# Selectivity in Vinyl Azide Reactions; Decomposition of Azidocinnamates with Olefinic *ortho*-Substituents

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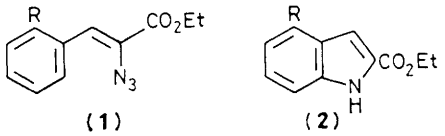
Thermal decomposition of vinyl azides (**1a**—**c**) gives isoquinolines (**3**), benzazepines (**4**), or aziridines (**5**) and (**6**) by preferential reaction at the unsaturated substituent; removal of this unsaturation as in the epoxides (**1d**, **1e**) leads exclusively to 4-substituted indoles.

A wide range of nitrogen heterocyclic compounds can be synthesised by the intramolecular reactions of nitrenes and their azide precursors.[1] In some cases there is more than one reaction pathway available; for example, the vinylnitrenes



(1) (2)

**a**; R = $CH{=}CH_2$
**b**; R = $CH{=}^{t}CHPh$
**c**; R = $CH_2CH{=}CH_2$
**d**; R = $CH(O)CHPh$
**e**; R = $CH_2CH(O)CH_2$

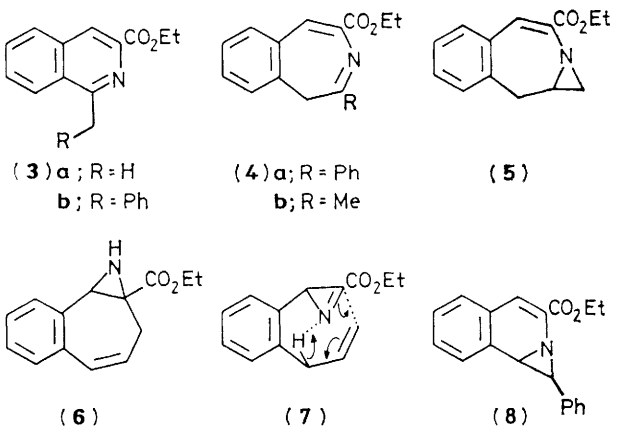
derived from mono-*ortho*-substituted azidocinnamates (**1**) can cyclise onto the free *ortho*-position to give indoles (**2**) or interact with the substituent to give six- or larger membered rings. Thermal decomposition of the azides (**1**, R = Br, Cl, OMe, Me) is known to give exclusively the corresponding indoles (**2**) in high yield,[2] and we have recently shown that isoquinolines can also be formed from the azides (**1**, R = alkyl), in addition to indoles, by interaction with the alkyl substituent.[3] The presence of iodine increases the preference for interaction with the substituent,[3] and in attempts to increase this selectivity further, we have investigated the effect of substituents, R, containing olefinic bonds. We now report that the products resulting from the decomposition of such azides (**1a**—**c**) are formed by selective (*ca.* 9:1) interaction with the unsaturated substituent in preference to the aromatic ring.

2-Vinylbenzaldehyde[1] was condensed with ethyl azidoacetate under the usual conditions[3] to give the azidocinnamate (**1a**) as an unstable oil, $\nu_{max}$ 2120 and 1710 $cm^{-1}$, which decomposed slowly on standing at 5 °C. Heating in toluene caused rapid decomposition with the formation of one major product (75%) identified as ethyl 1-methylisoquinoline-3-carboxylate (**3a**), m.p. 104 °C. The 4-vinylindole (**2a**) was also isolated as a minor product (<10%).

The styryl substituted azidocinnamate (**1b**), m.p. 69—70 °C, was more thermally stable than (**1a**). Decomposition in boiling toluene for 2 h gave the indole (**2b**) (10%), m.p. 173—174 °C, the 1-benzylisoquinoline (**3b**) (35%), m.p. 94 °C, and the benz[*d*]azepine (**4a**, or the 5*H*-tautomer) (35%) as an oil, b.p. 160 °C/0.3 mmHg (Kugelrohr).

Decomposition of the allyl azidocinnamate (**1c**) in toluene for 1.5 h gave four products identified as the indole (**2c**) (10%), m.p. 89—91 °C, the benzazepine (**4b**, or the 5*H*-tautomer) (20%) and the tricyclic aziridines (**5**) (35—40%) and (**6**)† (30—35%) [$\nu_{max}$ ($CCl_4$) 3300 and 1720 $cm^{-1}$; $^1H$ n.m.r. ($CDCl_3$, 250 MHz) δ 1.34 (3H, t, *J* 7 Hz), 2.11 (1H, br. s, exchange with $D_2O$), 2.50 (1H, dd, *J* 8, 15 Hz), 2.91 (1H, dd, *J* 5.7, 15 Hz), 3.23 (1H, br. s), 4.31 (2H, AB, q of q), 6.05 (1H, ddd, *J* 5.7, 8, 11.5 Hz), 6.59 (1H, d, *J* 11.5 Hz), and 7.05—7.65 (4H, m)]. No ethyl 1-vinylisoquinoline-3-carboxylate was observed. The relative yields of thermolysis products were temperature dependent: thus when the azide (**1c**) was decomposed at higher temperatures in boiling xylene or decalin, the yields of (**2c**) and (**6**) increased with increasing temperature, whilst those of (**4b**) and (**5**) decreased correspondingly.

† The compounds (**5**), (**6**), and (**2c**) are unstable to chromatography. The yields quoted are based on n.m.r. spectra of the products obtained immediately after thermolysis.



(3)a; R = H
b; R = Ph

(4)a; R = Ph
b; R = Me

(5)

(6) (7) (8)

Formation of all of these products can be explained by a temperature-dependent competition between cycloaddition and decomposition of the azide group; intramolecular cycloaddition to the double bond gives a triazoline, whilst loss of nitrogen leads to the azirine–nitrene equilibrium. The latter pathway is the minor one at lower temperatures but is favoured with increasing reaction temperature. The nitrene can cyclise to an indole (**2**) or add to the side-chain double bond to give an aziridine (*e.g.* **5**) which can in turn rearrange to a benzazepine (**4**) (see below). The azirine can, in the *o*-allyl case only, undergo an intramolecular ene reaction (**7**) to give the aziridine (**6**).‡ Loss of nitrogen from the triazoline, accompanied by 1,2-hydrogen shift, gives an isoquinoline (**3**).

When the double bond of the substituent was 'protected' by epoxidation, indoles were the major products of decomposition of the azidocinnamates. Thus, the azide (**1d**), m.p. 86—88 °C, prepared by epoxidation of (**1b**) with 3-chloroperbenzoic acid in dichloromethane, gave the 4-substituted indole (**2d**) (80%), m.p. 153.5—155 °C, on heating in toluene. Similarly, the azide (**1e**), prepared from (**1c**), gave the indole (**2e**) in quantitative yield.† Decomposition of the azide (**1d**) in tetrahydrofuran in the presence of triethyl phosphite (1.1 mol. equiv.) at 25 °C took a different course, and the aziridine (**8**) was isolated as the major product (40%); the coupling constant (3 Hz) for the aziridine protons suggests that they are *trans*. The aziridine (**8**) is presumably formed by attack of the phosphite on the azide to give an iminophosphorane intermediate, which then undergoes intramolecular nucleophilic attack on the epoxide. Iminophosphoranes are known to react intermolecularly with epoxides to form aziridines.[7] On heating in toluene for 2 h, the aziridine (**8**) was quantitatively converted into the benzazepine (**4a**), suggesting that in the formation of (**4a**) from the azide (**1b**), the aziridine (**8**) could well be an intermediate.

Thus a general pattern emerges in that the products from azidocinnamates containing an unsaturated *ortho*-substituent are derived from selective interaction with the substituent in preference to the free *ortho*-position of the aromatic ring, even when this entails the formation of a seven-membered ring. However, when the possibility for such interaction is

‡ Ene reactions involving carbon–nitrogen double bonds are rare (ref. 5); two examples involving azirines have been reported (ref. 6), but as far as we are aware the intramolecular version has not been described previously.

removed by epoxidation of the double bond, cyclisation to the aromatic ring is the exclusive reaction.

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