Conformational Effects in Spiro-fused Azirines

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Analysis of the n.m.r. spectra of azirines (**5**)—(**8**) together with the *X*-ray crystal structure of (**7**) reveals that a requirement for near-coplanarity of three bonds at the spiro centre results in conformational anchoring of the five-membered ring.

Intermolecular addition of *N*-nitrenes to alkynes has been shown to give 2*H*-azirines by rearrangement, it is thought, of the initially formed 1*H*-azirines (Scheme 1).[1] We have examined the intramolecular version of this reaction by oxidation of (**1**)—(**4**) and find the corresponding spiro-azirines (**5**)—(**8**) are produced as crystalline solids. The yields of (**7**) and (**8**) are quantitative but (**5**) (79%) and (**6**) (90%) are more reactive and are accompanied by acetic acid addition products (**9**) and (**10**), respectively. There are striking and unexpected differences in chemical shifts of the protons on the five-membered ring in *e.g.* azirine (**5**) by comparison with the corresponding protons in the acetoxyaziridine (**9**): in (**5**) these protons resonate at δ 1.75 (*J* 13.9, 9.3, and 1.3 Hz), 2.65 (*J* 13.9, 10.9, 9.6, and 2.8† Hz), 3.03 (*J* 17.5, 9.6, and 1.3 Hz),

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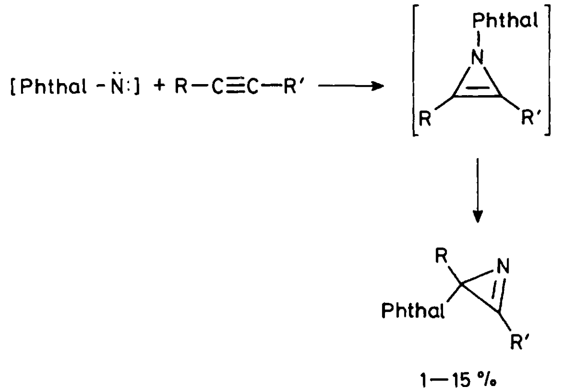
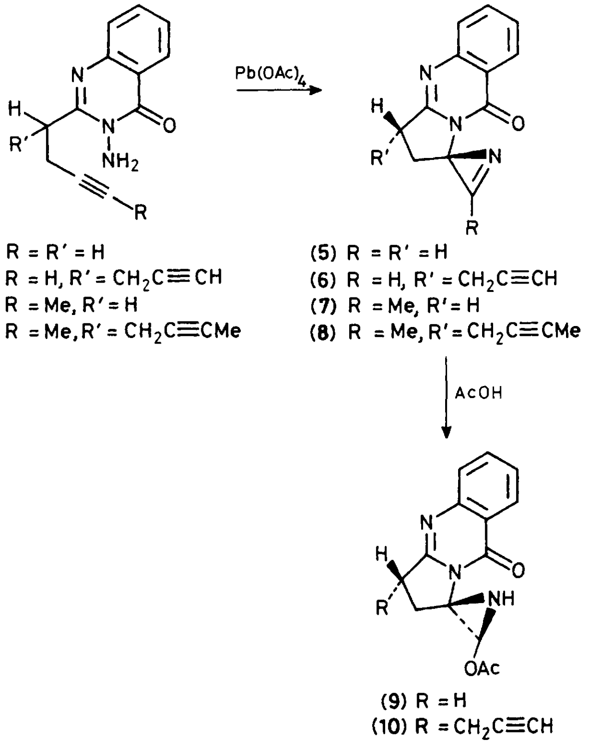
† This coupling constant is a long-range one with the azirine ring H δ 10.41 (*J* 2.8 Hz): see K. Isomura, M. Okada, and H. Taniguchi, *Tetrahedron Lett.*, 1969, 4073.



Phthal = phthalimido
R = H, alkyl; R' = alkyl

Scheme 1

and 3.47 (*J* 17.5, 10.9, and 9.3 Hz) whereas in (**9**) these protons resonate (at 90 MHz) as two triplets (each two protons) at δ 2.31 and 3.08 (a 400 MHz spectrum shows that these four protons are non-equivalent).



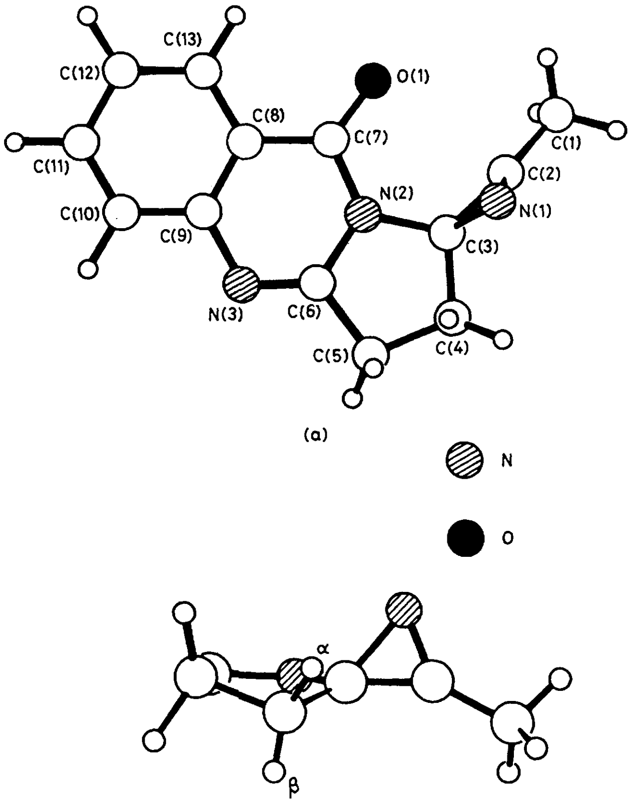


Figure 1

The results of an *X*-ray crystallographic determination on the structure of (**7**)‡ are shown in Figure 1(a): Figure 1(b) is part of this structure viewed perpendicular to the azirine ring with the quinazolone ring residue removed for clarity. It is clear from Figure 1(b) that the C–C bond of the azirine ring is nearly coplanar with the two bonds of the five-membered ring to the spiro-centre [summation of the angles between these bonds gives a value of 358(1.2)°]. Examination of the four azirine ring containing structures in the Cambridge crystallographic data file[2] shows that all of these exhibit the same effect with a similar near-coplanarity of azirine C–C bond and substituent bonds at the 3-position.§ In azirines, the abnormal length of the C–N bond [2a] together with the magnitude of $J(^{13}C\text{–}H)$ at C(3)[3] have been interpreted as evidence for increased p-character in the C–N bond and increased sp^2-character at C(3). The near-coplanarity at C(3) in the azirine crystal structures available is consistent with this conclusion.

Analysis of chemical shifts and coupling constants in the

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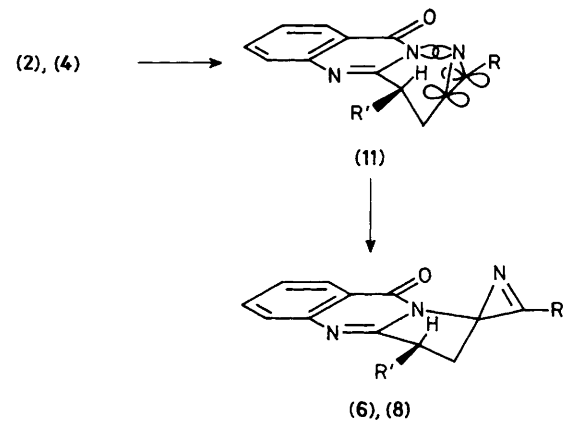
‡ *Crystal data:* $C_{13}H_{11}N_3O$, $M = 225.25$, monoclinic, $a = 8.345(2)$, $b = 13.354(3)$, $c = 10.405(6)$ Å, $\beta = 106.9(1)°$, $U = 1109.4$ Å^3 [cell determined by least squares refinement of diffractrometer measurements of zero and upper layer reflections and from oscillation photographs (*c*)], space group $P2_1/n$ (alt. $P2_1/c$ No. 14), $Z = 4$, $D_x = 1.348$ g cm^{-3}. The crystals were colourless prisms, $\lambda(\text{Mo-}K_\alpha) = 0.7107$ Å, $\mu(\text{Mo-}K_\alpha) = 0.52$ cm^{-1}. The intensities of 2314 unique reflections ($7 \leqslant 2\theta \leqslant 50°$, $+h$ $+k$ $\pm l$) 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 795 reflections with $I \geqslant 2.5\sigma(I)$. 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] The number of variables refined by full matrix least squares was restricted owing to the limited amount of intensity data available. The methyl hydrogen atoms and the atoms of the phenyl groups were refined as rigid groups but the hydrogen atoms on C(4) and C(5) were allowed to refine for position and isotropic motion. Final cycles employed a weighting parameter $g(0.00052)$ $\{w = [1/\sigma^2(F) + g(F)^2]\}$ and gave the final residual indices $R\{= \Sigma|(|F_o|-|F_c|)|/\Sigma|Fo|\}$ 0.0748 and $R_w\{= [\Sigma w(|F_o|-|F_c|)^2/\Sigma w|F_o|^2]^{\frac{1}{2}}\}$ 0.0694. The final difference Fourier map was featureless, and an analysis of the weighting scheme over $|F_o|$ and $\sin\theta/\lambda$ was satisfactory. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

§ It is not surprising that this effect was overlooked since the deformation required to achieve this near-coplanarity is not large and only by viewing the crystal structures perpendicular to the azirine ring is the effect visible.



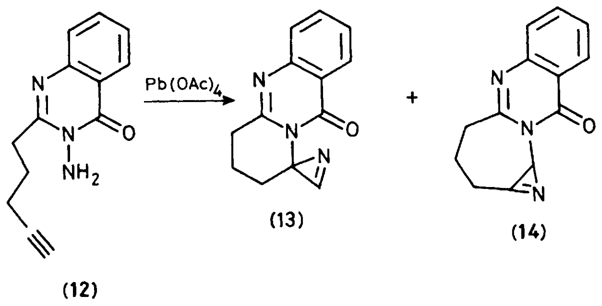
Scheme 2

n.m.r. spectra of (**5**)—(**8**) is in agreement with a common conformation in each case which is the same as that in Figures 1(a) and 1(b) with the relative configurations at the two carbons adjacent to the quinazolone ring in (**6**) and (**8**) as indicated. Noteworthy is the large shielding in (**7**) of H_α (δ 1.73) [the C(4)–H_α bond is nearly coplanar with the C–N azirine ring bond, Figure 1(b)] by comparison with H_β (δ 2.61).[4]

The stereospecificity in formation of (**6**) and (**8**) is of interest. If intramoleculuar *N*-nitrene addition to the triple bond proceeds analogously to the recently proposed pathway for intramolecular addition to alkenes,[5] then the rigid boat-shaped 1*H*-azirine (**11**) in Scheme 2 would result, within which alignment of orbitals required for 1,2-migration is good (even if this migration, construed as a 1,3-sigmatropic rearrangement, is not concerted). This migration would also deliver (**6**) and (**8**) directly in their stable conformations.

Acetoxyaziridines (**9**) (oil) and (**10**) m.p. 128—131°C (decomp.) are assigned the configurations shown at the acetoxy-bearing carbon atoms with the assumption of attack of acetate anion on the azirine C=N from the side of the azirine ring opposite to the quinazolone.

Oxidation of the quinazolone (**12**) proceeds quantitatively to give a mixture of azirines (**13**) and (**14**)¶ in a 9:4 ratio respectively.



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¶ Both (**13**) and (**14**) have definable conformations which will be described in due course.