluoroketen, which is intercepted with ammonia *in situ* to avoid oligomerisation[37], was obtained similarly:

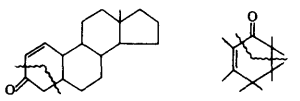


Other methods for the generation of intermediate ketens with interception *in situ* are also known. For example, Ziegler and Sterk[38] confirmed the intermediate formation of ketens in the thermolysis of β-diketones with the aid of infrared spectroscopy and also subsequent solvolysis:



Ziegler et al.[30] also suggested the intermediate formation of ketens in the dehydration of benzylmalonic acid with acetic anhydride.

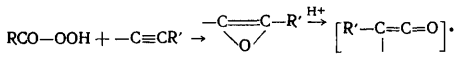
The formation of ketens following the electron bombardment of conjugated cyclohexenones has been observed mass-spectrometrically[40] (the wavy line indicates the keten fragment formed):



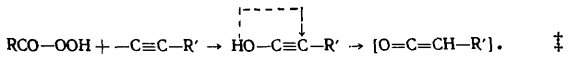
According to Schneibaum[41], the oxidation of certain acetylenes with nitrobenzene is accompanied by the intermediate formation of ketens, which are intercepted *in situ* by solvolysis:

$$C_6H_5NO_2 + -C\equiv C- \rightarrow C_6H_5NO + \left[\rangle C=C=O\right] \rightarrow \text{solvolysis products.}$$

A "keten" mechanism has also suggested[42] for the reaction of substituted acetylenes with per-acids; according to this view, the hypothetical acetylene α-oxide rearranges to a keten, which undergoes solvolysis *in situ*:

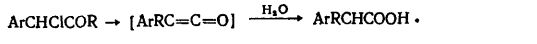


We believe that the intermediate formation of ketens in this reaction can be explained also in a different way—by the oxidation of acetylene to alkyn-1-ol with subsequent El'tekov rearrangement:

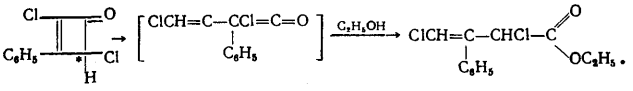


Such a mechanism can explain satisfactorily the intermediate formation of monosubstituted ketens only, while the mechanism proposed by Stille and Whitehurst[42] is suitable also for disubstituted ketens *in situ*.

Richard[43] suggested the intermediate generation of a keten to account for the conversion of α-halogeno-ketones into acids in the course of the Favorskii rearrangement:



In the alcoholysis of optically active dichlorophenylcyclobutenone, Jenny and Roberts[44] isolated a racemic ester:

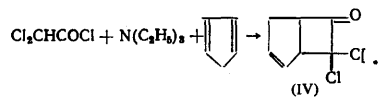


They explained the racemisation by the intermediate formation of a keten in which the asymmetric carbon atom of the initial keten ceases to be asymmetric by virtue of its transition to an sp^2-hybridised state.

3. CYCLOADDITION OF KETENS *IN SITU*

a. Cycloaddition to the C=C Bond

Activated olefins, for example, cyclic dienes are used as a rule to intercept ketens *in situ*. Products of 1,2-cycloaddition are then formed in high yield. Thus the intermediate formation of dichloroketen from dichloroacetyl chloride and triethylamine was confirmed for the first time, and the use of cyclopentadiene[15] as an "interceptor" permitted the synthesis of 7,7-dichlorobicyclo[3,2,0]hept-2-en-6-one(IV)



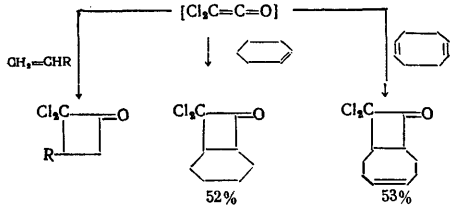
Further reactions of compound (IV) led to a new synthesis of tropolone.

The corresponding bicyclic dibromo-analogue was synthesised[36] similarly, both dehalogenation of tribromoacetyl bromide with zinc and the reaction of dibromoacetyl chloride with triethylamine being used for the generation of the intermediate dibromoketen.

Monosubstituted intermediate ketens add *in situ* to cyclic dienes by the same mechanism[45].

Non-activated olefins also react with ketens *in situ* forming cyclic products, electrophilic substituents in the keten molecules favouring its interception by the olefin.

For example, dichloroketen reacts more vigorously *in situ* than does dimethylketen under the same conditions. Cyclopentene[46], cyclohexene[47], cyclo-octadiene[47], styrene[47], and ethyl vinyl ether[47] are used as "intercepting" agents. In all cases cyclobutanones are formed. The yields of the corresponding reactions involving the interception of dichloroketen *in situ* are given below:

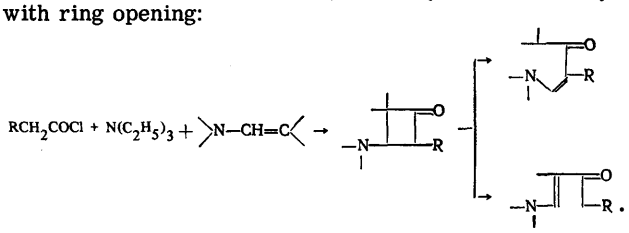


where the yields are 19, 31, and 45% for R = C_6H_5, C_3H_7, and OC_2H_5 respectively.

The choice of the method of generation of intermediate ketens in the presence of olefins is determined both by the nature of the olefin and the activity of the keten and the duration of its existence as a monomer. In the case of olefins which are not polymerised in the presence of zinc halides, the method of generation of ketens *in situ* by the dehalogenation of α-halogeno-acid halides is suitable. Otherwise, for example, when vinyl ethers are used as interceptors for ketens *in situ*, the method of generation based on the reaction of substituted acetyl chlorides with trialkylamines is more convenient, provided of course that the ketens themselves are not polymerised *in situ* in the presence of the amine and (or) its hydrochloride at a rate comparable to the rate of interception[5,47].

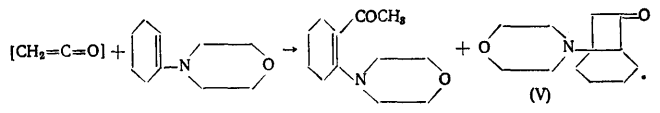
It has been mentioned[48] that the addition of dichloroketen *in situ* to indene (in a yield of 12%) leads to the formation of the corresponding 4,5-benzotropolone as a result of further reaction of the adduct.

Enamines add to aldoketens *in situ* with formation of β-aminocyclobutan-2-one derivatives which can be converted, under the reaction conditions, into acyclic amide vinylogues with ring opening:



‡ RCO–OOH + –C≡C–R′ → H–O–C≡C–R′ → [O=C==CH–R′] (Ed. of Translation).

In the reactions of ketens *in situ* with 1-morpholinocyclohexene (as the interceptor), the presence in the reaction mixture of a bicyclic addition product (V) has been confirmed[49] by infrared spectroscopy, but 2-acetyl-1-morpholinocyclohexene was isolated as the main product:

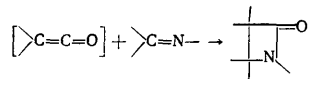


(V)

b. Cycloaddition to Multiple Carbon–Nitrogen Bonds

The addition of stable ketens to reagents containing a double or triple carbon–nitrogen bond can be achieved successfully only under very severe conditions and only a highly polarised C=N bond takes part in the reaction.

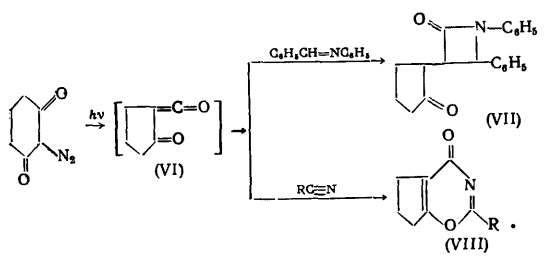
In contrast, ketens *in situ* add to both C=C and C=N bonds under mild conditions with formation of cyclic products. The addition of intermediate ketens to azomethines leads to the formation of β-lactans[50]:



The synthesis of β-lactams by cycloaddition to ketens *in situ* has been widely investigated[51-54] in connection with its employment for the synthesis of penicillins, the molecules of which contain condensed β-lactam rings. The chlorides of phthaloyl and succinyl glycine, which are introduced into the reaction with triethylamine in the presence of the corresponding azomethines, are used as a source of ketens in this case.

The photolysis of β-diazocarbonyl compounds[55] is also used for the synthesis of α-lactams via ketens *in situ*[55]. It has been noted that ketens with electronegative substituents (for example, *p*-chloro- and *p*-nitro-phenylketens) enter into the cycloaddition reaction at the C=N bond of the intercepting agent either with difficulty or do not react at all (in contrast to the effect of substituents of the same type on the cycloaddition of ketens *in situ* to olefins).

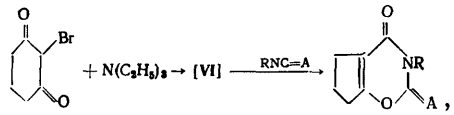
Intermediate α-oxoketens have a marked tendency to undergo 1,4-cycloaddition of reagents with multiple bonds[56], but in the reaction with anils 1,2-cycloadducts are nevertheless formed, albeit in a low yield. For example, β-oxoketen (VI) reacts *in situ* with benzylidene-aniline, forming a β-lactam(VII):



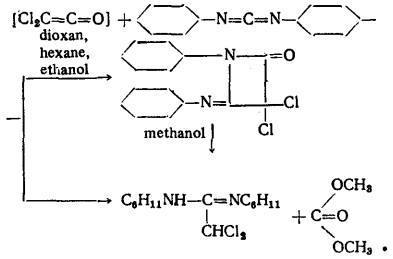
(VI) (VII) (VIII)

On the other hand, in the reaction of the keten (VI) *in situ* with nitriles a 1,4-cycloaddition product is formed—a condensed oxo-1,3-oxazine (VIII).

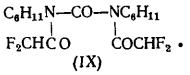
The reactions of the intermediate keten (VI) with isocyanates and isothiocyanates has been investigated by Selvarajan et al.[57], ketens being generated *in situ* by the reaction of triethylamine with 2-bromocyclohexa-1,3-dione;



where A = O or S, and



Difluoroketen reacts *in situ* with carbodi-imide forming acylated dicyclohexylureas (IX)[16]:



(IX)

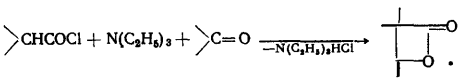
In this case the 1,4-cycloaddition product is obtained in a yield of the order of 25%.

Hull[16] noted that carbodi-imides add to ketens *in situ* with the cleavage of only one C=N bond; if the process is carried out in boiling dioxan, hexane, or ethanol the 1,1-adduct is a β-lactam, but if the solvent is methanol the final reaction product is a substituted dichloroacetamidine produced, according to the author, as a result of the solvolysis of the β-lactam formed initially.

c. Cycloaddition to the Carbonyl Group

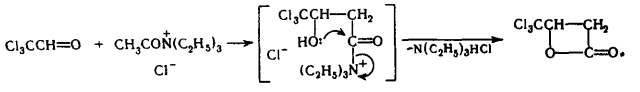
Stable ketens add to the carbonyl group of aldehydes and ketones with formation of β-lactones. These reactions take place only in the presence of various catalysts, which polarise the carbonyl group of the aldehyde or ketone. As a rule such catalysts are Lewis acids[3,58-61]. Evidently catalysts of this type are unsuitable for the reactions *in situ* of aldehydes or ketones with ketens generated by the action of trialkylamines on acid chlorides, since the Lewis acids would be immediately neutralised by the amines. Therefore, in the synthesis of β-lactones via ketens *in situ*, generated in this way, only highly polarised carbonyl components which do not require additional activation by a catalyst are employed as interceptors.

Thus β-trichloromethyl-β-propiolactone was synthesised[62] in 92% yield from acetyl chloride, triethylamine, and chloral. The replacement of acetyl chlorides by methanesulphonyl chloride made it possible to synthesise the corresponding β-sultone derivative[63]. Borrmann and Wegler[64] showed that this synthesis of β-lactones is general. The authors used the chlorides of acetic, dichloroacetic, and ring-substituted phenoxyacetic acids for the generation of the intermediate ketens and polyhalogeno-substituted aldehydes and ketones as intercepting agents:



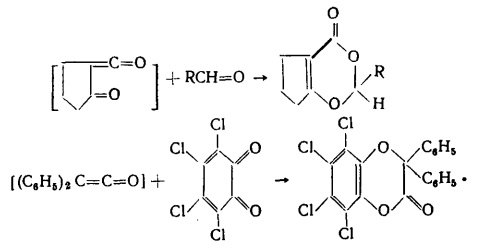
When optically active highly basic tertiary amines (for example brucine) are used for the generation of ketens *in situ*, it is possible to obtain[65] optically active β-lactones with one or two asymmetric carbon atoms.

Although at first sight the "keten" mechanism of the synthesis of β-lactones from substituted acetyl chlorides and tertiary amines in the presence of carbonyl intercepting agents appears to be the most likely, we believe that this process can also be explained in a different way[66], omitting the intermediate generation of the keten. Thus it may be supposed that the quaternary salt formed by reaction of the amine with the acid chloride, which has a hydrogen atom with enhanced lability in the α-position relative to the carbonyl, adds initially to the highly polarised carbonyl group of the intercepting agent; subsequently the alcoholic hydroxyl is acylated intramolecularly with the elimination of triethylamine hydrochloride and the closure of the β-lactone ring (shown below in the synthesis of β-trichloromethyl-β-propiolactone as an example:



This mechanism is supported, for example, by the fact that the yield of diketen in this reaction is negligible, becoming zero at sufficiently high dilution. Nevertheless, as will be shown below, the dimerisation of ketens *in situ* is strongly catalysed by tertiary amines and their salts. This should undoubtedly result in a decrease of the yield of β-lactone if an intermediate keten forms in the reaction. On the other hand, the absence from the reaction medium of diketen as a side product can be accounted for by the lower rate of its formation from the keten *in situ* compared with the rate of interception of the latter by the carbonyl compound. This view is confirmed by the finding that the yields of other β-lactones (except β-trichloromethyl-β-propiolactone) are not so high[64] although the formation of keten dimers as side products is not reported.

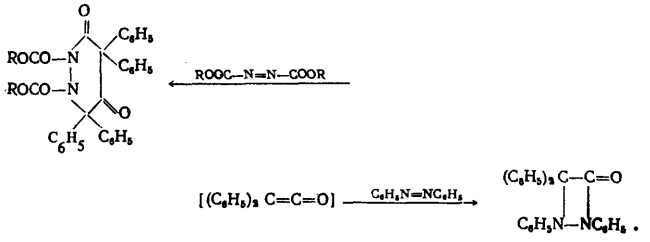
So far there is no convincing evidence in favour of any one of the mechanisms of the synthesis of β-lactones from acid halides, trialkylamines, and carbonyl compounds discussed above. On the other hand, when other methods are used for the generation of intermediate ketens in the presence of carbonyl compounds, β-lactones are not formed. Thus, when ketens are generated *in situ* by the thermolysis or photolysis of α-diazo-carbonyl compounds in the presence of aldehydes[56] or quinones[67,68], only 1,4-cycloaddition products having the structure of oxodioxans are isolated:



It is noteworthy that such a comparison of the reactivity of ketens generated *in situ* by two different methods in the presence of aldehydes is not entirely valid, since in the examples quoted the ketens, whose formation was suggested, have different structures; furthermore carbonyl compounds with insufficiently polarised carbonyl groups were employed as intercepting agents in these investigations[56,67,68]. This probably in fact accounts for the preferential 1,4-cycloaddition rather than 1,2-cycloaddition.

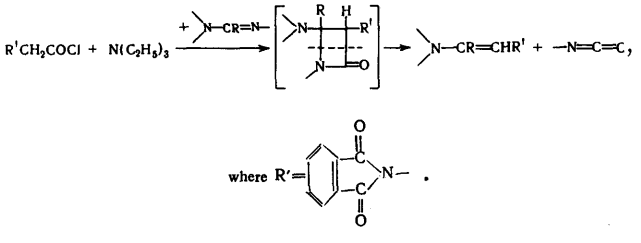
d. Cycloaddition to the N=N Bond

The cycloaddition of stable ketens, for example diphenylketen, to azo-compounds is achieved only on ultraviolet irradiation with formation of 1 : 1 adducts having the structure of 1,2-diazacyclobutan-3-one[69,70]. In contrast, the reaction of azo-compounds with the intermediate diphenylketen generated *in situ* by the photolysis of α-diazocarbonyl compounds leads to both 1 : 1 [71] and 2 : 1 [68] adducts:

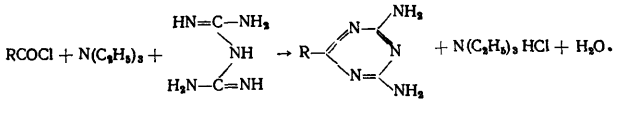


e. Cycloaddition to Amidines, Guanidines, and Urea Derivatives

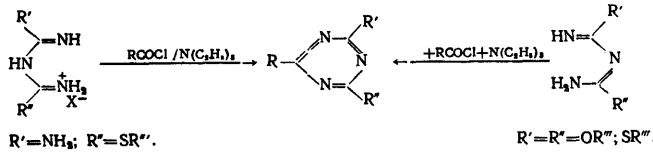
The addition *in situ* of intermediate ketens to amidines fully substituted at the nitrogen atom probably takes place at the C=N bond with formation of β-lactams[72]; the authors believe that further degradation of the lactams in fact results in the formation of the final products—an enamine and an isocyanate; in this case the reaction of the chloride of phthaloylglycine with triethylamine was employed to generate the keten; in the presence of azomethines, the reaction[51-54] (see preceding page) led to the formation of β-lactams in high yields:



When acid chlorides react with diguanidine in the presence of triethylamine, derivatives of 1,3,5-triazine are formed[73,74]:



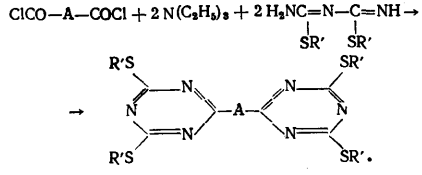
The corresponding 1,3,5-triazines are produced also when derivatives of biuret and dithiobiuret and *S*-alkylguanylisothiuronium salts are used as the intercepting agents[75]:



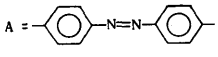
However, it should be noted that not only the chlorides of mono- and di-substituted acetic acids, in which a hydrogen atom is retained in the α-position, but also the halides

of acids lacking the capacity to serve as a source of intermediate ketens, for example trichloroacetyl chloride, substituted benzoyl chlorides, and the chlorides of $\alpha\beta$-unsaturated acids, were used in these reactions. These findings suggest that the synthesis of trazines under conditions of this kind may not in fact be accompanied by the formation of ketens as intermediate structures.

The interaction of dicarboxylic acid chlorides with triethylamine in the presence of dithiobiuret derivatives leads to the formation of the corresponding bistriazines [75]:

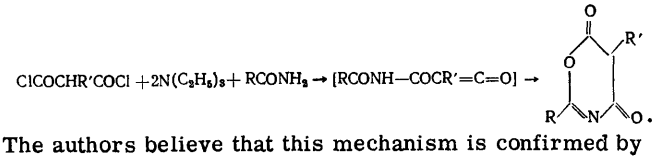


When A = $(CH_2)_n$, this process may be accompanied by the intermediate formation of a keten or a bisketen, while with

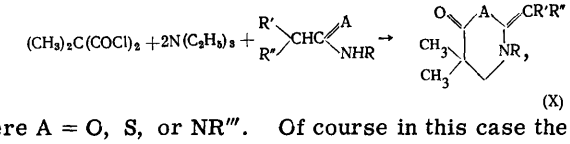


intermediate ketens are not formed.

Ziegler and coworkers [76,77] proposed a "keten" mechanism for the synthesis of dioxo-1,3-oxazines by the interaction of unsubstituted or monosubstituted malonic acid chlorides with amides in the presence of triethylamines:

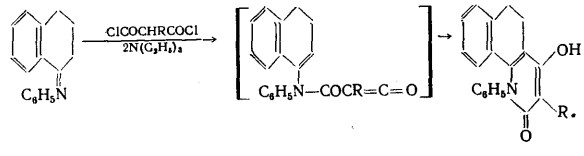


The authors believe that this mechanism is confirmed by the fact that they were unable to achieve analogous reactions with disubstituted malonyl dichlorides. However, some time later Martin et al. [78] synthesised successfully a number of derivatives of 1,3-oxazine, 1,3-thiazine, and pyrimidine (X) by the interaction of disubstituted malonyl dichlorides with amides, thioamides, and amidines in the presence of triethylamine:

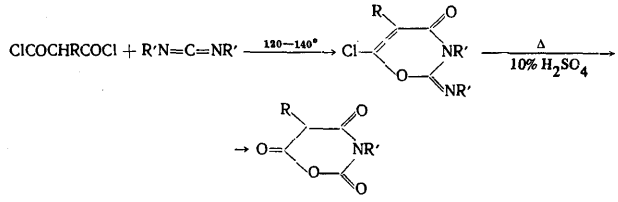


(X)

where A = O, S, or NR'''. Of course in this case the intermediate formation of a keten cannot occur. Furthermore in the reaction of butyramide with dimethylmalonyl dichloride the derivative of dioxo-1,3-oxazine (X, A = O, R' = R'' = CH_3, are obtained both in the presence [in this case R = $COCH(CH_3)_2$] and in the absence (R = H) of triethylamine. However, the formation of ketens in the reaction of monosubstituted malonyl dichlorides with tertiary amines is confirmed not only by the formation of 2-pyridones when ketimines and azomethines are employed as "interceptors" but also by infrared spectroscopic data [79-81]:



It is suggested [82] that the synthesis of barbituric acids by the cycloaddition of monosubstituted malonyl dichlorides to carbodi-imides also takes place by a "keten" mechanism:



where R = H or alkyl and R' = H or C_6H_5.

4. CYCLIC DI- AND TRI-MERISATION

Reactions involving cycloaddition to ketens *in situ* are complicated by their polymerisation, which is usually limited to di- and tri-merisation. These side processes are most significant in the generation of ketones from acid chlorides under the action of trialkylamines.

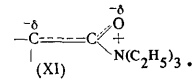
Even in the early studies by Staudinger [83,84] it was noted that stable ketens polymerise in the presence of tertiary amines. It would appear that this must be an indication of the interaction of ketens with trialkylamines, but there is still not single view concerning the nature of this interaction.

Wedekind [85,86] isolated in low yields weakly basic compounds which, according to their composition, appeared to be the products of the addition of triethylamine to keten in proportion of 1 : 1 ("ketenium" compounds) or 2 : 1 ("ketenates"). The following mesomeric structures with pentavalent nitrogen were attributed to the "ketenium" compounds:



Wedekind's results were not examined further for almost 30 years until Miller and Johnson [87] disproved the existence of the "Wedekind ketenium bases", having shown that the "ketenium" compounds are in fact the diethylamides of the corresponding acids, formed as a result of the presence of an admixture of diethylamine in the initial triethylamine. This accounts for both the low yield of Wedekind's "ketenium" compounds and their "anomalous" (according to Wedekind) reactivity.

Pracejus and Oehme [88] were unable to detect by infrared spectroscopy the interaction of trialkylamines with ketens and the possible structure of the adduct (XI) presented below was rejected on the basis of spectroscopic data:



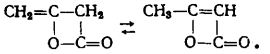
(XI)

However, subsequent kinetic investigation and the measurement of the isotope effect in the alcoholysis of ketens in the presence of tertiary amines enabled Tille and Pracejus [89] to attribute the structure (XI) to the postulated keten–amine complex.

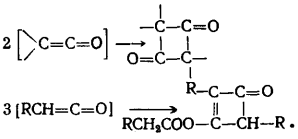
Di- and tri-merisation of ketens *in situ* is observed in all the methods of their formation without exception [2,3,5,90-92]. The catalysis of these processes by tertiary amines and their salts was investigated in greatest detail [93]. The study of the polymerisation of ketens *in situ* and the dependence of the structure of the keten dimers and trimers on the method of their formation permits controlled synthesis of products with a specified degree of polymerisation [94].

The dimer of the simplest keten (diketen) is obtained in high yield from keten *in situ* in the interaction between acetyl chloride and trialkylamines[93]. It is noteworthy that the rate of dimerisation of keten *in situ* is higher than the rate of dimerisation of the stable keten.

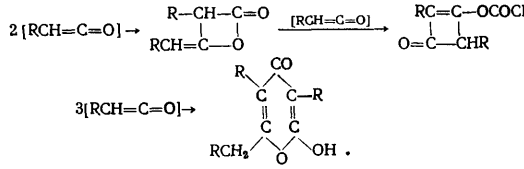
With the aid of modern methods for the investigation of structures (nuclear magnetic resonance[95], isotope methods[96]), it was possible to resolve the long-standing controversy concerning the structure of diketen and to demonstrate that it is a β-lactone:



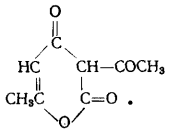
Later it was established[94] that, with the exception of keten itself, which is readily converted into the β-lactone even in the absence of catalysts, other ketens dimerise spontaneously *in situ* to cyclobutane-1,3-diones[95] or trimerise with formation of 3-hydroxycyclobutenone derivatives[97]:



Tertiary amines and their salts catalyse both the dimerisation *in situ* of the intermediate aldoketens, formed in the reaction between acid chlorides and tertiary amines, to β-lactones[98] and their trimerisation to 3-acylhydroxybutenones[99] (with R = alkyl) or pyranones (with R = aryl)[100]:



In addition in the case of an unsubstituted keten formed *in situ* in the interaction between acetyl chloride and triethylamine there is a possibility of further dimerisation of the diketen with formation of a tetramer—dehydroacetic acid (XII)[101]:

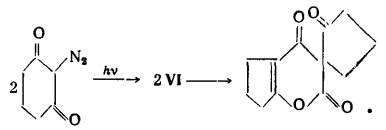


(XII)

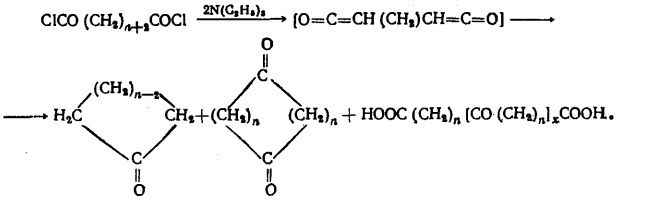
Ketens formed in the dehalogenation of α-halogeno-acid halides with zinc dimerise *in situ* in a different way. Here, the zinc halide formed in the reaction favours the dimerisation of the ketens to β-lactones with both R = alkyl and R = aryl[95].

Ketens derived from α-diazo-carbonyl compounds dimerise *in situ* in the presence of silver and copper catalysts for the Wolff rearrangement with formation of cyclobutane-1,3-diones[68].

Stetter and Kiehs[102] showed that the dimer of the intermediate keten derived from 2-diazodihydroresorcinol is a spiropyranone:



Acid dichlorides of the type $ClCO-(CH_2)_nCOCl$ react with tertiary amines in an unusual way. The intermediate bisketens formed in this case are converted into a mixture of cyclic ketone and diketone; furthermore, the formation of a polymer was observed[17-21] but its structure was not established:



Certain biologically active natural compounds previously difficult to obtain were synthesised by this method (muscone, civetone, and others). The concentration of the reactants plays a decisive role in this synthesis: for example, with sebacyl dichloride cycloketones can be isolated only when the reaction is carried out in highly dilute ethereal solutions.

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