Slow Inversion in Aziridines: Investigation of Invertomer Ratios

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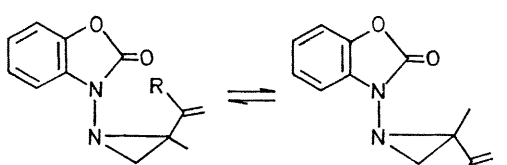
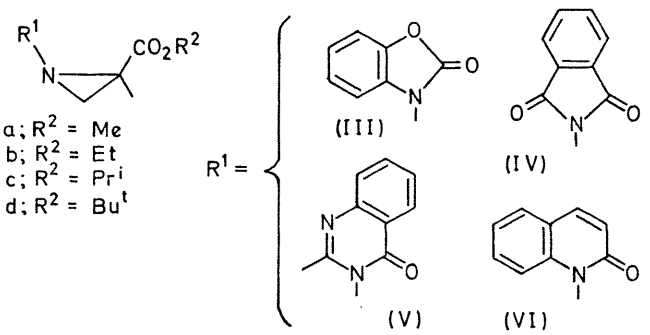
Summary Invertomer ratios in aziridines (III—VI; a—d), conveniently measured at room temperature by n.m.r., reveal an unexpected attraction between heterocycle and ester which increases with the size of the latter.

RECENTLY it was reported that the ratio of invertomers a : b was 1·4 : 1 for (I) and 1 : 11 for (II) from measurement of peak areas of the respective invertomers in the n.m.r. spectra.[1] That the vinyl group is less sterically demanding than the methyl group is also the conclusion from conformational analysis in the cyclohexane ring system.[2]

The value of using the slow inversion phenomenon in aziridines as a probe for the relative sizes of groups depends upon the absence of attractive (or repulsive) interactions other than those which are steric in origin. Aziridines (III—VI; a—d) were prepared by oxidation of the parent heterocyclic *N*-amino-compounds in the presence of the appropriate methacrylate ester.[3] Interpretation of the (room temperature) n.m.r. spectra of these aziridines is usually simple and accuracy in determination of the invertomer ratios is limited only by integration methods. In most cases, both families of peaks can be seen, thus providing multiple checks on the ratios. Assignments of peaks to particular invertomers follow from the common, although unequal, effect of heterocycles (III)—(VI) upon aziridine ring substituents. In particular, aziridine ring methyl groups and alkyl groups of all esters are shielded when *cis* to





the heterocycle: *e.g.* in (VI a—d) there is a difference of 0·6 p.p.m. in τ for aziridine ring methyl groups *cis* and *trans* to the heterocycle. The converse is observed for aziridine ring protons; those *cis* are deshielded relative to those *trans* to the heterocycle.

The Table lists the ratios of invertomer with ester *cis*/*trans* to the aziridine ring nitrogen substituent obtained from measurement of areas of various peaks in the n.m.r. spectra of aziridines (III—VI; a—d). The unexpected conclusion is that a definite preference for a *cis* relationship appears between the N-heterocycle and the ester as the size of the latter is increased, contrary to what is expected from steric considerations.[4] In addition, the same effects as those described above are present in the corresponding acrylate derived aziridines which lack the ring methyl group. The ratio of ester *cis*/*trans* to the heterocycle increases as its size increases, *e.g.* from 1 : 6 to 1 : 3 for (IVa) to (IVd) (H replacing the aziridine ring methyl group). It is reasonable to suppose in this case that the major invertomer is that with ester and heterocycle *trans*.

TABLE

	a	b	c	d	
(III)	0·7	0·9	1·1	1·5	Spectra run in $CDCl_3$
(IV)	1·8	2·2	2·8	3·5	solution using a Varian
(V)	2·1	2·4	2·9	3·3	A60A or Bruker 90MHz
(VI)	1·9	2·2	2·5	3·1	Spectrospin.

An explanation of this effect is a dipolar attraction between the ester carbonyl oxygen and the electrophilic carbon(s) of the heterocyclic substituent (*e.g.* the lactam carbonyl carbon) whose time-averaged proximity increases as the size of the alkyl group of the ester increases.† Only in the case of (IIIa) and (IIIb), does the ring methyl group appear to be 'smaller' than the ester, a consequence of the reduced electrophilicity of the lactam carbon and lone pair electron repulsion between the oxygens of (III) and the ester oxygens.

The above results vitiate against the use of (III)—(VI) as aziridine nitrogen substituents for determination of simple steric effects. However, they suggest that invertomer ratios in suitably designed aziridines offer a potentially quantitative method for comparing interactions between substituents, steric or otherwise.

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† A less likely explanation is increasing repulsion between the ester group and the aziridine nitrogen lone pair in the invertomer where both are *cis*.

[1] R. S. Atkinson and C. W. Rees, *J. Chem. Soc.*, (*C*), **1969**, 772.
[2] R. J. Ouellette, K. Liptak, and G. E. Booth, *J. Org. Chem.*, 1966, **31**, 546.
[3] D. J. Anderson, T. L. Gilchrist, D. C. Horwell, and C. W. Rees, *Chem. Comm.*, **1969**, **146**.
[4] Values in the cyclohexane series of conformational energy preference with increasing ester size are sparse and inconclusive. See N. L. Allinger and E. L. Eliel. 'Topics in Stereochemistry,' Vol. 1, Interscience, New York, p. 208.