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FOUR- AND SIX-MEMBERED HETEROCYCLES FROM 1,2- AND 1,4-CYCLOADDITIONS TO KETENIMINES

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Cycloadditions of thiobenzophenone to ketenimines illustrate the possibility of multiple modes of reaction across various centres of the cumulene depending on the substituents at nitrogen and carbon as well. 1,2-Cycloaddition across the C=C bond of the cumulene to give iminothietanes, as well as two types of 1,4-cycloaddition, one involving the C=N bond of the cumulene and the N-aryl group to give benzothiazines, the other involving the C=C bond of the cumulene and the C-vinyl to give iminothiacyclohexenes, have been observed. The variable siteselectivity in ketenimine-thioketone cycloadditions appears to be determined by a balance between steric and electronic effects, the latter being interpreted in terms of frontier MO's of the cumulene. Cycloadditions of electron-poor heteroenes (tosylisocyanate, N-dicyanomethylene-p-chloroaniline, sulfur dioxide) offer other examples of variable siteselectivity which produce four- and six-membered heterocycles. On the other hand, vinylketene although more reactive than vinylketenimine, appears to undergo exclusively 1,2-cycloaddition across the C=C bond of the cumulene to give four-membered adducts. The possibility of stereochemical variables in ketenimine cycloadditions increases the value of these heterocumulenes as intermediates for the synthesis of heterocycles.

Introduction

That cycloadditions to cumulenes[1] provide a direct and versatile entry to a variety of heterocycles and offer stimulating arguments for mechanistic and theoretical studies, is well documented by the numerous articles which currently appear in the literature. Among the many heterocumulenes which have been used as cycloaddition partners, ketenimines[2,3,4] have appeared somewhat later than ketenes, isocyanates, carbodiimides, isothiocyanates, etc., probably because they are less reactive and the available methods for their preparation are in most cases scarcely efficent. Therefore, the potential role of these cumulenes as intermediates for the synthesis of heterocyclic systems has been little explored. Of course, given the mentioned drawbacks, the synthetic value of these heterocumulenes may be considered as much as they are proved to display a peculiar reactivity and lead to compounds otherwise unaccessible.

I will report in this lecture new examples of cycloaddition of 2π-electron systems to substituted ketenimines and show that owing to the possibility of multiple modes of reaction, these heterocumulenes are useful intermediates for the preparation of a variety of heterocycles of different ring sizes. I will limit the description of each reaction to the formation of a prototype of the heterocyclic system which is obtained, while other derivatives are reported in the original papers. Therefore, for semplicity of presentation, in many cases numbering refers to types of compounds rather than to a single derivative.

It may be useful, to begin with, to recall a few properties of ketenimines which anticipate their reactivity. Ketenimines, like ketenes, are π-isoelectronic with allenes and possess two π-systems, one orthogonal to the other (Fig. 1). However, although the reactions of the two heterocumulenes parallel in some respect those of allene, there are considerable differences of reactivity. This may be accounted for by the unequal -electron distribution in the three systems which arise, on one side from the intrinsic higher electronegativity of oxygen and nitrogen with respect to carbon, on the other from the possibility of interaction of the orbital of the heteroatom containing the lone-pair with the parallel orbitals of the C-C moiety. In fact, calculations of the p-electronic population on each atom[4] and spectroscopic data,[5] mainly from ^{13}C NMR, indicate that allene can be conveniently described by a single covalent structure, whereas polar resonance forms contribute signifi-

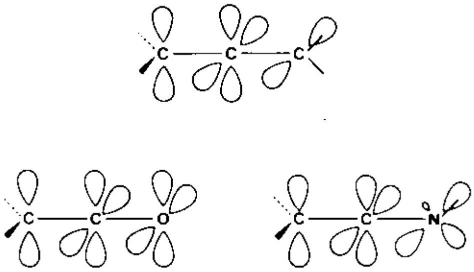
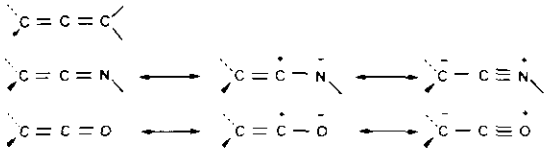


Fig. 1 π-Orbitals of allene, ketene, and ketenimine cantly to the ground state of ketenimine and ketene. These polar structures show that a positive and negative charge is located at the central and terminal carbon respectively.



An inspection of the frontier MO's diagram[4] of the three cumulenes is also very instructive (Fig. 2). Ketene has a very low energy LUMO and high energy HOMO which possess large coefficients at the central and terminal carbon respectively. The frontier orbitals of ketenimine have similar coefficients as those of ketene but the energy of the LUMO is higher and that of the HOMO is lower. Frontier orbitals of allene are even less accessible. These characteristics suggest a sequence of decreasing reactivity from ketene, to ketenimine, to allene and the tendency of the two heterocumulenes to react as electrophiles at the central carbon and as nucleophiles at the terminal carbon.

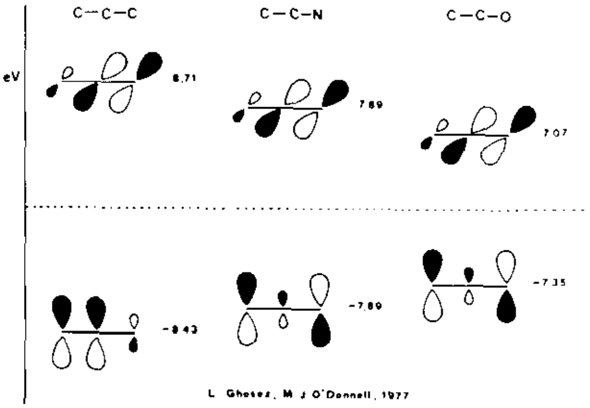
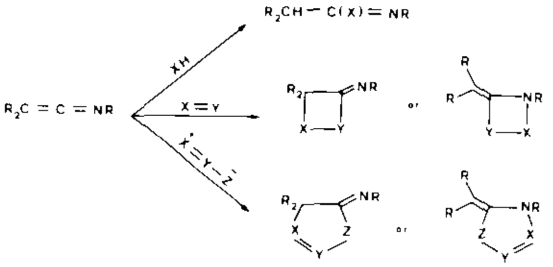


Fig. 2 *Frontier MO's of allene, ketene, and ketenimine (Ref. 4)*

Accordingly, ketenimines are known to undergo 1,2-additions[2] by nucleophiles such as alkoxides and amines[6] at the central carbon and by electrophiles such as chlorine and hydrogen chloride[7] at the terminal carbon (Scheme 1). They also undergo thermally and photochemically *induced* 1,2-cycloadditions by 2π and 4π electron systems to give four and five-membered heterocycles. Addition across the C=C bond is the ru- while addition across the C=N bond is limited to a few cases.

Scheme 1



A harvest of significant examples of four- and five-membered heterocycles derived from cycloaddition of the indicated compounds to ketenimines is presented in Tables 1 and 2.

Table 1

Four-membered Heterocycles from Ketenimines

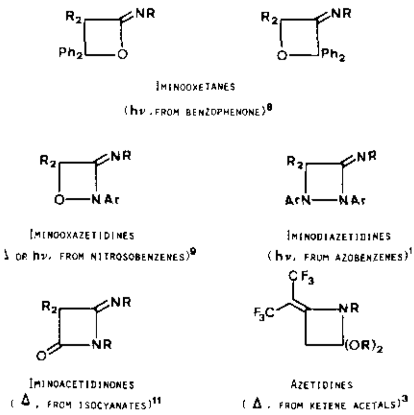
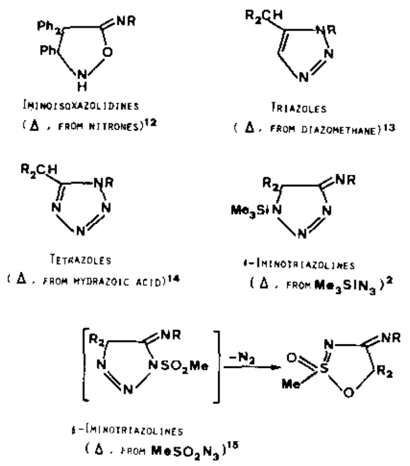


Table 2

Five-membered Heterocycles from Ketenimines

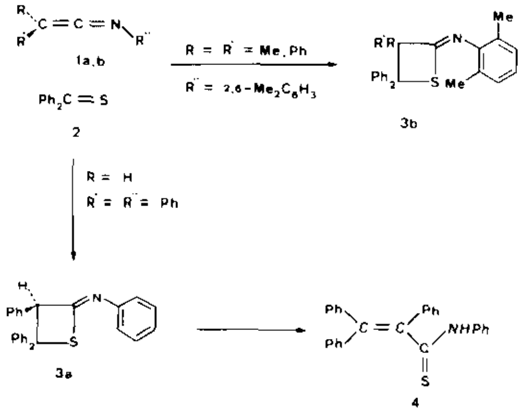


We have restricted our studies on ketenimine reactions within the limits of cycloadditions with 2π electron systems. The main attention was given to variations of siteselectivity produced by changes of the stereoelectronic characteristics of the cumulene as well as by the electron-donor and electron-acceptor character of the ketenophile.

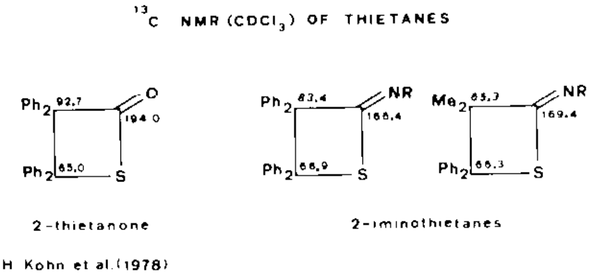
1. Reactions with Thiobenzophenone. Reactions of ketenimines with thioketones are those more extensively investigated in our Laboratory[16] since 1977 and whose characteristics summarize quite significantly the various facets of ketenimine cycloadditions.

1.A. 1,2-Cycloaddition. Formation of 2-Iminothietanes. Phenylketene-N-phenylimine **1a** undergoes[17] thermal 1,2-cycloaddition by thiobenzophenone **2** across the C=C bond of the cumulene to give 2-iminothietane **3a** which subsequently rearranges to thioacrylamide **4a** *(Scheme 2). Also dimethyl- and diphenylketenimines* **1b** afford the corresponding 2-iminothietanes **3b** provided that the group R" flanking nitrogen is an ortho-dimethyl substituted aryl group, as shown, or an alkyl group. The stereochemistry of this cycloaddition is identical to that of ketene-thioketone cycloaddition which in fact leads to 2-thietanone,[18] both reactions showing a siteselectivity which directs the nucleophilic sulfur of the thione to become bonded to the central electrophilic carbon of the cumulene. ^{13}C-NMR spectroscopy appears very useful for the routine identification of these thietanes (Scheme 3), whose spectra are in fact characterized by two signals corresponding to the non-equivalent quaternary carbons C(3) and C(4) of the heterocyclic ring and by a low field peak for the carbonyl or azomethine carbon. Interestingly, substitution of the phenyls at C(3) by methyls reduces the difference between the signals of C(3) and C(4), but still two peaks are observed.

Scheme 2



Scheme 3



The structure of 2-iminothietanes **3** was unequivocally assigned by X-ray analysis[19] (Fig. 3). Of relevance are the long S-C(4) bond distance (1.868 Å) and the puckering of the four-membered ring. It is likely that this non-planar arrangement releaves the angular strain and steric repulsions which would occur from eclipsed substituents in a strictly planar conformation and provides compounds 3 with high thermal stability. Therefore, the ring opening of 3-monosubstituted 2-iminothietanes 3a to thioacrylamides 4 (Scheme 4) which occurs during the work-up operations of the reaction mixtures and prevents adducts 3a to be isolated in a pure state, may be ascribed to the possibility of releasing hydrogen from C(3), rather than to the intrinsic thermal instability of the thietane ring. Whether the rearrangement

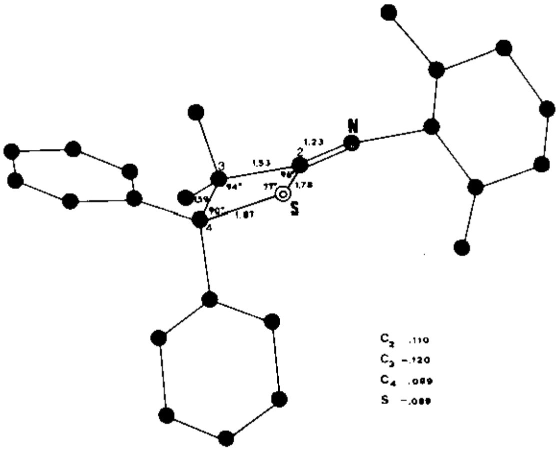
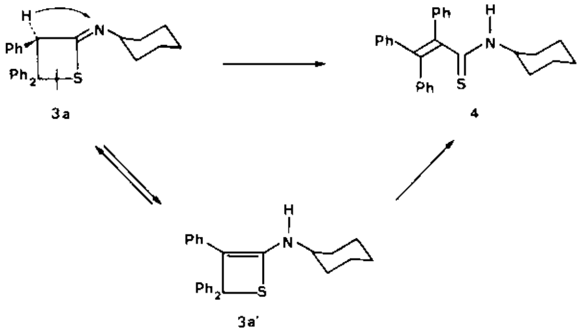


Fig. 3 Schematic view with relevant bond distances (Å) and angles (degrees) of 2-(2,6-dimethylphenylimino)-3,3-dimethyl-4,4-diphenylthietane. Deviations of the atoms of the four-membered ring from the mean plane are indicated in a separated column (Ref. 19).

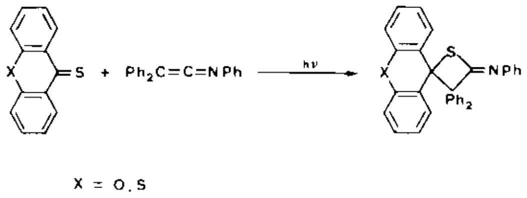
Scheme 4



3a → 4a occurs in one step by S-C(4) bond cleavage in concert with migration of hydrogen from carbon to nitrogen, or stepwise through an iminothietene 3a', is a point which deserves further studies.

Spiro-2-iminothietanes have been obtained from *photochemically* induced cycloadditions of cyclicthiones (thiantrone, xantene thione, and thioxantene thione) to *N*-arylketenimines.[21] (Scheme 5).

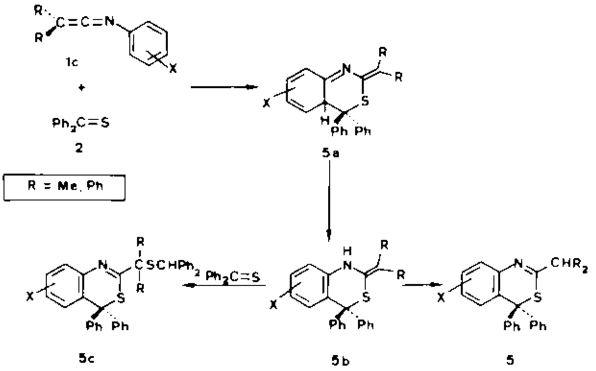
Scheme 5



H. J. T. Bos et al., Tetrahedron Lett., 4343 (1977)

1.B. 1,4-Cycloaddition. Formation of 4H-3,1-Benzothiazines. From *thermal* reactions between thiobenzophenone 2 and dimethyl- and diphenylketenimines 1c whose nitrogen is flanked by a *meta* or *para* substituted aryl group, the 1:1 adducts isolated in more than 80 % yields, resulted to be 4H-3,1-benzothiazines 5[16,17] (Scheme 6). The formation of products 5 can be formulated as a 1,4-cycloaddition of the C=S bond of the thione across the C=N bond of the cumulene and the C=C bond of the *N*-aryl group to give a six-membered ring condensed with a cyclohexadiene, *viz*. the bicyclic heteropolyene system 5a, whose aromatization by hydrogen migration leads to the observed product 5. While the formation of 5a constitutes a mechanistic problem which will be considered in a moment, other pathways which exclude 5a as an intermediate along the reaction pathway from reactants 1c and 2 to benzothiazine 5, are hardly conceivable.

Scheme 6

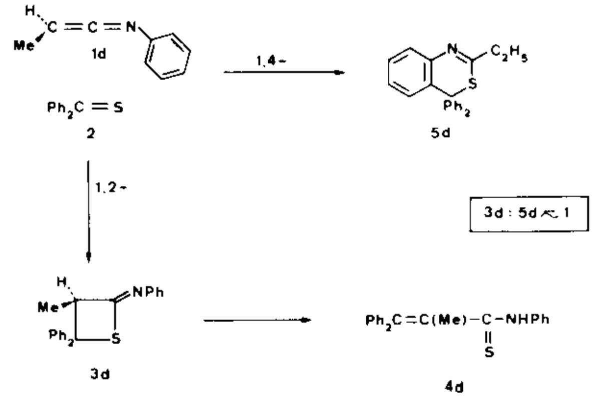


An indirect evidence for the existence of 5a, or 5b, comes from the formation of the bis-adduct 5c as sideproduct of 5. This is consistent with the addition of a second molecule of thioketone 2 to the exocyclic C=C bond of 5a, or 5b as shown, in competition with hydrogen migration to give benzothiazine 5.

Since benzothiazines 5 do not have spectroscopic characteristics to allow an unequivocal structural assignment, this was obtained from an X-ray analysis[22] which, by the way, represents the first structure determination of a 4H-3,1-benzothiazine system.

1.C. Concurrent 1,2- and 1,4-Cycloadditions. Mechanism of Formation of 2-Iminothietanes and 4H-3,1-Benzothiazines. Unlike ketenimines of type 1a and 1b which undergo sitespecific 1,2- or 1,4-cycloaddition, methylketene-*N*-phenylimine 1d follows both pathways to give 2-iminothietane 3d and 4H-3,1-benzothiazine 5d in almost equal amounts[17] (Scheme 7). Both adducts 3d and 5d are satisfactorely stable at room temperature, but on heating 2-iminothietane 3d rearranges to thioacrylamide 4d whereas benzothiazine 5d remains unaltered. The exclusive conversion of 3d to 4d although *ortho* positions of the *N*-phenyl ring are equally available for the rearrangement to benzothiazine 5d, indicates that the formation of products 5d and 3d is kinetically controlled without subsequent conversion of the one into the other.

Scheme 7



The kinetics[23] of the 1,2- and 1,4-cycloadditions reveal that both reactions occur at comparable rates in solvents of different polarity and have activation parameters characterized by relatively small activation energies and large and negative activation entropies (Table 3). However, there are significant differences between the values of these parameters in the two reactions and the variations of rate to changes of substituents are in opposite directions since electron-donor groups on nitrogen of ketenimine decrease the rate of the 1,2-cycloaddition but increase that of the 1,4-cycloaddition. Substitution at carbon exerts a dramatic effect on the rate of the 1,2-cycloaddition as shown by the relative reactivity between phenylketene-*N*-

-mesitylimine (9.5) and the diphenyl derivative (0.001) (Table 4).

Table 3

Cycloadditions of $Ph_2C{=}S$ to Ketenimines

1,1-Cycl. $Me_2C{=}C{=}N{\cdot}PhMe$

Solvent	CCl_4	CH_2Cl_2	Me_2CO	MeCN
rel. rate	1.78	1.0	0.95	2.38

$E_a = 7.6$ kcal/mol $\Delta S^{\neq} = -49$ e.u.

1,2-Cycl. $Me_2C{=}C{=}N{\cdot}Mes$

Solvent	CCl_4	CD_2Cl_2	$CDCl_3$
rel. rate	2.20	1.14	1.0

$E_a = 14.8$ kcal/mol $\Delta S^{\neq} = -32$ e.u.

Table 4

Cycloadditions of $Ph_2C{=}S$ to Ketenimines (CCl_4)

1,2-Cycl.

	$Ph(H)C{=}C{=}N{\cdot}Ph$	$Ph(H)C{=}C{=}N{\cdot}Mes$	$Ph(H)C{=}C{=}N{\cdot}Me$	$Ph_2C{=}C{=}N{\cdot}Mes$
rel. rate	7.3	9.5	1.0	0.001

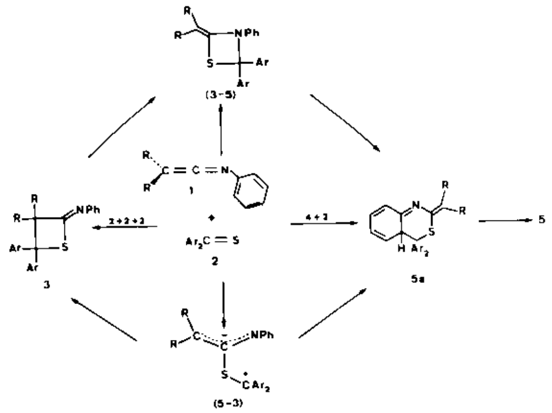
1,1-Cycl.

	$Me_2C{=}C{=}N{\cdot}PhOMe$	$Me_2C{=}C{=}N{\cdot}PhMe$	$Me_2C{=}C{=}N{\cdot}Ph$	$Ph_2C{=}C{=}N{\cdot}Ph$
rel. rate	2.0	1.6	1.0	0.1

Therefore, among various mechanistic possibilities (Scheme 8) preference is given to a Scheme where 3 and 5a are formed through two independent pathways by concerted mechanisms, rather than through multi-step processes involving the zwitterion (5-3) or the 1,3-thiazetidine (3-5) as intermediates. Accordingly, interaction diagrams[23] between frontier MO's indicate as most probable two pericyclic processes, viz. a $[_{\pi}4_{s}+_{\pi}2_{s}]$ between the C=S of the thione and the heterodiene system constituted by the C=N of the cumulene and the C=C bond of the N-aryl group (1,4-cycloaddition), and a $[_{\pi}2 +_{\pi}2 +_{\pi}2]$ involving the two orthogonal π systems of the cumulene and the lone-pair on sulfur (1,2-cycloaddition). The latter formulation is similar to the six-electron symmetry-allowed $[_{\pi}2_{s}+_{\pi}2_{s}+_{\pi}2_{s}]$ process[24a] which currently relied upon to rationalize the concerted cycloadditions of 2π systems to C=C bond of ketene, as an alternative to the classical, equally symmetry-allowed, $[_{\pi}2_{s}+_{\pi}2_{a}]$ process.[24b]

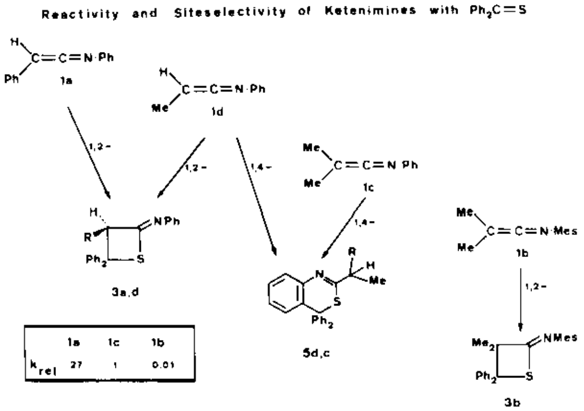
The reactivity order for the various types of ketenimines and the accompanying

Scheme 8



variations of siteselectivity can be interpreted in terms of competition between these two pericyclic processes whose relative extents depend on a balance of steric and electronic effects (Scheme 9). In phenylketene-*N*-phenylimine 1a, where the C=S of the thione can easily reach the C=C bond of the cumulene by approaching the molecule from the unsubstituted side, electronic effects determine a high reactivity and direct siselectivity across the C=C bond to give iminothietane 3a (R = Ph). In methylketene-*N*-phenylimine 1d, however, the importance of the electronic factors must be somewhat reduced so that the rate of the 1,2-cycloaddition decreases in favor of the 1,4-cycloaddition and iminothietane 3d (R = Me) and benzothiazine 5d (R = H) are formed competitively in almost equal amounts. In dimethylketene-*N*-phenylimine 1c, and in diphenyl derivatives as well, where substituents at carbon of the cumulene hinder the

Scheme 9

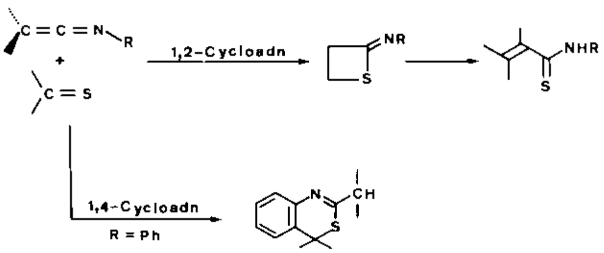

Reactivity and Siteselectivity of Ketenimines with Ph$_2$C=S

	1a	1c	1b
k_{rel}	27	1	0.01

approach of the thione from both sides of the C=C bond, the 1,2-cycloaddition becomes a very high energy process which gives way to the 1,4-cycloaddition across the heterodiene system C=N-C=C to give benzothiazine 5c (R = Me). When also this mode of reaction is inhibited by *ortho* substituents in the *N*-aryl group, such as in dimethylketene-*N*-mesitylimine 1b, the 1,2-cycloaddition across the C=C bond of the cumulene takes place, although at very low rate, to give iminothietane 3b.

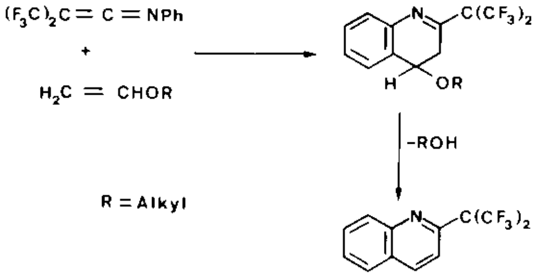
1.D. Other Examples of 1,4-Cycloaddition to Ketenimines. While the formation of 2-iminothietanes 3 constitutes buth a further example of 1,2-cycloaddition across the C=C bond of ketenimine which fits in the usual reactivity scheme of cumulenes, the formation of benzothiazines 5 through a 1,4-cycloaddition which involves the C=N bond of the cumulene and the C=C bond of the *N*-aryl group, is more attractive (Scheme 10).

Scheme 10



In fact examples of this stereochemical variable in ketenimine cycloadditions are less common. One concerns the reaction between trifluoromethylketene-*N*-phenylimine and vinyl ethers to give fluorinated quinolines[3] (Scheme 11), another one is provided by the reactions of dimethyl- and diphenylketene-*N*-phenylimines with ynamines to give again substituted quinolines[25] (Scheme 12). Finally, very significant is the behavior of vinylketenimines, a new class of heterocumulenes, described by Ghosez and collaborators. For instance, vinylmethylketene-*N*-tolylimine undergoes[26] (Scheme 13) two 1,4-cycloadditions at different sites, one across the C=N and the C=C of the *N*-aryl group by electron-donor ketenophiles, *e.g.* 1-diethylamino-2-phenylacetylene, the other one across the dienic system formed by the C=C of the cumulene and the vinyl group by electron-acceptor ketenophiles, *e.g.* dimethyl acetylenedicarboxylate.

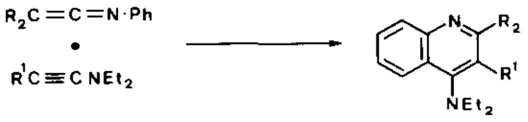
Scheme 11



R. Gambaryan, Russian Chem. Rev., 45, 630 (1976)

Very attractively, the presence of the vinyl group attached to carbon of kete-

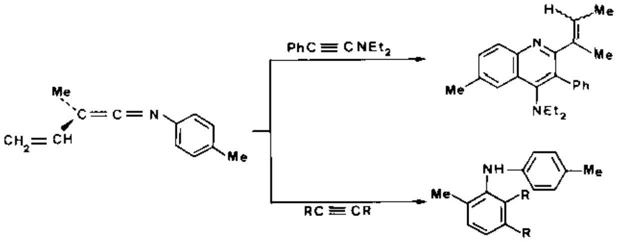
Scheme 12



R and R' = Me, Ph

L. Ghosez, C. de Perez, Angew. Chem. Int. Edn., 10, 184 (1971)

Scheme 13



R = CO_2Me

L. Ghosez et al., J. Am. Chem. Soc., 95, 5417 (1973)

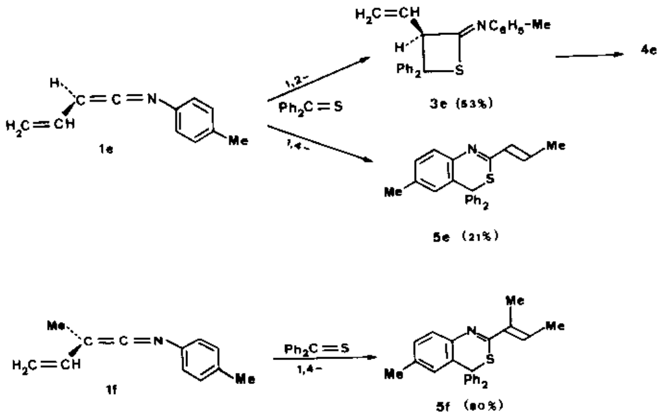
nimine discloses the possibility of a new stereochemical variable in cycloadditions with thioketones.

1.E. 1,2- and 1,4-Cycloadditions to Vinylketenimines. Formation of Vinylthietanes, Vinylbenzothiazines, and Thiacyclohexeneimines. Cycloadditions of thiobenzophenone 2 to vinylketenimines occur at different sites of the cumulene and involve both the N-aryl and C-vinyl groups.[27] The results are summarized in the following Schemes.

Vinylketene-N-tolylimine 1e (Scheme 14) undergoes 1,2-cycloaddition across the C=C bond of the cumulene to give the 3-vinyl-2-iminothietane 3e (53 %) and 1,4-cycloaddition across the C=N of the cumulene and the C=C bond of the N-tolyl group to give the 2-vinyl-4H-3,1-benzothiazine 5e (21%). Iminothietane 3e rearranges on heating to the highly unsaturated thioamide 4e whereas benzothiazine 5e is thermally stable. The larger amount of 3e with respect to 5e (ca. 2.5 : 1 ratio) indicates that also for a monosubstituted vinylketenimine, e.g. 1e, the 1,2-cycloaddition is preferred over the 1,4-process. In this reaction the thioketone 2 reveals its electron--donor character since of the two possible 1,4-cycloadditions, preference is given to that involving the N-aryl group, as observed for the electron-rich dienophile ynamines.[26]

From the reaction of vinylmethylketene-N-tolylimine 1f, however, the vinylbenzothiazine 5f is isolated in 80 % yield. Evidently, as observed for C-phenylketenimine 1a, substitution at the terminal carbon of a vinylketenimine inhibits the 1,2-cycloaddition in favor of the 1,4-process, thereby confirming the importance of steric effects on the siteselectivity of these reactions.

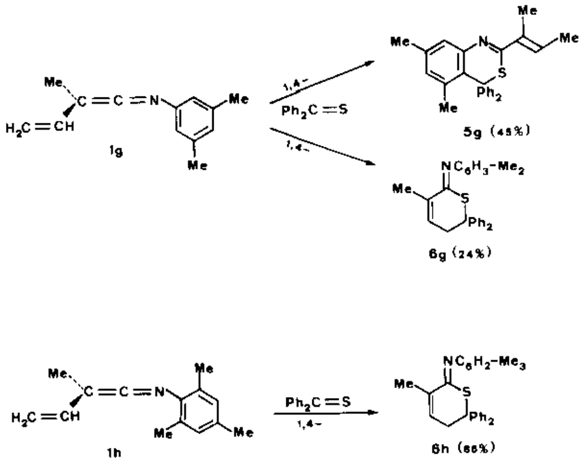
Scheme 14



It was very interesting to notice that also meta substitution in the N-aryl group of the vinylketenimine affects the stereochemical choice of the cycloaddition. In fact vinylmethylketene-N-(3,5-dimethylphenyl)imine 1g (Scheme 15) undergoes the two sitedifferent 1,4-cycloadditions, one involving the N-aryl group to give the benzothiazine 5g, the other one involving the C-vinyl to give the six-membered ring adduct thiacyclohexene-2-imine 6g in ca. 2:1 ratio.

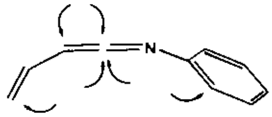
Finally, when also the two ortho positions of the N-aryl group are blocked by methyls as in vinylmethylketene-N-mesitylimine 1h, the 1,4-cycloaddition across the

Scheme 15



C=C bond of the cumulene and the C-vinyl takes place to give the thiacyclohexene-2-imine **6h**.

From an overview of the reactions of vinylketenimines with thiobenzophenone **2** it appears that this class of heterocumulenes offers to thioketones the choice of three different sites for cycloaddition, viz. the C=C bond of the cumulene for a 1,2-cycloaddition, the heterodiene system C=N-C=C(aryl) for a 1,4-cycloaddition, and finally the diene system C=C-C=C(vinyl) for another 1,4-cycloaddition. It is worth noting that in our approach the reaction of vinylketenimines with a single partner can be directed to produce three types of heterocycles. Each of these possesses an exocyclic unsaturated function, viz. C=C and C=N bond, which may be used for further synthetic transformations.



1.F. Interpretation of the Siteselectivity in Ketenimine-Thioketone Reactions by MO's Reasonings. It is now time to looking at what we called the electronic factors which are in part responsible for the variation of siteselectivity in ketenimine-thioketone cycloadditions. To do that on a qualitative ground, let us consider a molecular orbital diagram of ketenimines constructed using data from STO-3G calculations[23,28] and PES[28] (Fig. 4). The relevant MO's of the model ketenimine $H_2C=C=NH$ are the two occupied MO's very close in energy (the NHOMO ψ_1 being mainly π_{CN} mixed with some π_{CH_2} in an antibonding manner; the HOMO ψ_2 being mainly n_N with a substantial contribution π_{CC} in an antibonding manner) and the two empty MO's having also similar energies (the LUMO ψ_3^* is mainly π_{CN}^* and the NLUMO ψ_4^* is mainly π_{CC}^*). The HOMO ψ_2 and the LUMO ψ_3^* are the MO's involved in [2+2] cycloadditions across the C=C bond. For the relatively high and low energies respectively of ψ_2 and ψ_3^* it is understandable why there is a preferential siteselectivity toward this centre, provided that steric factors are negligible.

The interaction of ψ_1 and ψ_3^* MO's with proper orbitals of the co-planar N-phenyl ring[29] creates two new orbitals Φ_1 and Φ_3^* which are at higher and lower energies respectively. Therefore, when steric effects inhibit the [2+2] process, these orbitals are available for a [4+2] reaction. Finally, also the presence of a vinyl group at the terminal carbon creates a new set of orbitals since ψ_2 mixes with π_{CC} in an antibonding way to give χ_2 higher in energy and ψ_4^* mixes with π_{CC}^* in a bonding way to give χ_4^* lower in energy. These new orbitals account for the 1,4-cycloaddition across the C=C of the cumulene and the vinyl group when steric factors inhibit the electronically favored 1,2-cycloaddition.

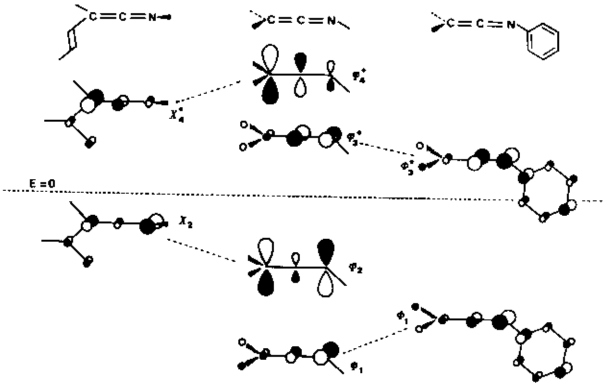
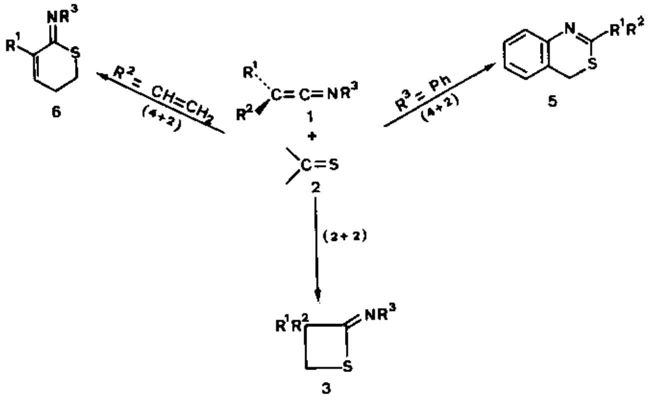


Fig. 4 Frontier MO's of ketenimine $H_2C=C=NH$ (center), N-phenyl derivative (right), and C-vinyl derivative (left).

In conclusion, the interaction of substituents with the orthogonal π-systems of the cumulene creates new sets of orbitals which possess proper energies and symmetries to allow different siteselective cycloadditions. The relevance of the empty or occupied orbitals of the cumulene, and consequently the siteselectivity, depends on the electron-donor or electron-acceptor character of the other partner of the reaction, a point which can be decided after the construction of the MO's interaction diagram for each reaction. Of course, this interpretation holds on the assumption that the reactions under study are pericyclic processes.

1.G. Heterocycles fro Ketenimine-Thioketone Cycloadditions. An Overview. The results presented in the preceeding Sections show that ketenimines display a polyvalent character as cycloaddition partner with thioketones (Scheme 16) since they undergo 1,2- and 1,4-cycloaddition which allow the construction of three types of sulfur hetero-

Scheme 16

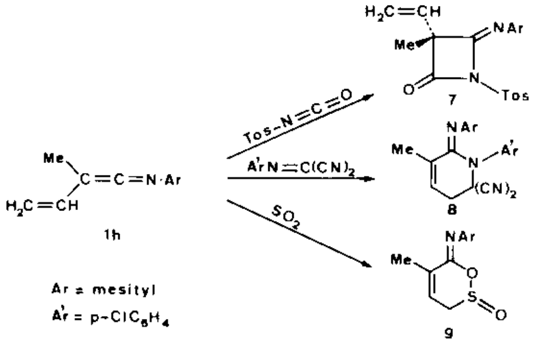


cycles, viz. the four-membered ring thietanes 3, the six-membered ring thiazines 5, and the six-membered ring thiacyclohexenes 6. In most of the cases examined, the reactions are sitespecific in favor of one of these pathways, although the occurrence of two competitive modes of cycloaddition has been observed in some cases.

2.A. Reactions of Vinylketenimines with Electron-Poor Heteroenes. The tendency of vinylketenimines to undergo sitevariable cycloadditions is under study using electron-poor heteroenes which are expected (Sect. 1.F.) to be quite reactive and give 1,2-cycloaddition across the C=C bond of the cumulene or 1,4-cycloaddition involving the vinyl group.

Vinylmethylketene-*N*-mesitylimine 1h (Scheme 17) undergoes[30] 1,2-cycloaddition by the strong electron-acceptor heterocumulene *p*-toluenesulfonylisocyanate to give the 4-iminoacetidinone 7, as reported[10] for other ketenimine-isocyanate cycloadditions, whereas with the less strong acceptors *N*-dicyanomethylene-*p*-chloroaniline and sulfur dioxide the 1,4-cycloaddition prevails to give the six-membered adducts azacyclohexene-2-imine 8 and 3-dihydro-6-imino-1,2-oxathiin-2-oxide 9, respectively.

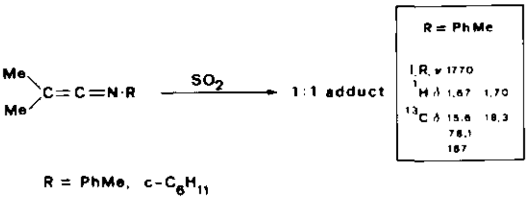
Scheme 17

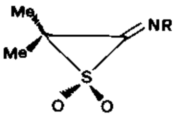


The 1,4-cycloaddition between the vinylketenimine 1f acting as a diene and the oxygen-sulfur bond of sulfur dioxide to give the cyclic sulfinic ester 9 parallels similar reactions of vinylallenes[31] and certain dienes[32] with sulfur dioxide. This periselectivity, however, is quite rare whereas that usually observed is the cheletropic $[{}_{\pi}4_{s} + {}_{\omega}2_{s}]$ process[33] which leads to five-membered ring sulfones (sulfolene reaction).

2.B. Reactions of Ketenimines with Sulfur Dioxide. In the course of an extensive investigation on the reactivity of various ketenimines toward sulfur dioxide, we have observed[34] that dimethylketenimines 1b react with liquid sulfur dioxide to give 1:1 adducts (*ca*. 90 % yield) (Scheme 18) whose significant spectroscopic characteristics were (R = PhMe) a very strong IR(CCl_4) absorption at 1770 cm^{-1}, ^{1}H NMR($CDCl_3$) peaks at 1.67 and 1.70 ppm (2 Me), ^{13}C NMR($CDCl_3$) signals at 15.6 and 18.3 ppm (two primary carbons) and at 78.6 and 166.9 ppm (two quaternary carbons). The structure which *is better compatible with these spectroscopic properties is that of the four-membered ring 1,2-oxathietan-4-imine-2-oxide 10 (β-sultine) which possesses two diastereotopic methyls at C(3) as required by the NMR spectra,and an exocyclic C=N bond as indicated by the low field signal in the ^{13}C NMR spectrum and the 1770 cm^{-1} absorption in IR which is in the range of the values reported for iminolactones.[11,35] On the other hand, the three-membered ring structure of iminothiirane-1,1-dioxide 11 (episulfone) appears unjustified since owing to its symmetry, it requires the equivalence of the two methyls at C(3).

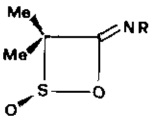
Scheme 18





11

episulfone



10

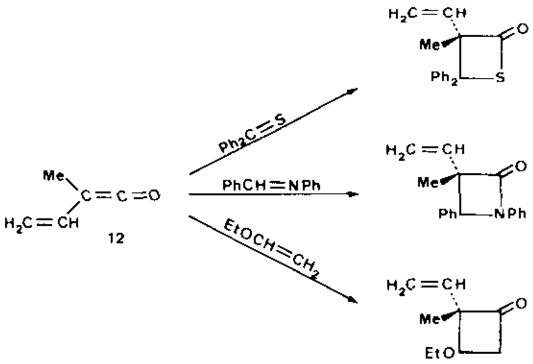
β-sultine

Should the oxathietanimine structure be correct, these results fill in a relevant gap of the literature, viz. the preparation of stable β-sultines, a class of cyclic sulfinic esters which have been hitherto elusive,[36] and provide an unequivocal example of /‾2+2_/ cycloaddition to SO_2, a long pursued reaction whose occurrence has been advocated in some cases from indirect evidence.[37]

Conclusion

The cycloadditions between ketenimines and 2π electron systems offer a flexible way for the synthesis of four- and six-membered ring heterocycles, thus increasing the value of these cumulenes as intermediates for heterocycles. The scope of these reactions appears quite wide and compensates for some drawbacks of ketenimines such as their low reactivity and difficulty of preparation in a pure state. On the other hand, ketenes although more reactive than ketenimines,[4] appear less flexible intermediates since undergo preferentially 1,2-cycloaddition across the C=C bond. For instance, unlike vinylmethylketenimine 1f, vinylmethylketene 12 reacts (Scheme 19) with thiobenzophenone, benzalaniline, and ethyl vinyl ether to give invariably the corresponding four-membered ring adducts.[38]

Scheme 19



Acknowledgments

The collaboration of those who have contributed to the development of the work described in this lecture has been highly appreciated : they are individually recognised in the cited references. I wish also to thank C.N.R. (Rome) for financial support and the Laboratory of the Carbon Compounds containing Heteroatoms (Bologna) for a Research Grant and for making available instrumentations and facilities.

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