The Relationship Between Rotational Barriers in Amides and Nitrogen Inversion Barriers in Related Amines

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Summary Certain bicyclic amines have high nitrogen inversion barriers but their *N*-acetyl and *N*-benzoyl derivatives have normal amide rotational barriers.

THE kinetics of rotation about the N–CO bond of amides have been extensively studied,[1] but apart from *N*-acylaziridine systems[2] no results have been reported which demonstrate the effect of an increased nitrogen inversion barrier upon the amide rotational barrier. We have therefore investigated amide rotational barriers, using standard n.m.r. techniques, for the bicyclic amine derivatives (**1**)—(**6**), since it is known that nitrogen inversion barriers are abnormally high[3] in the corresponding tertiary amines.

In all cases the free energy barriers for rotation about the N–CO bond (Table) are comparable with those found for *NN*-dimethylacetamide ($\Delta G^{\ddagger}_{298}$ 18·2 kcal mol^{-1})[4] and *NN*-dimethylbenzamide ($\Delta G^{\ddagger}_{298}$ 15·5 kcal mol^{-1}).[5] Furthermore the barrier to rotation about the N–S bond of the trichloromethylsulphenamide (**7**) is also comparable with those found for *NN*-dibenzyltrichloromethylsulphenamide ($\Delta G^{\ddagger}$ 14·9 kcal mol^{-1})[6,7] and trichloromethylsulphenylazetidine ($\Delta G^{\ddagger}$ 12·1 kcal mol^{-1}).[6] Since few details are available of accurate measurements of nitrogen inversion-barriers in the corresponding amines, details of the free energy barriers to nitrogen inversion in the amines (**8**), (**9**), and (**10**) are also included in the Table. The results agree well with those

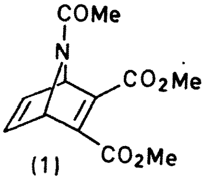
TABLE

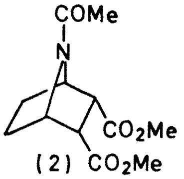
Spectral parameters and free energies of activation for rotation about the N–CO *bonds of compounds* (**1**)—(**6**) *and the* N–S *bond of compound* (**7**), *and nitrogen inversion for compounds* (**8**)—(**10**)

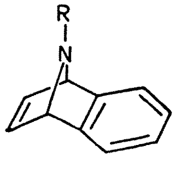
Compound	Solvent	$\nu_A - \nu_B{}^a$/Hz (±1)	$k_c{}^b$/s^{-1}	$T_c{}^b$/°C (±2)	$\Delta G^{\ddagger}_c$/kcal mol^{-1} (±0·3)	$P_1{}^c$ (±0·03)	$P_2{}^c$ (±0·03)
(**1**)	$CDCl_3$	26	58	+70	17·4		
(**2**)	$CDCl_3$	45	100	+58	15·9		
(**3**)	$CDCl_3$	38	84	+90	18·1		
(**4**)	$CDCl_3$	47	104	+52	16·0		
(**5**)	$CDCl_3$	47	104	+75	17·2		
(**6**)	$CDCl_3$	53	118	+35	15·1		
(**7**)	$CDCl_3$–$CFCl_3$ (1 : 1) ..	34	76^d	−12	12·9^d	0·75	0·25
(**8**)	$CDCl_3$	40	89^d	+26	14·8^d	0·20	0·80
(**9**)	$CDCl_3$	39·5	88^d	−18	12·6^d	0·10	0·90
(**10**)	C_5D_5N	40	89	+17	14·3	0·40	0·60

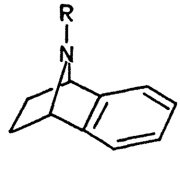
[a] For bridgehead protons of compounds (**1**)—(**7**) and the *N*-benzylmethylene protons of compounds (**8**)—(**10**). [b] The rate constant k_c is based upon comparison of observed and theoretical spectral line shapes of appropriate pairs of coalescing signals at the temperature T_c where the two lines just coalesce to a broad singlet. [c] Mole fractions, P_1 refers to the conformer giving a signal at low field. [d] The rate constant k_c, and therefore $\Delta G^{\ddagger}_c$, refer to the process conformer 1 → conformer 2.

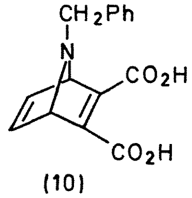
previously reported,[3] except that it is clear that the results reported for amino-acids, analogous to (**10**), are anomalously high, owing presumably to protonation of the nitrogen atom in non-basic solvents. Thus it is clear from the results in the Table that although nitrogen inversion barriers in these bicyclic amines are approximately twice those found for simple tertiary amines, these high nitrogen inversion barriers have no effect on amide rotational barriers. The results reported for *N*-acylaziridines[2] are atypical for amides since conjugation in three-membered ring systems may be either of the amide or acylcyclopropane type.

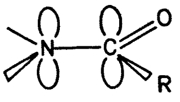

(1)

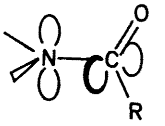

(2)

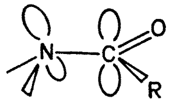

(3) R = COMe
(4) R = COPh
(8) R = CH$_2$Ph

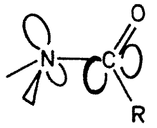

(5) R = COMe
(6) R = COPh
(7) R = SCCl$_3$
(9) R = CH$_2$Ph


(10)


(11a) $E_N = +I$
$E_\pi = -E$.


(11b) $E_N = +I$
$E_\pi = 0$


(11c) $E_N = 0$
$E_\pi = -0{\cdot}66E$


(11d) $E_N = 0$
$E_\pi = 0$

Although intuitively the amide rotational barrier might have been expected to decrease with an increasing tendency for the nitrogen atom to adopt a pyramidal geometry the following simple argument shows that this is not a correct viewpoint. Four limiting amide geometries (**11a**—**d**)† may be recognised; the first pair (**11a** and **b**) have a trigonal nitrogen atom with its *p*-orbital parallel (**11a**) and orthogonal (**11b**) to the *p*-orbital on the carbonyl carbon atom, the second pair (**11c** and **d**) have a pyramidal nitrogen atom with the non-bonding sp^3 orbital in a plane either parallel (**11c**) or orthogonal (**11d**) to the plane containing the *p*-orbitals of the carbonyl group. The amide geometry shown in (**11a**) is generally believed, on the basis of structural evidence, to represent the normal amide geometry and the geometry (**11d**) represents the probable transition state for rotation about the N–CO bond. It has been pointed out,[8] on the basis of simple MO treatment, that whereas the amide delocalisation energy ($E_\pi = -E$) is maximised in (**11a**) it would only be reduced by one third ($E_\pi = -0{\cdot}66E$) in the geometry (**11c**), although it would be zero in (**11b** and **d**). On the other hand the change in energy associated with nitrogen geometry in going from (**11d**) to (**11b**) would be equal to the nitrogen inversion barrier [$E_N = 0$ in (**11d**) and I (**11b**)] and it is assumed that the energy associated with the nitrogen geometry (E_N) changes in a similar way in going from (**11c**) to (**11a**). Thus from the above argument the amide rotational barrier for a planar amide would be $E - I$ and for an amide having a pyramidal nitrogen atom it would be $0{\cdot}66E$. Since I is typically *ca.* 6—7 kcal mol^{-1} and the amide rotational barrier is 15—18 kcal mol^{-1}, E would be 21—25 kcal mol^{-1} which is consistent with a rotational barrier of 14—17 kcal mol^{-1} in an amide having a pyramidal nitrogen atom. Following this reasoning one would not expect to find that an enhanced nitrogen inversion barrier would necessarily result in a change in the amide rotational barrier, and this conclusion is in accord with the results summarised in the Table. The results for the sulphenamide (**7**) further show that the argument also applies to the case of $p\pi$–$d\pi$ bonding.

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† The geometry (**11d**) in this discussion implies both that shown in the formula and the alternative geometry in which the nitrogen substituents are synclinal with respect to the carbonyl oxygen atom.

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