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METHYLENE NON-EQUIVALENCE DERIVING FROM SLOW RING INVERSION IN 3,5-DIETHYLTETRAHYDRO-1,3,5-THIADIAZINE

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The protons of methylene groups are rendered non-equivalent when one methylene is attached to a chiral centre, or when no plane of symmetry passes through the carbon atoms of two methylene groups in the same molecule. Numerous examples have been observed, e.g. $MeC\underline{H}_2$ in acetaldehyde diethylacetal[1], and $PhC\underline{H}_2$ in 1-benzyl-trans-2,6-dimethylpiperidine.[2] However, they do not include a case where the chirality results solely from the slow chair-chair inversion of a six-membered ring, and we now report such an example.

The room temperature NMR spectrum (100 MHz) of 3,5-diethyltetrahydro-1,3,5-thiadiazine (1) in $CFCl_3/CDCl_3$ (1:1) shows the expected sharp singlets for the 2- and 6-protons and for the 4-protons at $\tau = 5.76$ and 6.14 respectively, and the usual A_2X_3 ethyl group pattern with $\tau_{CH_2} = 7.14$, $\tau_{CH_3} = 8.96$, and $J = 7$ Hz. At -70° (Table and Figure) the ring protons appear as two overlapping AB quartets, the methyl group protons remain a simple triplet (showing that nitrogen inversion is still fast on the NMR time scale), but the methylene protons of the ethyl groups appear as two sextuplets, showing their non-equivalence. This was confirmed by spin-decoupling; irradiation at the methyl resonance frequency collapsed the methylene signals to an AB quartet. This non-equivalence arises because, in the non-inverting ring, the nitrogen atoms are centres of chirality regardless of the conformations of the ethyl groups [cf. (2)]. The free energy of activation for the ring inversion process can be calculated to be ca. 12.1 Kcal/Mole from the coalescence of the various methylene proton signals (Table), which may be compared with 10.9 Kcal/Mole for 1,3-diethylhexahydropyrimidine[3] and 12.3[4] or 12.1 Kcal/Mole[5] for 1,3,5-triethylhexahydro-1,3,5-triazine.

A similar observation would be expected for 1,3-diethylhexahydropyrimidine. The low temperature spectrum of this has been reported by Riddell;[3] the methylene protons of the ethyl group do not show obvious non-equivalence although their signal is somewhat broadened. Riddell[6] has observed non-equivalence of the bridge methylene protons in the low temperature NMR spectrum of (3).

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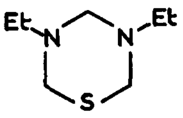
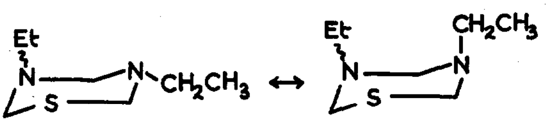
TABLE Coalescence Data from 100 MHz Spectrum of (1)

Methylene Group	$\Delta\nu$ (Hz)	$\Delta\bar{\nu}$ (Hz)	J_{AB} (Hz)	T_C (K)	$\Delta G^{\ddagger}$ (Kcal/Mole)
2,6-protons	58.5	46.9	13.0	250 ± 3	12.1 ± 0.1
4-protons	36.5	25.2	13.8	246 ∓ 3	12.1 ∓ 0.1
ethyl group	38.0	26.9	13.4	246 ± 2	12.1 ∓ 0.1



(1)



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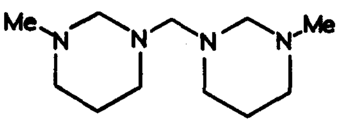

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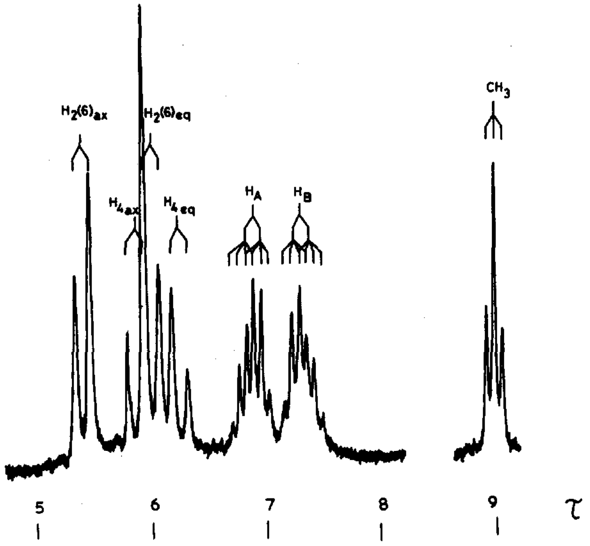

FIG. NMR spectrum (100 MHz) at -70° of 3,5-diethyltetrahydro-1,3,5-thiadiazine (1). Note: the downfield doublets of both AB quartets are attributed to the axial protons in line with previous assignments for six-membered rings containing sulphur.[7]

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