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CYCLOADDITION OF HETEROFUNCTIONALIZED ALLENES WITH *tert*-BUTYLTHIOACRYLONITRILE. DETERMINATION OF ACTIVATION PARAMETERS FOR DIRADICAL INTERMEDIATE FORMATION AND THE DETECTION OF REVERSIBLE RING CLOSURE

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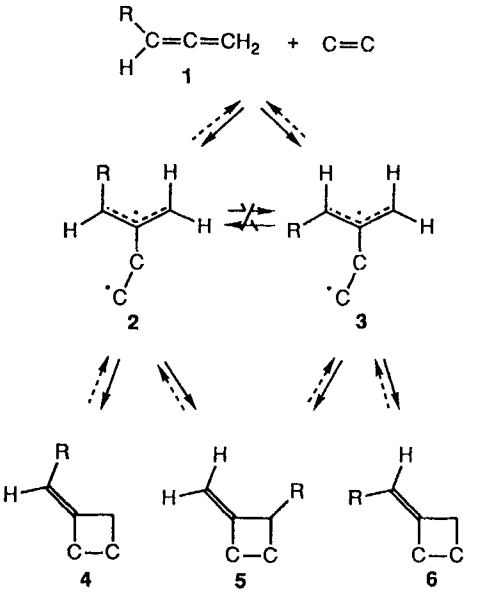
The cycloaddition reactions of 4-methylphenylthio-, methoxy-, 4-methoxyphenyl-, phenyl-, chloro- and cyanoallene with *tert*-butylthioacrylonitrile (BTA) in toluene-d_8 solution were investigated. The relative reactivity sequence of these substituted allenes is 4-methylphenylthio ~ methoxy- > 4-methoxyphenyl- > phenyl- > chloro- > cyanoallene. Activation parameters were measured for diradical intermediate formation of BTA with 4-methylphenylthio-, methoxy- and 4-methoxyphenylallene, giving average values of E_a and $\Delta S^{\ddagger}$ of 14·2–16·8 kcal mol^{-1} and *ca.* −33 eu, respectively. The relative reactivity sequence is consistent with a FMO allene-HOMO, BTA-LUMO dominant interaction for diradical intermediate formation. However, the regioselectivity of attack on the substituted allene appears to be thermodynamically controlled. The formation of the diradical intermediates in these cycloaddition processes appears to be irreversible. However, the ring closure of the diradical intermediates formed from 4-methylphenylthio-, methoxy- and 4-methoxyphenylallene is reversible under the conditions of the kinetic experiments. The kinetically controlled ring closure of the diradical intermediates is allyl radical SOMO controlled, while the final cycloadduct distribution is thermodynamically controlled.

INTRODUCTION

Over the past decade, studies in the authors' laboratories have focused on several features of the two-step, diradical intermediate [2 + 2] cycloaddition reactions of substituted allenes. These include gaining an understanding of the factors controlling the relative reactivity and regioselectivity of attack on the substituted allene in the diradical intermediate-forming process, the stereochemistry of formation of the diradical intermediates, the possible reversibility of diradical intermediate formation, internal rotation processes in the diradical intermediates that result in the loss of stereochemistry originally present in the reactants and the regioselectivity and possible reversibility of ring closure. The overall mechanistic scheme for the [2 + 2] cycloaddition process is illustrated opposite, where the dashed arrows represent rarely observed processes.

Although much information has been obtained on the factors governing the relative extents of the formation of the stereoisomeric diradical intermediates **2**



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and **3**,[1-3] much less has been learned about the factors governing the other aspects of the overall cycloaddition process. Reversibility in diradical intermediate formation has been observed so far only in two cases, those involving the cycloaddition of 1,1-dimethylallene (11DMA) with diethyl maleate, which results in the formation of *trans*-diester products as the major products and isomerization of the diethyl maleate to diethyl fumarate (which does not occur in the absence of the 13DMA),[2] and in the cycloaddition of enantioenriched 1,3-dimethylallene (13DMA) with 1,1-diphenylethene, which results in racemization of the 13DMA.[4] In both of these reactions, highly sterically congested intermediates are formed, resulting in steric congestion destabilization of the diradical intermediates. The studies that have been carried out in the authors' laboratories have not detected reversible ring closure in the formation of the cycloadducts, although reversible ring closure has been reported in the cycloadducts derived from the cycloaddition of methoxyallene with acceptor–donor, 1,1-disubstituted radicophiles, and activation parameters have been measured for the cycloadduct ring-opening process.[5]

The factors controlling the regioselectivity of ring closure have not been apparent. FMO control predicts ring closure at C-1 (the substituted carbon atom of the allyl radical portion of the intermediate), which possesses the largest coefficient in the SOMO, whereas thermodynamic control predicts that ring closure should occur at C-3.[7] Steric effects might also play an important role. The regioselectivities observed in the ring closure of the diradical intermediates formed in the [2 + 2] cycloaddition reactions of selected alkyl and heterofunctionalized allenes with 1,1-dichloro-2,2-difluoroethene,[6] which occurs in competition with [2 + 2] cyclodimerization,[6] and the [2 + 2] cycloaddition with diethyl fumarate[2] are given in Table 1. The regioselectivities of ring closure vary widely, both in the individual reactions of certain substituted allenes and between different reactions of a given substituted allene. Notable reversals of regioselectivity with an individual allene are evidenced in the diethyl fumarate cycloadditions reactions and in the cyclodimerization reactions of phenyl-, methoxy-, chloro- and phenylthioallene. Notable reversals of regioselectivity within the same type of cycloaddition reactions are exhibited by comparison of the regioselectivities of the cyclodimerization reactions of phenyl- and cyanoallene. (There is no evidence to indicate that the ring closure of the diradical intermediates formed in these reactions is reversible.)

In an attempt to avoid the competitive cyclodimerization of the highly reactive heterofunctionalized allenes, a more reactive radicophile was sought in order to observe only the [2 + 2] cycloaddition process. For this study, *tert*-butylthioacrylonitrile (BTA) was selected. BTA reacts cleanly with methoxy-, 4-methylphenylthio-, 4-methoxyphenyl-, phenyl-, chloro- and cyanoallene to form only [2 + 2] cycloaddition products. No cyclodimerization of the heterofunctionalized allenes is observed. The cycloaddition reactions of BTA with methoxy-, 4-methylphenyl- and 4-methylphenylthioallene occur with sufficient ease that the rates of reaction could be monitored by NMR spectroscopy, which also allowed for the detection of reversible ring closure and equilibration of the cycloadducts.

Table 1. Regioselectivities of ring closure of diradical intermediates formed in the [2 + 2] cycloaddition reactions of substituted allenes with 1,1-dichloro-2,2-difluoroethene (1122), diethyl fumarate (DEF) and [2 + 2] cyclodimerization (CD)

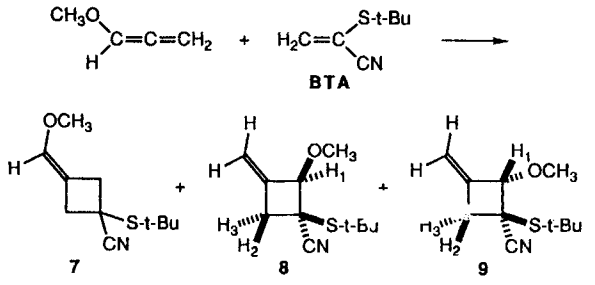
Allene	Radicophile	C-1 : C-3 ring-closure ratio
$C_2H_5CH=C=CH_2$	1122	17 : 83
	DEF	56 : 44
$(CH_3)_2C=C=CH_2$	1122	14 : 86
	DEF	13 : 87
	CD	17 : 83
$C_6H_5CH=C=CH_2$	1122	55 : 45
	DEF	15 : 85
	CD	100 : 00
$CH_3OCH=C=CH_2$	1122	30 : 70
	DEF	53 : 47
$ClCH=C=CH_2$	1122	33 : 67
	DEF	16 : 84
	CD	53 : 47
$NCCH=C=CH_2$	1122	11 : 89
	CD	30 : 70
$C_6H_5SCH=C=CH_2$	1122	38 : 62
	CD	65 : 35

RESULTS

Cycloaddition of methoxyallene with *tert*-butylthioacrylonitrile (BTA)

The cycloaddition of methoxyallene with BTA was carried out in toluene-d_8 solution in a sealed NMR tube. After heating at 120 °C for 2 h, the NMR spectrum of the reaction mixture showed the complete disappearance of the methoxyallene and the presence of peaks belonging only to the three cycloadducts **7**–**9**. There was no evidence for the formation of any other product, or oligomerization of the reactants or the products. The **7**:**8**:**9** ratio in the initial reaction mixture was 4·03 : 1·00 : 6·77. After the reaction mixture had been further heated at 160 °C for 36 h, only cycloadduct **7** was present.

The attempted column chromatographic separation of the mixture of cycloadducts resulted in extensive decomposition. However, fractions containing only **7** and **8**, and **7** and **9** were obtained which allowed for the complete assignment of the NMR resonances of the

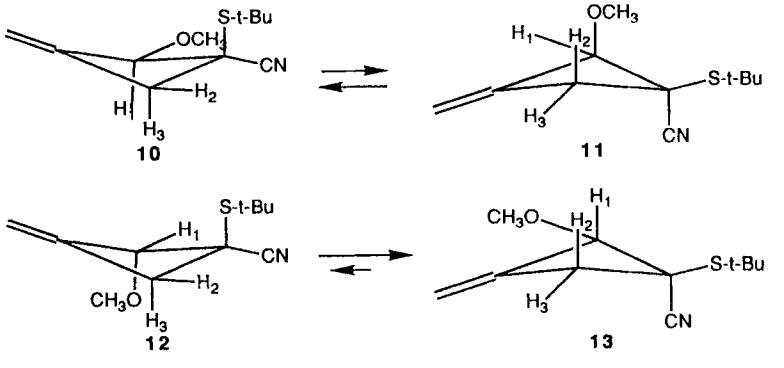


individual cycloadducts utilizing extensive decoupling and integration experiments. The structure of **7** was readily apparent from the appearance of only a single vinyl proton at low field in the NMR spectrum. The protons attached to the ring carbon atoms appeared as a complex multiplet. The assignment of the stereochemistry in **8** and **9** was made difficult because of the lack of vicinally related pairs of protons attached to the ring carbon atoms. The assignment of the stereochemistry was made on the basis of a conformational analysis of **8** and **9**. In the *Z*-cycloadduct (*Z* being defined as having the two groups of highest polarizability attached to C-2 and C-3 on the same face of the four-membered ring) the two conformations **10** and **11** should both be extensively populated; in each structure one of the larger groups (OCH_3 or S-*t*-Bu) is oriented in the preferred pseudo-equatorial direction. In this case H-2 and H-3 will both extensively occupy the pseudo-axial and pseudo-equatorial positions in one of the two conformations, resulting in an expected small difference in their chemical shifts on a time-averaged basis. In contrast, in the *E*-cycloadduct **9**, conformation **13** is expected to much more extensively populated than **12**, resulting in an expected large difference between the chemical shifts of pseudo-axial H-2 and pseudo-equatorial H-3 in **13**. In **8** $\Delta\delta$ is 0·17 ppm, whereas in **9** $\Delta\delta$ between H-2 and H-3 is 0·49 ppm. Further, when a mixture of **7** and the *Z*-cycloadduct **8** is heated at 100 °C, **8** rapidly disappears with he concomitant formation of **9**, which then more slowly undergoes isomerization to **7** (see Table 2). This is suggestive that **8** has the *Z*-stereochemistry in which one of the larger groups must be oriented in the pseudo-axial direction which undergoes isomerization to the more thermodynamically stable **9** in which both of the large groups are oriented pseudo-equatorially.

Table 2. Relative concentrations of **7**, **8** and **9** derived on heating a mixture of **7** and **8**

		Cycloadduct		
Temperature (°C)	Time (h)	**7**	**8**	**9**
–	0	1·00	0·92	0·00
100	2	1·00	0·76	0·16
120	2	1·00	0·44	0·43
120	40·5	1·00	0·18	0·38
120	64·5	1·00	0·12	0·17
120	131	1·00	0·00	0·10

The kinetics of the reaction of methoxyallene with BTA were monitored in the following manner. Solutions of methoxallene, BTA and an internal standard (for NMR integration purposes) in bromobenzene-d_5 were placed in NMR tubes. The contents of the tubes were triply freeze-degassed (liquid nitrogen) and the tubes were sealed under high vacuum. The NMR tubes were then placed in the NMR spectrometer which had been equilibrated at the desired temperature. NMR spectra were recorded periodically using a 1 PULSE KINETICS EXPERIMENT program. The individual NMR spectra were integrated and the concentrations of the methoxyallene and BTA were calculated. Excellent second-order kinetic plots were obtained. Figure 1 shows a stacked-plot output of the NMR spectra for the kinetic run at 80 °C. Table 3 lists the rate constants determined at the various temperatures and Table 4 lists the activation parameters for the disappearance of the methoxyallene (formation of the diradical intermediates in the cycloaddition process).



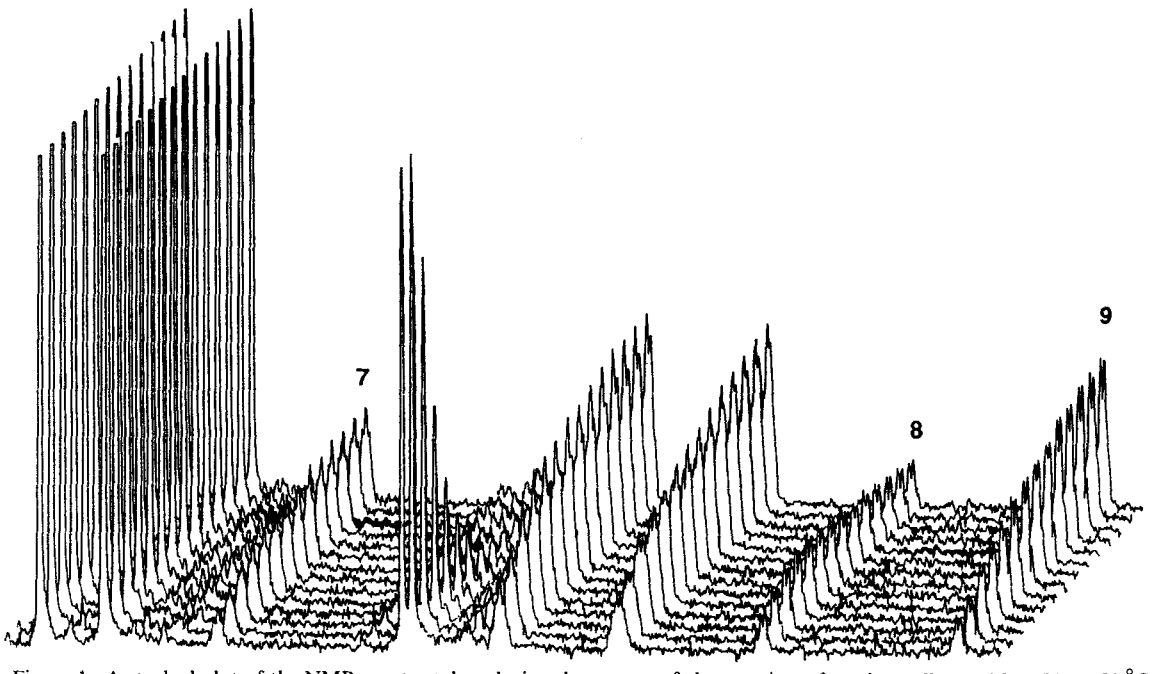


Figure 1. A stacked plot of the NMR spectra taken during the course of the reaction of methoxyallene with BTA at 80 °C

Table 3. Second-order rate constants for diradical intermediate formation in the cycloaddition reactions of MEOA, MPTA and MEPA with BTA

Allene	Temperature (°C)[a]	k_2 (l mol^{-1}s^{-1})
MEOA	80·0	$2{\cdot}72 \times 10^{-4}$
	90·0	$5{\cdot}15 \times 10^{-4}$
	100·0	$6{\cdot}17 \times 10^{-4}$
	110·0	$1{\cdot}76 \times 10^{-3}$
MPTA	80·0	$3{\cdot}00 \times 10^{-4}$
	90·0	$6{\cdot}59 \times 10^{-4}$
	100·0	$8{\cdot}32 \times 10^{-4}$
	110·0	$1{\cdot}56 \times 10^{-3}$
MEPA	80·0	$1{\cdot}35 \times 10^{-4}$
	90·0	$2{\cdot}70 \times 10^{-4}$
	100·0	$3{\cdot}60 \times 10^{-4}$
	110·0	$9{\cdot}59 \times 10^{-4}$

[a] Estimated uncertainty, ±0·5 °C.

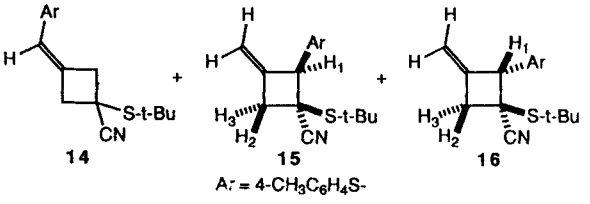
Table 4. Activation parameters for diradical intermediate formation in the cycloaddition reactions of MEOA, MPTA and MEPA with BTA[a]

Allene	E_a (kcal mol^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (eu)
MEOA	15·7	15·0	−32·5
MPTA	14·1	13·4	−36·5
MEPA	16·8	16·1	−30·9

[a] Estimated uncertainties ±1·0 kcal mol^{-1} and $\tilde{2}$ eu.

Cycloaddition of 4-methylphenylthioallene with BTA

The reaction of 4-methylphenylthioallene with BTA in toluene-d_8 solution at 120 °C cleanly produces only a mixture of the three cycloadducts **14**–**16**. After further heating at 160 °C for 36 h, only **14** was present. There is no evidence for any polymerization of the reactants or cycloadducts. Attempted chromatographic separation of the mixture of cycloadducts resulted in extensive decomposition and loss of the cycloadducts; however, small amounts of fractions were obtained containing **14** and **15**, and **14** and **16**.



The structure of **14** was immediately evident from its NMR spectrum, which showed the presence of a single vinyl proton. The stereochemistry of **15** and **16** was assigned on the basis of the relative $\Delta\delta$ values between H-2 and H-3, being 0·31 ppm in **15** and 0·42 ppm in **16**, and the observation that on heating the mixture of **14** and **15**, **15** undergoes rapid isomerization to **16**, which undergoes further slower isomerization to **14**.

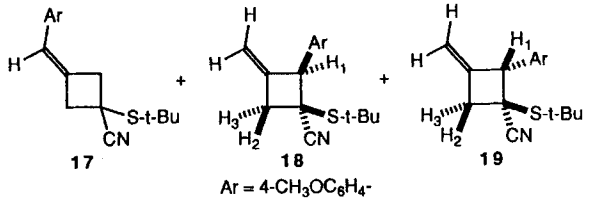
This is similar to the behavior of the methoxyallene–BTA cycloadducts and indicates that **15** possesses the *Z*-stereochemistry and **16** the *E*-stereochemistry.

When the isomerization of the mixtures of **14** and **15**, or **14** and **16**, was carried out in the presence of an excess of methoxyallene, there was no indication of the formation of any of the cycloadducts **7**–**9** derived from methoxyallene with BTA. This indicates that although the cycloadducts undergo ring opening to the initially formed diradical intermediates, the diradical intermediates do not undergo cleavage to 4-methoxyphenylallene and BTA, the latter of which should have been trapped by the essentially equally reactive methoxyallene.

The rate constants for the reaction of 4-methylphenylthioallene with BTA could be conveniently determined at various temperatures by NMR as described above for the reaction of methoxyallene with BTA. The NMR spectra recorded at early times during the kinetic runs indicated the predominant formation of **15** and **16**, with subsequent isomerization of **15** to **16**, and then **16** to **14**. The rates constants are given in Table 3 and the activation parameters in Table 4.

Cycloaddition of 4-methoxyphenylallene with BTA

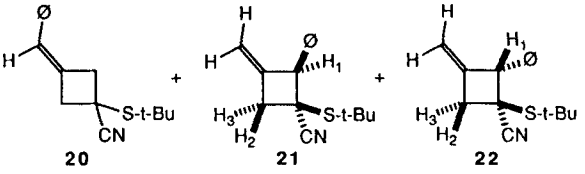
The reaction of 4-methoxyphenylallene with BTA in toluene-d_8 solution at 100 °C for 2 h resulted in the complete disappearance of the allene (by NMR) with the formation of only the three cycloadducts **17**, **18** and **19** in a ratio of 1·00:1·16:0·48. The mixture of cycloadducts could not be separated by chromatographic techniques. However, the NMR spectrum of the mixture of the cycloadducts was well enough resolved that the NMR spectra of the three cycloadducts could be easily distinguished. The stereochemistry of **18** and **19** could not be assigned on the basis of the relative $\Delta\delta$ values of H-2 and H-3. The stereochemistry was assigned on the basis of the relative chemical shifts of H-1 attached to C-2, being at much higher field (δ 4·29, pseudo-axial) in **19**, in which the conformation similar to **13** should be overwhelmingly populated, compared with δ 4·95 (pseudo-equatorial) in **18**. Further evidence for this assignment is derived from the stacked-plot NMR spectra from the kinetic runs, in which **18** anad **19** are preferentially formed at the beginning of the reaction, with **18** rapidly isomerizing to **19** and further isomerization of **19** to **17**.



The rate constants for the reaction of 4-methoxyphenylallene with BTA could be conveniently determined by the NMR techniques described above. The rate constants are given in Table 3 and the activation parameters in Table 4.

Cycloaddition of phenylallene with BTA

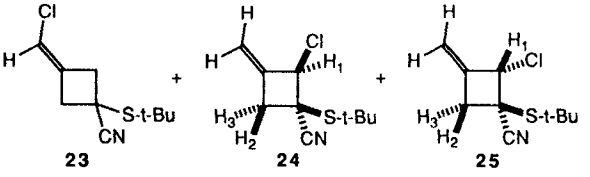
The cycloaddition of phenylallene with BTA occurs considerably more slowly than do the reactions with the other substituted allenes described above. The reaction required heating the reaction mixture at 160 °C for several hours in order attain complete reaction of the phenylallene. Under these conditions, the reaction cleanly produces a mixture of only two cycloadducts, assigned structures **20** and **22**. After further heating of the reaction mixture at 160 °C only **20** was present. There was no evidence for the presence of cycloadduct **21** in any of the NMR spectra taken of the reaction mixture at intermediate degrees of completion of the reaction.



The mixture of cycloadducts was partially separated into a pure fraction of **20** and a mixture of **20** and **22** by column chromatography on silica gel. The structure of **20** was readily assigned on the basis of the appearance of a single vinyl proton in the NMR spectrum. The *E*-stereochemistry of **22** was assigned on the basis of the kinetic and thermodynamic properties of the *E*- and *Z*-stereoisomers of the ring-substituted cycloadducts described above.

Cycloaddition of chloroallene with BTA

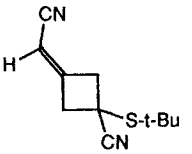
The cycloaddition of chloroallene with BTA occurs very slowly, requiring heating for several hours at 160 °C for completion, producing a 3·08:1·00 mixture of two cycloadducts assigned structures **23** and **25**. Column chromatography on silica gel resulted in the isolation in low yields of a pure fraction of **23** and a mixture of **23** and **25**. The structure of **23** was readily apparent from its NMR spectrum, which showed the



presence of a single vinyl proton. The stereochemistry of the cycloadduct assigned structure **25** is based on the relatively large $\Delta\delta$ between H-2 and H-3 of 0·49 ppm, and the kinetic and thermodynamic observations described above for the other mixtures of cycloadducts.

Cycloaddition of cyanoallene with BTA

The cycloaddition of cyanoallene with BTA at 160 °C for 4 h produced in high yield a single cycloadduct assigned structure **26** on the basis of the appearance of only a single vinyl proton in the NMR spectrum of the cycloadduct.



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DISCUSSION

Analysis of the relative reactivities of the heterofunctionalized allenes

The relative reactivities of methoxy-, 4-methylphenylthio- and 4-methoxyphenylallene can be assessed directly from their rate constants. For the less reactive substituted allenes phenyl-, chloro- and cyanoallene, whose rate constants for reaction with BTA could not be conveniently measured by the NMR techniques used for the rate measurements with the more reactive substituted allenes, an attempt was made to measure relative reactivities by competitive reaction techniques; however, the NMR spectra of the resulting reaction mixtures were very complex, indicating that cross-cyclodimerization had occurred in addition to the desired cycloaddition with BTA (self-cyclodimerization appears not to have occurred by comparison of the NMR spectra of the reaction mixtures with those of the known cyclodimers).[6] From the quantitative and qualitative observations, the relative reactivity sequence can be assigned as 4-methylphenylthio- ~ methoxy- > 4-methylphenyl- > phenyl- > chloro- > cyanoallene.

One of the objectives of this study was to gain an understanding of the factors that control the relative reactivity and the regioselectivity in diradical intermediate formation. In a related study, the orbital energies and coefficients of the HOMOs and LUMOs of a number of substituted allenes were calculated for appropriate models of methoxy- and ArS-substituted allenes, and for chloro- and cyanoallene[7] (no good simple model for phenylallene was found from the results of these calculations).[7] The calculated values for the energies and the coefficients of the HOMOs and LUMOs in the substituted allenes used in this study are given in Table 5.

It must be noted that in chloro- and cyanoallene the largest coefficient in both the HOMO and the LUMO resides on C-1, whereas in the other heterosubstituted allenes the largest coefficients in the HOMOs and LUMOs reside on C-2. The results of these calculations suggest that if the regioselectivity of diradical intermediate formation were controlled by FMO interactions, C—C bond formation at C-1 should have been observed with chloro- and cyanoallene. In all cases C—C bond formation has occurred at C-2 of the heterofunctionalized allenes (it is possible that C—C bond formation at C-1 is kinetically faster and is reversible, thus not resulting in observable cycloadduct formation; however, this does not seem reasonable in the light of all of the results of our previous studies). A similar observation has been made in the free-radical, chain addition of benzenethiol to the same heterosubstitued allenes, i.e. the benzenethiyl radical attacks exclusively at C-2 of the substituted allenes.[7] These observations were interpreted in terms of thermodynamic, and not kinetic, control of intermediate formation, the more thermodynamically stable substituted allyl radicals being formed as intermediates instead of the corresponding substituted vinyl radicals which would be predicted to be formed from chloro- and cyanoallene under FMO control.[7] This also appears to

Table 5. HOMO and LUMO energies and coefficients[a] for heterofunctionalized allenes and SOMO coefficients for heterofunctionalized allyl radicals[b]

Heterofunctionalized allenes				
Substituent	E_{HOMO} (eV)	E_{LUMO} (eV)	C-1	C-2
OH	−9·261	+5·409	0·492	0·542
			0·831	0·721
SH	−8·909	+4·877	0·369	0·428
			0·818	0·721
Cl	−10·156	+3·176	0·475	0·466
			0·801	0·766
CN	−10·555	+2·963	0·522	0·440
			0·561	0·748

Heterofunctionalized allyl radicals[c]		
Substituent	C-1	C-3
OH	−0·703	+0·575
SH	−0·607	+0·440
Cl	−0·642	+0·578
CN	−0·601	+0·636

[a] Upper coefficients are of the HOMO and the lower coefficients are of the LUMO.
[b] Taken from Ref. 7.
[c] The substituted allyl radicals having *syn* stereochemistry.

be the case in the formation of the diradical intermediates in the cycloaddition reactions of the heterofunctionalized allenes with BTA described in this study.

Although the regioselectivity of diradical intermediate formation is not FMO controlled, the relative reactivity sequence reflects orbital energy FMO control. There is a reasonable correspondence of the relative reactivity with the energy of the HOMO of the heterofunctionalized allene, the reactivity decreasing with the lowering in the energy of the HOMO (initially one might have argued that the energies of the LUMOs show a better correlation with the relative reactivities of the substituted allenes; however, if this were the case the reactivity sequence would be reversed). Thus, the relative reactivity sequence of the heterofunctionalized allenes toward diradical intermediate formation with BTA appears to be allene-HOMO, BTA-LUMO controlled, but the regioselectivity of attack is thermodynamically controlled (this is consistent with prior suggestions in the literature for reactions involving free-radical addition to substituted ethenes,[8] and the results of theoretical calculations in the authors' laboratories on 1,1-disubstituted ethenes and comparison with their relative reactivities toward alkyl free-radical addition[9]). This suggests that the transition state for diradical intermediate formation is sufficiently well developed that thermodynamic and kinetic control both play important roles in determining the relative reactivity and regioselectivity of attack. This is reasonable considering the overall thermodynamics of the diradical intermediate-forming process.

The formation of the diradical intermediates appears to occur irreversibly, as evidenced by the observation that in the studies on the equilibration of the cycloadducts derived from 4-methylphenylthioallene carried out in the presence of the equally reactive methoxyallene, no cycloadducts of methoxyallene could be detected at the end of the equilibration reaction. The lack of reversibility in diradical intermediate formation is attributed to the high degree of stability afforded the radical center by the cyano and *tert*-butylthio groups in the akyl radical portion of the intermediates, and the high positive heat of formation of the central allene carbon (34 kcal mol^{-1})[10] which is lost during diradical intermediate formation.

Regioselectivity of ring closure of the diradical intermediates

The stacked-plot output of the NMR spectra in Figure 1 shows some very interesting changes in the relative amounts of the three cycloadducts **7**–**9** during the course of the reaction. Initially, **8** and **9** are the predominant cycloadducts formed. However, during the course of the reaction **8** rapidly undergoes isomerization to predominantly **9**, which is the more thermodynamically stable of the two. With longer reaction times **8** disappears and **9** undergoes a slow isomerization to the most thermodynamically stable cycloadduct **7**. This is demonstrated even more clearly when the pure cycloadducts are heated. When a mixture of **7** and **8** is heated at 120 °C in toluene-d_8 there is a fairly rapid disappearance of **8** with a concomitant increase in **9**, which is then followed by a decrease in both the relative concentrations of **8** and **9** relative to **7** (see Table 4). After heating at 160 °C for several hours only **7** remained. Similarly, when the mixture of **7** and **9** was heated there was a small initial formation of **8** followed by the disappearance of both **8** and **9** with only **7** being present at the end of the reaction. These data indicate that **8** and **9** are the kinetically favored products, and that **7** is the thermodynamically favored product. Similar results were observed in the stacked-plot output of the NMR spectra obtained during the cycloaddition reactions of 4-methylphenylthio- and 4-methoxyphenylallene with BTA.

These observations are fully consistent with the results of the theoretical calculations carried out on the heterofunctionalized allyl radicals[7] and the corresponding 1- and 3-substituted propenes.[7] The results of the calculations on the substituted allyl radicals indicate that the largest coefficient in the SOMO appears at the heterofunctionalized carbon atom, except in the 1-cyanoallyl radical in which the largest coefficient is at C-3, thus predicting that in an FMO-controlled ring closure, ring closure should preferentially occur at C-1. This is what is observed in the ring-closure reactions of the diradical intermediates formed in the cycloaddition reactions of methoxy-, 4-methoxyphenyl- and 4-methylphenylthioallene with BTA. This is the first instance in which we have observed FMO control in a reaction of a heterofunctionalized allyl radical intermediate.

The results of the calculations on the 1- and 3-substituted propenes indicate that the 1-substituted propenes are lower in energy than the corresponding 3-substituted propenes.[7] The isomerization of the 3-substituted propenes **8** and **9** to the 1-substituted propene **7** is consistent with a thermodynamically driven process. Similar behavior is observed with the cycloadducts derived from 4-methylphenylthio- and 4-methoxyphenylallene with BTA. The lack of observation of such isomerization reactions of the cycloadducts derived from phenyl-, chloro- and cyanoallene with BTA precludes the drawing of any conclusions pertaining to kinetic versus thermodynamic preferences in the ring closure of the diradical intermediates formed in those cycloaddition reactions.

Analysis of the activation parameters

One of the objectives of this study was to determine the activation parameters for diradical intermediate formation for comparison with the activation parameters

of a concerted [4 + 2] cycloaddition process. Of particular interest was the effect of a concerted cycloaddition process versus a two-step, non-concerted process on the E_a and the $\Delta S^{\ddagger}$ values for the two different types of processes. One might have expected that in concerted processes the E_a values would be smaller because of the formation of two bonds versus one bond in the transition state, and that the $\Delta S^{\ddagger}$ values for the concerted processes might be more negative because of the greater restrictions in motion of the reactants in approaching the transition state versus that for the non-concerted processes.

The E_a values measured in this study for the [2 + 2] cycloaddition of the heterofunctionalized allenes (13·4–16·1 kcal mol^{-1}) with BTA are slightly less than those measured for the gas-phase concerted cycloaddition reactions [it might be argued that a comparison between the results of the gas-phase studies cannot be compared with the results of the solution-phase studies described in this paper; it must be pointed out that a highly non-polar solvent (toluene-d_8) was used as a solvent and low concentrations of the reactants were used]. The activation parameters have been measured for the gas-phase [4 + 2] cycloaddition reactions of acrolein with cyclopentadiene (E_a = 15·2 kcal mol^{-1}, log A = 6·2), butadiene (E_a = 19·7 kcal mol^{-1}, log A = 6·2) and isoprene (E_a = 18·7 kcal mol^{-1}, log A = 6·0).[11] One wonders how this can be, in view of the fact that in the concerted [4 + 2] processes two σ bonds are being formed with the loss of two π bonds, whereas in the two-step, diradical intermediate [2 + 2] cycloaddition reactions of the substituted allenes only one σ bond is being formed with the loss of two π bonds. However, in the diradical intermediate formation process with a substituted allene, the very positive heat of formation of the allenic carbon atom (+34 kcal mol^{-1})[10] is reduced to *ca* +10 kcal mol^{-1} for the vinyl carbon atom that is formed in the process, and a resonance-stabilized substituted allyl radical-containing intermediate is formed which must offset the energy gained by the formation of the second bond in the concerted process.

The similarity of the $\Delta S^{\ddagger}$ values for the [4 + 2] concerted and the two-step, diradical intermediate [2 + 2] cycloaddition processes with substituted allenes also seems unusual. However, recent molecular modelling calculations on the conformations of the approach of 1,3-dimethylallene to the 1,2-disubstituted radicophiles *N*-phenylmaleimide and dimethyl fumarate,[12] the monosubstituted radicophiles acrylonitrile and methyl acrylate[13] and the 1,1-diubstituted radicophile 1,1-dichloro-2,2-difluoroethene[4] all proceed via reaction channels of highly constrained conformations of the two reactants in their approach to the activated complexes for diradical intermediate formation. That is, the orientation of the radicophile in space on approaching the allene is restricted, as is also the case in the concerted [4 + 2] processes.

CONCLUSION

The transition states for the formation of diradical intermediates in the [2 + 2] cycloaddition reactions of the heterofunctionalized allenes involved in this study must occur sufficiently late along the reaction coordinate that the regioselectivity of initial bond formation is thermodynamically controlled, yet sufficiently early that the relative reactivity of the heterofunctionalized allenes is FMO HOMO-allene controlled. The kinetically controlled regioselectivity of ring closure of the diradical intermediates is FMO allyl radical SOMO controlled, but the final cycloadduct distributions are thermodynamically controlled.

EXPERIMENTAL

Synthesis of tert-*butylthioacrylonitrile (BTA).*[14] Sodium methoxide (0·4 g), 2-methyl-2-propanethiol (14·2 ml) and 2-chloroacrylonitrile (10 ml) were placed in a 50 ml round-bottomed flask and stirred for 6 h at 30 °C. The mixture was transferred into a 250 ml round-bottomed flask containing 17 g of potassium bromide in 120 ml of dimethylformamide. The reaction mixture was stirred overnight at room temperature. After continuing stirring for a further 4 h at 100 °C, the reaction was worked up by diluting the reaction mixture with water and extracting with three 20 ml portions of diethyl ether. The ether extract was washed three times with 20 ml of saturated aqueous sodium sulfate and dried over magnesium sulfate. The solvent was removed on a rotary evaporator and the residue was distilled under reduced pressure at 46–47·5 °C (3 mm HG) giving 5·2 g (28·3%) of a colorless liquid. ^{1}H NMR ($CDCl_3$): δ 1·42 (s, 9 H), 6·25 (d, J = 0·27 Hz, 1 H), 6·42 (d, J = 0·27 Hz, 1 H).

Cycloaddition reaction of methoxyallene with BTA. Methoxyallene[15] (66 mg, 0·8 mmol), 150 μl (134 mg, 0·948 mmol) of BTA and 10 mg of hydroquinone in 0·3 ml of toluene-d_8 were placed in an NMR tube. The contents of the tube were triply freeze-degassed, and the tube was sealed under vacuum. The sealed NMR tube was heated at 120 °C for 2 h. The NMR spectrum of the resulting reaction solution indicated the formation of **7**, **8** and **9** in a ratio of 4·03 : 1·00 : 6·77. When the reaction mixture was heated at 160 °C for 30 h, only **7** was present. The volatiles were pumped off from the crude reaction mixture on a vacuum line and the residue was subjected to column chromatography on silica gel. Two fractions were obtained: a mixture of **7** and **8** in 6·4% and 5·5% yields, respectively, and a mixture of **7** and **9** in 10·2% and 30·3% yields, respectively.

7: Colorless liquid. ^{1}H NMR ($CDCl_3$): δ 5·91 (m, J_{ave} = 2·3 Hz, 1 H), 3·6 (s, 3 H), 3·52 (dddd, J = 15·85, 3·11, 0·89, 2·36 Hz, 1 H), 3·43 (dddd, J = 15·05, 3·18, 0·91, 1·91 Hz, 1 H), 3·11 (dddd,

$J = 15{\cdot}86$, 3·32, 0·48, 2·50 Hz, 1 H), 3·05 (dddd, $J = 15{\cdot}05$, 3·20, 0·48, 2·28 Hz, 1 H), 1·48 (s, 9 H). EI-MS (on mixture of **7** and **8**): no parent ion observed, major fragment ions at m/z 155(100), 124(26·2) and 57(100). CI-MS (isobutane): m/z 268 ($M^{+\cdot} + 57$, 21·0), 212 ($M^{+\cdot} + 1$, 100).

8: Colorless liquid. ^{1}H NMR ($DCCl_3$): δ 5·30 (dddd, $J = 0{\cdot}95$, 2·34, 2·30, 2·91, Hz, 1 H), 5·09 (dddd, $J = 0{\cdot}95$, 2·51, 2·50, 1·80 Hz, 1 H), 4·77 (m, $J_{ave} = 2{\cdot}56$ Hz, 1 H), 3·54 (s, 3 H), 3·20 (dddd, $J = 15{\cdot}73$, 2·88, 2·35, 0·28 Hz, 1 H), 3·03 (overlapping with vinyl isomer, $J = 15{\cdot}76$ Hz, 1 H), 1·47(s, 9 H).

9: Colorless liquid. ^{1}H NMR ($CDCl_3$): δ 5·24 (dddd, $J = 0{\cdot}88$, 2·27, 2·28, 2·86 Hz, 1 H), 5·05 (dddd, $J = 0{\cdot}90$, 1·92, 2·63, 2·53 Hz, 1 H), 4·31 (dddd, $J = 0{\cdot}5$, 2·1, 1·67 Hz, 1 H), 3·54 (s, 3 H), 3·27 (dddd, $J = 15{\cdot}47$, 1·91, 2·34, 2·59 Hz, 1 H), 2·78 (dddd, $J = 15{\cdot}46$, 0·60, 2·76, 2·76 Hz, 1 H), 1·47 (s, 9 H).

Cycloaddition reaction of 4-methylphenylthioallene with BTA. 4-Methylphenylthioallene[6] (154 mg, 0·948 mmol) of was reacted with BTA (0·948 mmol) as described above at 120 °C for 2 h. The NMR spectrum of the reaction mixture showed the presence of only the three cycloadducts **14**, **15** and **16** in a ratio of 8·0:4·2:1·0. The volatiles were removed on a vacuum line and the residue was subjected to chromatographic separation on silica gel giving mixtures of **14** and **15** (3·3% and 5·1%) and **14** and **16** (51·2% and 28·1%). When the reaction was carried out at 160 °C for 30 h, only **14** was present in the reaction solution.

14: Yellow liquid. ^{1}H NMR (from the mixtures of **14** and **15** and of **14** and **16**) ($CDCl_3$): δ 7·46–7·13 (m, 4 H), 6·07 (m, $J_{ave} = 2{\cdot}26$ Hz, 1 H), 3·58 (dddd, $J = 16{\cdot}31$, 3·33, 1·61, 1·68 Hz, 1 H), 3·54 (dddd, $J = 16{\cdot}97$, 1·68, 2·38, 3·43 Hz, 1 H), 3·19 (ddd, $J = 16{\cdot}35$, 2·31, 3·01 Hz, 1 H), 3·13 (ddd, $J = 16{\cdot}97$, 3·17, 2·92 Hz, 1 H), 2·33 (s, 3 H), 1·49 (s, 9 H). HR EI-MS (on mixture of **14** and **15**): calculated for $C_{17}H_{21}NS_2$, 303·1115; found, 303·1120.

15: Yellow liquid. ^{1}H NMR (from mixture of **14** and **15**) ($CDCl_3$): δ 7·15 (m, 4 H), 5·29 (m, $J = 2{\cdot}72$, 2·43, 2·60 Hz, 1 H), 5·14 (m, $J = 2{\cdot}11$, 2·5 Hz, 1 H), 4·97 (dddd, $J = 2{\cdot}72$, 2·87, 3·26 Hz, 1 H), 3·55 (m, $J = 2{\cdot}11$, 2·43 Hz, 1 H), 3·24 (dddd, $J = 2{\cdot}49$; 2·5, 1·88, 2·36 Hz, 1 H), 2·33 (s, 3 H), 1·56 (s, 9 H).

16: Yellow liquid. ^{1}H NMR (from mixture of **14** and **16**) ($CDCl_3$: δ 7·15–7·46 (m, 4 H), 5·31 (ddd, $J = 1{\cdot}26$, 2·55, 5·09 Hz, 1 H), 5·14 (ddd, $J = 2{\cdot}66$, 2·71 Hz, 1 H), 4·42 (q, $J = 2{\cdot}70$ Hz, 1 H), 3·49 (ddd, $J = 15{\cdot}62$, 2·5, 4·75 Hz, 1 H), 3·07 (dt, $J = 13{\cdot}41$, 2·67 Hz, 1 H), 2·34 (s, 3 H), 1·44 (s, 9 H). HR EI-MS (from mixture of **14** and **16**): calculated for $C_{17}H_{21}NS_2$, 303·1115; found, 303·1114.

Synthesis of 4-methoxyphenylallene. To 4-methoxyphenylmagnesium bromide, prepared from 4-methoxyphenyl bromide (0·083 mol) and magnesium chips (4 g, 0·17 mol) in 25 ml of diethyl ether in a 100 ml round-bottomed flask, was added 0·24 g of copper (I) bromide followed by 3·29 g (0·047 mol) of methyl propargyl ether in 20 ml of diethyl ether. The reaction mixture was stirred for 20 min at 5–15 °C. The reaction was worked up by the slow addition of an aqueous solution of 0·75 g of potassium cyanide and 7·5 g of ammonium chloride in 25 ml of water with vigorous stirring. The ether layer was removed and the aqueous layer was extracted three times with 20 ml of diethyl ether. The combined ether solution was dried ($MgSO_4$) and the ether was removed on a rotary evaporator. The residue was distilled (b.p. 71–75 °C/1·3 mm Hg) giving a colorless liquid. ^{1}H NMR ($CDCl_3$): δ 3·68 (s, 3 H), 5·02 (d, $J = 6{\cdot}81$ Hz, 2 H), 6·02 (t, $J = 6{\cdot}81$ Hz, 1 H) and 6·76 and 7·12 (AA'XX' ms, 2 H each). HR EI-MS: calculated for $C_{10}H_{10}O$, 146·0732; found, 146·0729.

Cycloaddition reaction of 4-methoxyphenylallene with BTA. 4-Methoxyphenylallene (70 mg, 0·48 mmol), 0·948 mmol of BTA and 10 mg of hydroquinone in 0·3 ml of toluene-d_8 in a sealed NMR tube were heated at 100 °C for 2 h. The NMR spectrum of the reaction mixture showed the presence of only the three cycloadducts **17**, **18** and **19** in a ratio of 1·00:1·16:0·48. Attempted chromatographic separation of the mixture of cycloadducts on silica gel resulted in only the isolation of a mixture of the three cycloadducts.

19: Colorless liquid. ^{1}H NMR (from mixture of the three cycloadducts) ($CDCl_3$): δ 6·82–7·03 (m, 4 H), 6·16 (quintet, $J_{ave} = 2{\cdot}40$ Hz, 1 H), 3·64 (m, 1 H), 3·58 (m, 1 H), 3·39 (ddd, $J = 3{\cdot}08$, 3·08, 16·54 Hz, 1 H), 3·23 (ddd, $J = 16{\cdot}36$, 2·65, 3·01 Hz, 1 H), 3·76 (s, 3 H), 1·46 (s, 9 H). EI-MS: no parent ion could be detected. HR CI-MS (ammonia): calculated for $C_{17}H_{21}NOS$, 287·1344; found, 287·1346.

18: ^{1}H NMR ($CDCl_3$): δ 6·88–7·32 (m, 4 H), 5·15 (dddd, $J = 0{\cdot}82$, 2·59, 1·88, 2·64 Hz, 1 H), 5·02 (m), 4·84 (m), 3·78 (s, 3 H), 1·30 (s, 9 H).

19: ^{1}H NMR ($CDCl_3$): δ 6·88–7·32 (m, 4 H), 5·10 (dddd, $J = 0{\cdot}82$, 2·56, 1·86, 2·73 Hz, 1 H), 4·95 (dq, $J = 0{\cdot}84$, 2·65 Hz, 1 H), 4·29 (quintet, $J_{ave} = 2{\cdot}84$ Hz, 1 H), 3·15–3·48 (s, 3 H), 3·45 (ddd, $J = 2{\cdot}13$, 15·57, 2·67 Hz, 1 H), 3·15 (ddd, $J = 1{\cdot}14$, 15·68, 2·42 Hz, 1 H), 1·40 (s, 9 H).

Cycloaddition reaction of phenylallene with BTA. Phenylallene[15] (87 mg, 0·75 mmol) and 0·948 mmol of BTA were initially heated at 100 °C for 2 h, then at 120 °C for 2 h, and finally at 160 °C for 4 h, whereupon the reaction had gone to completion. The NMR spectrum of the reaction solution indicated the formation of only the two cycloadducts **20** and **22**. Pure **20** was iso-

lated by column chromatography on silica gel in 14·6% yield. A mixture of **20** and **22** was also obtained (24·17% and 9·86% yield, respectively). When the reaction was carried out at 160 °C for 30 h, only **20** was present.

20: ^{1}H NMR ($CDCl_3$): δ 7·14–7·32 (m, 5 H), 6·27 (m, J_{ave} = 2·22 Hz, 1 H), 3·84 (dm, J = 16·55 Hz, 1 H), 3·66 (ddddd, J = 16·37, 3·23, 1·66, 1·72, 2·37 Hz, 1 H), 3·46 (ddd, J = 16·61, 3·0, 3·03 Hz, 1 H), 3·29 (ddd, J = 16·33, 2·79, 2·79 Hz, 1 H), 1·52 (s, 9 H): HR EI-MS: calculated for $C_{16}H_{19}NS$, 257·1238; found, 257·1237.

22: Colorless liquid. ^{1}H NMR (from mixture of **20** and **22**) ($CDCl_3$): δ 7·23–7·42 (m, 5 H), 5·17 (dddd, J = 0·86, 2·58, 1·93, 2·71 Hz, 1 H), 5·02 (dddd, J = 0·85, 2·14, 2·35, 3·03 Hz, 1 H), 4·39 (m, J =), 3·52, (dddd, J = 15·81, 1·73, 2·58, 3·09 Hz, 1 H), 3·29 (dddd, J = 15·65, 1·19, 2·55, 3·05 Hz, 1 H), 1·45 (s, 9 H).

Cycloaddition reaction of chloroallene with BTA. Chloroallene[16] (62 mg, 0·87 mmol) and BTA were heated at 100 °C for 2 h. Analysis by NMR spectroscopy indicated that no rection had occurred. After further heating at 120 °C for 2 h and then finally at 160 °C for 4 h, the NMR spectrum of the reaction solution indicated the formation of only **23** and **25** in a ratio of 3·08 : 1·00. Pure **23** (6·05%) and a mixture of **23** and **25** (32·5% and 15·19%, respectively) were isolated by column chromatography on silica gel.

23: Colorless liquid. ^{1}H NMR ($CDCl_3$): δ 5·94 (m, J_{ave} = 2·51, Hz, 1 H), 3·49–3·58 (m, 2 H), 3·10 (ddd, J = 17·3, 3·20, 3·26 Hz, 1 H), 3·09 (ddd, J = 16·2, 2·95, 2·96 Hz, 1 H), 1·49 (s, 9 H). EI-MS: no parent ion was detected. CI-MS (isobutane): m/z 272 ($M^{+\cdot}$ + 57, 27), 216 ($M^{+\cdot}$ + 1, 100), 189 (63·9).

25: Colorless liquid. ^{1}H NMR (from mixture of **23** and **25**) ($CDCl_3$): δ 5·34 (dddd, J = 1·64, 2·45 2·64, 3·26 Hz, 1 H), 5·18 (dddd, J = 1·66, 2·55, 2·35, 2·36 Hz, 1 H), 4·87 (ddd, J = 0·51, 2·62, 4·91 Hz, 1 H), 3·46 (dddd, J = 15·79, 2·57, 2·08, 2·69 Hz, 1 H), 2·97 (dddd, J = 15·79, 0·52, 2·65, 2·71 Hz, 1 H), 1·51(s, 9 H).

Cycloaddition reaction of cyanoallene with BTA. Cyanoallene[17] (43 mg, 0·69 mmol) was reacted with 0·948 mmol of BTA at 100 °C for 2 h. The NMR spectrum of the reaction solution indicated that no reaction had occurred. After being heated at 120 °C and finally at 160 °C for 4 h, the NMR spectrum of the reaction solution indicated the formation of only one cycloadduct, **26**.

26: ^{1}H NMR ($CDCl_3$): δ 5·34 (quintet, J_{ave} = 2·48 Hz, 1 H), 3·77 (dddd, J = 17·86, 3·46, 2·55, 2·47 Hz, 1 H), 3·66 (dddd, J = 17·76, 3·52, 2·19, 2·12 Hz, 1 H), 3·35 (dddd, J = 17·87, 3·47, 0·73, 2·86 Hz, 1 H), 3·24 (dddd, J = 17·76, 3·38, 0·76, 2·40 Hz, 1 H), 1·46 (s, 9 H). HR EI-MS: calculated for $C_{11}H_{14}N_2S$, 206·0878; found, 206·0876.

Kinetic study. BTA (0·948 mmol), 1 molar equivalent of the allene, 10 mg of hydroquinone, an internal standard (anisole or dibenzyl ether, for NMR integration purposes) and 0·3 ml of bromobenzene-d_5 were placed in an NMR tube. The contents of the tube were triply freeze-degassed (liquid nitrogen) and the tube was sealed under vacuum. The NMR tube was placed in the NMR spectrometer, which had been allowed to equilibrate at the desired temperature. After a short delay to allow temperature equilibration of the sample, the NMR spectrum of the reaction mixture was periodically recorded using a 1 PULSE KINETICS EXPERIMENT program. The NMR spectra were integrated and the concentrations of the reactants were calculated. The estimated uncertainty in temperature is ±0·5 °C.

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