Conformational Analysis of *N*-[3,4-Dihydro-4-oxoquinazolin-3-yl]aziridines

Robert S. Atkinson*, John Fawcett, David R. Russell, and Gary Tughan
Department of Chemistry, Leicester University, Leicester LE1 7RH, U.K.

The *X*-ray crystal structure of the aziridine (**7a**) shows that the preferred orientation around the N–N bond has the lone pairs of electrons on adjacent nitrogens eclipsed; the rotamer equilibria around the N–N bonds in the two stereoisomers (**7a**) and (**7b**) suggest that this is also the preferred conformation for these substituted hydrazines in solution.

The cyclopropylcarbinyl cation is at its most stable in the bisected conformation (**1**) in which stabilisation of the cation by delocalisation of the cyclopropyl ring bonds is at a maximum.[1] Experimental evidence for the preferred conformation of the cyclopropylcarbinyl anion is lacking† but calculations suggest that there is a slight preference for the perpendicular conformation (**2**) (sp^2-hybridisation for the carbanion assumed).[3]

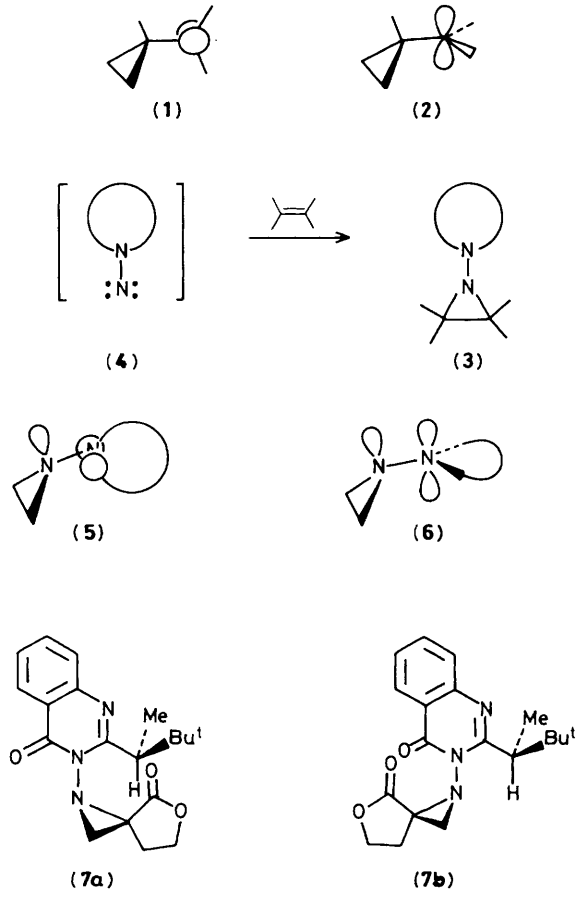
Our interest has been in the related problem of the preferred conformation of aziridines of the general formula (**3**) which are obtained by addition of the heterocyclic *N*-nitrenes (**4**) to alkenes.[4] Invariably in these aziridines, (**3**), the nitrogen of the heterocycle is sp^2-hybridised. Consideration of (**3**) as a substituted hydrazine would suggest that the most stable conformation would be the bisected one (**5**) since it is in this conformation that repulsion between electron pairs is at a minimum. The perpendicular conformation (**6**), however, is that which would minimise possible unfavourable interactions between the aziridine ring bonds and the sp^2-hybridised heterocyclic ring nitrogen lone pair.

In this communication we report that aziridine stereoisomer (**7a**) shows a preference for the perpendicular arrangement (**6**) in the crystalline state and present evidence that this is the preferred conformation in solution also.

The spiro-fused aziridines (**7a**) and (**7b**) are obtained by oxidation of the corresponding *N*-aminoquinazolone in the presence of α-methylene-γ-butyrolactone.[5] An *X*-ray crystal structure determination of the stereoisomer (**7a**) is shown in Figure 1 and a view which shows the eclipsing of the lone pairs on adjacent nitrogens is shown in Figure 2, which has the plane of the quinazolone ring horizontal and the N–N bond projecting towards the viewer.‡

The other (oily) stereoisomer (**7b**) shows an n.m.r. spectrum at 300 MHz and room temperature in which there are broadened signals typical of a system undergoing a conformational change close to the coalescence temperature. At −40 °C, well-resolved spectra of both these conformers were obtained and the ratio of the two was *ca.* 1:1.

A number of factors suggest that these conformers of (**7b**) are rotamers around the N–N bond and not invertomers.[8] Thus the barrier which separates these two conformations is calculated from data at the coalescence temperature to be *ca.* 14 kcal mol^{-1} (1 kcal = 4.142 kJ) which is 7 kcal mol^{-1} lower than that expected for inversion in aziridines of this type. Neither the bulky substituent at C-2 of the quinazolone nor the spiro-ring fusion to the aziridine ring in (**7b**) would be expected to bring about a reduction in the inversion barrier in (**7b**) of this magnitude. Thus the aziridines (**8**) (one stereoisomer) and (**9**) have inversion barriers of 21 kcal mol^{-1} and >21 kcal mol^{-1}, respectively [(**9**) exists as a 5:1 ratio of invertomers and the symmetry of the phthalimido ring means that no rotamers around the N–N bond will be visible].



† Simple cyclopropylcarbinyl carbanions are prone to ring open to the corresponding allylcarbinyl anions, see ref. 2.

‡ *Crystal data:* $C_{19}H_{21}N_3O_3$, M = 339.39, monoclinic, space group $P2_1/n$ (Alt. $P2_1/c$, No. 14), a = 10.503(2), b = 27.399(6), c = 6.401(12) Å, β = 103.9(1)°, U = 1788.33 Å, Z = 4, D_x = 1.23 g cm^{-3}, λ(Mo-K_α) = 0.7107 Å. The intensities of 3051 reflections with $7 < 2\theta < 54$ and $\pm h$, $\pm k$, $+l$ 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 1809 reflections with $I \geq 3\sigma(I)$. The structure was solved using the TREF direct methods option of SHELXS 84.[6] All subsequent calculations were carried out using the computer program SHELX.[7] All hydrogen atoms were located from a difference Fourier map and the positional and isotropic thermal parameters were refined independently. All other atoms were refined anisotropically. The final cycles of refinement employed a weighting scheme $w = 1/[\sigma^2(F_0) + 0.00093(F_0)^2]$ and gave the final residual indices $R\{=\Sigma|(|F_0|-|F_c|)|/\Sigma|F_0|\}$ 0.0400 and $R_w\{=[\Sigma w(|F_0|-|F_c|)^2/\Sigma w|F_0|^2]^{\frac{1}{2}}\}$ 0.0426. The remaining difference Fourier map was featureless and an analysis of the weighting scheme over $|F_0|$ and sinθ/λ 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.

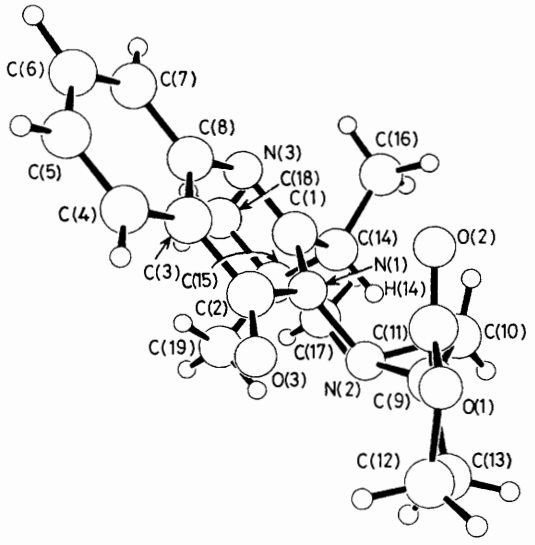


Figure 1. *X*-Ray structure of (**7a**).

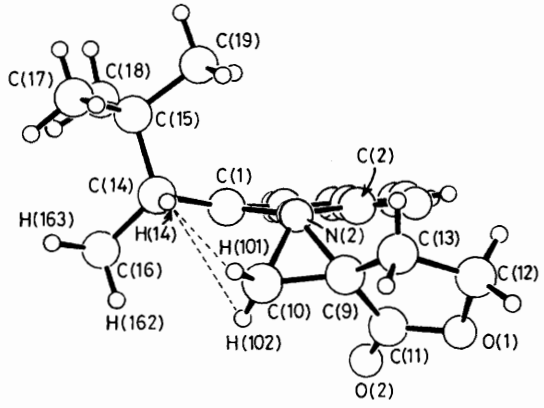
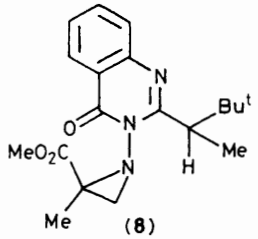
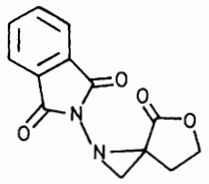


Figure 2. *X*-Ray structure of (**7a**) viewed along the N–N bond. The dotted lines connect hydrogen atoms separated by little more than their van der Waals' radii.

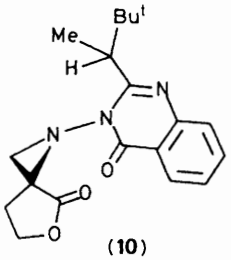
That (**7b**) exists as a 1 : 1 ratio of rotamers but (**7a**) as a single rotamer is explicable from inspection of Figure 1. Compound (**7a**) has the methine hydrogen of the chiral C-2 substituent and both aziridine ring protons just outside their combined van der Waals' radii.§ It is clear that interchange of this methine hydrogen with the methyl group on this chiral substituent, *i.e.* formally changing from (**7a**) → (**7b**), will introduce steric interaction at this point. On the other hand, models suggest that in the other rotamer, formed by rotation around the N–N bond through 180°, interaction of the chiral substituent with the lactone ring may be more unfavourable with (**7a**) than with (**7b**).



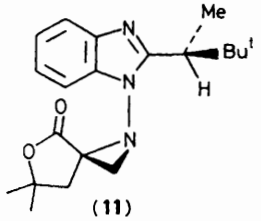
(**8**)



(**9**)



(**10**)



(**11**)

The existence of a 1 : 1 rotamer ratio for (**7b**) and a single rotamer for (**7a**) would be difficult to reconcile with bisected conformations, *e.g.* (**10**) for these rotamers; the more stable conformation of (**3**) is, therefore, the perpendicular arrangement both in the crystalline state and also in solution.¶

The *X*-ray structure of (**11**)[9] shows that the preferred conformation around the N–N bond does not have the electron pairs as nicely eclipsed as in (**7a**) [the angle between the two planes containing these lone pairs is *ca.* 20° in (**11**) compared with 1° for (**7a**)]. It appears that there is some rotation away from the eclipsed conformation in (**11**) to relieve steric interactions between the lactone ring and the chiral substituent at position 2 which would otherwise result.

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6 G. M. Sheldrick, SHELXS 84, personal communication.
7 G. M. Sheldrick, SHELX 76, Program for Crystal Structure Determination, University of Cambridge, 1976.
8 See footnote in ref. 5.
9 R. S. Atkinson, J. Fawcett, D. R. Russell, and G. Tughan, *J. Chem. Soc., Chem. Commun.*, 1986, 832.

§ The quinazolone C-2 atom is tilted slightly out of the plane of the remainder of this ring presumably to accommodate the methine C–H–aziridine ring proton interaction.

¶ Alkanoylated aminocyclopropanes (having sp^2-hybridised N) retrieved from the Cambridge Crystallographic Data Centre show a similar preference for the perpendicular conformation.