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Fluorinated Ketenimines

N.P.Gambaryan

Methods of obtaining imines of fluorinated ketens are surveyed, together with their dimerisation and nucleophilic addition. Cycloaddition at the carbon-nitrogen bond and 1,4-dipolar cycloaddition involving the aromatic ring are most characteristic of fluorine-containing *N*-arylketenimines. A two-stage mechanism is suggested, involving intermediate formation of small rings. The Review concludes with 92 references.

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I. INTRODUCTION

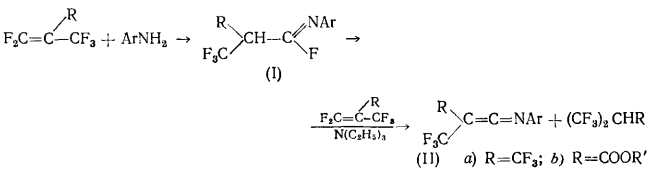
Imines of ketens were first obtained by Staudinger[1] in 1920, but their chemical properties have been studied only during recent years. Trialkylketenimines are unstable, so that the diaryl and mainly the triaryl derivatives have been investigated. Replacement of alkyl by trifluoromethyl groups greatly improves the stability both of ketens and of their imines, and hence imines of bistrifluoromethylketen provide a convenient model for studying the properties of aliphatic ketenimines.

Imines of ketens are of interest as dehydrating agents in peptide synthesis, as coreagents in oxidations with dimethyl sulphoxide, and especially as substrates in numerous cycloadditions with nucleophilic multiple bonds and dipolar compounds. The great variety of reactions involving cycloaddition is due to the fact that triarylketenimines react not only at the C=C and C=N bonds of the cumulative system but also at carbon or nitrogen with involvement of the aromatic rings, behaving in the latter reactions formally as dienes or nitrogen heterodienes. As a result, diverse carbocyclic and heterocyclic compounds are made available.

Reviews[2,3] have appeared during recent years, covering methods of preparation and reactions of ketenimines, but they contain hardly any information on fluorine-containing ketenimines. Nevertheless, fluoroketens and their imines exhibited a characteristic general feature of organofluorine compounds: the electron-accepting character of trifluoromethyl groups increases the electrophilic activity of bistrifluoromethylketen and its imines, which become capable of many reactions quite uncharacteristic of their unfluorinated analogues. Fluoroketens have been surveyed in Ref. 4. The present Review is concerned mainly with imines of bistrifluoromethylketen as the most readily available and thoroughly studied fluorinated ketenimines. Special attention is paid to *N*-aryl derivatives, since they reveal the effects of electron-donating and electron-accepting substituents on the activity of the cumulative bond system. Furthermore, the reactions of *N*-arylketenimines involving the aromatic ring are most interesting.

II. METHODS OF PREPARATION

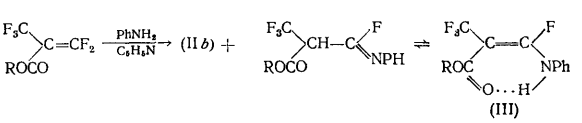
A broad study of ketenimines became possible only after a simple general method of preparation was developed in 1973.[5,6] The latter was based on the reaction of perfluoroalkenes with primary amines, the result of which was determined by the ratio of the reactants. With perfluoroisobutene and perfluoromethacrylic esters excess of the amine gives difficultly separable mixtures of products. With excess of the alkene in the presence of catalytic quantities of triethylamine, on the other hand, excellent yields of the corresponding *N*-arylketenimines (II) are obtained in a single stage:



(II) *a*) R=CF_3; *b*) R=COOR′

Thus a mixture of a fluoroalkene and triethylamine is a mild dehydrofluorinating agent, in which triethylamine acts as a carrier of hydrogen fluoride from the imidoyl fluoride (I) to the fluoroalkene. When pyridine is used instead of triethylamine, the reaction ceases at the stage of the imidoyl fluoride (I).

It is interesting that perfluoromethacrylic esters yield not only the imidoyl fluorides (I) but also the isomeric enamines (III):

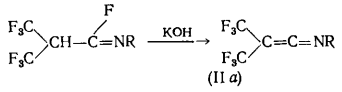


(III)

The comparative stability of the latter (III) is obviously due to the presence of an intramolecular hydrogen bond between the amino-group and the alkoxycarbonyl group. This is confirmed by the fact that the ratio of the latter to the former isomer increases with decrease in the ability of the solvent to form a hydrogen bond[6,7].

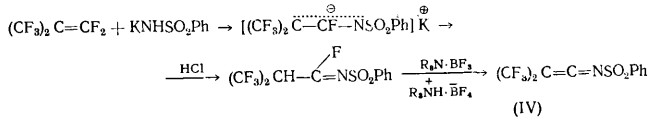
A second general method for preparing fluorinated ketenimines is the dehydrofluorination of imidoyl fluorides with powdered caustic potash in ether, which has been used to

obtain the most diverse *N*-aryl-, *N*-alkyl- †, and *N*-cycloalkyl-ketenimines[5] ‡:



(II *a*)

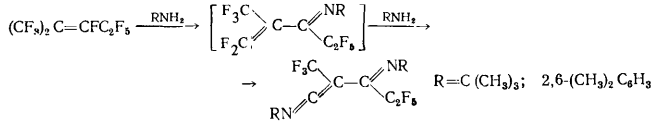
Such weak nucleophiles as benzenesulphonamide do not react with perfluoroisobutene. *N*-Benzenesulphonylbistrifluoromethylketenimine can be obtained as a stable adduct with potassium fluoride by treating perfluoroisobutene with the potassium salt of benzenesulphonamide; the free ketenimine (IV) is obtained by the action on the imidoyl fluoride of a mild dehydrofluorinating agent, such as the complex of triethylamine with boron trifluoride[9,10]:



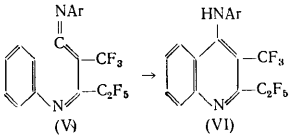
(IV)

N-*p*-Nitrophenylbistrifluoromethylketenimine can be prepared similarly from the imidoyl fluoride only by means of this complex[11].

The reaction of fluoroalkenes with primary amines extends even to perfluoroisohexene[12]:

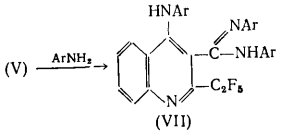


N-Arylketenimines (V) in which an *ortho*-position is unsubstituted, especially when the ring contains electron-donor substituents, are cyclised under the reaction conditions to fluorinated quinolines (VI):



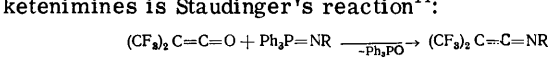
(V) (VI)

In the presence of a large excess of an aromatic amine the ketenimine (V) undergoes further reaction, ultimately with formation of the quinoline (VII)[13]:

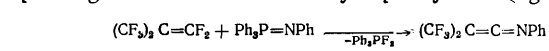


(VII)

A less general method for preparing bistrifluoromethylketenimines is Staudinger's reaction[14]:



Bistrifluoromethylketen can be replaced by perfluoroisobutene, which reacts with tetraphenylphosphine imide, replacing two fluorine atoms by a phenyliminо-group §[15]:

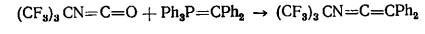


† Hexafluoroisobutyronitrile reacts with triethylamine to form a stable adduct[8], which can be regarded as a salt of the unsubstituted imine of bistrifluoromethylketen $(CF_3)_2C:C:NH.NH_3$.

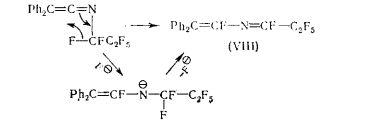
‡ The dehydrohalogenation of imidoyl halides is a general method for preparing unfluorinated ketenimines[2].

§ This reaction illustrates the analogy between the carbonyl and difluoromethylene groups[4,16,17].

The Staudinger reaction can be used also to obtain ketenimines having an *N*-perfluoroalkyl group[18]:

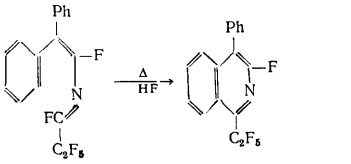


In contrast to perfluoro-t-butyl isocyanate, perfluoropropyl isocyanate, which contains mobile α-fluorine atoms, reacted with the yields to give the azabutadiene (VIII), obviously as a result of isomerisation of the intermediate ketenimine with migration of fluorine[18]:

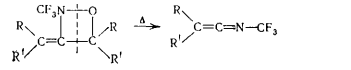


(VIII)

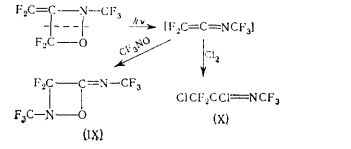
This rearrangement of a heterocumulene into a heterodiene can occur via a four-membered cyclic transition state or as a result of attack by a fluoride ion on the central carbon atom. An analogous isomerisation is found with bistrifluoromethylketen[19]. When heated, the azabutadiene (VIII) undergoes dehydrofluorination with ring closure, which provides a simple method for preparing a fluorinated isoquinoline[18]:



Ketenimines in which a trifluoromethyl group is attached to the nitrogen atom are formed also by pyrolysis of products of the cycloaddition of trifluoronitrosomethane to allenes[20]:

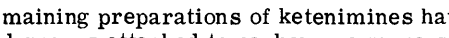


Ketenimines having fluorine atoms adjacent to the multiple bond, like the corresponding ketens, are unstable, and their formation in such a reaction can be judged from isolation of the cycloadduct (IX) or the chlorinated product (X) [21]:

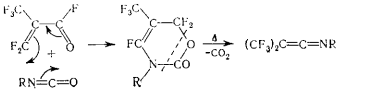


(IX) (X)

Iminosulphuranes are analogous to iminophosphoranes in reacting with bistrifluoromethylthioketen to form *N*-alkyl- and *N*-phenyl-bistrifluoromethylketenimines[22]:

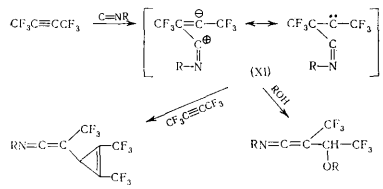


The remaining preparations of ketenimines having perfluoroalkyl groups attached to carbon are more specific in character. Thus *N*-alkylbistrifluoromethylketenimines are formed in the pyrolysis of a cycloaddition product of an isocyanate and perfluoromethacryloyl fluoride[23]:

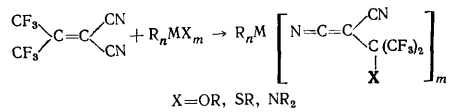


Ketenimines containing a cyclopropenyl substituent are obtained by the interaction of perfluorobutyne with isonitriles in inert solvents; in the presence of an alcohol the

intermediate equimolecular adduct (XI) reacts, not with another hexafluorobutyne molecule, but with the alcohol[24,25]:



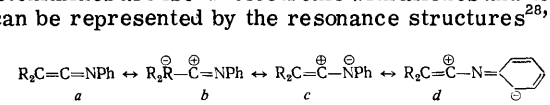
Finally, ketenimines containing *N*-organometallic groups are formed by the 1,4-addition of organo-silicon, -germanium, -tin, and -boron compounds to bistrifluoromethylmethylenemalononitrile[26,27]:



X=OR, SR, NR_2

III. CHEMICAL PROPERTIES

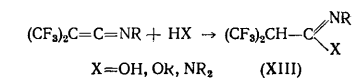
Ketenimines are iso-π-electronic with allenes and ketens, and can be represented by the resonance structures[28,29]



(XII)

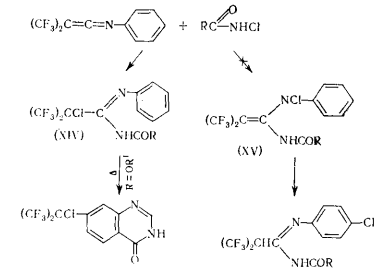
As the ketens, the electrophilic character of the central atom can be strengthened by attaching electron-donor substituents to the carbon atom. Furthermore, the structural features of ketenimines permit the reactivity of the heterocumulative bond system to be changed by attaching electron-donor or electron-acceptor substituents also to the nitrogen atom, the latter enhancing the electrophilic character. The most active electron acceptors exert in principle the same influence on the reactivity of ketenimines as does electrophilic catalysis, bringing their activity close to that for ketenimmonium salts[30]. Furthermore, the structure (XII*d*) indicates the possibility of reactions involving the aromatic ring of *N*-arylketenimines, in which the latter behave formally as 1,4-heterodienes— cf. (XXVII).

In conformity with the above, bistrifluoromethylketenimines react far more readily than unfluorinated ketenimines with water, alcohols, and amines to give the corresponding derivatives of hexafluoro-α-hydroisobutyric acid (XIII)[31]:



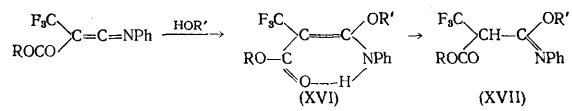
X=OH, Ok, NR_2 (XIII)

This reaction does not answer the question—important for the chemistry of heterocumulenes—at which of the cumulative bonds the nucleophiles add on, since products of addition at the C=N bond, not stabilised by a hydrogen bond (Section II), would have immediately isomerised into the more stable end-products (XIII) ¶. However, the formation of the α-chlorohexafluoroisobutyramidines (XIV)[44] when the anil of bistrifluoromethylketen is treated with *N*-chloro amides indicates addition at the ethylenic bond in the ketenimine, since the product (XV) of addition at the C=N bond would have isomerised with migration of chlorine into the aromatic ring[33]:

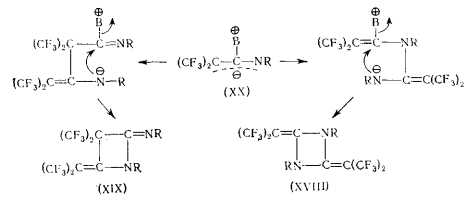


Cyclisation of the amidines (XIV) on being heated is a good method for the preparation of quinazolines.

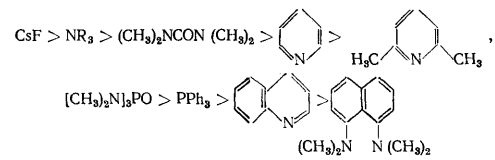
It is interesting that products formed by addition at the C=N bond in ketenimines — aminoacetals (XVI) — can be detected in the reactions of the anil of an alkyl trifluoro-β-*N*-phenyliminomethacrylate with alcohols; they rearrange comparatively slowly to imidic esters (XVII), a process which is irreversible[6], in contrast to the isomerisation of enamines into imidoyl fluorides (Section II):



In contrast to trialkylketenimines, *N*-alkyl- and especially *N*-aryl-bistrifluoromethylketenimines are stable, remaining unchanged even on prolonged heating †. However even such weak bases‡ as oxiran, dimethylformamide, benzylidenaniline, triethyl phosphate, pyridine, etc. cause rapid dimerisation of *N*-arylketenimines into symmetrical (XVIII) or unsymmetrical (XIX) dimers[11,31]:



Dimerising agents form the reactivity sequence



in which only the nitrogen heterocycles give rise to the symmetrical dimer (XVIII).[11] Comparison shows that the activity of a dimerising agent is determined mainly by its nucleophilicity, not its basicity. For example, such a strong base but weak nucleophile as naphthalene-1,8-bisdimethylamine[34] dimerises ketenimines more slowly than does the considerably less basic but more nucleophilic Hexametapol, triphenylphosphine, and tetramethylurea. Similarly,

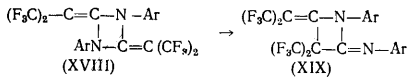
¶ Results on the addition of dialkyl phosphites at the C=N bond in the anil of bistrifluoromethylketen[32] are unreliable.

† *N*-t-Butylimines of fluorinated ketens on being heated decompose into isobutene and the corresponding nitrile[14].

‡ The poorer stability of unfluorinated ketenimines may be due to autocatalysis, since they themselves are quite strong bases. The basicity of imines of fluorinated ketens is depressed by the electron-accepting action of the trifluoromethyl groups.

lutidine dimerises ketenimines more slowly than does pyridine[11]. The greater importance of the nucleophilicity of dimerising agents is consistent with the hypothesis that dimerisation begins with nucleophilic attack on the central carbon atom of the ketenimine to form the zwitterion (XX).

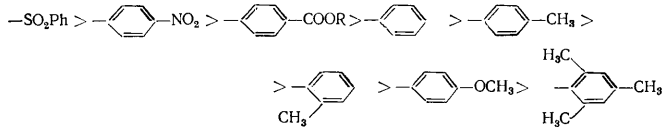
Unsymmetrical dimers are thermodynamically more stable than the symmetrical compounds, in accordance with which the latter rearrange into the former even under the influence of such weak bases as Hexametapol, tetramethylurea, pyridine, lutidine, and quinoline[11] §:



(XVIII) (XIX)

It is interesting that *para*-substituents in the aromatic ring have the same effect on the rate of rearrangement of symmetrical into unsymmetrical dimers as on the activity of the ketenimines.

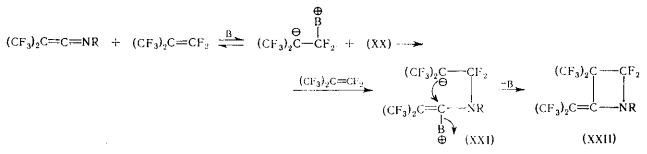
The relative activities of fluorinated ketenimines have been studied in nucleophilic addition, dimerisation, and cycloaddition involving the aromatic ring. The anils of alkyl trifluoro-β-*N*-phenyliminomethacrylates are more active than the anil of bistrifluoromethylketen[6], since alkoxycarbonyl groups are stronger electron acceptors than is the trifluoromethyl group[37]. As already stated with regard to the effect of *N*-substituents, increasing the electron density on the nitrogen should diminish the electrophilic activity of the central carbon atom of the cumulative system. Indeed, the activities of *N*-substituted bistrifluoromethylketenimines are antiparallel to the basicities of the nitrogen in them[11]:



where the *N*-benzenesulphonyl derivative is the most active, and the *N*-alkyl compounds are the least active. The activity of imines of fluorinated ketens depends not only on the basicity of the nitrogen atom but also on the bulk of the reactant and of the substituent, especially in cycloadditions. Thus *N*-phenylbistrifluoromethylketenimine adds methanol and ethanol in 1–2 h, whereas with t-butyl alcohol the reaction is not complete after 6 months[44]; *N*-mesitylbistrifluoromethylketenimine adds alcohol considerably more slowly than does *N*-phenylketenimine, and is dimerised with immeasurably greater difficulty than any other ketenimine[11]; and *N*-*o*-tolybistrifluoromethylketenimine dimerises more slowly than does the *para*-isomer.

It is interesting that the presence of perfluoroisobutene slows down by more than 99% the dimerisation of imines of fluorinated ketens under the influence of tertiary amines. Perfluoroisobutene not only tends to inhibit dimerisation but also recaptures the mesomeric anion (XX); the resulting carbanion (XXI) undergoes cyclisation to the azetidine (XXII) with regeneration of the tertiary amine. Thus the extremely electrophilic character of perfluoroisobutene enables it to compete successfully with ketenimines both in bonding the amine and in recapturing the betaine (XX).

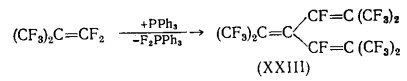
Dimerisation is suppressed, and the main reaction product is the corresponding azetidine (XXII)[38]:



(XXI) (XXII)

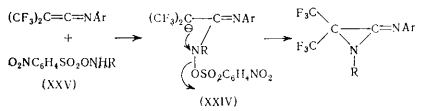
The same result is obtained in the presence of alkali-metal fluorides. Such mixed dimerisation of ketenimines with perfluoroisobutene provides an excellent method for preparing fluorinated azetidines.

Triphenylphosphine is more active than tertiary amines in catalysing the dimerisation of activated alkenes and the Michael reaction[39,40]. However, it cannot be used to catalyse the cycloaddition of perfluoroisobutene to ketenimines: perfluoroisobutene reacts not only in preference to the ketenimine but also irreversibly, being converted ultimately into the conjugated triene (XXIII) ¶:



(XXIII)

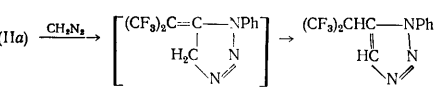
In the synthesis of azetidines the carbanion (XXI) is stabilised by intramolecular nucleophilic substitution of the group B with closure of the four-membered ring. Nucleophilic elimination of imines of fluorinated ketens is accomplished similarly but at the ethylenic bond of the ketenimine. The carbanion (XXIV) is then obtained by the action of substituted amides (XXV) on the fluorinated ketenimines.



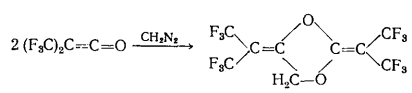
(XXV) (XXIV)

It is interesting that the direction of the reaction is predetermined by the nature of the leaving group: whereas chlorine migrates to the anionic centre of the molecule—cf. (XV)–the sulphonyloxy-group is readily detached with closure of the three-membered ring.

Nucleophilic elimination and formation of the unsymmetrical dimer (XIX) are among the few examples of cycloaddition at the ethylenic bond in imines of fluorinated ketens. Almost all cycloadditions involving unfluorinated ketenimines, on the other hand, take place at the ethylenic bond in the heterocumulene[2] †. An exception is the reaction of triarylketenimines with diazomethane[43]. Imines of fluorinated ketens also react with diazomethane at their C=N bond[44].



Bistrifluoromethylketen gives with diazomethane a cyclic trimer as a result of the reaction of both keten molecules at the carbonyl group[45]:

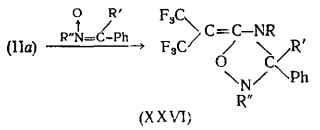


§ Symmetrical dimers of ketens (cyclobutanediones) isomerise into the unsymmetrical dimers in the presence of aluminium chloride; the reverse rearrangement takes place in the presence of bases[35]. Symmetrical dimers of unfluorinated ketenimines have not been described; for the only examples of unsymmetrical dimers see Ref. 36.

¶ Perfluorocyclobutene and butadiene give a 1 : 1 adduct with triphenylphosphine[41,42].

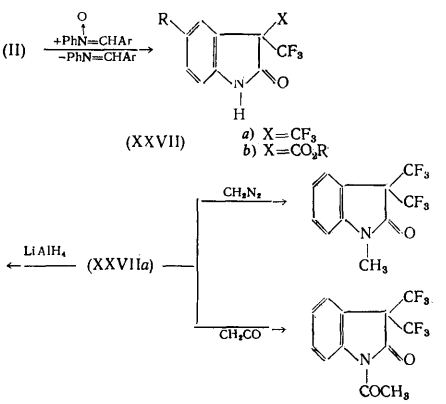
† Since hardly any information is available on aliphatic ketenimines[2], imines of bistrifluoromethylketen must be compared with those of aromatic ketens.

With nitrones unfluorinated ketenimines give products resulting from addition at the ethylenic bonds[46]. Imines of fluorinated ketens, on the other hand, form with triphenyl and *N*-methyl-α-phenyl nitrones cyclic adducts at the C=N bond — oxa-2,4-diazolidines (XXVI)[47]:



(XXVI)

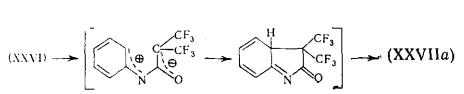
In the cycloadditions discussed hitherto the fluorinated ketenimines have behaved as 1,2-dipolar compounds. As already mentioned — cf. (XII) and (XV) — however, with *N*-arylketenimines reactions involving the aromatic ring are also possible, in which these derivatives behave formally as 1,4-dipolar compounds. An example of this type is the unusual reaction undergone by imines of fluorinated ketens with α-aryl *N*-phenyl nitrones, in which fluorinated oxindoles (XXVII) have already formed on cooling[48], instead of cycloaddition products:



(XXVII) a) X=CF_3 b) X=CO_2R

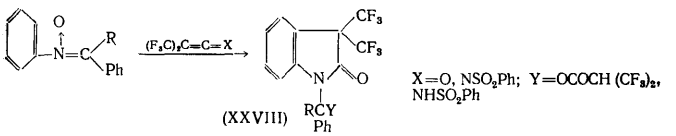
The structure of (XXVII*a*) is confirmed by cross synthesis, as well as by its chemical reactions. The oxindole (XXVII*a*) is formed also from oxadiazolidines (XXVI: R = C_6H_5). On standing for a long time or on being heated in a solvent, the latter compounds break down into the oxindole (XXVII*a*) and the corresponding Schiff bases. Isolation of products of the 1,3-cycloaddition of triphenyl and *N*-methyl α-phenyl nitrones to *N*-arylbistrifluoromethylketenimines and their conversion into the oxindole (XXVII*a*) suggest that reaction with the latter nitrones may involve the formation of unstable oxadiazolidines, which decompose so easily into an oxindole and an imine that they cannot be detected even by spectroscopic methods.

Thus nitrones are ultimately donors of oxygen in their reactions with *N*-arylbistrifluoromethylketenimines, which is unusual for nitrones. The mechanism of this peculiar reaction of oxygen transfer can be represented[47]:



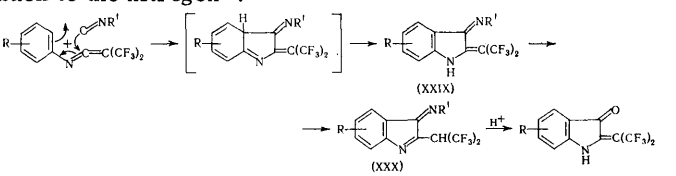
The betaine is stabilised by cyclisation at an *ortho*-position in the aromatic ring.

Substituted oxindoles (XXVII) are formed eventually also by the reaction of *N*-benzenesulphonylbistrifluoromethylketenimine and bistrifluoromethylketen[47] with *N*-phenyl nitrones, which, in contrast to the above reactions, involves the phenyl group of the nitrone:



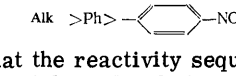
(XXVIII)

Indole derivatives are obtained also by reaction between *N*-arylbistrifluoromethylketenimines and isocyanides[49]. The indogenimines (XXIX) formed by 1,4-dipolar addition under very mild conditions then isomerise into iminoindolenines (XXX), whose hydrolysis involves migration of hydrogen back to the nitrogen[49]:



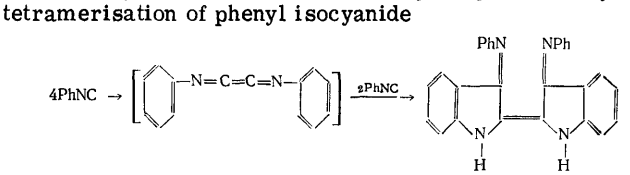
(XXIX) (XXX)

Reactions with isocyanides, similarly to nucleophilic addition and cyclodimerisation, are accelerated by electron-acceptor substituents in the aromatic ring of bistrifluoromethylketenimines, but restrained by electron-donor substituents. Whether in the imino-group or in the benzene ring, substituents have the opposite effect on the rate of isomerisation of indogenides into indolenines: indogenimines obtained from methoxyketenimine and alkyl isocyanides are the least stable. The reactivities of isocyanides with *N*-arylbistrifluoromethylketenimines fall in the sequence[50]



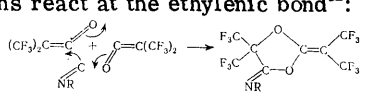
It is interesting that the reactivity sequence of isocyanides with nucleophilic acetylenic bonds is just the reverse[51]. This clearly indicates a difference in reaction mechanisms: whereas isocyanides react as nucleophiles with extremely electrophilic organofluorine compounds‡, they react as electrophiles with nucleophilic alkynes.

Unfluorinated triarylketenimines react with isocyanides only on irradiation, when heated, or in the presence of a catalyst. The reaction may involve the aromatic ring, the nitrogen atom, or a carbon atom, its direction being governed by the substituents in the aryl rings[53,54]. Only the tetramerisation of phenyl isocyanide



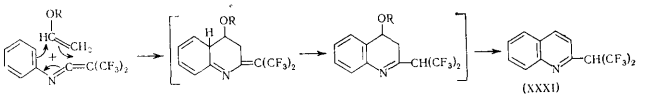
is accomplished at room temperature and without external assistance[49,54,55].

Bistrifluoromethylketen gives with isocyanides, as with diazomethane, a cyclic trimer in which both keten molecules have reacted at the carbonyl group[45], whereas unfluorinated ketens react at the ethylenic bond[52]:



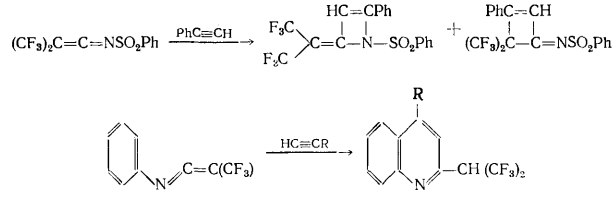
‡ The nucleophilicity of the carbene carbon atom is less in aryl than in alkyl isocyanides[52], and decreases on the introduction of electron-accepting substituents into the aromatic ring.

Ordinary alkenes are insufficiently nucleophilic and do not react with imines of fluorinated ketens. With especially nucleophilic vinyl ethers, however, *N*-arylbistrifluoromethylketenimines react even at room temperature, yet again by 1,4-cycloaddition with the ultimate formation of a fluorinated quinoline (XXXI)[56]:



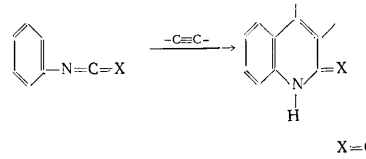
(XXXI)

Imines of fluorinated ketens react similarly with ethoxy- and phenyl-acetylenes (only the especially active *N*-*p*-nitrophenyl- and *N*-benzenesulphonyl-ketenimines react with the latter without heating). *N*-Benzenesulphonylbistrifluoromethylketenimine, which does not contain a conjugated bond system, gives a mixture of cyclic adducts formed at the C=N and C=C bonds, whereas *N*-arylketenimines react as nitrogen heterodienes with involvement of the aromatic ring[31,56]:



Various reactions of *N*-arylbistrifluoromethylketenimines involving the aromatic ring can be accomplished with good yields, usually with cooling or at room temperature, and provide a convenient method for preparing fluorinated heterocycles. The Reviewer considers reactions of this type most interesting, and will therefore discuss them in somewhat greater detail.

Apart from the processes discussed above, several other reactions have been discovered during recent years, usually achieved also under mild conditions, in which the cumulative or the azomethine bond with an attached aromatic ring behaves as a nitrogen heterodiene. Examples are the reactions of phenyl isocyanate[57–59] and of *N*-arylketenimines[60,61] with nucleophilic alkynes:

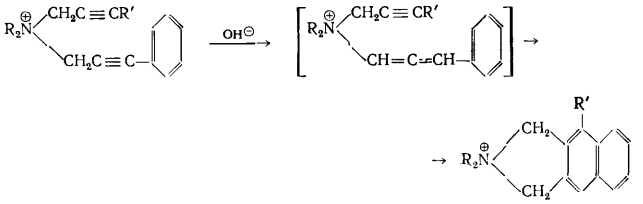


X=O, CPh_2

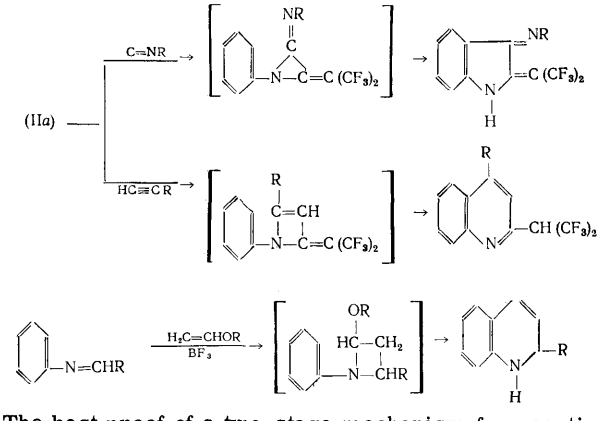
Formation of a quinoline ring by the reaction of vinyl ethers § with Schiff bases (in the presence of boron trifluoride)[62–64]



or with ammonium salts[65,66] has been widely studied. An ethylenic bond to which an aromatic ring is attached can also react as a diene under mild conditions[67,68]. Examples are the reaction of styrene with perfluorothioacetone[69] and the intramolecular cyclisation of amines and ammonium salts containing an *N*-arylprop-2-ynyl group[70,71]:



All these reactions are structurally similar to Diels–Alder reactions. Their mechanism has not been established, yet they have usually been regarded, in view of the isolation of final products to be expected from a mechanism of diene synthesis, as fresh examples of the Diels–Alder reaction¶. This approach seems unsound. Indeed, it is improbable that, under such mild conditions, an aromatic ring would react as a double bond of a diene. Typical Diels–Alder reactions represent concerted ($\pi 4_S + \pi 2_S$) addition, requiring very specific orientation of the reactants. They are therefore characterised by high negative entropies of activation: the pre-exponential factors in the rate constants are smaller by factors of 10^5–10^6 than would follow from collision theory[73,74]. Compensation for these rigorous demands on mutual reactant orientation is usually provided by a favourable energy balance in the reaction, with the disappearance of two double bonds and the formation of two σ-bonds. Such compensation is absent from reactions involving an aromatic ring, since they entail loss of the aromatic stabilisation energy. Yet they are usually accomplished under far milder conditions than are typical Diels–Alder reactions, which casts still greater doubt on the identification of these two types of processes. A two-stage rather than a synchronous mechanism is more probable for such reactions, involving intermediate formation of small rings subsequently stabilised by reaction with the aromatic ring†: e.g.



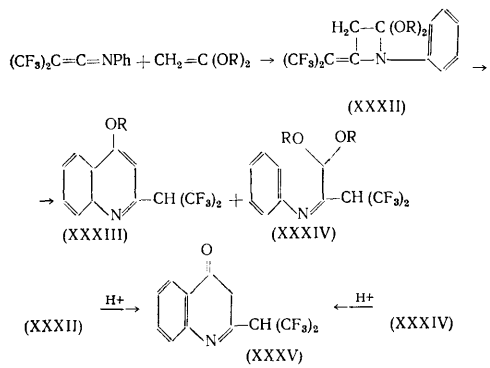
The best proof of a two-stage mechanism for reactions involving the aromatic ring would be isolation of compounds containing small rings and their conversion into the final heterocycles. However, this is not the simplest of tasks,

§ Isocyanides also react like alkenes with Schiff bases[72].

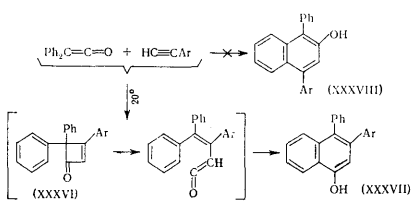
¶ An alternative mechanism with intermediate formation of cyclobutanone followed by isomerisation to a six-membered ring has been discussed[75].

† Such changes are well known with three-membered[76–79] and four-membered[80–85] rings.

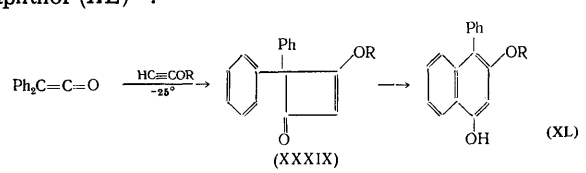
since small rings are very reactive[86,87]. Indeed, few data are available on the isolation of small rings in reactions of this type. Despite numerous attempts in the case of imines of fluorinated ketens, for example, only in a reaction with a keten acetal could a fairly stable product of cycloaddition at the C=N bond — the azetidine (XXXII) — be isolated. On prolonged storage at room temperature this azetidine is converted into the ethoxyquinoline (XXXIII) and the linear anil (XXXIV). Concentrated sulphuric acid converts both (XXXII) and its linear isomer into hexafluoroisopropyl-4-quinolone (XXXV)[56]:



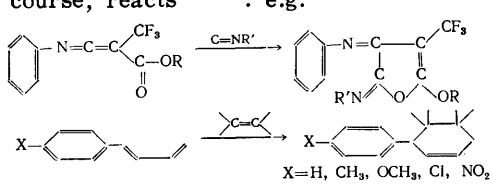
In the reaction of diphenylketen with arylacetylenes the intermediate product—cyclobutene (XXXVI)—could not be isolated, but the final formation of the 1-naphthol (XXXVII) instead of the 2-naphthol (XXXVIII) provided a forcible argument in support of a two-stage process[88]:



With the more reactive ethoxyacetylene, indeed, the cyclobutenone (XXXIX) could be isolated and converted into the 1-naphthol (XL)[84]:



Indirect support for a two-stage mechanism of "diene synthesis" involving an aromatic ring is that, when another conjugated multiple bond is present as well as the ring, this bond, of course, reacts[50,68,89]: e.g.



Over the years the number of reactions that are structurally similar to Diels–Alder reactions has so increased and their variety is so great that it would be naive to suppose that they all have the same mechanism. Both concerted and two-stage mechanisms have many variations. Formation of the two bonds may not be altogether simultaneous in a concerted mechanism[73,90]. Initial formation of charge-transfer molecular complexes is possible[91,92]. The first stage of two-stage reactions may produce betaines, perhaps in equilibrium with small rings. However, a covalent structure is more probable for the intermediate products, since substituents of the first and second kinds in the aromatic ring would have had a far greater effect in the case of betaines than is observed[73] ‡.

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Thus both in nucleophilic addition and in cycloaddition not only are imines of fluorinated ketens more reactive than unfluorinated ketenimines but they also undergo reactions that are unknown with the latter compounds. Another distinguishing feature of the fluorinated imines is that most cycloadditions involve the methine bond, not the ethylenic bond as with the unfluorinated analogues (perhaps because of steric factors, which are especially important in cycloaddition). Because the methine bond is less polar than the carbonyl bond, imines of bistrifluoromethylketen are less reactive than bistrifluoromethylketen itself. Reactions involving the aromatic ring, which are structurally similar to the Diels–Alder reaction but obviously occur by a completely different mechanism, extend significantly the synthetic possibilities of ketenimines.

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‡ For example, the rate of reaction of *N*-arylbistrifluoromethylketenimines with isocyanides decreases by factors of only 3–5 when an alkoxycarbonyl group is replaced by methyl.

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