Concerted Rotational-inversion Process in 5-Acyl-10,11-dihydrodibenz[*b*,*f*]azepines

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Summary Detailed analysis of the temperature-dependent ^{1}H n.m.r. spectra of 5-acyl-10,11-dihydrodibenz[*b*,*f*]azepine (*N*-acyliminobibenzyl) derivatives suggests the occurrence of three conformational equilibria—rotation of the ethano-bridge section, rotation of the amide C–N bond, and inversion of the central seven-membered ring; ring inversion and amide rotation occur in a novel, concerted manner.

PREVIOUSLY we have noted differences between the ^{1}H n.m.r. spectra of *N*-alkyl and *N*-acyl derivatives of 10,11-dihydrodibenz[*b*,*f*]azepine without any detailed interpretation.[1] We now present both complete analyses of the spectra, and temperature-dependent studies which provide evidence for a hitherto unknown concerted rotational-inversion process.

The ^{1}H n.m.r. spectrum of 5-acetyl-10,11-dihydrodibenz-[*b*,*f*]azepine (*N*-acetyliminobibenzyl) (**1a**) shows a remarkable variation with temperature. At −60° all the protons of the ethano-bridge are non-equivalent and thus form an ABCD system which gives rise to two groups of peaks centred at *ca.* δ 2·8 and 3·3. As the temperature is raised

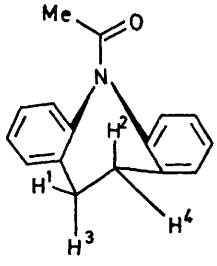


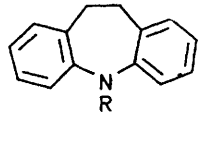
FIGURE. $J_{1,2} = 5{\cdot}1$, $J_{1,3} = -15{\cdot}8$, $J_{1,4} = 8{\cdot}7$ Hz.

the ABCD spectrum is transformed into an AA'BB' system (T_c *ca.* room temp.) which appears as two symmetrical groups of absorptions at δ 2·85 and 3·43. A further increase in temperature leads to a broadening of the AA'BB' absorptions which eventually coalesce to a single absorption (T_c 112°).

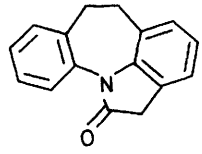
Of the two coalescence processes involved the first, ABCD → AA'BB', is complex and ill-defined and it was not possible to determine a value for the activation energy; however, for the process AA'BB' → A_4 the value of $\delta\nu_{AB}$ was found to be 56·7 Hz, and from this and the coalescence temperature, the free energy of activation ($\Delta G^{\ddagger}$) for the process may be calculated as 19·9 kcal mol^{-1}.

A full analysis of the AA'BB' spectrum provides values for the $^3J_{HH}$ couplings of the ethano-protons (see Figure). Application of the Karplus-type equation appropriate to rotation of the ethano-bridge fragment[2] between two equivalent conformations gives a dihedral angle (φ) of *ca.* 45°. This value indicates that the ethano-bridge is twisted out of a symmetrical staggered conformation, *cf.* metacyclophane.[3]

We interpret these spectra in terms of restricted rotation about the amide C–N bond and an inversion of the central seven-membered azepine ring. At low temperatures the amide fraction adopts a fixed planar conformation which has the effect of "freezing" the conformation of the seven-membered ring. This follows since ring flip would involve gross steric interaction between the planar amide group and the abutting aromatic protons at the 4- and 6-positions. As the temperature is raised the amide rotational barrier is overcome, removing the steric restrictions imposed on the ring inversion by the planar amide group; rapid ring flip occurs resulting in the collapse of the AA'BB' to an A_4 system.



(1) a; R = Ac
b; R = Me
c; R = $COCH_2Cl$
d; R = CO_2Et



(2)

Since $\delta\nu_{AB}$ for the coalescence ABCD → AA'BB' is much smaller than that of AA'BB' → A_4 the process ABCD → AA'BB' → A_4 may equally well be considered as a co-operative phenomenon in which ring-flip must be preceded by rotation of the amide group to a non-planar conformation. When the amide group is held in a rigidly planar conformation, as in the annelated derivative (**2**), ring inversion involves mainly the ethano-bridge and the least substituted aromatic ring. There is no longer a requirement for movement of the planar amide group across the interfering *ortho*-protons and, in agreement with prediction, the ^{1}H n.m.r. spectrum of (**2**) shows the ethano-bridge protons as a single line down to −60°. Similarly, *N*-alkyl derivatives, *e.g.* (**1b**), exhibit very low barriers to ring inversion as shown by the single line (A_4) absorptions of the ethano-bridge protons down to −100°.

Other *N*-acylated iminobibenzyl derivatives, *e.g.* (**1c**), (**1d**), exhibit temperature-dependent n.m.r. spectra similar to those obtained for (**1a**). In these cases the amide

rotation may also be followed by observing the methylene protons of (**1c**) and (**1d**). At low temperatures these are non-equivalent but become isochronous on warming [coalescence temperatures *ca.* 30 and $-5°$ for (**1c**) and (**1d**), respectively].

The conformations of the 5*H*-dibenz[*b*,*f*]azepine (iminostilbene), and of the related iminobibenzyl ring system have not been studied, which is surprising in view of their extensive pharmacological applications.[4]

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