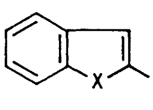
Synthesis and Thermal Ring-cleavage Fragmentation of 2-Azido-1-methylindole and 2-Azidobenzo[*b*]furan

Elisabetta Foresti,[a] **Piero Spagnolo,**[b,*] **and Paolo Zanirato**[c,*]
[a] *Dipartimento di Chimica 'Ciamician,' Via Selmi n° 2, 40126 Bologna, Italy*
[b] *Istituto di Chimica, Università della Basilicata, Via N. Sauro n° 85, 85100 Potenza, Italy*
[c] *Dipartimento di Chimica Organica, Viale Risorgimento n° 4, 40136 Bologna, Italy*

Mild thermal fragmentation of 2-azido-1-methylindole and 2-azidobenzo[*b*]furan leads to an *ortho*-quinoidal enimine or enone intermediate respectively through a ring-cleavage reaction of the corresponding nitrene.

Aromatic five-membered ring heterocycles can undergo thermal ring-cleavage fragmentation when an azido substituent is generated at C-2.[1,2] Such a reaction, in fact, appears to be general, but the reported examples in which there is good evidence for the ring-cleavage products are rather limited. Moreover, the mechanism of these cleavage fragmentations is generally unknown and the question of whether the azides themselves or initially formed nitrenes are actually involved remains unresolved.

Recently we have provided evidence that mild thermal decomposition of 2-azidobenzo[*b*]thiophene (**1a**) probably leads to a singlet nitrene intermediate (**2a**) which can add to olefin double bonds and undergo a ring-opening reaction to give the *ortho*-quinoidal enethione (**3a**).[3] We now report our



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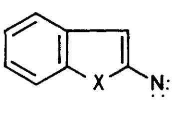

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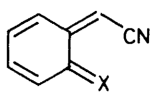
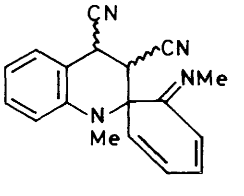


(**3**)

a; X = S **b**; X = NMe **c**; X = O

preliminary results from a related study carried out with 2-azido-1-methylindole (**1b**) and 2-azidobenzo[*b*]furan (**1c**). At the outset of this work the chemistry of 2-azido-indoles (or -pyrroles) had not been explored. However, shortly after the present work had been accomplished, a number of 1-substituted 2-azido-3-formylindoles were reported to exhibit smooth thermal ring-opening fragmentation.[4] Several 2-azido substituted furans are known; these compounds are reported to be thermally labile and undergo ring-cleavage reactions;[1,5] however, no examples of 2-azidobenzofurans can be found in the literature. The azide (**1b**)[*] was prepared in 70% yield by direct metallation of 1-methylindole with butyl-lithium followed by treatment of the resulting 2-lithium derivative with toluene-*p*-sulphonyl azide and subsequent fragmentation of the intermediate triazene lithium salt.[6]



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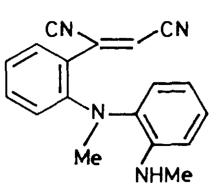
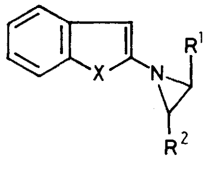
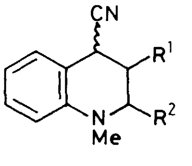


(**5**)



(**6**) **a**; $R^1 = CO_2Me$, $R^2 = H$, X = NMe
b; $R^1 = CN$, $R^2 = H$, X = NMe
c; $R^1 = R^2 = CO_2Me$, X = NMe
d; $R^1 = SiMe_3$, $R^2 = H$, X = NMe
e; $R^1 = CO_2Me$, $R^2 = H$, X = O

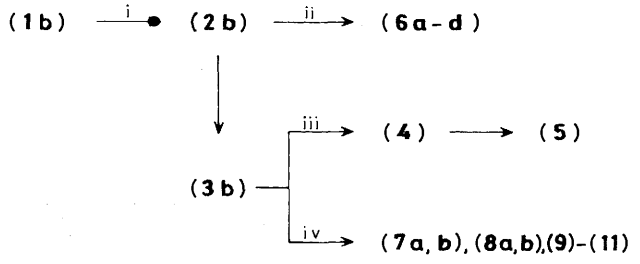


(**7**) **a**; $R^1 = CO_2Me$, $R^2 = H$
b; $R^1 = CN$, $R^2 = H$
(**8**) **a**; $R^1 = H$, $R^2 = CO_2Me$
b; $R^1 = H$, $R^2 = CN$

Table. Product yields (%)[a] for the decomposition of the azide (**1b**) in neat alkenes at room temperature

Alkene	Aziridine*	Tetrahydroquinoline*
Methyl acrylate	(**6a**) (78)	[(**7a**) + (**8a**)] (17)
Methyl acrylate[b]	(**6a**) (55)	[(**7a**) + (**8a**)] (40)
Acrylonitrile	(**6b**) (25)	[(**7b**) + (**8b**)] (35)
Dimethyl fumarate[c]	(**6c**) (25)	(**9**) (43)
Vinyltrimethylsilane	(**6d**) (41)[d]	—
trans- But-2-ene	—	(**10**) (6)[d]
cis- But-2-ene	—	(**11**) (5)[d]

[a] Isolated yields based on the starting azide (**1b**). [b] Reaction carried out at 60 °C. [c] Reaction carried out in benzene in the presence of 2 molar equiv. of the alkene. [d] The diamine (**5**) (40—45%) was also obtained. * See footnote †.



Scheme. *Reagents and conditions*: i, 25—60 °C, $-N_2$; ii, acrylonitrile, methyl acrylate, dimethyl fumarate, or vinyltrimethylsilane; iii, +(**3b**), *cis*- and *trans*- but-2-ene, vinyltrimethylsilane, or benzene; iv, methyl acrylate, acrylonitrile, *cis*- and *trans*- but-2-ene, or dimethyl fumarate

The azide (**1b**) in benzene exhibited first-order decomposition at 60 °C with a half-life of *ca.* 45 min[†] leading substantially to the diamine (**5**) (60%), whose structure was supported by spectral data and was confirmed by an *X*-ray crystal structure determination (details will be reported in the full paper). Compound (**5**) was probably formed by isomerisation of the imine (**4**) initially produced by cyclodimerization of the enimine (**3b**) resulting from ring-opening fragmentation of the azide (**1b**). A similar cyclodimerization process has been previously shown to occur with the enimine (**3**; X = NPh, CN = H), arising from valence isomerisation of 1-phenylbenzazetine.[7] When the azide (**1b**) was allowed to decompose in methyl acrylate at room temperature suppression of the diamine (**5**) occurred in favour of the aziridine (**6a**) (78%) and a regioisomeric mixture of the tetrahydroquinolines (**7a**) and (**8a**) (17%). Similar results were obtained from thermolysis of (**1b**) in neat acrylonitrile or in benzene containing 2 molar equiv. of dimethyl fumarate (Table and Scheme). Under the same conditions the azide (**1b**) in vinyltrimethylsilane gave the aziridine (**6d**) (41%) and the diamine (**5**) (35%), whereas in *trans*- or *cis*- but-2-ene compound (**5**) was produced as a major product together with small amounts of the tetrahydroquinolines (**10**) and (**11**) respectively (see Table and Scheme). As can be seen in the Table the formation of aziridines at the expense of the corresponding tetrahydroquinolines and/or the diamine (**5**) can be favoured by an increase in the electrophilic character of the alkene. No triazolines, which might have resulted from cycloaddition of the azide (**1b**) to the alkene present,[8] were detected although they might be expected to survive our very mild reaction conditions. Triazolines, however, are known to undergo thermal fragmentation to aziridines.[8,9] From this evidence it may be inferred that a nitrene rather than a triazoline is the intermediate leading to aziridine formation. On this basis we suggest that unimolecular

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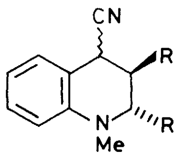
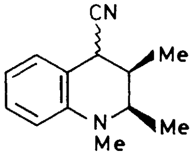
[*] Structural assignment of all new compounds was made on the basis of ^{13}C and/or ^1H n.m.r., i.r., and mass spectral data.

[†] Under the same conditions the azide (**1a**) exhibits a half-life of *ca.* 140 min.[3]

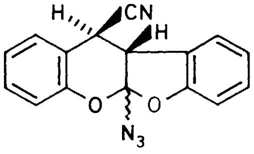


(9) R = CO_2Me
(10) R = Me



(11)

decomposition of the azide (**1b**) initially affords the singlet nitrene (**2b**). In the presence of the appropriate alkene the nitrene (**2b**) would give the aziridines (**6a**—**d**) and/or would undergo a ring-opening reaction to give the *ortho*-quinoidal enimine (**3b**). This intermediate (**3b**) would then undergo cyclodimerization and/or cycloaddition reaction with the alkene leading to the tetrahydroquinolines (**7a**,**b**), (**8a**,**b**), and (**9**)—(**11**) (see Scheme). An increase in the reaction temperature would favour ring-opening of the nitrene (**2b**). This is suggested by the remarkable increase in the yield of the quinolines (**7a**) and (**8a**) at the expense of the aziridine (**6a**), which was observed when the azide (**1b**) was allowed to react with methyl acrylate at 60 °C (Table). However, the occurrence of the presumed nitrene (**2b**) was apparently suppressed when the azide (**1b**) was decomposed in methyl propiolate at room temperature. Under these conditions compound (**1b**) exhibited only cycloaddition to the alkyne triple bond to give a 75:25 mixture of the triazoles (**12a**)* and (**12b**)* respectively.



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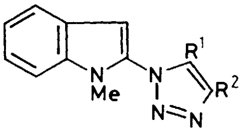

(12) **a**; $R^1 = H$, $R^2 = CO_2Me$
b; $R^1 = CO_2Me$, $R^2 = H$

2-Azidobenzo[*b*]furan (**1c**)* was obtained in 70% yield by a procedure similar to that employed for the azide (**1b**). The first-order decomposition of (**1c**) in benzene at 60 °C was found to occur *ca.* three times faster than that of (**1b**) and give the azide (**13**) (50%)* in addition to small amounts of an unidentified isomeric compound. Interestingly, the azide (**1c**) was found to be converted into (**13**) even upon being stored in a freezer at −20 °C. In methyl acrylate at room temperature this azide (**1c**) gave the aziridine (**6e**) (30%)* and an unknown oily compound. Thus, it would appear that the azide (**1c**), analogously to (**1a**,**b**), initially gives a nitrene intermediate (**2c**). Ring-opening of (**2c**) would afford the *ortho*-quinoidal enone (**3c**) which would then add to the furan ring of unchanged azide (**1c**) to afford ultimately the azide (**13**). The observed increase in the decomposition rates on passing from the azide (**1a**)[3] to (**1b**) and (**1c**) might result from a progressive capability of the heterocyclic ring to donate electron-density to the electron-deficient nitrogen of the ensuing singlet nitrene (**2a**—**c**).

Experimental

Preparation of the Azides (**1b**,**c**).—A solution of 1-methylindole (0.06 mol) in dry diethyl ether (100 ml) was added dropwise with stirring at room temperature to 1.6M butyllithium in hexane (40 ml). The reaction mixture was stirred and refluxed for 8 h, after which it was cooled at −70 °C and a solution of tosyl azide (6.5 mmol) in ether (200 ml) was added dropwise. The resulting mixture was stirred for 5 h at −70 °C and then allowed to reach 0 °C. The yellow triazene salt which had formed was filtered off and washed with dry ether. This salt was then suspended in dry ether and treated with a solution of tetrasodium pyrophosphate decahydrate (6.5 mmol) in water. After the mixture had been stirred overnight the ether layer was separated and the aqueous solution extracted with pentane. The combined organic layers were dried and evaporated. Chromatography of the residue on Florisil column using hexane as eluant gave *2-azido-1-methylindole* (**1b**) (42 mmol, 70%), m.p. 40—42 °C; $\nu_{max.}$ 2 150 cm^{-1} (N_3); *m/z* 172 (M^+) and 144 ($M - N_2$).

2-Azidobenzo[b]*furan* (**1c**) was similarly prepared from benzofuran in *ca.*70% yield: $\nu_{max.}$ 2 130 cm^{-1} (N_3); *m/z* 159 (M^+) and 131 ($M - N_2$).

Thermal Decomposition of the Azide (**1b**) *in the Presence of Alkenes.*—A solution of the azide (**1b**) (2 mmol) in 4 ml of methyl acrylate, acrylonitrile, vinyltrimethylsilane *trans*-, *cis*-butene, or in benzene containing dimethyl fumarate (2 mol equiv.) was allowed to stand in a sealed tube at room temperature for *ca.* 3—7 days [until t.l.c. showed the absence of the azide (**1b**)]. The residue obtained after careful evaporation of the excess of olefin was chromatographed on a silica gel column using hexane with increasing amounts of diethyl ether (up to 100%) as eluant.

Acknowledgements

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† See footnote on p. 1355.