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THE EFFECT OF HYDROGEN BONDING ON THE RING-CHAIN TAUTOMERISM OF OXAZOLIDINES

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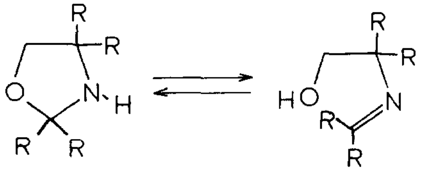
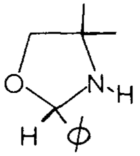
It is well known that oxazolidines and Schiff bases are in mobile equilibrium in solution (2, 3). The methods available for the study of these equilibria have been severly limited because in all cases assumptions had to be made in order to interpret the data collected (2). It seemed to us that nuclear magnetic resonance spectroscopy was ideally suited to probe this equilibrium, I $\rightleftarrows$ II. During the course of our investigation a report of a similar equilibrium in oxazines has appeared (4, 5), which compliments our work.

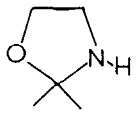


I II

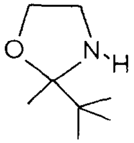
The oxazolidines III, IV and V were prepared by standard methods (6, 7) and their physical properties (b. p. and m. p.) agreed with literature values. The n. m. r. spectra (38° C) of each of the three oxazolidines as pure liquids (III at 69° C) were easily explained if the liquids were regarded as mixtures of the open (Schiff base) and closed (oxazolidine) forms with equilibrium constants of 1.99, 1.40 and 0.47, respectively.



III



IV



V

In III, the equilibrium constant was determined by comparison of the areas of the single proton geminal with the phenyl group. In the oxazolidine, the signal occurred (CCl_4 with internal TMS) at τ= 4.45 while in the Schiff base the signal appeared at τ= 1.68. In IV, the closed form exhibited a signal at τ= 8.80 while the open form had two signals, one at τ= 8.39 (broadened singlet) and the other at τ= 8.22 (a triplet or two overlapping doublets). Similarly in V, the closed form showed two singlets one at τ= 9.05 (t-butyl) and the other at τ= 8.92 (methyl) while the open form showed a singlet at τ= 8.92 (t-butyl) and a triplet or two doublets at τ= 8.20.

The most striking effects on the equilibrium constant were observed on changes in solvent. Cursory examination of the equilibrium constants in various solvents indicated that the equilibrium constants (or $\Delta G°$) were related to the ability of the solvent to hydrogen bond with -OH acids. It is well known that hydrogen bonding primarily manifests its action in $\Delta H°$ as illustrated by recent studies (8, 9). We then undertook a temperature study in a variety of solvents (1 mole of III per 20 moles of solvent) and have summarized the results in TABLE 1 in the form

TABLE 1

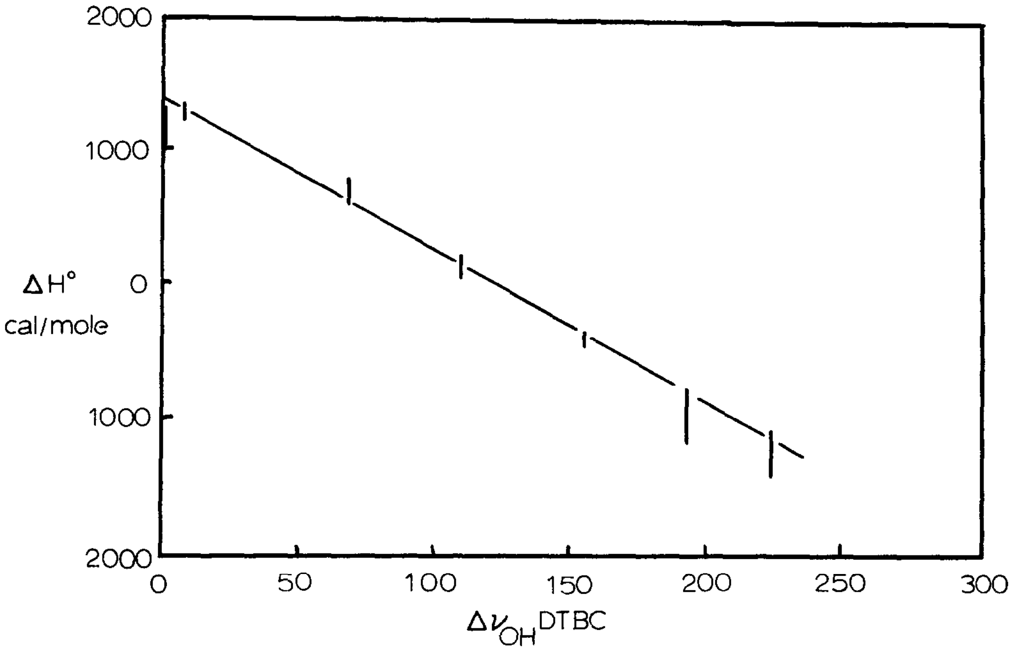
SOLVENT (Temp. Range of Exp. °C)	$K_{311}{}^{a}$	$\Delta G°_{311}$ (Cal/mole)	$\Delta H°^{a}$ (Cal/mole)	$\Delta\nu_{OH}$ DTBC (cm^{-1})	$\Delta S°_{311}{}^{a}$ (e.u.)
CARBON TETRACHLORIDE (-2.5 to 71)	0.53 ± .05	395	1154 ± 150	0	2.7 ± 0.7
CHLOROFORM (-17 to 83)	0.58 ± .04	338	1269 ± 56	8^{b}	3.0 ± 0.7
DIMETHYLCARBONATE (6 to 94)	1.25 ± .11	-138	675 ± 106	69	2.7 ± 0.7
ACETONITRILE (14.5 to 77)	1.61 ± .12	-293	1145 ± 108	87	4.7 ± 0.5
ACETONE (-17 to 50)	2.38 ± .20	-537	97 ± 89	110	2.0 ± 0.6
TETRAHYDROFURAN (-43 to 62.5)	1.98 ± .11	-423	- 425 ± 45	156	0.0 ± 0.4
DIMETHYLACETAMIDE (38 to 117)	8.3 ± 1.1	-1313	-967 ± 212	193	1.2 ± 1.0
DIMETHYLSULFOXIDE (38 to 117)	9.6 ± 1.0	-1400	-1213 ± 186	224	0.7 ± 1.0

a. Error limits are evaluated at the 95% confidence level
b. Estimated from Ref. 8.

of K, $\Delta G°$ (at 38° C), $\Delta H°$ (least squares analysis of ln K vs 1/ T) and $\Delta S°$ (at 38° C).

From previous studies of heteroassociation of di-t-butyl carbinol (DTBC) with a variety of bases in CCl_4 solution (10) we had available measures of relative hydrogen bonding abilities of our solvents as bases with a common acid (DTBC) in CCl_4 as revealed by the shift of the -OH stretching frequency, $\Delta\nu_{OH}$, for DTBC. Figure 1 indicates the good correlation of $\Delta\nu_{OH}$ DTBC and $\Delta H°$ confirming that in the equilibrium I $\rightleftarrows$ II solvent association with the free -OH group of the Schiff base plays a major role, with only acetonitrile exhibiting anomalous behavior. Interpretation became more difficult since a plot of $\Delta G°$ versus $\Delta\nu_{OH}$DTBC yields a linear relationship with acetonitrile becoming well behaved and tetrahydrofuran exhibiting anomalous behavior. We are examining more solvents and a greater variety of oxazolidines in an effort to understand this anomaly.

FIGURE 1



We have examined the neat oxazolidines III and IV at various temperatures and found $\Delta H°$ (cal/ mole) to be 4000 ± 300 and 1900 ± 70 while $\Delta S°$ (eu) to be 12.1 ± 1.0 and 6.8 ± 0.3, respectively. The two methyl groups of the Schiff base of IV coalesce to give a single broad signal at about 120° C.

An important aspect of this investigation is that it may shed light on the behavior of some diterpene alkaloids such as veachine which is known to isomerize to garryine (11, 12). Examination of model systems which contain N-alkyl oxazolidines for this purpose is planned.

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