Flash-pyrolysis of 1-Vinylbenzotriazoles

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1-Vinylbenzotriazoles give indoles on flash vacuum pyrolysis, but depending on the vinyl substituents side reactions leading to *N*-phenylketenimines or benzonitrile are observed. The latter process occurs with 1,2-disubstituted vinyl groups and an azatrimethylenemethane is suggested as an intermediate. Ketenimine formation is associated with vinyl groups bearing an α-hydrogen and is the only pathway observed for 1-(2-methylprop-1-enyl)benzotriazole which does not give 3,3-dimethyl-3*H*-indole.

The formation of carbazoles by photolysis and pyrolysis of 1-arylbenzotriazoles, the Graebe–Ullmann synthesis, has found wide application.[1] Surprisingly, reports of the analogous formation of indoles from 1-vinylbenzotriazoles are limited. The photochemical reaction appeared to be inefficient[2] but Wender and Cooper[3] have described a much improved modification of this procedure. Katritzky *et al.*[4] have recently described a mass spectral investigation of the flash pyrolysis of vinyl benzotriazoles which indicates that *N*-phenylketenimines are the primary products but that indoles may be formed at higher temperatures. This last report prompts us to report our studies of the preparative scale flash pyrolysis of vinylbenzotriazoles which confirm the practicability of this route to indoles and identify some of its limitations.

Vinylbenzotriazoles are attractive precursors to indoles because of their availability by a variety of routes.[2–7] Triazoles (**1a**), (**1b**), and (**9**) were obtained in 20, 9, and 25% yields, respectively, by thermal (polar, Markovnikov) addition of 1-chlorobenzotriazole to styrene, heptene, and cyclohexane in dichloromethane, followed by chromatographic separation of the desired benzotriazol-1-yl substituted adducts and dehydrohalogenation with potassium t-butoxide in t-butyl alcohol or DMF.[5] The low yield is the result of the addition step which gives mainly the 2-substituted chloroalkylbenzotriazole by attack of the ambident benzotriazolyl anion through N-2 on the intermediate chloronium ion.

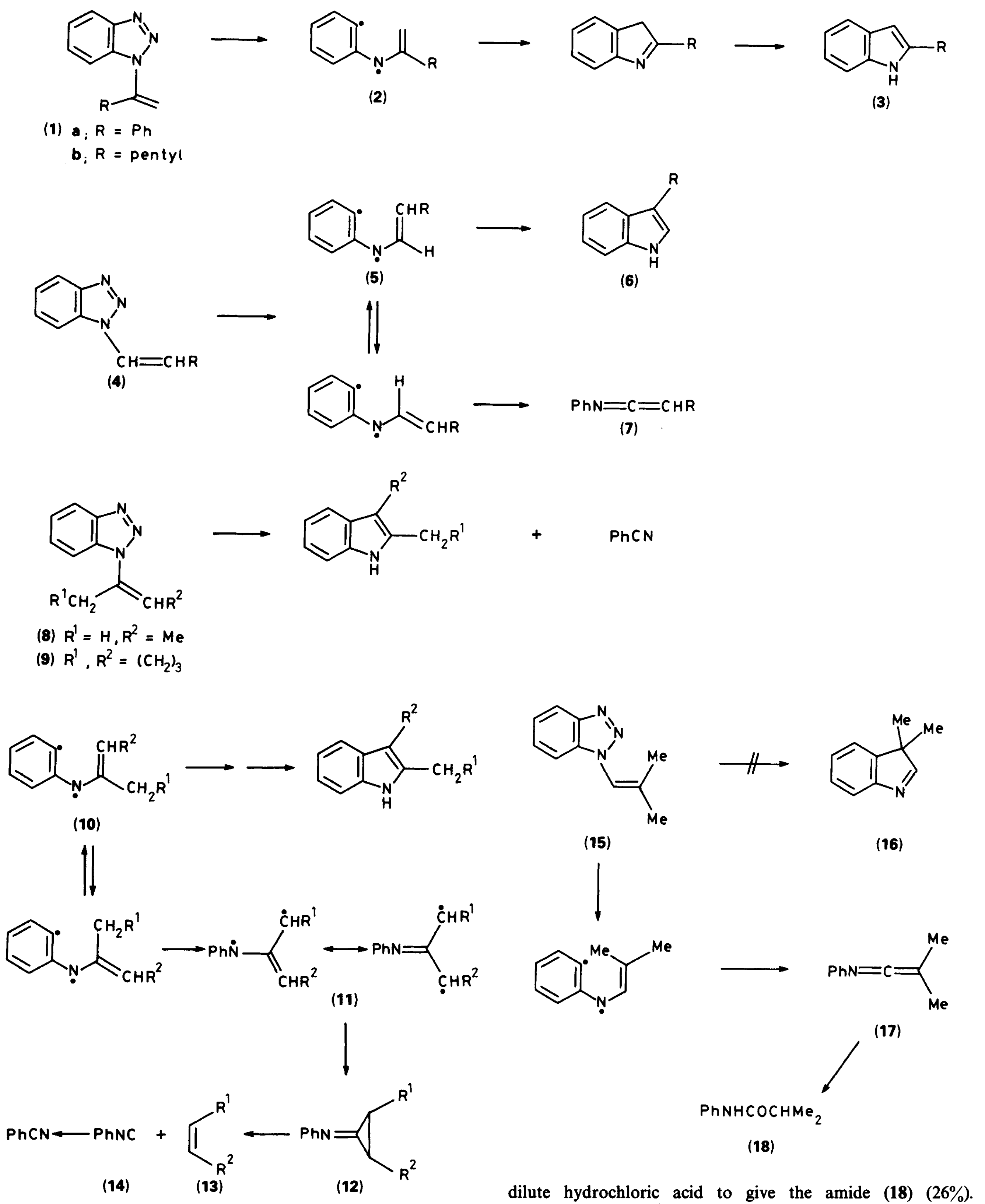
The regiochemistry of the addition of 1-chlorobenzotriazole to monosubstituted alkenes is reversed under conditions of u.v. irradiation. Thus photochemical addition of 1-chlorobenzotriazole to heptene gave the anti-Makovnikov adduct (benzotriazol-1-yl isomer only) which on dehydrohalogenation yielded (**4**; R = pentyl) (36%), as a mixture of *E* and *Z* isomers. We believe that this addition proceeds by homolysis of the benzotriazole–chlorine bond and addition of the benzotriazolyl radical to the alkene. The resulting radical then abstracts a chlorine atom from chlorobenzotriazole and leads to an inefficient radical chain mechanism for the addition.[6]

Vinylbenzotriazoles can also be obtained by base catalysed isomerisation of allylbenzotriazoles.[2] Thus 1-(1′-methylallyl)-benzotriazole and 1-(2′-methylallyl)benzotriazole gave triazoles (**8**) and (**15**) in 81 and 44% yields, respectively. Compound (**4**; R = CO_2Et) was obtained quantitatively by nucleophilic addition of benzotriazole anion to ethyl propiolate[3] and represents a further approach to vinylbenzotriazoles. Finally, the availability of 1-(1-alkenyl)benzotriazoles is extended considerably by the use of 1-(benzotriazolylmethyl)triphenylphosphonium chloride and of 1-(1-trimethylsilylalkyl)benzotriazoles in Wittig reactions and Peterson olefinations, respectively.[7]

Flash-pyrolysis of vinylbenzotriazoles (**1a**, **b**) at 600 °C/10^{-2} Torr gave the 2-substituted indoles (**3**; R = Ph, pentyl) in 67 and 56% yields, respectively, presumably by closure of the diradicals (**2**) and aromatisation of the resulting 3*H*-indoles. Vinylbenzotriazole (**4**; R = pentyl) gave 3-pentylindole (**6**; R = pentyl), but in somewhat lower yield (42%). In this case, examination of the crude pyrolysate by GC/MS revealed a trace of *N*-phenylheptanamide possibly resulting from hydrolysis of the keteneimine (**7**) formed by intramolecular transfer of the α-vinylic hydrogen to the aryl radical centre in the initial diradical (**5**). In their mass-spectral/flash pyrolysis studies Katritzky and co-workers[4] identified ketenimines as the products of pyrolysis of 1-vinyl- and 1-styryl-benzotriazoles (**4**; R = H, Ph) below 700 °C and indoles at higher temperature and concluded that the indoles were probably formed *via* the ketenimines. The formation of indoles from (**1**; R = Ph, pentyl), in which ketenimine formation is precluded by the lack of an α-vinyl hydrogen, indicates that ketenimines are not necessarily intermediates in indole formation and, indeed, direct collapse of the initial diradical is a more reasonable mechanism. No 2-pentylindole was observed in the pyrolysis of (**4**; R = pentyl), although Katritzky *et al.* report the formation of both 2- and 3-phenylindoles in the pyrolysis of 1-styrylbenzotriazole (**4**; R = Ph).[4] Surprisingly, compound (**4**; R = CO_2Et) gave no trace of ethyl indole-3-carboxylate; an insoluble polymeric product was obtained.

Cyclohexenylbenzotriazole (**9**) gave tetrahydrocarbazole as expected, but in only 44% yield. Unexpectedly, the major product was benzonitrile (53%). The dimethylvinylbenzotriazole (**8**) gave 2,3-dimethylindole (34%), the major product again being benzonitrile (63%). An explanation for this observation is given in the Scheme. Depending on its conformation, the diradical (**10**) can collapse to give the indole or undergo intramolecular hydrogen-transfer to give the azatrimethylenemethane (**11**) and hence the iminocyclopropane (**12**). Cheletropic fragmentation of (**12**) would furnish the alkene (**13**) and PhNC, rearrangement of which to PhCN at high temperature is well precedented.[8] Some support for this mechanism comes from the NMR spectrum of the crude pyrolysate from (**9**) which showed signals at δ 5.66, 2.31, and 1.82 ppm, which correspond to cyclopentene. Close examination of the pyrolysate from (**1b**) by GC/MS also reveals a trace of PhCN. Thus, as expected, the relative sizes of substituents on the vinyl group appear to control the conformational populations of the intermediate diradical (**10**). When R^1 is large relative to R^2, indole formation is favoured.

In an attempt to obtain a 3*H*-indole, the isobutenylbenzotriazole (**15**) was pyrolysed (675 °C). The resulting unstable pyrolysate showed a singlet (6 H) in the ^{1}H NMR



Scheme.

spectrum at δ 1.75 ppm, but the 3*H*-indole structure was ruled out by the observation of a strong IR absorption at 2 000 cm^{-1}. The data are in accord with the ketenimine structure (**17**), support for which comes from treatment of the pyrolysate with dilute hydrochloric acid to give the amide (**18**) (26%). Formation of the ketenimine in this case is in agreement with the mass spectral studies reported by Katritzky *et al.* and again correlates with the presence of an α-vinyl hydrogen.

Flash-pyrolysis of vinylbenzotriazoles provides a simple route to substituted indoles, although side reactions of the intermediate diradical impose limitations and lead to lowering of yields in some cases.

Experimental

^{1}H NMR spectra were obtained on a Perkin-Elmer R34 Spectrometer (220 MHz) or a Bruker WM 250 (250 MHz) spectrometer with tetramethylsilane as the internal reference. Gas chromatography/mass spectrometry was carried out using a VG 7070E mass spectrometer coupled to a capillary column with type OV 1 packing. New compounds were characterised by high resolution mass spectrometry and were judged to be pure by TLC and NMR spectroscopy. All were subsequently converted to known, fully characterised, compounds.

Preparation of 1-*Vinylbenzotriazoles.*—1-(Benzotriazol-1-yl)-1-phenylethene (**1a**), m.p. 46.5–48 °C,[5] and (benzotriazol-1-yl)-cyclohexene (**9**), m.p. 45–46 °C,[3] were obtained by elimination of hydrogen chloride from the appropriate 1-chlorobenzotriazole–alkene adduct as described previously.

1-(Benzotriazol-1-yl)-2-methylpropene (**15**) (44%) and 2-(benzotriazol-1-yl)but-2-ene (**8**) (88% as a 65:35 mixture of *E* and *Z* isomers) were obtained by base-catalysed isomerisation (1M potassium t-butoxide in DMSO) of 3-(benzotriazol-1-yl)-2-methylprop-1-ene and 3-(benzotriazol-1-yl)but-1-ene respectively.[2]

Ethyl 3-(benzotriazol-1-yl)propenoate (**4**; R = CO_2Et) was prepared as described by Wender and Cooper.[3]

2-(*Benzotriazol*-1-*yl*)*hept*-1-*ene* (**1b**).—A mixture of 1-chlorobenzotriazole (3.825 g, 25 mmol) and heptene (3.07 g, 31.25 mmol) in dichloromethane was allowed to stand for 6 days. The resulting solution was washed with 2M sodium hydroxide (50 ml) and water (25 ml) and then dried over magnesium sulphate and evaporated. The residual oil was chromatographed on silica gel and the desired 2-(benzotriazol-1-yl)-1-chloroheptane was eluted as a pale yellow oil with 20% ether in petroleum. The less polar 2-(benzotriazol-2-yl)-1-chloroheptane was eluted first and discarded. Bulb-to-bulb distillation gives a colourless oil, b.p. 200 °C/0.2 Torr (9.2%) (Found: *m/z* 253.1155 and 251.1180. $C_{13}H_{18}N_3Cl$ requires *m/z* 253.1160 and 251.1189); δ($CDCl_3$) 8.09 (1 H, d, *J* 8.8 Hz), 7.57–7.47 (2 H, m), 7.38 (1 H, dt, *J* 7.3 and 1.4 Hz), 4.98–4.87 (1 H, m), 4.17–3.98 (2 H, m), 2.35–2.13 (2 H, m), 1.42–0.80 (9 H, m).

The 2-(benzotriazol-1-yl)-1-chloroheptane (0.5 g, 2 mmol) was stirred with potassium t-butoxide (0.46 g, 4 mmol) in dry t-butyl alcohol (50 ml) at 30 °C for 6 h. The resulting solution was poured into water (100 ml) and extracted with ether (3 × 50 ml). The combined ethereal extracts were washed with 2M hydrochloric acid (50 ml) and water, and dried ($MgSO_4$). Evaporation and bulb-to-bulb distillation gave (**1b**) as a colourless oil (94%), b.p. 200 °C/0.25 Torr (Found: *m/z* 215.1423. $C_{13}H_{17}N_3$ requires *m/z* 215.1422); δ($CDCl_3$) 8.09 (1 H, d, *J* 8.3 Hz), 7.69 (1 H, d, *J* 8.3 Hz), 7.55–7.36 (2 H, m), 5.42 (1 H, s), 5.28 (1 H, s), 2.91 (2 H, t, *J* 7.4 Hz), 1.53–1.45 (2 H, m), 1.34–1.28 (4 H, m), 0.85 (3 H, t, *J* 6.9 Hz).

1-(*Benzotriazol*-1-*yl*)*hept*-1-*ene* (**4**; R = *pentyl*).—A solution of heptene (4.31 g, 44 mmol) and 1-chlorobenzotriazole (5.37 g, 35 mmol) in dichloromethane (40 ml) was irradiated at −10 °C in a Pyrex glass apparatus using a Hanau 150 W mercury immersion lamp. After 8.5 h, the solution was washed with 2M sodium hydroxide (60 ml) and water (50 ml), and then dried ($MgSO_4$). Removal of the solvent gave an oil which, after bulb-to-bulb distillation at 200 °C/0.2 Torr, afforded 1-(benzotriazol-1-yl)-2-chloroheptane (3.15 g, 36%) (Found: *m/z* 253.1153 and 251.1181. $C_{18}H_{18}N_3Cl$ requires *m/z* 253.1160 and 251.1180); δ($CDCl_3$) 8.00 (1 H, d, *J* 8.3 Hz), 7.60–7.27 (3 H, m), 4.85 (2 H, t, *J* 6.7 Hz), 4.54–4.34 (1 H, m), 1.92–0.66 (11 H, m).

1-(Benzotriazol-1-yl)-2-chloroheptane (0.76 g, 3 mmol) and potassium t-butoxide (0.34 g, 3 mmol) were stirred in t-butyl alcohol (75 ml) for 3 h at 30 °C. The mixture was then poured into water (300 ml) and extracted with ether (3 × 75 ml). After washing with 2M hydrochloric acid (75 ml) and water (75 ml) and drying over magnesium sulphate, the combined ethereal extracts were evaporated and the residue subjected to bulb-to-bulb distillation at 200 °C/0.15 Torr to give 1-(benzotriazol-1-yl)hept-1-ene as a pale yellow oil (0.63 g, 97%) (75:25 mixture of *E* and *Z* isomers) (Found: *m/z* 215.1428. $C_{13}H_{17}N_3$ requires *m/z* 215.1422); δ($CDCl_3$) 8.05 (1 H, d, *J* 8.0 Hz), 7.66–7.34 (3 H, m), 7.29 (0.75 H, *E* isomer, d, *J* 14.7 Hz), 6.99 (0.25 H, *Z* isomer, d, *J* 8.8 Hz), 6.50 (0.75 H, *E* isomer, m), 5.84 (0.25 H, *Z* isomer, m), 2.46–2.20 (2 H, m), 1.63–0.76 (9 H, m).

Flash-Pyrolyses of Vinylbenzotriazoles.—Flash pyrolyses were carried out by distillation of the vinylbenzotriazole (100 mg/h) at 1–2 × 10^{-2} Torr through a silica tube (30 cm × 1.5 cm i.d.) maintained at 600 °C. The pyrolysate was collected on a cold surface (−78 °C) placed close to the end of the tube. After warming to room temperature, the pyrolysate was removed with dichloromethane and the products isolated as described below.

(a) 1-(Benzotriazol-1-yl)-1-phenylethene (**1a**) (300 mg) gave, after preparative TLC on alumina with 30% dichloromethane–petroleum as eluant, 2-phenylindole (175 mg, 67%), identical with an authentic sample (m.p., IR, and NMR).

(b) 2-(Benzotriazol-1-yl)hept-1-ene (**1b**) (200 mg) gave, after purification by preparative TLC on alumina with dichloromethane as eluant, 2-pentylindole[9] (97 mg, 56%) as a colourless oil (Found: *m/z* 187.1371. Calc. for $C_{13}H_{17}N$: *m/z* 187.1361); δ($CDCl_3$) 7.80 (1 H, br s), 7.51 (1 H, d, *J* 6.2 Hz), 7.30–6.97 (3 H, m), 6.21 (1 H, s), 2.68 (2 H, t, *J* 7.6 Hz), 1.74–0.86 (9 H, m).

(c) 1-(Benzotriazol-1-yl)hept-1-ene (**4**; R = pentyl) (240 mg) gave, after preparative TLC on alumina with 20% dichloromethane–petroleum as eluant, 3-pentylindole[10] (88 mg, 42%) as a colourless oil (Found: *m/z* 187.1367); δ($CDCl_3$) 7.87 (1 H, br s), 7.61 (1 H, d, *J* 7.5 Hz), 7.35–7.05 (3 H, m), 6.95 (1 H, d, *J* 1.8 Hz), 2.74 (2 H, t, *J* 7.5 Hz), 1.77–0.85 (9 H, m). Analysis of the crude pyrolysate by GC/MS revealed a low intensity peak corresponding to *N*-phenylheptanamide, *m/z* (205 (M^+), 135, 94, 93, and 77.

(d) 1-(Benzotriazol-1-yl)cyclohexene (**9**) (220 mg) gave a pyrolysate which was condensed at −196 °C. After warming to room temperature this was dissolved in dichloromethane, and the solution was evaporated and subjected to bulb-to-bulb distillation at 100 °C/0.2 Torr to give benzonitrile (60 mg, 53%), identical (TLC, IR, and NMR) with an authentic sample. Sublimation of the residue (180 °C/0.2 Torr) gave tetrahydrocarbazole (82 mg, 44%), m.p. 119 °C, identical with an authentic sample. When the crude pyrolysate was removed from the cold surface below −10 °C with carbon tetrachloride and the solution was analysed by NMR spectroscopy, signals were observed at δ 5.66 (2 H, br s), 2.31 (4 H, br t), and 1.80 (2 H, m). These are identical with those reported for cyclopentene.[11]

(e) 1-(Benzotriazol-1-yl)-2-methylpropene (**8**) (300 mg) gave a pyrolysate which showed an IR absorption at 2 218 cm^{-1} and was shown by GC/MS to contain benzonitrile and 2,3-dimethylindole. Bulb-to-bulb distillation (100 °C/0.2 Torr) of the crude pyrolysate gave benzonitrile (113 mg, 63%), identical with an authentic specimen (TLC, IR, and NMR). The residue was sublimed (130 °C/0.15 Torr) to give 2,3-dimethylindole (87 mg, 34%), m.p. 105–107 °C, identical with an authentic sample.

(f) 1-(2-Methylprop-1-enyl)benzotriazole (**13**) (280 mg) gave a yellow oil, ν_{max} 2 910, 2 000, 1 583, 1 478, 1 370, 760, and 683 cm^{-1}; δ($CDCl_3$) 7.52–7.11 (8 H, m) and 1.75 (6 H, s) corresponding to keteneimine (**17**).[12] Purification by preparative TLC on alumina gave isobutyrylanilide (**18**) (26%), identical with a sample prépared from aniline and isobutyryl chloride.

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