

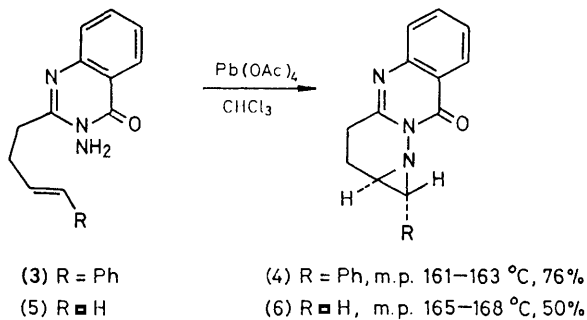
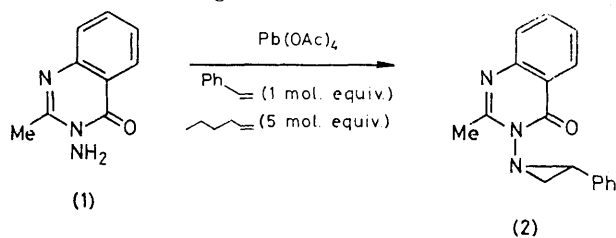
Intramolecular Reactions of *N*-Nitrenes: Evidence for Non-concerted Addition to Alkenes

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Summary Intramolecular *N*-nitrene addition in 2-(hepta-1,6-diene-4-yl)-3-aminoquinazolone derivatives gives aziridines stereospecifically in good yield; the regio-specificity (or lack of it) is rationalised in terms of a non-concerted addition proceeding by electrophilic attack of the nitrene on the alkene double bond *via* a 7-membered transition state.

HETEROCYCLIC *N*-nitrenes exhibit a high degree of discrimination in their reactions with alkenes. Oxidation of 2-methyl-3-aminoquinazolone¹ (**1**) with lead tetra-acetate in the presence of styrene (1 mol. equiv.) and hex-1-ene (5 mol. equiv.) yields only the aziridine (**2**), as shown by n.m.r. analysis.

A secondary interaction between the heterocycle and π -electron-containing substituents has been shown to be



important in the reactions of similar *N*-nitrenes with dienes, acrylates, and styrenes² and this stabilising interaction must be associated with the greater trapping efficiency of styrene to give (**2**).

We have studied the intramolecular additions of *N*-nitrenes to alkenes with the intention of imposing geometric constraints which would effectively prohibit the 'secondary' effects of π -electron substituents and, at the same time, offer entropic assistance for additions to alkenes.

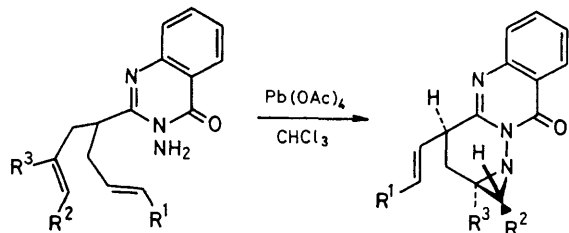
Having established that efficient addition could be achieved in the cases of (**3**) and (**5**), attention was turned to a series of 3-aminoquinazolones having bifurcated side-chains designed to allow the study of *competitive* intramolecular additions (again, without complications due to secondary interactions).

The results of the intramolecular additions described herein can be summarised as follows. (a) Addition of the nitrene to the alkene is not a concerted reaction but proceeds stepwise, probably *via* a fully developed dipolar species. (b) Attack of the nitrene (acting as an electrophile) is stereoelectronically controlled and proceeds exclusively *via* a 7-membered ring transition state. (c) In every case examined, the reaction appears to be stereospecific.

Thus, oxidation of (**7**) gives the aziridine (**8**) (90%); three chiral centres are created in this addition and yet only one stereoisomer, apparently, is formed. Similarly, oxidation of (**9**) yielded a single stereoisomer (**10**) (89%). A competitive reaction for the nitrene between the two alkenes in oxidation of (**11**) produced the aziridines (**12**) and (**13**) in a 1:1 ratio (n.m.r. spectrum of crude reaction product).[†] This is a surprising result and is totally at variance with the results of the intermolecular competition between hexene and styrene described above. Similarly, a 1:1 ratio of (**15**) and (**16**) was obtained from the reaction of (**14**) despite the inherently more nucleophilic character of the methyl-substituted double bond.

Oxidation of (**17**) was particularly informative since examination of the n.m.r. spectrum of the crude product indicated only the presence of (**18**): the aziridine formed by attack on the β -methyl-substituted double bond.

[†] It is implicit in this discussion that conformational preferences of the side-chains do not have a significant influence on the nitrene selectivity.



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|---|---|
| (7) $R^1 = R^2 = \text{Ph}, R^3 = \text{H}$ | (8) $R^1 = R^2 = \text{Ph}, R^3 = \text{H}$
m.p. 208–210 °C |
| (9) $R^1 = R^2 = R^3 = \text{H}$ | (10) $R^1 = R^2 = R^3 = \text{H}$
m.p. 155–157 °C |
| (11) $R^1 = \text{Ph}, R^2 = R^3 = \text{H}$ | (12) $R^1 = R^3 = \text{H}, R^2 = \text{Ph}$
m.p. 145–147 °C |
| (14) $R^1 = R^3 = \text{H}, R^2 = \text{Me}$ | (13) $R^1 = \text{Ph}, R^2 = R^3 = \text{H}$
m.p. 137–140 °C |
| (15) $R^1 = \text{Me}, R^2 = R^3 = \text{H}$
m.p. 146.5–147.5 °C | (16) $R^1 = R^3 = \text{H}, R^2 = \text{Me}$
oil |
| (17) $R^1 = R^2 = \text{H}, R^3 = \text{Me}$ | (18) $R^1 = R^2 = \text{H}, R^3 = \text{Me}$
m.p. 153–155 °C |

A transition state for these nitrene \ddagger additions as shown in (19), analogous to that previously used³ to explain intramolecular nitrene additions to substituted benzenoid rings, accounts for the regioselectivity (or lack of it) in the above reactions. Thus a transition state in which the formation of one C–N bond is almost complete will give rise, in the case of (11) and (14), to a similar secondary carbonium ion, irrespective of which double bond is attacked. The regio-specificity of addition in the case of (17) is the result of tertiary carbonium ion formation at the β -carbon.

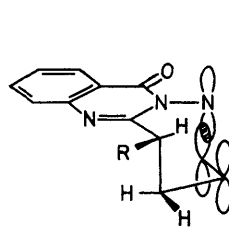
In every case studied so far, it appears that only one stereoisomer is formed. For three of these aziridines, complete analysis of the 400 MHz ^1H n.m.r. spectra has been carried out. The results are consistent with stereospecific *cis*-addition to the alkene and a *cis*-relationship of the aziridine ring and the substituted allyl side-chain [(20), in which it will be noted that the substituted allyl side-chain assumes a pseudo-equatorial configuration].

\ddagger When the oxidation of (5) is carried out in the presence of an excess of styrene, intermolecular trapping by styrene is preferred, giving the corresponding aziridine. This observation implies that inter- and intra-molecular additions both involve the same nitrene intermediate.

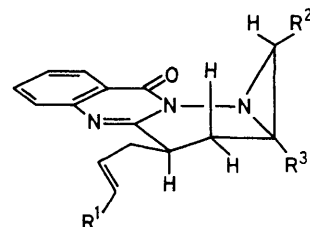
¹ D. J. Anderson, T. L. Gilchrist, D. C. Horwell, and C. W. Rees, *J. Chem. Soc., C*, 1970, 576.

² R. S. Atkinson and J. R. Malpass, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2242.

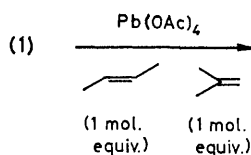
³ R. S. Atkinson, J. R. Malpass, and K. L. Woodthorpe, *J. Chem. Soc., Chem. Commun.*, 1981, 160.



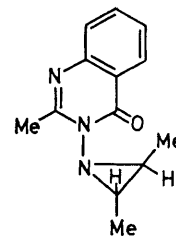
(19)



(20)



(1)



(21)

A competitive intermolecular addition of the nitrene derived from (1) to an equimolar mixture of *trans*-but-2-ene and 2-methylpropene in chloroform gives only the aziridine (21) from n.m.r. examination of the crude reaction mixture.

Clearly there is a reversal of alkene reactivity in passing from the non-concerted addition of nitrenes derived from (14) and (17) to the (presumably concerted) intermolecular nitrene addition giving (21). In a suitably designed system, this changeover in alkene reactivity could be used to define the necessary geometry for concerted nitrene addition.

We thank Dr. O. Howarth (University of Warwick) and the S.R.C. for the 400 MHz n.m.r. spectra and the S.R.C. for studentships (to K.L.W. and K.L.S.).

(Received, 23rd March 1981; Com. 318.)