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Rates and Products of the Thermal Decomposition of 5-Azidoisothiazoles

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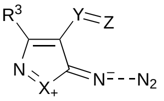
5-Azidoisothiazoles have been thermolysed in *p*-xylene solutions to yield bicyclic products; there are appreciable neighbouring group effects on the reaction rates.

Both azidobenzenes and the α-azides of five-membered heteroaromatics thermolyse when heated in solution, but there are important differences in both reaction products and rates. Whereas simple azidobenzenes thermolyse slowly,[1] the heterocyclic α-azides normally undergo ring opening.[3,4] A further important difference between azidobenzenes and these heterocyclic α-azides relates to neighbouring group effects from such *ortho* substituents as nitro and formyl. In the azidobenzenes, an *ortho* nitro group is known to increase the thermolysis rate by 1060-fold, and an *ortho* formyl one by 29-fold.[11] In both cases, a cyclic product results.[1] The stabilization provided by the ring hetero-atom (represented by **3**) places a high negative charge on the inner azido nitrogen atom, which must inhibit the formation of the bridging bond represented in the transition state **4**.



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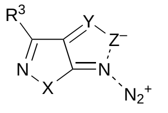

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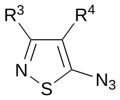
(X = NPh, O, S)

In this paper we explore the possibility that suitable 4-substituents in 5-azidoisothiazoles might exert large neighbouring group effects.

We have synthesized the azides **5a–g**, which were fully characterized by ^{1}H and ^{13}C NMR and IR spectroscopy, as well as by mass spectroscopy.



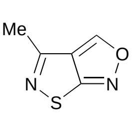
5a R^3 = Me, R^4 = H
b R^3 = Me, R^4 = CN
c R^3 = Me, R^4 = CHO
d R^3 = Me, R^4 = NO_2
e R^3 = Ph, R^4 = CN
f R^3 = MeS, R^4 = CN
g R^3 = $MeSO_2$, R^4 = CN

The decay of the azido band in the IR spectrum was monitored, and all the decompositions were smoothly first-order. Rate constants are presented in Table 1, and the activation parameters for **5a** in Table 2 (for both Tables see full text).

The four 5-azido-4-cyano compounds **5b**, **5e**, **5f** and **5g** were chosen in order to see what effect substituents at position 3 in the ring might exert on the rate. The methyl, phenyl and methylsulfanyl groups had virtually no effect, whereas the strongly electron-withdrawing methylsulfonyl group reduced the rate by about 30%. An interesting feature of the reaction rates is the seven-fold increase when a 4-cyano group is introduced into 5-azido-3-methylisothiazole. In our studies of other α-azido heterocycles the cyano group has generally had the opposite effect on rates.[5,11,12,14] With the 5-azidoisothiazoles, we must assume that 4-substituents such as formyl and nitro, which have similar inductive and resonance properties to cyano, will cause a rate increase of similar magnitude. In fact, these two groups do cause moderately large rate enhancements. These two neighbouring group effects are larger than those observed with 5-azidoisoxazoles,[12] but substantially smaller than those measured for azidobenzenes.[11]

As expected, **5c** furnished 4-methylisothiazolo[5,4-*c*]isoxazole **6** and **5d** yielded 6-methylisothiazolo[4,5-*c*]-1,2,5-oxadiazole 1-oxide **7** upon thermolysis.

Thermolysis of 5-azido-3-methylisothiazole **5a** in 2,3-dimethylbutadiene as solvent yielded the triazoline **8**; we did not obtain any derivative of the expected ring-opened cyano thione **9**.



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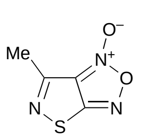

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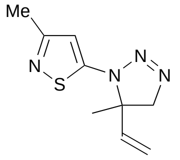

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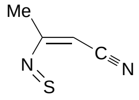

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Thermolyses of the azides **5f** and **5g** in the diene did not lead to isolation of triazolines, but moderately good yields of the corresponding primary amine were identified. This result appeared to demonstrate that a nitrene intermediate had been formed in the unimolecular decomposition of the azide.

Techniques used: IR, ^{1}H and ^{13}C NMR, low- and high-resolution mass spectrometry

References: 21

Schemes: 2

Table 1: First-order rate constants for thermal decomposition of 5-azidoisothiazoles in *p*-xylene solution

Table 2: Arrhenius data for thermolysis of **5a** in *p*-xylene solution

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