Hindered Rotation about C–N Bonds: Equilibration of Diastereomeric Rotational Isomers

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Summary The equilibration of diastereomeric rotational isomers of 4,6-diamino-1,2-dihydro-2-methyl-1-(*o*-tolyl)-*s*-triazine hydrochloride (I), and 5-methyl-3-α-naphthyl-2-thiohydantoin (II) has been followed by integration of their n.m.r. spectra, and the activation parameters for hindered rotation about C–N bonds have been calculated.

IF a compound exhibits atropisomerism[1] and also contains an asymmetric centre, the rotational isomers are diastereomers and have different physical properties. Provided that the barrier to rotation is sufficiently high it should be possible to separate the rotational isomers by standard procedures for the separation of the components of a mixture. We now report two compounds in which the magnitude of the energy barrier is such as to allow rotational isomers (as enantiomeric pairs) to be investigated by n.m.r. spectrometric techniques.

Normal work-up procedures after synthesis yielded predominantly one of the rotational isomers of 4,6-diamino-1,2-dihydro-2-methyl-1-(*o*-tolyl)-*s*-triazine hydrochloride[2] (I), and 5-methyl-3-α-naphthyl-2-thiohydantoin[3] (II). Recrystallization of (I) from ethanol yielded an isomeric mixture containing about 88% of the thermodynamically preferred isomer, whereas recrystallization of (II) from ethanol yielded a mixture containing about 87% of the thermodynamically less stable isomer.

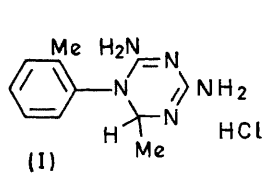
The equilibration of the initially predominant isomer of (I) in trifluoroacetic acid was followed over the temperature range 22·5—52° by measuring the rate of change in the relative intensities of the 2-methyl doublets of the predominant isomer (δ 1·762, *J* 6·1 Hz) and its rotamer (δ 1·578, *J* 6·1 Hz) by repeated integration of the 100 MHz n.m.r. spectrum. At equilibrium, the concentration ratio of these isomers was 1·64 : 1·00, respectively. The rate of conversion of the initially predominant isomer of (II) in pyridine into the equilibrium ratio (1·00 : 1·18) was measured over the range 24—78° by repeated integration of the overlapping 5-methyl doublets of the two forms, the initially predominant form absorbing at δ 1·505 (*J* 7·0 Hz) and its rotamer at δ 1·575 (*J* 7·0 Hz).

Activation parameters for the forward and reverse reactions (Table) reveal considerable steric restriction to rotation in these compounds. The rotational barriers are comparable to those reported for many highly hindered 2,2′-substituted biphenyls.[4] High conformational stability resulting from hindered rotation about an aryl C–N bond has also been observed in a number of *ortho*-substituted *N*-acyl-*N*-alkyl derivatives of aniline and 1-naphthylamine.[5] At present, the significance of the difference between the activation entropies of (I) and (II) is not clear, but solvent effects may contribute. A similar range of activation entropies has been found for hindered biphenyls.[4]

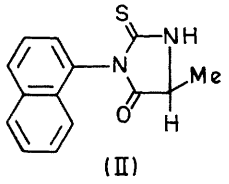
Activation parameters at 298K *for equilibration of diastereomeric rotational isomers*

		E_a[c]	Log *A*	$\Delta H^{\ddagger}$[c]	$\Delta G^{\ddagger}$[c]	$\Delta S^{\ddagger}$[d]
(I)[a]	A	23·5 ± 1·3	12·13 ± 0·90	22·9	24·4	− 5·0
	B	23·5 ± 1·3	12·35 ± 0·90	22·9	24·1	− 4·0
(II)[b]	A	21·1 ± 0·4	9·55 ± 0·28	20·5	25·6	−16·8
	B	21·1 ± 0·4	9·48 ± 0·28	20·5	25·7	−17·2

[a] Obtained by analysis of the rate of equilibration in trifluoroacetic acid of the more preferred isomer.
[b] Obtained by analysis of the rate of equilibration in pyridine of the less preferred isomer.
[c] kcal. mole^{-1}.
[d] Entropy units.
Error limits quoted are standard deviations.



(I)



(II)

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[3] Prepared by the method of H. K. Pujari and M. K. Rout, *J. Indian Chem. Soc.*, 1954, **31**, 937.
[4] D. M. Hall and M. M. Harris, *J. Chem. Soc.*, 1960, 490.
[5] For leading references see M. M. Harris, *Progr. Stereochem.*, 1958, **2**, ch. 5.