

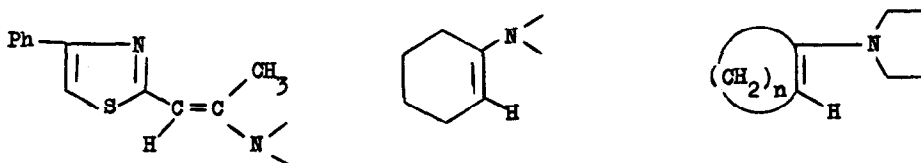
NMR SPECTRAL STUDIES ON CYCLIC ENAMINES*

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In an earlier paper¹ we had shown that the chemical shifts of the vinyl proton in the enamines of 4-phenyl-2-thiazolylaceton varied with the ring size of the amine component. The signal due to the vinyl proton in I occurred 0.41 ppm higher field compared to that in the NMR spectrum of II. This was rationalized on the basis of more effective conjugation by the nitrogen in a 5-membered ring. The



I	—N<	= pyrrolidine	V	—N<	= pyrrolidine	IX	n = 3
II		piperidine	VI		piperidine	X	n = 4
III		morpholine	VII		morpholine	XI	n = 5
IV		hexamethylenimine	VIII		hexamethylenimine	XII	n = 6
						XIII	n = 10

chemical shift of the olefinic proton in IV was intermediate between those seen for this signal in I and II. The vinyl protons in II and III had the same chemical shifts, signifying that basicity had a negligible role.

The present report deals with the extension of our study to the enamines of a number of cyclic ketones with cyclic secondary bases. The NMR data are assembled in the table.

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TABLE

Chemical shifts (cps downfield from TMS internal standard at 60 MC)
of vinyl protons^a of enamines in CCl₄ solution

Ketone	Amine component			
	Pyrrolidine	Piperidine	Morpholine	Hexamethyl- enimine
Cyclopentanone	235	255	261	
Cyclohexanone	248	272	274	255
	260 ^b	280 ^b	276 ^b	
	250 ^c		273 ^c	
	256 ^d			
Cycloheptanone	262	285		
Cyclooctanone	245	269		
Cyclododecanone	238	258		

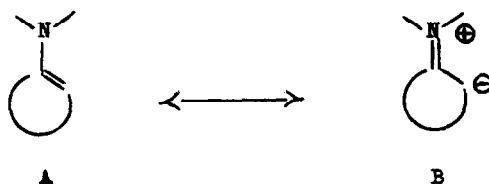
^a line shapes were in agreement with what have been reported in the case of respective cycloalkenes by G.V. Smith and H. Kriloff, J. Am. Chem. Soc., 1963, 85, 2016.

^b in benzene; ^c as neat liquid (ref. 3); ^d in CDCl₃.

An earlier paper² reported little difference in the chemical shifts of the enamine protons in 1-morpholino- and 1-pyrrolidinocyclohexenes in benzene solution. But Gurowitz and Joseph³ noted that in the NMR spectra of these as neat liquids, the same order of differences in chemical shifts were observed as what we had subsequently found for I and III. In the present study, it can be seen that there are minor differences in the chemical shifts of any enamine in different solvents; however, the relative order for the series V → VIII is the same as found earlier for the corresponding thiazolylacetone enamines¹.

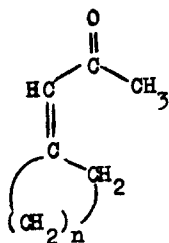
An inspection of the first vertical column of the table reveals an even more interesting variation of the chemical shift of the proton with ring size of the

ketone. The enamine XI from cycloheptanone has the lowest field signal for the vinyl proton. The chemical shifts of the olefinic protons in such enamines would depend on the electron density at the carbon terminus and hence on the extent of contribution of the canonical structures A and B to the resonance hybrid. It is evident therefore that as the ring size is varied, maximum conformational



hindrance for the contribution from B is offered by the 7-membered ring. The 6- and 8-membered alicycles permit more conjugation while this is allowed most in the 5- and 12-membered rings. A reverse order has been experimentally established by Turner and Garner⁴ and Gope *et al*⁵ for the endo / exo ratio of equilibrated mixtures of 1-methylcycloalkene and methylenecycloalkanes. However, the equilibration of 1-cycloalkenylacetone and 1-cycloalkylideneacetone would be a nearer analogy for the examples presented by us. It has been shown⁴ that at equilibrium, in the 5-membered case, the exo- isomer XIV predominates over the endo XV; the reverse is true for the 6-membered analogues XVI and XVII. Increased steric inhibition to effective resonance in cyclohexylideneacetone relative to the cyclopentene series has been invoked to explain this observation. By extrapolating our data on the enamines, it can be predicted that in the cycloheptane series, the endo isomer XIX will predominate over the exo isomer XVIII at equilibrium.

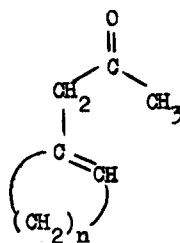
The data shown in the table allow another speculation. The nucleophilic reactivity of an enamine will depend, at least in part, on the electron availability at the carbon terminus. Hence the chemical shifts of the vinyl protons can be an index of the reactivity of enamines. Pyrrolidine enamines are known to be more reactive than morpholine or piperidine enamines² and this is borne out by the NMR data. It can also be expected that cycloheptanone enamines



XIV n = 3

XVI n = 4

XVIII n = 5



XV n = 3

XVII n = 4

XIX n = 5

would be generally less reactive than those of cyclopentanone or cyclohexanone and that 1-piperidinocycloheptene would be the least nucleophilic among all the enamines reported in this paper. It would be interesting to check this by compiling kinetic data on the relative reactivities of such enamines.

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