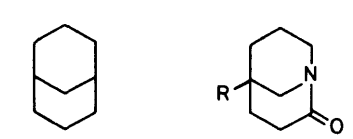
Conformation of 5-Phenyl-1-azabicyclo[3.3.1]nonan-2-one, a Bridgehead Amide

By GEO. L. BUCHANAN
(*Department of Chemistry, University of Glasgow, Glasgow* G12 8QQ)

Summary The ^{1}H n.m.r. spectrum of 5-phenyl-1-azabicyclo[3.3.1]nonan-2-one reveals *W*-coupling between only one of the C(9) protons and the equatorial protons on C(6) and C(8), from which it is concluded that the lactam ring has the boat conformation.

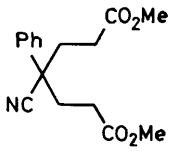
IT is well established[1] that in all but a few cases bicyclo[3.3.1]nonanes (**1**) prefer the chair–chair to the chair–boat conformation, notwithstanding the apparent proximity of the *endo*-hydrogens on C(3) and C(7) in the former. Molecular models of the related (but little known[2]) bridgehead amides of type (**2**) suggest that efficient p–π overlap is only consistent with the chair–boat conformation. It is therefore of interest to discover which of these factors is dominant. Other workers[2] have concluded recently that, for compound (**2**), the chair–boat conformation is preferred, but since their evidence was slender we now report some work on the 5-phenyl derivative, which gives, unambiguously, the same conclusion.

The cyano-diester (**4**) was converted into the 2-piperidone (**5**) in 35% overall yield by successive reduction (Ni–H_2), hydrolysis, and thermal cyclisation. The product was esterified (CH_2N_2), selectively reduced to the piperidine (**6**) by the method of Borch,[3] and, without isolation, the corresponding amino-acid was cyclised ($SOCl_2$–Et_3N) to 5-phenyl-1-azabicyclo[3.3.1]nonan-2-one (**3**) [in 10% overall yield from compound (**5**)], m.p. 73 °C (light petroleum) (*m/e* 215·1305; Calc. for $C_{14}H_{17}ON$, *M*, 215·1306); $\nu_{CO}(CCl_4)$ 1695 cm^{-1}; δ_C(CO) 184 p.p.m. A comparison with *N*-methyl-2-piperidone (**7**) [$\nu_{CO}(CCl_4)$ 1650 cm^{-1}; δ_C(CO) 169 p.p.m.] indicates that compound (**3**) is a non-planar amide.

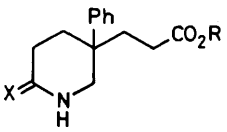


(1)

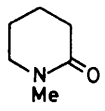
(2) R = H
(3) R = Ph



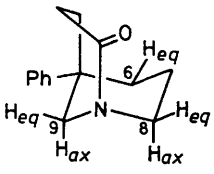
(4)



(5) X = O, R = H
(6) X = H_2, R = Me



(7)



(8)

The ^{1}H n.m.r. of compound (**3**) shows the four protons adjacent to the N atom as the lowest field aliphatic signals. At 360 MHz these signals are 8-H_{eq} δ 4·2 (split m), 9-H_{eq} 3·74 (ddd, $J_{9eq,\ 9ax}$ 13·2, $J_{9eq,\ 6eq}$ 3·0, $J_{9eq,\ 8eq}$ 1·3 Hz), 9-H_{ax} 3·2 (d, $J_{9ax,\ 9eq}$ 13·2 Hz), 8-H_{ax} 2·77(m), and 6-H_{eq} 1·9 (m). Irradiation at δ 3·7 (9-H_{eq}) collapsed the 9-H_{ax} signal to a singlet and simplified the 8- and 6-H_{eq} signals. Conversely, decoupling the 8-H_{eq} proton removed the 1·3 Hz coupling from 9-H_{eq}, and decoupling the 6-H_{eq} proton (δ *ca.* 1·9) reduced the 9-H_{eq} signal to a broadened doublet by virtual elimination of the 3 Hz coupling. As expected, decoupling 8-H_{ax} left the 9-H_{eq} and 9-H_{ax} signals unaffected, but collapsed the 8-H_{eq} signal to a tight multiplet.

The absence of *W*-coupling, which involves the proton at position 4, indicates structure (**8**) as the conformation of the bridgehead amide and supports the earlier conclusion for the structure of compound (**2**).

We are grateful to Dr. D. S. Rycroft (University of Glasgow) for the ^{13}C n.m.r. spectra and to Dr. I. H. Sadler (University of Edinburgh) for the high-field n.m.r. experiments.

(*Received*, 18*th May* 1981; *Com.* 597.)

[1] G. L. Buchanan, 'Topics in Carbocyclic Chemistry,' Vol. 1, ed. D. Lloyd, Logos Press, London, 1969, p. 215.
[2] H. K. Hall, R. G. Shaw, and A. Deutschmann, *J. Org. Chem.*, 1980, **45**, 3722.
[3] R. F. Borch, *Tetrahedron Lett.*, 1968, 61.