Rates and products from thermolysis of 5-azidoisoxazoles in solution

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Thermolysis in solution of 5-azidoisoxazoles with formyl, acetyl or *N*-phenylimino in the 4-position led to the formation of bicyclic products; in the absence of such 4-substituents, ring-opening resulted and in two instances the expected nitrosoalkene intermediate was successfully trapped with 2,3-dimethylbuta-1,3-diene.

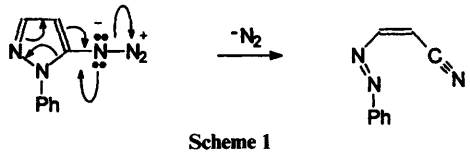
Rate measurements indicate that there are small neighbouring group effects exerted by those 4-substituents which lead to cyclization, and it is argued that these effects are necessarily small in these 5-azidoisoxazoles. Nevertheless, these small effects appear to play a key role in directing the reaction towards cyclization instead of ring-opening.

With ring substituents which cannot exert neighbouring group effects, electron-withdrawing groups at position 4 reduce the reaction rate, while electron-donating groups increase it. Substituents at position 3 have little effect on rate. These results are interpreted in terms of a nitrene-like transition state which is substantially stabilized by electron release from the heteroaromatic ring.

Introduction

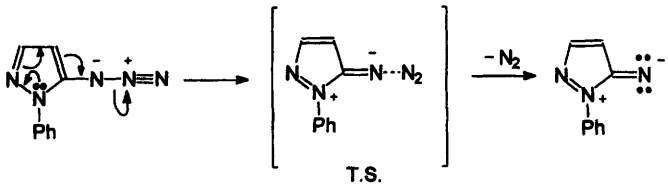
Recently, we reported the rates and products from thermolysis of 5-azidopyrazoles in solution.[1] The rates were strikingly different from those reported in the extensive literature[2,3] on azidobenzenes, in two respects. First, a typical 5-azidopyrazole, the 1-phenyl-3-methyl derivative, reacted 3655 times as fast at 80 °C as does azidobenzene. Secondly, the large neighbouring group effect (1060-fold)[4] exerted by the nitro substituent on the azidobenzene thermolysis could not be detected in the corresponding 5-azido-4-nitropyrazole.

The very high thermolysis rates for α-azides of the five-membered heterocycles have become well known in recent years.[1,5,6] One explanation with wide currency is that ring-opening is concerted with nitrogen loss (Scheme 1), so that the high-energy nitrene species is not actually formed.



Scheme 1

All the 5-azidopyrazoles we studied did ring-open, but we pointed out[1] that this might occur after the rate-determining step had produced a nitrene. We advanced an alternative explanation of the very high reaction rates, in which the transition state is substantially stabilized by internal electrostatic attraction (Scheme 2).



Scheme 2

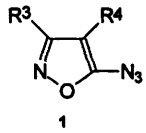
We also noted that 4-substituents in the pyrazole ring exerted appreciable effects on the thermolysis rates, the increases being in the order CH=N–NHPh ≅ CH=CHCO$_2$Et > Ph > CH=NPh > H > CHO ≅ CN > NO$_2$. We deferred an explanation of this order until further information had been obtained.

We now report studies of both rates and products of the thermolyses of 5-azidoisoxazoles. There are significant differences in their behaviour from that of the 5-azidopyrazoles. Taken together, the two sets of data have allowed us to identify some of the factors which determine the rates and products found in these thermal decompositions.

Results and discussion

Products

Anderson and Muchmore[7] have very recently reported that the 5-azidoisoxazole-4-carbaldehyde **1a** cyclized on thermolysis to yield the isoxazolo[5,4-*c*]isoxazole **2a**. We confirm this cyclization to form a second isoxazole ring (see structures **2a–c**) with all our 5-azidoisoxazole-4-carbaldehydes (**1a–c**), and have also isolated a corresponding isoxazolo[5,4-*c*]isoxazole, **2d**, from the thermolysis of the 4-acetylazide **1d**.



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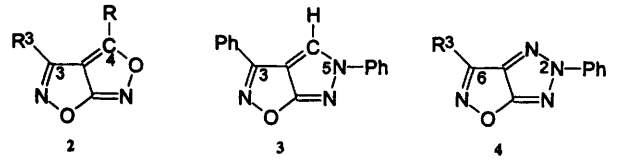
	R^3	R^4		R^3	R^4
a:	Ph	CHO	**h:**	Me	H
b:	Bu^t	CHO	**i:**	Me	Me
c:	CO_2Et	CHO	**j:**	Ph	H
d:	Ph	COMe	**k:**	H	Ph
e:	Ph	CH=NPh	**l:**	H	*p*-MeOC$_6$H$_4$
f:	Me	N=NPh	**m:**	Ph	CN
g:	Ph	N=NPh	**n:**	Me	NO_2

Similarly, the 4-(*N*-phenyliminomethyl)azide **1e** thermolysed in solution to yield the pyrazolo[4,3-*d*]isoxazole **3**. The 5-azidoisoxazoles with 4-phenylazo substituents (**1f,g**) proved to be too unstable to isolate, the products actually obtained being the corresponding phenyltriazolo[4,5-*d*]isoxazoles **4a** and **4b**.

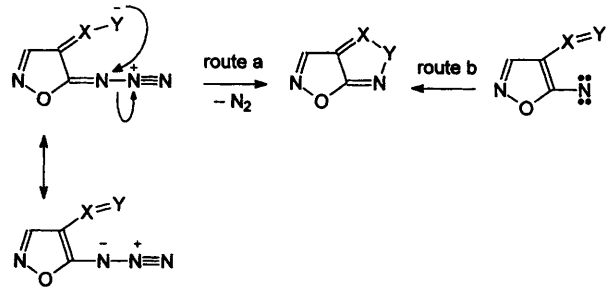
The pathway to these cyclized products can be formulated as



	R^3	R
a:	Ph	H
b:	Bu^t	H
c:	CO_2Et	H
d:	Ph	Me

	R^3
a:	Me
b:	Ph

either a π-electron reorganization implying neighbouring group participation (Scheme 3, route a) or as an internal capture of a nitrene (Scheme 3, route b). Anderson and Muchmore[7]

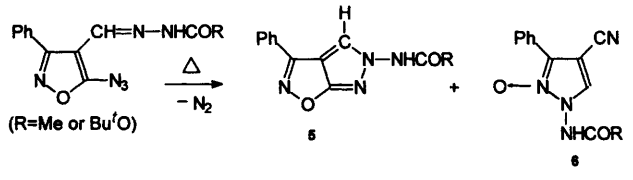


Scheme 3

favoured route b for their cyclizations of this type, which they found to occur not only with the 4-carbaldehyde **1a** but also with some of its oxime and hydrazone derivatives.

These alternative routes can be distinguished in terms of reaction rates, which we shall discuss shortly. For the moment, we wish to emphasize that none of the 5-azidoisoxazole thermolyses we have discussed up to this point has involved the ring-opening reaction analogous to Scheme 1. These results are in sharp contrast with those we obtained with 5-azidopyrazoles,[1] where ring-opening was the invariable result even in the presence of such 4-substituents as formyl, *N*-phenyliminomethyl and nitro.

Nevertheless, with certain 4-substituents in 5-azidoisoxazoles, the pyrolyses do lead to products *via* ring-opening. Anderson and Muchmore have isolated the pyrazole **6** as well as the cyclized product **5** (see Scheme 4) and have other such examples



Scheme 4

from 5-azido-4-oximoisoxazoles. The product **6** is clearly derived *via* the ring-opened nitrosoalkene and, since **5** and **6** did not interconvert thermally, they must arise by separate pathways.

With our present selection of 5-azidoisoxazoles (**1a–n**), ring-opening seems likely to occur when there is no 4-substituent, or if the 4-substituent is methyl, aryl or cyano. In the cases of the 4-substituent being hydrogen, phenyl or *p*-anisyl, a new cyano group could be detected in the infrared spectrum near 2220 cm^{-1} as the thermolysis progressed. Trapping experiments, using 2,3-dimethylbuta-1,3-diene, were performed with both 5-azido-3-phenylisoxazole (**1j**) and 5-azido-4-phenylisoxazole (**1k**) and oxazines **7a** and **7b** respectively were isolated. The structures of

Table 1 Neighbouring group effects of 4-substituents on rates of thermolysis of 5-azidoisoxazole in *p*-xylene solution at 80 °C

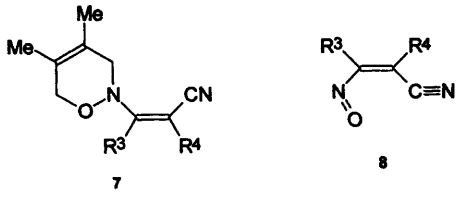
R^3	R^4	$k_1/10^{-5}$ s^{-1}	k_{rel}	Hammett[a] σ_p^-
Ph	H	4.33	1	0
	CN	0.855[b]	0.20	0.88
	CHO	8.53[c]	1.97	1.03
	COMe	20.8	4.79	0.84
	CH=NPh	83.0[c]	19.2	0.54
Me	H	3.84[c]	1	0
	NO_2	2.29	0.60	1.24

[a] Values of σ_p^- are taken from ref. 13. [b] Obtained from extrapolation of data obtained at higher temperatures (see Table 3). [c] Average value from duplicate or triplicate runs (see Table 3).

Table 2 General substituent effects on rates of thermolysis of 5-azidoisoxazoles in *p*-xylene at 80 °C

R^3	R^4	$k_1/10^{-5}$ s^{-1}
Me	H	3.84
Ph	H	4.33
Me	Me	48.6
H	Ph	69.8
H	*p*-Anisyl	174
Ph	CHO	8.53
Bu^t	CHO	9.30
CO_2Et	CHO	5.19

these adducts clearly identify the corresponding nitrosoalkenes **8a** and **8b** as the intermediates.



	R^3	R^4
a:	Ph	H
b:	H	Ph

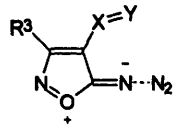
There are two possible routes for the thermolyses of 5-azidoisoxazoles to follow. We now look at the reaction rates for information on what determines whether ring-opening will occur.

Reaction rates

The rate constants for thermolysis of the azides in *p*-xylene solution at 80 °C are presented in Tables 1 and 2. The substituents at the 3-position had little effect on rate and will be discussed later. On the other hand, there is an 88-fold range of rates for the various 4-substitutions.

The influence of 4-substituents. Many of our azidoisoxazoles have thermolysed to produce a new fused ring (see Scheme 3) and it is unlikely in these cases that the transition state has any significant features of the ring-opened nitrosoalkene (*e.g.* **8**). In our view, the transition state leading to cyclized products can be stabilized by two possible factors, and the sum of these stabilizations will determine the reaction rate.

The first of these factors is conjugative stabilization of a nitrene intermediate (see structure **9**). We have recently suggested[1] that this stabilization is very large. Secondly, there is neighbouring group participation, for which the electron distribution shown in **10** has been proposed.[8] Many of our 4-substituents (formyl, acetyl, nitro and phenyliminomethyl)



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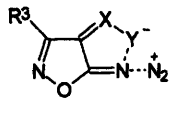
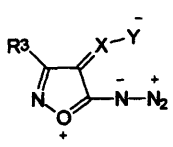


10

are known to act as neighbouring groups in thermolyses of azidobenzenes.[2]

This model (**10**) of the neighbouring group effect (see also Scheme 3) involves bonding from the negatively charged terminal atom of the 4-substituent to the inner azido nitrogen. The latter should not therefore itself carry negative charge if this bond donation from the neighbouring group is to be effective. Assuming that this model for transition state stabilization is correct, then the stabilization provided in **9** is not compatible with neighbouring group participation. It follows that if stabilization by conjugation is high, the neighbouring group effect must be small or even negligible. The neighbouring group effect is further disadvantaged by the presence of the 3-substituent. It is well documented[2,9,10] for azidobenzenes that the rate enhancement provided by a neighbouring group is considerably reduced if a flanking substituent forces it out of the ring plane. This type of inhibition of conjugation has been demonstrated by infrared spectroscopy for the nitro group in 3,5-dimethyl-4-nitroisoxazole.[11]

In the five-membered ring, the wider angles will result in smaller steric effects than in substituted benzenes. Thus, a significant degree of conjugation by the 4-substituents in our 3-substituted-5-azidoisoxazoles will remain, and those of –R type must reduce the transition state stability. Their conjugation with the ring oxygen atom (canonical structure **11**) reduces the ability of this atom to produce the stabilization depicted in **9**, and at the same time reduces the contribution by **10**.



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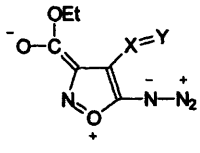

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Conjugative effects at the 4-position of isoxazole are known to be very large in the absence of steric effects.[12] In principle, an –R type 3-substituent (*e.g.* ethoxycarbonyl) could also destabilize the transition state (see structure **12**) but since conjugative effects at the 3-position are reckoned to be small,[11,12] this destabilization is perhaps less significant than the others we have discussed.

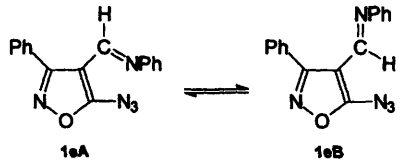
The experimentally determined effects on thermolysis rate of –R type 4-substituents are gathered together in Table 1. With 5-azido-4-cyano-3-phenylisoxazole we see the adverse electronic effect of the cyano group: this compound thermolyses five times more slowly than 5-azido-3-phenylisoxazole. The cyano group, being linear, is unable to bond to the nitrenoid centre and the contribution from **10** is therefore negligible.

This same adverse electronic effect must also operate when the 4-substituent is formyl, acetyl or phenyliminomethyl. Nevertheless, these azides all thermolyse faster than 5-azido-3-phenylisoxazole. These rate increases we ascribe to a neighbouring group effect: there has been enough stabilization provided by direct bonding to the reaction centre (as in structure **10**) to over-compensate for the conjugative destabilization of **9**.

The destabilization of **9** by cooperative conjugation will not be a constant term. If we ignore steric effects, it can be estimated, very approximately, from the Hammett σ_p-values[13] shown in Table 1. Thus, the cyano group provides a fair measure of the effect for acetyl and formyl, but overestimates for phenyliminomethyl and underestimates for nitro. The rate observed with the 4-nitro compound is actually less than that for the azide with no 4-substituent (see last two entries in Table 1), though not by as much as expected. There must be a small neighbouring group effect which partly offsets the adverse conjugative one.

The neighbouring group effects are generally very small, whereas in azidobenzenes the rate enhancements produced by formyl, phenyliminomethyl, acetyl and nitro are 28.8, 60.1, 413 and 1060 respectively.[4] Reasons for the small size of the effects in 5-azidoisoxazoles have already been given above. A direct comparison of the neighbouring group abilities in azidobenzenes and isoxazoles cannot be made with our data, partly because the conjugative destabilization of the isoxazole transition state cannot be quantified, and partly because the 3-substituent in the isoxazoles is exerting a steric effect whose size will depend on the geometry of the 4-substituent. It is not practicable, with existing methodology, to synthesize 5-azidoisoxazoles with –R type substituents in the 4-position and no substituent in the 3-position.

Despite the unfavourable context for neighbouring group participation in the thermolyses of 5-azidoisoxazoles, two of the 4-substituents have exerted appreciable effects. When the 4-phenylazo group was present, the azide decomposed during synthesis at 0 °C. The result is not unexpected, this azo function being more than 30 times better than any other neighbouring group.[4] A more interesting case is provided by phenyliminomethyl, which has assisted the azidoisoxazole thermolysis more than expected from its modest ability in azidobenzene. Part of this rate enhancement in the isoxazole is because this imino group produces much less conjugative destabilization of the transition state than the other neighbouring groups. There may also be a conformational advantage for such an unsymmetrical group (see Scheme 5). Whereas in azidobenzenes the flanking



1eA 1eB

Scheme 5

phenyl group would have twisted the 4-substituent out of the ring plane, in the five-membered ring where steric effects are smaller, the presence of the 3-phenyl group may actually assist the neighbouring group effect by increasing the proportion of the active conformation **1eA** over the unreactive one **1eB**.

We now turn to the 4-substituents which cannot provide neighbouring group assistance. 5-Azido-3,4-dimethylisoxazole and 5-azido-4-phenylisoxazole both have high rates of decomposition. These rates must be due to electronic factors, and not to steric ones, because the *p*-anisyl group is not larger than phenyl but does cause a further 2.49-fold increase in rate (see Table 2). While this electronic effect—known to be large for alkyl and aryl groups at the 4-position[11,12]—may be stabilizing a nitrene-like transition state, it could also be argued that it stabilizes a transition state resembling the ring-opened nitrosoalkene (see **8**). The 4-phenyl compound, like its 3-phenyl isomer, does actually ring-open and we have trapped the nitrosoalkene (see Experimental). The extent to which ring-opening has progressed at the transition state is unknown. While *ab initio* calculations on 5-azidoisoxazole (see below) indicate little ring-opening at that stage, this conclusion may not apply when the ring is heavily substituted.

The influence of 3-substituents. Rate constants have been measured for 5-azidoisoxazole-4-carbaldehydes with phenyl, *tert*-butyl or ethoxycarbonyl in the 3-position (see Table 2). In these sterically congested trisubstituted compounds, the interplay of steric and conjugative factors is probably complex.

Table 3 Rate constants and activation parameters for thermolysis of selected 5-azidoisoxazoles in nitrobenzene and *p*-xylene solution

Substituent in 5-azidoisoxazole	T/°C	$k_1/10^{-5}$ s^{-1}	Arrhenius parameters[a]
3-Me (nitrobenzene)	80.0	3.51, 3.54	E_a 126.8 ± 0.5 kJ mol^{-1}
	90.0	11.2, 11.5	ln$A$ 32.9 ± 1.4 s^{-1}
	100.0	35.4, 35.9	S_a 18.8 ± 1.3 J K^{-1} mol^{-1}
	110.0	101, 105	
3-Me (*p*-xylene)	70.0	1.24	E_a 124.1 ± 1.1 kJ mol^{-1}
	80.0	3.70, 3.98	ln$A$ 32.2 ± 3.2 s^{-1}
	90.0	13.2, 13.6	S_a 12.5 ± 3.1 J K^{-1} mol^{-1}
	100.0	37.3, 38.1	
	110.0	110, 115	
4-Ph (*p*-xylene)	60.0	6.02, 6.08[b]	E_a 118.3 ± 0.6 kJ mol^{-1}
	70.0	20.5, 20.9	ln$A$ 33.0 ± 1.7 s^{-1}
	80.0	68.5, 71.0	S_a 20.0 ± 1.8 J K^{-1} mol^{-1}
	90.0	201, 206	
3-Ph-4-CHO (*p*-xylene)	70.0	2.20, 2.25	E_a 121.6 ± 1.7 kJ mol^{-1}
	80.0	8.61, 8.41, 8.58[c]	ln$A$ 32.0 ± 5.2 s^{-1}
	90.0	24.0, 24.0	S_a 11.3 ± 5.1 J K^{-1} mol^{-1}
	100.0	68.9, 74.6	
3-Ph-4-CH=NPh[d] (*p*-xylene)	50.0	2.55, 2.66	E_a 105.6 ± 1.2 kJ mol^{-1}
	60.0	8.52, 8.80	ln$A$ 28.8 ± 3.4 s^{-1}
	70.0	25.8, 26.1	S_a −14.9 ± 3.7 J K^{-1} mol^{-1}
	80.0	82.4, 83.0, 83.7	
	90.0	186, 189	
3-Ph-4-CN (*p*-xylene)	90.0	3.01, 3.07	E_a 132.7 ± 0.8 kJ mol^{-1}
	100.0	9.32, 9.38	ln$A$ 33.5 ± 2.7 s^{-1}
	110.0	28.9, 29.5	S_a 23.8 ± 2.3 J K^{-1} mol^{-1}
	120.0	84.4, 88.8	

[a] Errors are expressed as 90% confidence levels. The error in S_a is calculated by dividing the error in E_a (in J) by the lowest experimental temperature (in K). [b] In acetonitrile solvent, $k_1 = 6.41 \times 10^{-5}$ s^{-1}. [c] The rate constant evaluated from decay of the carbonyl band was 2.4% higher, which is for practical purposes the same value. [d] This compound had two well-resolved bands in the IR spectrum, at 2134 and 2151 cm^{-1}, and of almost equal intensity. The rate constants given above are from decay of the 2134 cm^{-1} band. In the three runs at 80 °C, rate constants were also evaluated at the other band, and gave values within 0.0, 2.4 and 6.0% of those reported above.

The –R type ethoxycarbonyl group reduces the rate, as expected from our consideration of competing conjugation (see structure **12**). It is not clear whether the small size of the effect is due to steric inhibition, or to the general insensitivity of the 3-position to conjugative effects.[11] *Ab initio* calculations (see below) find no significant changes in charge at this 3-position on going from reactant to transition state.

Arrhenius parameters. One possible explanation for the rather small neighbouring group effects we have observed is that we have chosen a family of azides whose energies and entropies of activation are linearly related, with an isokinetic temperature[14] close to our experimental ones. However, the E_a and S_a values do not stand in a linear relationship to one another (see Table 3).

The phenyliminomethyl group, which is the only moderately effective neighbouring group included in Table 3, has produced the expected low energy of activation and negative entropy of activation. The formyl group, although it does exert a very small neighbouring group effect, has a small positive S_a value, which may indicate that separation of the nitrogen molecule is well advanced at the transition state.

Solvent effects. Comparison of the rates and Arrhenius parameters for thermolysis of 5-azido-3-methylisoxazole in *p*-xylene and nitrobenzene shows that the change from a non-polar to a polar solvent has almost no effect (see Table 3).

A comparison with 5-azidopyrazoles

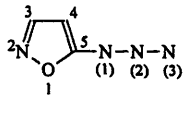
There are now sufficient data available to compare the thermolysis rates and products from 5-azidoisoxazoles and 5-azidopyrazoles. The first-order rate constants, for thermolysis in *p*-xylene solution at 80 °C, of 5-azido-3-methyl-1-phenylpyrazole and 5-azido-3-methylisoxazole, are 16.7×10^{-5} and 3.84×10^{-5} s^{-1} respectively. The difference is not large, but it is in the expected order (N > O) for conjugative release of charge from the ring heteroatom to stabilize the nitrene-like transition state. To accord with our earlier arguments, the 5-azidopyrazoles should show even smaller neighbouring group effects from 4-substituents than do the 5-azidoisoxazoles. We have already reported[1] that there are no discernible neighbouring group effects for the azidopyrazoles. The only effects on rate of 4-substituents in the pyrazole ring are related to their ability to donate or withdraw electron density.

Although the neighbouring group effects of –R type 4-substituents in the 5-azidoisoxazoles are quite small, we suggest that the partial development of the new bond shown in structure **10** plays an important role in steering the transition state to cyclized products such as **2–5**. In the absence of any neighbouring group effect, ring-opening is the inevitable result. The two pathways, of ring-opening and cyclization, must be very finely balanced, to judge by the isolation of both types of products by Anderson and Muchmore[7] (see Scheme 4). These authors believe that 'the formation of the bicyclic structures involves a nitrene' but we take the view that a bridged nitrenoid transition state is involved, even if the degree of bonding from the neighbouring group be weak. Such a transition state would not be expected to pass on to a free nitrene intermediate.

In support of our view, it is to be noted that the introduction of an exceptionally good neighbouring group, phenylazo, at the 4-position of 5-azido-3-methyl-1-phenylpyrazole leads to the ring-closed pyrazolotriazole instead of the ring-opening observed for all other 5-azidopyrazoles.

Ab initio calculations

Our colleagues D. Sengupta and M. T. Nguyen have recently carried out *ab initio* calculations at the 6-31G(d,p)/MP2 = Full level for the thermal decomposition of α-azidoheterocycles. The calculations for 5-azidoisoxazole **13** find that, at the transition



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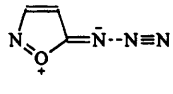

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state, the N-1 to N-2 bond has stretched by 42%, whereas the O-1 to C-5 bond has stretched only 3.7%. These findings are not consistent with the ring-opening mechanism (Scheme 1) and indicate that the transition state is nitrene-like. The calculated atomic charges show a large degree of transfer of charge from O-1 to the azido group on passing from reactant to transition state, and the C-5 to N-1 bond has developed 43% double-bond character. Thus, the canonical structure **14**, which we have implied throughout this paper to represent the π-electron distribution at the transition state, is reasonably realistic, though it does not indicate the electron donation from C-4 which is revealed by the calculations.

Similar conclusions were reached from *ab initio* calculations on eight other five-membered aromatic heterocycles with an α-azido group. These results are consistent with the general mechanism shown in Scheme 2.

Importantly, the *ab initio* calculations show that the point charge at O-1 in **14** remains negative in the transition state despite the charge transfer which has occurred. The point charge also remains negative when nitrogen is present at ring position 1, and only for sulfur is there a positive point charge. The electrostatic stabilization we have previously postulated[1] is, then, not an acceptable explanation for the stability of the transition states in most azidoheterocycle thermolyses. The low energies of these transition states are to be explained in terms of a high level of electron transfer from the heterocyclic ring to the azido nitrogens, so that the incipient nitrene is substantially stabilized.

Experimentally, both in the present work with 5-azidoisoxazoles and our earlier work[1] with 5-azidopyrazoles, we have observed only small effects of substituents at C-3 on the thermolysis rates, but large effects of substituents at C-4. These results are consistent with the *ab initio* calculation of virtually no charge change between reactant and transition state at the 3-position, whereas there are appreciable changes at the 4-position.

Experimental

General

Mps were determined using a Reichert Thermovar apparatus. IR spectra of the products were recorded with a Perkin-Elmer 1620 FT spectrometer, using KBr pellets unless otherwise specified. NMR spectra were measured on a Bruker WM-250 or AMX-400 spectrometer, using $CDCl_3$ solutions unless otherwise stated. *J* Values are quoted in Hz. Low resolution mass spectra were measured with a Hewlett Packard 5989A spectrometer and high resolution ones with a Kratos MS50 TC machine, both operated at 70 eV and in EI mode unless specified otherwise. Chemical ionization (CI) mass spectra used methane as the reagent gas. 5-Amino-3-methylisoxazole and 5-amino-3,4-dimethylisoxazole were purchased from the Maybridge Chemical Company.

Synthesis of azides

Through nucleophilic substitutions of chloroaldehydes (azides 1a,b,c). To an ice-cooled solution of the corresponding chloroaldehyde[15,16] (20 mmol) in dry DMF (100 cm^3) was added 5 equiv. of sodium azide, and the solution was stirred at 0 °C for 1 h. The reaction mixture was then poured into ice–water (400 cm^3) and extracted with diethyl ether (4 × 100 cm^3). The combined extracts were washed with water (4 × 50 cm^3), dried ($MgSO_4$), and evaporated to yield the crude azide, which was crystallized from diethyl ether–hexane.

5-Azido-3-phenylisoxazole-4-carbaldehyde **1a**.—Yield 80%, mp 46–48 °C (lit.,[7] 49.5–51 °C); ν_{max}/cm^{-1} 2134s (N_3) and 1688s (CO); δ_H(400 MHz) 7.45–7.55 and 7.75 (5 H, m + dd, Ph) and 9.76 (1 H, s, CHO); δ_C 104.1 (C-4, $^2J_{CH}$ 28), 126.6, 128.9 (×2) and 131.0 (Ph), 163.6 (C-3, m), 166.2 (C-5, $^3J_{CH}$ 4.8) and 181.8 (CHO, $^1J_{CH}$ 181.4); *m/z* 214 ($M^{\bullet+}$, 9%), 186 ($M^{\bullet+} - N_2$, 14), 129 (17), 128 (33), 103 ($PhCN^{\bullet+}$, 27) and 77 (Ph^+, 100) (Found: $M^{\bullet+}$, 214.0492. $C_{10}H_6N_4O_2$ requires *M*, 214.0491).

5-Azido-3-tert-butylisoxazole-4-carbaldehyde **1b**.—Yield 85%, mp 31.5–33 °C (resolidifying above 45 °C and then decomposing near 115 °C); ν_{max}/cm^{-1} 2130s (N_3) and 1694s (CO); δ_H(250 MHz) 1.40 (9 H, s, Bu^t), and 9.75 (1 H, s, CHO); δ_C 27.8 and 33.9 (Bu^t), 104.2 (C-4), 167.9 (C-5), 171.1 (C-3) and 180.6 (CHO); *m/z* (CI) 195 (MH^+, 20%), 167 ($MH^+ - N_2$, 30), 125 (11) and 57 (100, $C_4H_9^+$) (Found: $M^{\bullet+}$, 194.0802. $C_8H_{10}N_4O_2$ requires *M*, 194.0804).

5-Azido-3-ethoxycarbonylisoxazole-4-carbaldehyde **1c**.—Yield 35%, mp 34 °C; ν_{max}/cm^{-1} 2172s (N_3), 1731s (ester CO) and 1688s (CHO); δ_H(400 MHz) 1.45 (3 H, t, Me), 4.51 (2 H, q, CH_2O) and 10.17 (1 H, s, CHO); δ_C 14.0 and 63.1 (Et), 105.6 (C-4, $^2J_{CH}$ 27), 155.3 (C-3), 158.8 (COO), 165.8 (C-5, $^3J_{CH}$ 7) and 183.7 (CHO, $^1J_{CH}$ 191); *m/z* (CI) 211 (MH^+, 100%) (Found: $M^{\bullet+}$, 210.0370. $C_7H_6N_4O_4$ requires *M*, 210.0389).

The precursor aldehyde for **1c** was synthesized from 3-ethoxycarbonyl-5-oxazolinone by reacting it with Vilsmeier reagent in the way described by Anderson.[15] It was obtained as a yellow oil in 56% yield; $\nu_{max}(CHCl_3)/cm^{-1}$ 1734s (ester CO) and 1698s (CHO); δ_H(400 MHz) 1.46 (3 H, t, Me), 4.54 (2 H, q, CH_2) and 10.2 (1 H, s, CHO); δ_C 13.9 and 63.2 (Et), 114.2 (C-4, $^2J_{CH}$ 28), 155.4 (C-3), 158.4 (ester CO), 160.4 (C-5) and 182.2 (CHO); *m/z* (CI) 204/206 (MH^+, 100/33%), 176/178 (MH^+ – CO, 21/7), 132 (20), 130 (20) and 96 (21).

Through diazo-transfer with tosyl azide (azides 1h,i,j). *5-Azido-3-methylisoxazole* **1h**.—General procedure. A solution of 5-amino-3-methylisoxazole (1.0 g, 10 mmol) and tosyl azide (1.97 g, 10 mmol) in dry THF (40 cm^3) was added dropwise to a suspension of NaH (11 mmol) in THF (50 cm^3) at −30 °C. The black reaction mixture was stirred at room temp. overnight, then diluted with water (20 cm^3) and extracted with diethyl ether (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$) and chromatographed twice on silica gel with hexane–chloroform (1:1) as the eluent to give the azide **1h** as a pale-yellow oil (278 mg, 22%); ν_{max}(neat)/cm^{-1} 2139s (N_3) and 1609s; δ_H(400 MHz) 2.26 (3 H, s, Me) and 5.54 (1 H, s, 4-H); δ_C 11.9 (Me), 89.8 (C-4, $^1J_{CH}$ 184, $^3J_{CH}$ 3.4), 160.7 (C-5, $^2J_{CH}$ 8) and 162.2 (C-3, $^2J_{CH}$ 7 and 5). Attempts to obtain the mass spectrum led to polymerization on the probe under both EI and CI conditions.

5-Azido-3,4-dimethylisoxazole **1i**.—This compound was similarly prepared from 5-amino-3,4-dimethylisoxazole and purified by chromatography on silica gel with chloroform as the eluent; yield 24% (yellow oil); ν_{max}(neat)/cm^{-1} 2137s (N_3) and 1650s; δ_H(400 MHz) 1.79 (3 H, s, 4-Me) and 2.18 (3 H, s, 3-Me); δ_C 5.6 and 10.5 (2 Me), 97.9 (C-4, m), 155.1 (C-5, q, $^3J_{CH}$ 5), and 162.4 (C-3, m). The sample polymerized when attempts were made to obtain the mass spectrum.

5-Azido-3-phenylisoxazole **1j**.—This compound was similarly prepared from 5-amino-3-phenylisoxazole[17] and purified by chromatography on silica gel with hexane–ethyl acetate (4:1) as the eluent; yield 30% (pale-yellow crystals), mp 75–76 °C; ν_{max}/cm^{-1} 2144s (N_3) and 1606s; δ_H(250 MHz) 6.0 (1 H, s, 4-H) and 7.4–7.8 (5 H, 2 m, Ph); δ_C 87.4 (C-4, $^1J_{CH}$ 183), 126.7, 128.6, 129.0 and 130.5 (Ph), 161.4 (C-5, d, $^2J_{CH}$ 7), 164.4 (C-3, m); *m/z* 186 ($M^{\bullet+}$, 13%), 128 (Ph-C^+=CHCN, 88), 103 ($PhCN^{\bullet+}$, 30), 101 (*m/z* 128 − HCN, 34), 77 (Ph^+, 100) and 51 ($C_4H_3^+$, 84) (Found: $M^{\bullet+}$, 186.0542. $C_9H_6N_4O$ requires *M*, 186.0542).

Miscellaneous methods. *4-Acetyl-5-azido-3-phenylisoxazole* **1d**.—A solution of methylmagnesium iodide was prepared from iodomethane (4.26 g, 30 mmol), magnesium turnings (0.72 g, 30 mmol), and a crystal of iodine in dry diethyl ether (40 cm^3) and then chilled to −15 °C while a solution of 5-chloro-3-phenylisoxazole-4-carbaldehyde (1.035 g, 5 mmol) in diethyl ether (20 cm^3) was added. The reaction mixture was brought to room temp., poured into ice–water (500 cm^3) and acidified with aqueous NH_4Cl. After extraction with diethyl ether (5 × 100

cm^3), the combined ether extracts were dried ($MgSO_4$) and evaporated to give 1-(5-chloro-3-phenylisoxazol-4-yl)ethanol as a yellow oil (1.072 g, 96%); ν_{max}(neat)/cm^{-1} 3402s (OH).

A solution of this compound (1.0 g, 4.5 mmol) in acetic anhydride (20 cm^3) was added dropwise to one of chromic oxide (1.3 g, 9 mmol) in acetic anhydride (50 cm^3) and the whole was stirred for 30 min. The reaction mixture was extracted with diethyl ether (4 × 100 cm^3) and the combined extracts were washed with aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated. The residue was chromatographed on silica gel with diethyl ether–light petroleum (1:1) as the eluent to give 4-acetyl-5-chloro-3-phenylisoxazole as a pale-yellow oil (0.86 g, 87%); ν_{max}(neat)/cm^{-1} 1693s (C=O).

Reaction of this chloro-compound with sodium azide in the usual way (see azides **1a–c** above) afforded the crude azide **1d** which was purified *via* chromatography on silica gel with diethyl ether–light petroleum (1:1) as the eluent (768 mg, 90%), mp 80 °C (decomp.); ν_{max}/cm^{-1} 2175s, 2149s (N_3) and 1680s (C=O); δ_H(400 MHz) 2.33 (3 H, s, Me) and 7.4–7.6 (5 H, 2 m, Ph); δ_C 30.1 (Me), 104.6 (C-4, m), 127.8, 128.3, 129.2 and 130.3 (Ph), 163.3 (C-5, s), 164.4 (C-3, t, $^3J_{CH}$ 4) and 190.0 (CO, $^2J_{CH}$ 6); *m/z* 228 ($M^{\bullet+}$, 0.8%), 200 ($M^{\bullet+}$ − N_2, 6), 103 ($PhCN^{\bullet+}$, 8), 77 (Ph^+, 20), 51 (13) and 43 ($MeCO^+$, 100) (Found: $M^{\bullet+}$, 228.0648. $C_{11}H_8N_4O_2$ requires *M*, 228.0647).

5-Azido-3-phenyl-4(N-phenyliminomethyl)isoxazole **1e**.—The azido-aldehyde **1a** (0.80 g, 3.7 mmol) was allowed to react overnight with aniline (0.35 g, 3.7 mmol) and a few drops of acetic acid in ethanol (15 cm^3) in an ice-cooled bath. The yellow crystalline precipitate was filtered off, and was shown by ^1H NMR spectroscopy to be a 9:1 mixture of the azide **1e** and the secondary amine 3-phenyl-5-(*N*-phenylamino)isoxazole-4-carbaldehyde. After crystallization from diethyl ether–light petroleum (1:1), pure **1e** was obtained (766 mg, 70%), mp 89–91 °C; ν_{max}/cm^{-1} 2154s (N_3) and 1625m (C=N); δ_H[$(CD_3)_2SO$, 400 MHz] 7.18, 7.24 and 7.39 (5 H, d + t + t, NPh), 7.5–7.6 and 7.75–7.8 (5 H, 2 m, Ph) and 8.26 (1 H, s, CH=N); δ_C[$(CD_3)_2SO$] 102.9 (C-4, $^2J_{CH}$ 10), 120.8, 126.3–130.6 and 150.9 (2 Ph), 149.4 (CH=N, $^1J_{CH}$ 162), 161.6 (C-5, $^3J_{CH}$ 7) and 163.4 (C-3, $^3J_{CH}$ 6); *m/z* 289 ($M^{\bullet+}$, 3.3%), 261 ($M^{\bullet+}$ − N_2, 75), 128 (27), 105 (27), 104 ($PhN^+{\equiv}CH$, 73), 77 (Ph^+, 100) and 51 ($C_4H_3^+$, 30) (Found: $M^{\bullet+}$, 289.0962. $C_{16}H_{11}N_5O$ requires *M*, 289.0964).

5-Azido-4-phenylisoxazole **1k**.—A solution of 5-amino-4-phenylisoxazole[18] (1.0 g, 6.2 mmol) in trifluoroacetic acid (20 cm^3) was treated with solid sodium nitrite (2.2 g, 31 mmol) at 0–5 °C and then with sodium azide (2.0 g, 31 mmol) at −10 °C. The reaction mixture was then stirred for 2 h at room temp. before being diluted with water (50 cm^3) and extracted with chloroform. The extracts were dried ($MgSO_4$), evaporated, and the crude product chromatographed on silica gel. Elution with hexane–ethyl acetate (9:1) gave the pure azide **1k** (127 mg, 11%), mp 62–72 °C (decomp.); ν_{max}/cm^{-1} 2142s (N_3), 1626s and 1599s; δ_H(400 MHz) 7.28, 7.40 and 7.50 (5 H, t + t + d, Ph) and 8.49 (1 H, s, 3-H); δ_C 104.0 (C-4), 126.2, 127.6 (×2) and 129.0 (Ph), 151.6 (C-3) and 154.6 (C-5); *m/z* 186 ($M^{\bullet+}$, 12%), 158 ($M^{\bullet+}$ − N_2, 14), 130 (33), 129 (24), 128 [$H\dot{C}$-C^+(CN)Ph, 24], 103 (93) and 77 (Ph^+, 100) (Found: $M^{\bullet+}$, 186.0547. $C_9H_6N_4O$ requires *M*, 186.0542).

5-Azido-4-(4-methoxyphenyl)isoxazole **1l**.—5-Amino-4-(4-methoxyphenyl)isoxazole was made by adapting the method used for the 4-phenyl compound by Eiden, Seemann and Nagar.[18] A solution of NaOEt (65 mmol) in ethanol (50 cm^3) was treated dropwise with a solution of *p*-methoxybenzyl cyanide (7.72 g, 52.5 mmol) and ethyl formate (6.0 g, 80 mmol), with the temperature held below 25 °C during the addition and then overnight. The precipitated α-formyl nitrile was collected and washed with diethyl ether before being dissolved in the minimum volume of aqueous methanol and then treated with a solution of hydroxylamine hydrochloride (6.95 g, 100 mmol) in water (10 cm^3). This reaction mixture was left overnight and the precipitate of 5-amino-4-(4-methoxyphenyl)isoxazole was collected (2.235 g, 22%), mp 135.6–138.7 °C; ν_{max}/cm^{-1} 3358s, 3193s (NH_2) and 1650s; δ_H[$(CD_3)_2SO$, 400 MHz] 3.76 (3 H, s, OMe), 6.88 (2 H, s, NH_2), 6.93 and 7.39 (4 H, 2 d, *p*-anisyl) and 8.47 (1 H, s, 3-H in isoxazole); δ_C[$(CD_3)_2SO$] 55.1 (OMe), 91.9 (C-4), 114.2, 123.5, 126.5 and 156.9 (*p*-anisyl), 151.0 (C-3, $^1J_{CH}$ 181) and 164.8 (C-5, $^3J_{CH}$ 5); *m/z* 190 ($M^{\bullet+}$, 100%), 175 ($M^{\bullet+}$ − Me, 41), 174 ($M^{\bullet+}$ − NH_2, 39), 173 (22), 159 ($M^{\bullet+}$ − OMe, 12), 147 ($M^{\bullet+}$ − HCNO, 92), 146 (41), 135 (61), 134 (61), 132 ($M^{\bullet+}$ − HCNO − Me, 84), 119 (20), 104 (19), 77 (36), 76 (30) and 51 (21).

This amine was diazotized and treated with sodium azide in the same way as the 4-phenyl amine above. Chromatography on silica with dichloromethane elution gave the pure azide **1l** (15%) which was recrystallized from diethyl ether, mp 101 °C (decomp.); ν_{max}/cm^{-1} 2153s (N_3) and 1605s; δ_H(400 MHz) 3.82 (3 H, s, OMe), 6.93 and 7.42 (4 H, 2 d, *p*-anisyl) and 8.42 (1 H, s, 3-H in isoxazole); δ_C 55.3 (OMe), 103.7 (C-4), 114.3, 120.0, 127.5 and 158.9 (*p*-anisyl), 151.5 (C-3, $^1J_{CH}$ 185.5) and 153.6 (C-5); *m/z* 216 ($M^{\bullet+}$, 34%), 188 ($M^{\bullet+}$ − N_2, 97), 173 ($M^{\bullet+}$ − N_2 − Me, 45), 171 (100), 157 ($M^{\bullet+}$ − N_2 − OMe, 30), 133 (84), 115 (61), 103 (79) and 77 (62) (Found: $M^{\bullet+}$, 216.0639. $C_{10}H_8N_4O_2$ requires *M*, 216.0647).

5-Azido-4-cyano-3-phenylisoxazole **1m**.—A suspension of 5-chloro-3-phenylisoxazole-4-carbaldehyde[15] (2.07 g, 10 mmol) and hydroxylamine-*O*-sulfonic acid (1.13 g, 10 mmol) in water (25 cm^3) was stirred at room temp. for 2 d and then heated at 50 °C for 1 h. The solution was extracted with diethyl ether (1 × 100 and 2 × 50 cm^3), and the combined extracts were dried ($MgSO_4$). After evaporation of the solvent the crude product was chromatographed on silica gel with chloroform–light petroleum (1:2) as the eluent to yield 5-chloro-4-cyano-3-phenylisoxazole (0.986 g, 48%), mp 42–44 °C; ν_{max}/cm^{-1} 2245s (CN); δ_H(400 MHz) 7.51–7.55 and 7.91 (5 H, m + d, Ph); δ_C 90.6 (C-4), 109.5 (CN), 125.4, 127.1, 129.3 and 131.9 (Ph), 162.5 (C-5, s) and 162.6 (C-3, t); *m/z* 204 ($M^{\bullet+}$, 14%), 169 ($M^{\bullet+}$ − Cl, 53), 141 (34), 77 (Ph^+, 96), 63 (51) and 51 (100).

A solution of this chloronitrile (0.986 g, 4.8 mmol) and sodium azide (1.30 g, 20 mmol) in dry DMF (40 cm^3) was stirred at 0 °C for 1 h. The reaction mixture was then poured into ice–water (100 cm^3) and extracted with diethyl ether (3 × 100 cm^3). The combined extracts were washed with water (2 × 100 cm^3), dried ($MgSO_4$), and evaporated to give the azide **1m** (785 mg, 77%), mp 98.5–100 °C; ν_{max}/cm^{-1} 2237m (CN), 2174s and 2140s (N_3); δ_H(CD_2Cl_2, 250 MHz) 7.4–7.5 and 7.80 (m + d, Ph); δ_C(CD_2Cl_2) 77.2 (C-4), 110.1 (CN), 126.2, 127.4, 129.5 and 132.0 (Ph), 163.1 (C-3, t) and 167.2 (C-5, s); *m/z* 211 ($M^{\bullet+}$, 9%), 153 [PhC^+=$C(CN)_2$, 28], 126 (27), 103 ($PhCN^{\bullet+}$, 54) and 77 (Ph^+, 100) (Found: $M^{\bullet+}$, 211.0499; $C_{10}H_5N_5O$ requires *M*, 211.0494).

5-Azido-3-methyl-4-nitroisoxazole **1n**.—To an ice-cooled solution of the azide **1h** (0.80 g, 6.45 mmol) in acetic anhydride (12 cm^3), nitric acid (0.4 cm^3, d = 1.42) was added dropwise. The reaction mixture was brought to room temp. for 2 h and then poured into ice–water (250 cm^3) and extracted with diethyl ether (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with chloroform as the eluent to give the azide **1n** as a pale-yellow oil (385 mg, 35%) which was crystallized from diethyl ether (127 mg, 12%), mp 67–68 °C; ν_{max}/cm^{-1} 2204s, 2135s (N_3) and 1601s; δ_H(400 MHz) 2.56 (s, Me); δ_C 12.15 (Me), 118.2 (C-4, br), 157.7 (C-3, q, $^2J_{CH}$ 7) and 160.7 (C-5, s); *m/z* 169 ($M^{\bullet+}$, 10%), 141 ($M^{\bullet+}$ − N_2, 3), 97 (16), 94 ($M^{\bullet+}$ − N_2 − NO_2 − H, 84), 57 ($MeCNO^{\bullet+}$, 43) and 43 ($HCNO^{\bullet+}$, 100) (Found: $M^{\bullet+}$, 169.0207. $C_4H_3N_5O_3$ requires *M*, 169.0236).

Attempted synthesis of 5-azido-3-methyl-4-phenylazoisoxazole **1f**.—5-Amino-3-methyl-4-phenylazoisoxazole was prepared from 5-amino-3-methylisoxazole by reaction with benzenediazonium chloride.[19] A solution of this amine (0.63 g, 3.1 mmol)

and tosyl azide (1.22 g, 6.2 mmol) in dry THF (25 cm^3) was added to a stirred suspension of NaH (6.2 mmol) in THF (20 cm^3) cooled to −30 °C. The reaction was left overnight at room temp. and then diluted with water (20 cm^3). The mixture was extracted with chloroform (3 × 100 cm^3) and the combined extracts were dried ($MgSO_4$), evaporated and chromatographed on silica gel with hexane–diethyl ether (8:1) as the eluent to afford 6-methyl-2-phenyltriazolo[4,5-*d*]isoxazole **4a** (0.25 g, 42%), mp 107–108 °C; δ_H(400 MHz) 2.64 (3 H, t, Me), 7.4, 7.5 and 8.1 (5 H, t + t + d, Ph); δ_C 10.8 (Me), 119.6, 128.7, 129.5 and 140.5 (Ph), 138.9 (C-6a, q, $^3J_{CH}$ 3), 150.5 (C-6, q, $^2J_{CH}$ 7) and 172.8 (C-3a); *m*/*z* 200 ($M^{\bullet+}$, 3.8%), 105 (PhN_2^+, 15), 77 (Ph^+, 100) and 51 ($C_4H_3^+$, 30).

Attempted synthesis of 5-*azido*-3-*phenyl*-4-*phenylazoisoxazole* **1g**.—5-Amino-3-phenyl-4-phenylazoisoxazole was prepared by diazo-coupling from 5-amino-3-phenylisoxazole.[19] The amino-azo compound (264 mg, 1 mmol) in dry THF (5 cm^3) was added dropwise to a suspension of NaH (1 mmol) in THF (10 cm^3). When the evolution of gas ceased, the mixture was cooled to −30 °C and treated with tosyl azide (182 mg, 0.92 mmol) dissolved in THF (5 cm^3). The precipitated tosyl amide was filtered off at room temp. and the filtrate was chromatographed on silica gel with diethyl ether–hexane elution to yield the starting amine (150 mg) and 2,6-diphenyltriazolo[4,5-*d*]isoxazole **4b** (40 mg, 15%), mp 129–130 °C (from hexane) (Found: C, 68.6; H, 3.8. $C_{15}H_{10}N_4O$ requires C, 68.67; H, 3.84%); δ_H(400 MHz) 7.45, 7.5–7.6 and 8.15–8.25 (10 H, t + m + m, 2 Ph); δ_C 119.8, 126.4, 127.9, 128.9, 129.3, 129.5, 131.6 and 140.6 (2 Ph), 137.7 (C-6a), 152.3 (C-6, $^3J_{CH}$ 4.5) and 173.4 (C-3a); *m*/*z* 262 ($M^{\bullet+}$, 4%), 129 (15), 105 (PhN_2^+, 7), 103 ($PhCN^{\bullet+}$, 4) and 77 (Ph^+, 100).

Products of azide thermolysis

General method. The azide (3–5 mmol) was refluxed in CCl_4 (50 cm^3) for 24 h, after which the solvent was removed. ^1H NMR analysis indicated that single products were formed. The crude material was then purified by recrystallization or by chromatography on silica gel. The results are as follows.

3-*Phenylisoxazolo*[5,4-*c*]*isoxazole* **2a**.—This compound was obtained by thermolysis of azide **1a**, and was purified by chromatography using diethyl ether–light petroleum (1:2) as the eluent; yield 43%, mp 139–140 °C (lit.,[7] 146–147 °C) (Found: C, 64.3; H, 3.3. $C_{10}H_6N_2O_2$ requires C, 64.52, H, 3.23%); ν_{max}/cm^{-1} 3111s and 1640s; δ_H(400 MHz) 7.5–7.6 and 7.87 (5 H, m + dd, Ph) and 8.71 (1 H, s, 4-H); δ_C 114.5 (C-3a, $^2J_{CH}$ 13.9), 126.0, 127.5, 129.4 and 132.0 (Ph), 150.8 (C-4, $^1J_{CH}$ 210), 153.9 (C-3, $^3J_{CH}$ 4.5) and 182.1 (C-6a, $^3J_{CH}$ 6.2); *m*/*z* 186 ($M^{\bullet+}$, 48%), 129 (13), 128 (37), 116 (13), 101 (11) and 77 (Ph^+, 100).

3-(tert-*Butyl*)*isoxazolo*[5,4-*c*]*isoxazole* **2b**.—This compound was obtained by thermolysis of azide **1b**, and was purified by crystallization from diethyl ether–hexane; yield 58%, mp 109 °C (Found: C, 57.7; H, 6.0. $C_8H_{10}N_2O_2$ requires C, 57.83; H, 6.02%); ν_{max}/cm^{-1} 3147m and 1621m; δ_H(400 MHz) 1.42 (9 H, s, Bu^t) and 8.45 (1 H, s, H-4); δ_C 28.7 and 33.6 (Bu^t), 114.8 (C-3a, $^2J_{CH}$ 13.5), 150.3 (C-4, $^1J_{CH}$ 210), 163.6 (C-3, $^3J_{CH}$ 4.5) and 181.9 (C-6a, $^3J_{CH}$ 6); *m*/*z* (CI) 167 (MH^+, 100%), 125 (23), 111 ($MH^+ - C_4H_8$, 14) and 57 ($C_4H_9^+$, 35).

3-*Ethoxycarbonylisoxazolo*[5,4-*c*]*isoxazole* **2c**.—This compound was obtained by thermolysis of azide **1c**, and was purified by chromatography using dichloromethane as the eluent; yield 72%, mp 35–37 °C (from Et_2O–EtOH–hexane) (Found: C, 45.9; H, 3.26. $C_7H_6N_2O_4$ requires C, 46.15; H, 3.29%); ν_{max}/cm^{-1} 3115s, 1748s (ester C=O) and 1647s; δ_H(250 MHz) 1.47 (3 H, t, Me), 4.53 (2 H, q, CH_2O) and 8.72 (1 H, s, 4-H); δ_C 14.0 and 63.5 (Et), 113.2 (C-3a, $^2J_{CH}$ 13), 147.9 (C-3), 152.4 (C-4, $^1J_{CH}$ 214), 157.4 (COO) and 182.4 (C-6a, $^3J_{CH}$ 6); *m*/*z* 182 ($M^{\bullet+}$, 8%), 137 ($M^{\bullet+}$ − EtO, 26), 111 (13), 110 ($M^{\bullet+} - CO_2Et$, 17), 96 (19), 78 (60) and 51 (100) (Found: $M^{\bullet+}$, 182.0330. $C_7H_6N_2O_2$ requires *M*, 182.0328).

4-*Methyl*-3-*phenylisoxazolo*[5,4-*c*]*isoxazole* **2d**.—This compound was obtained by thermolysis of azide **1d** and purified by chromatography using diethyl ether–light petroluem (1:1) as the eluent; yield 98%, mp 117–118 °C (Found: C, 65.8; H, 4.05. $C_{11}H_8N_2O_2$ requires C, 65.98; H, 4.03%); ν_{max}/cm^{-1} 1646s; δ_H(400 MHz) 2.79 (3 H, s, Me), 7.51–7.59 and 7.79–7.82 (5 H, 2 m, Ph); δ_C 14.1 (Me), 111.05 (C-3a, q, $^3J_{CH}$ 3), 126.7, 127.6, 129.3 and 131.6 (Ph), 154.6 (C-3, t, $^3J_{CH}$ 5), 163.25 (C-4, q, $^2J_{CH}$ 7) and 182.6 (C-6a, q, $^4J_{CH}$ < 1); *m*/*z* 200 ($M^{\bullet+}$, 6%), 142 (18), 103 ($PhCN^{\bullet+}$, 7), 94 (57), 91 (10), 77 (Ph^+, 42), 51 (30) and 43 ($MeCO^+$, 100).

3,5-*Diphenylpyrazolo*[4,3-*d*]*isoxazole* **3**.—This compound was obtained by thermolysis of azide **1e** and purified by chromatography using diethyl ether–light petroleum (1:1) as the eluent; yield 37%, mp 139–140 °C; ν_{max}/cm^{-1} 3136m, 3054m and 1614s; δ_H(400 MHz) 7.39 (1 H, t), 7.48–7.55 (5 H, m), 7.78 (2 H, d) 7.94–7.98 (2 H, m) and 8.14 (1 H, s, 4-H); δ_C 109.5 (C-3a, d, $^2J_{CH}$ 8), 118.2 (C-4, $^1J_{CH}$ 194), 120.2, 127.4–130.9 and 140.3 (2 Ph), 154.5 (C-3, t, $^3J_{CH}$ 4.5) and 176.6 (C-6a, d, $^3J_{CH}$ 9); *m*/*z* 261 ($M^{\bullet+}$, 48%), 260 (12), 219 ($M^{\bullet+}$ − NCO, 11), 128 ($M^{\bullet+}$ − PhCNO − CN, 38), 105 (PhN_2^+, 38), 104 (19), 77 (Ph^+, 100) and 51 (58) (Found: $M^{\bullet+}$, 262.0861. $C_{15}H_{10}N_4O$ requires *M*, 262.0855).

Trapping experiments

2-(2-Cyano-1-phenylethenyl)-3,6-dihydro-4,5-dimethyl-2*H*-oxazine 7a. The azide **1j** (465 mg, 2.5 mmol) and 2,3-dimethylbuta-1,3-diene (10 cm^3) were refluxed in an oil bath at 80 °C for 24 h. After removal of the excess of diene, the residue was chromatographed twice on silica gel, first with hexane–diethyl ether (3:1) and then with chloroform as the eluents, to give the product **7a** as a pale-yellow oil (47 mg, 8%), which according to TLC contained minor contaminants; ν_{max}(neat)/cm^{-1} 2212s (CN), 1597s and 1522s; δ_H(400 MHz) 1.54 and 1.62 (6 H, 2 s, 2 Me), 3.36 (2 H, s, CH_2N), 4.31 (2 H, s, CH_2O), 4.99 (1 H, s, vinyl H) and 7.45 (5 H, s, Ph); δ_C 13.6 and 15.4 (2 Me), 53.4 (CH_2N), 71.3 and 163.6 (C=C), 72.0 (CH_2O), 121.7 and 123.9 (Me–*C*=*C*–Me), 128.6, 128.8, 130.4 and 132.5 (Ph); *m*/*z* 240 ($M^{\bullet+}$, 11%), 155 (19), 128 (PhC^+=CHCN, 35), 102 ($PhC{\equiv}CH^{\bullet+}$, 16), 91 (82), 77 (Ph^+, 88) and 41 (100) (Found: $M^{\bullet+}$, 240.1257. $C_{15}H_{16}N_2O$ requires *M*, 240.1263).

2-(2-Cyano-2-phenylethenyl)-3,6-dihydro-4,5-dimethyl-2*H*-oxazine 7b. A solution of the azide **1k** (460 mg, 2.5 mmol) in 2,3-dimethylbuta-1,3-diene (10 cm^3) was refluxed in an oil bath at 80 °C for 2 h. After removal of the excess of diene, the residue was chromatographed twice on silica gel, the first time with chloroform and the second time with hexane–diethyl ether (2:1) as the eluents, to obtain the pure compound **7b** (160 mg, 27%), mp 148–149 °C; ν_{max}/cm^{-1} 3059m, 2186s (CN), 1626s and 1595s (C=C); δ_H(250 MHz) 1.65 and 1.75 (6 H, 2 s, 2 Me), 3.95 (2 H, s, CH_2N), 4.40 (2 H, s, CH_2O), 7.10 (1 H, s, vinyl H) and 7.18–7.40 (5 H, 2 m, Ph); δ_C 13.8 and 15.2 (2 Me), 53.9 (CH_2N), 72.0 (CH_2O), 81.4 and 143.4 (C=C, $^1J_{CH}$ 166), 119.2 (CN, $^3J_{CH}$ 12), 121.3 and 124.1 (Me–*C*=*C*–Me), 124.4, 126.1, 128.8 and 135.1 (Ph); *m*/*z* 240 ($M^{\bullet+}$, 100%), 155 (11), 142 [Ph(CN)C=CHN$^{\bullet+}$, 28], 115 (PhC^+–CN, 24) and 77 (Ph^+, 18) (Found: $M^{\bullet+}$, 240.1256. $C_{15}H_{16}N_2O$ requires *M*, 240.1263).

Kinetic measurement

Rates were obtained by monitoring the decay of the azido band near 2120 cm^{-1} in the infrared spectrum (see ref. 20). The runs, which were generally followed for two half-lives and sometimes for three, were strictly first-order throughout.

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