# Double Rate Processes in Substituted Tetrahydropyridazines: Rotational Barriers in Urethanes

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THE temperature-dependence of the nuclear magnetic resonance (n.m.r.) spectrum of the tetrahydropyridazine (I) has recently been described.[1] The interpretation of this spectrum required an unusually high energy barrier to ring inversion ($\Delta G^{\ddagger} = 18 \cdot 9$ kcal./mole at 97°c) and hindered rotation about the $N–CO_2Me$ bonds ($\Delta G^{\ddagger} = 14 \cdot 8$ kcal./mole. at −3°c). These interpretations were subsequently criticised on two counts.[2] The energy barrier assigned to the ring inversion process was considered to be too high and was said to be more in accord with the barrier expected for hindered rotation about the $N–CO_2Me$ bonds. The second criticism was based on an opinion that the two methyl signals observed at 35°c were of different intensities; our examination of the spectrum of (I) however shows that this is not correct.

As a result of our own studies of compounds similar to (I) we are now able to comment upon these two proposals,[1,2] but before doing so we present the results (see Table) of a study of the rotational barriers in urethanes by the n.m.r. method.[3]

gives a free-energy barrier to rotation for the $N–CO_2R$ bond in urethanes of the order of 16 kcal./mole at −3°c. This value may be compared with the corresponding values[4] ($\Delta G^{\ddagger} = 15–21$ kcal./mole at 25°c) for amides.
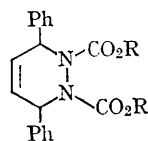


(I) R=Me
(II) R=Et
(V) R=Ph·CH$_2$
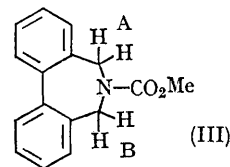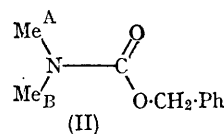
The free energies of activation ($\Delta G^{\ddagger}$ at −3°c) for $N–CO_2R$ bond rotation in (II) and (III) are similar to that originally assigned to the $N–CO_2Me$ rotation

TABLE

*Energy barriers to rotation about the* $N–CO_2R$ *bonds of* (II) *and* (III).

| Compound | Solvent | Coalescence temperature | $E_a$ (kcal./mole) | $\log_{10} A$ | $\Delta G^{\ddagger}(−3°c)$ (kcal./mole) |
|---|---|---|---|---|---|
| (II) | Deuterochloroform* | −1°c | 15·5 | 12·4 | 15·9 |
| (II) | Pyridine* | 19°c | 14·2 | 11·4 | 15·9 |
| (III) | Deuterochloroform | 16·5°c | 15·4 | 12·4 | 15·8 |

\* The separation of the low-temperature signals is temperature-dependent outside the limits where the separation is affected by the exchange process; an extrapolated linear variation with temperature has been assumed to obtain values for the signal separation ($\nu_A − \nu_B$) throughout the higher temperature range. Although this may lead to systematic errors in the values determined for the Arrhenius parameters the value of $\Delta G^{\ddagger}$ at a single temperature is relatively insensitive to this type of error.

The results in the Table were obtained by studying, at low temperatures, the coalescence of the two *N*-methyl resonances of (II) and the two ring methylene signals of (III). Hindered rotation associated with the $N–CO_2Me$ bond of the azepine derivative (III) causes the two methylene groups (III, A and B) to be non-equivalent, but each methylene group is represented by a single signal because ring inversion is rapid at the temperatures at which the rotational process can be studied. The examination of the compounds (II) and (I)

of (I) and support this assignment. The criticism[2] that the ester methyl signals of (I) are of different intensities at 35°c is unjustified; our examination of the n.m.r. spectrum of (I) shows that both these signals are of the same integrated intensity (within an experimental error of ±5%) and that the inequality in width, and therefore height, of these signals is due only to the low-temperature exchange process. The same remarks apply to the ester methylene signals of (IV) and (V). Finally the reported[1] coupling constants between

the vicinal ring protons of (I) (which are in accordance with our own observations) can only be consistent with the non-averaged coupling constants of a half-chair conformation. The unusually large energy barrier to ring inversion in

$NN'$-diacyltetrahydropyridazines has been independently observed by us[5] in a number of systems related to (I).

*(Received, March 15th, 1966; Com. 159.)*

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