Regiospecific Radical-induced Cleavage of Aziridines: Syntheses of Allylic Amines and Pyrrolidines

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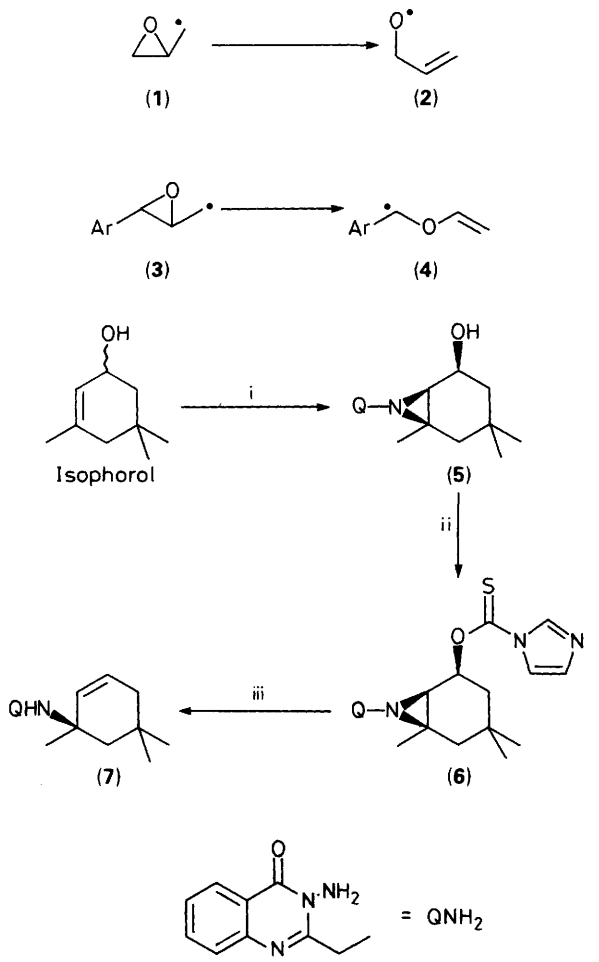
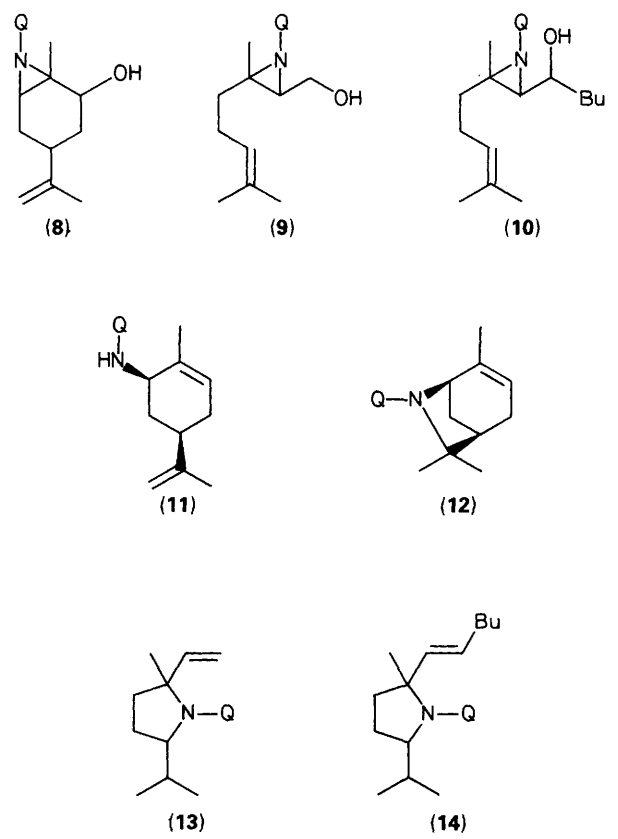
The radical-induced cleavage of a series of fused aziridines has been found to proceed regiospecifically to produce C–N bond cleavage, and the product radicals afford allylic amines or, in suitable cases, cyclise to form pyrrolidines.

Aziridines have been used as intermediates in organic chemistry far less than their oxygen counterparts, epoxides. This has resulted from the greater ease of accessing epoxides. Recently, interesting developments[1] have taken place in aziridine chemistry which promise greater exploitation of them as versatile intermediates in the near future. Our interest in the behaviour of reactive rings[2,3] in the presence of radicals has prompted us to investigate the behaviour of aziridines when a radical is formed on an atom adjacent to the ring. Specifically, we wished to probe the regiochemistry of



Scheme 1. *Reagents and conditions*: i, QNH_2, $Pb(OAc)_4$, CH_2Cl_2, room temp.; ii, thiocarbonyldiimidazole (2 equiv.), CH_2Cl_2, heat; iii, Bu^n_3SnH, AIBN, THF, heat.



cleavage of aziridines and whether the radicals produced on their cleavage could be utilized for further chemistry.

In the chemistry of small rings, one might imagine that a progression might exist on going from cyclopropanes *via* aziridines to epoxides. Under normal circumstances, it is known that epoxides undergo selective C–O bond fission under the influence of a radical on an adjacent atom[2,4] (**1**) → (**2**). With special substituents epoxides can undergo C–C bond cleavage[5] as seen in (**3**) → (**4**). Cyclopropanes on the other hand must suffer C–C bond cleavage, and the factors affecting the regiochemistry of cyclopropane cleavage have been discussed.[6,7] As yet, the radical-induced cleavage of aziridines remains untried. In order to test how aziridines would behave, we synthesised the aziridine (**5**) in racemic form from isophorol using the aziridination procedure[8] used by Atkinson. Reaction of (**5**) with thiocarbonyldiimidazole (2 equiv.) in dichloromethane, generated the imidazolide (**6**) *in situ* as judged by ^1H NMR. This was reacted with tributyltin hydride in tetrahydrofuran (THF) in the presence of a catalytic quantity of azoisobutyronitrile (AIBN), and gave rise to the allylic amine (**7**) in 78% yield (Scheme 1). As expected, no evidence for products resulting from C–C bond cleavage in the aziridine could be detected. This therefore constitutes a method of some potential for converting allylic alcohols *via* aziridination into allylic amines.

Investigating whether the obligatory nitrogen-centred radicals would cyclise onto appropriately placed reactive groups such as alkenes was a matter of great interest in the light of recent reports that nitrogen-centred radicals tend to add reversibly to alkenes with the equilibrium favouring non-addition.[9] In the light of these reports we synthesised the three aziridines (**8**), (**9**), and (**10**). On treatment as above the aziridine (**8**) gave rise to the allylic amine (**11**). No evidence for the bicyclic product (**12**) was found. For (**12**) to form however would require addition to an alkene carbon bearing two substituents, which might prove quite a steric challenge. With the aziridines (**9**) and (**10**) however, radical-induced aziridine cleavage led to formation of the pyrrolidines (**13**) and (**14**) respectively, albeit in disappointing yields (21% and 26% respectively). In these reactions no allylic amine could be isolated. Surzur[10] has discussed the differences between aminyl radicals and their protonated counterparts. One of the reported differences is that the protonated forms cyclise more efficiently. Mindful of this, we repeated the radical cleavage of (**9**) and (**10**) in the presence of a Lewis acid, magnesium bromide diethyl etherate, instead of a protic acid, and observed the production of (**13**) and (**14**) in a much higher yield (70% and 83% respectively).† We propose that this improved yield may be due to cyclisation of a magnesium-complexed radical, and that Lewis-acid catalysed radical cyclisations may be an area worthy of further exploration. The addition of the Lewis acid certainly transforms this reaction into a synthetically valuable process.

In conclusion, the cleavage of these aziridines by adjacent radicals is a clean and high yielding process which can be used to form allylic amines or diverted into heterocycle formation.

† Our attempts to use protic acid instead of Lewis acid led only to decomposition.

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