Chiral Aziridination of Alkenes

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Oxidation of the 2-substituted *N*-amainobenzimidazole (**5**) in the presence of prochiral alkenes gives aziridines stereoselectively: addition, to γ,γ-dimethyl-α-methylenebutyrolactone is stereospecific and the relative configuration of the two chiral centres in the product has been confirmed by a single crystal *X*-ray diffraction study and is in agreement with a transition state geometry resembling (**11**).

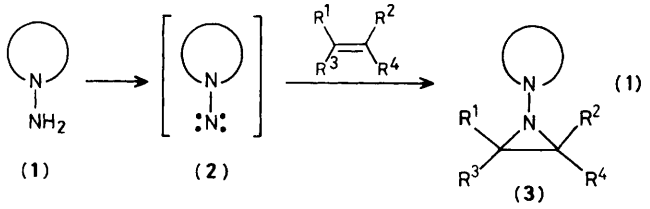
Epoxidation of alkenes followed by regio- and stereo-specific ring-opening of the epoxides is an invaluable routine in synthesis. The recent finding of Sharpless *et al.*[1] that epoxides can be obtained in high enantiomeric excess by epoxidation of prochiral allylic alcohols has broadened the scope of this routine to include synthesis of chiral products. By contrast, aziridination is still an unfamiliar term in the organic chemist's vocabularly in spite of the fact that, like epoxides, aziridines can easily be ring-opened in a controlled way.[2] Although some nitrenes R–N: add to alkenes directly,[3] the reactions are blighted by low yields and/or lack of stereospecificity, particularly at low concentrations of alkenes, and do not enjoy widespread use in synthesis of aziridines and their transformation products.

There is, however, a family of *N*-aminoheterocyclic compounds (**1**) whose oxidation generates the corresponding *N*-nitrenes (**2**) which are trapped by alkenes to give aziridines (**3**), often in good yields.[4] The singlet ground states of these nitrenes mean that their additions to alkenes are stereospecific and, unlike most other nitrenes which can be trapped intermolecularly, there is no competition from insertion of (**2**) into C–H bonds.[5] A further advantage in the use of (**2**) is their ambiphilic character: they react to give good yields of aziridines with *e.g.* styrene or methyl acrylate.[6]

To make use of aziridines (**3**) produced as in equation (1) would, in general, require that the heterocyclic ring be jettisoned by cleavage of the N–N bond[7] either in the aziridines (**3**) or, more expediently, in their ring-opened products.[8]

In this communication we show that the heterocycle in (**1**) can serve as more than just an appendage on the nitrene and can in practice be used to bring about efficient induction of chirality in aziridination of prochiral alkenes.[9]

N-Aminobenzimidazole is one member of the family (**1**) referred to above. Attempts to prepare benzimidazole (**4**) by the Phillips method[10] for construction of this ring system were



Scheme 1. *Reagents:* i, Bu^{t}CHMeCOCl–diethyl ether; iii, $POCl_3$–pyridine; iii, H_2NOSO_2mesityl.

unsuccessful but (**4**) was obtained and aminated to (**5**) by the procedure outlined in Scheme 1.

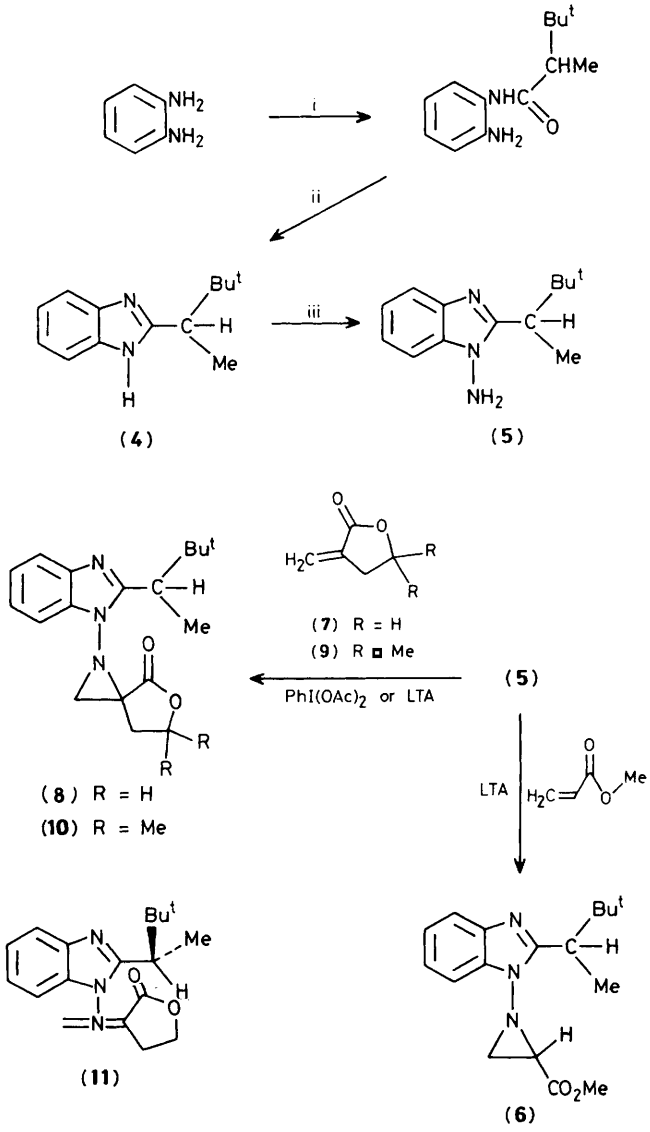
Oxidation of *N*-aminobenzimidazole (**5**) with lead tetra-acetate (LTA) in dichloromethane in the presence of methyl acrylate gave a 2.1:1 ratio of stereoisomers (**6**) (71%). However, a similar oxidation of (**5**) with phenyl iodosodiacetate in the presence of α-methylene-γ-butyrolactone (**7**) at room temperature gave a 5.3:1 ratio of stereoisomers (**8**) (from the 300 MHz spectrum of the crude product) from which the major product, m.p. 189—191 °C, was isolated (50%) by crystallisation. An identical ratio of stereoisomers of (**8**) was produced when LTA was substituted for phenyl iodosodiacetate suggesting that the free nitrene was involved in both cases.

Introduction of a *gem*-dimethyl group into the butyrolactone as in (**9**) and reaction of 2 mol equiv. of the latter with the *N*-nitrene derived from (**5**) results in formation of (**10**) (69% isolated) as a single stereoisomer: the other stereoisomer was not evident in the n.m.r. spectrum of the crude product.

Our rationale for the chiral induction in formation of these aziridines uses the '*syn*-selectivity' which is also a feature of these *N*-nitrene additions to alkenes.[11] Attack of the *N*-nitrene derived from (**5**) with butyrolactone (**9**) is believed to occur *via* a transition state geometry as shown in (**11**) in which the benzimidazole and butyrolactone are contained in parallel planes, the N–N(nitrene) bond is orthogonal to the plane containing the alkene π-electrons,[12] and there is an attractive secondary interaction between the C=O of the butyrolactone and the 2-position of the heterocycle.

The configuration of the newly-created chiral centre in (**10**) was established by *X*-ray crystallography (Figure 1)† and is in agreement with that predicted from the transition state model (**11**). Although both invertomers at the aziridine nitrogen of

† *Crystal data* for (**10**): $C_{20}H_{27}N_3O_2$, M = 341.40, monoclinic space group $P2_1/a$, a = 14.367(13), b = 18.574(16), c = 7.327(30) Å, β = 96.7(1)°, U = 1941.9 Å^3, Z = 4, D_c = 1.17 g cm^{-3}, λ(Mo-K_α) = 0.7107 Å, μ(Mo-K_α) = 0.43 cm^{-1}. The crystals were colourless prisms. The intensities of 1408 unique reflections ($2\theta < 50°$, $+h$, $\pm k$, $+l$) were measured on a Stoe STADI-2 Weissenberg diffractometer with graphite monochromated Mo-K_α radiation using an ω-scan technique. The data were corrected for Lorentz and polarisation effects, to yield 618 reflections with $I > 3\sigma(I)$. The structure was solved using the TREF direct methods option of SHELXS 84 (G. M. Sheldrick, SHELXS 84, personal communication). All subsequent calculations were carried out using the computer program SHELX (G. M. Sheldrick, SHELXS 76, Program for Crystal Structure determination, University of Cambridge, 1976). The hydrogen atom of positional interest (H15) was located and refined as a normal atom, all other hydrogen atoms were included in calculated positions for structure factor calculations. Final cycles employed a weighting parameter g(0.000336) $\{w = [1/\sigma^2 (F) + g(F)^2]\}$ and gave the final residual indices $R\{ = \Sigma'(|F_o| - |F_c|)/\Sigma|F_o|\}$ 0.098 and $R_w\{ = [\Sigma_w(|F_o| - |F_c|)^2/\Sigma_w|F_o|^2]^{\frac{1}{2}}\}$ 0.0944. The final difference Fourier map was featureless, and an analysis of the weighting scheme over $|F_o|$ and $\sin\theta/\lambda$ was satisfactory. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1, 1986.



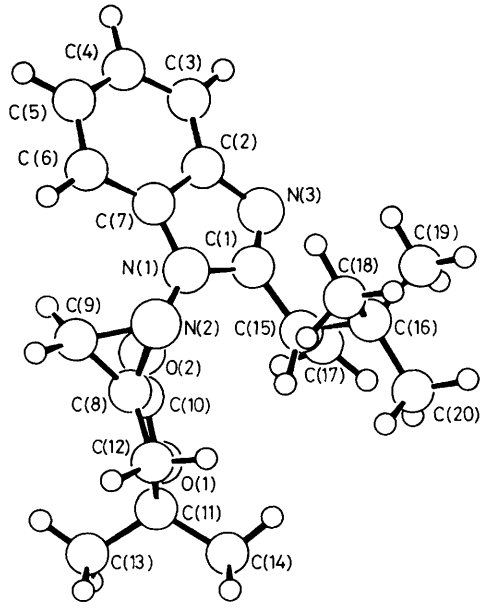


Figure 1. Molecular structure of (**10**).

(**10**) [and (**8**)] are present in solution (from n.m.r. spectroscopy) only the more abundant invertomer, which is apparently configurationally stable at nitrogen in the crystalline form,[13] was present in the crystal used in the *X*-ray study.

We suspect that the improved stereoselectivity in formation of aziridines (**8**) and (**10**) by comparison with (**6**) may be the consequence of the preference of methyl acrylate for the conformation shown [(**5**) → (**6**)].

The stereoselectivity of reaction of the nitrene derived from (**5**) with styrene and (*E*)-butene was also encouraging: a 5 : 1 ratio of stereoisomers was obtained in both cases. The major stereoisomer from addition to styrene was separated by crystallisation, m.p. 152—154 °C (61%), and that from addition to (*E*)-butene by chromatography (oil) (60%).

If (**5**) can be prepared as a single enantiomer then synthesis of chiral aziridines and their ring-opened products is in prospect.

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