Tetrahedron Letters No.5, pp. 429-432, 1967. Pergamon Press Ltd. Printed in Great Britain.

SOLVENT-DEPENDENT CHEMICAL SHIFTS OF exo-α-HYDROGEN RESONANCES IN NMR SPECTRA OF QUATERNARY PIPERIDINIUM SALTS(1)

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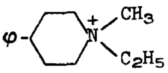
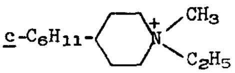
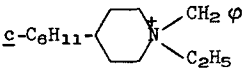
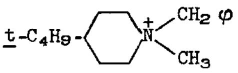
(Received 28 October 1966)

Following the example set by Closs,(2) numerous workers have used NMR spectroscopy in their studies of the stereochemistry of quaternization reactions of cyclic amines.(3) Most of these studies have been with piperidine derivatives.(3a-d) In general, the ratio of diastereomeric quaternary salts formed in a given reaction has been taken as equal to the intensity ratio of NMR bands due to similar exo-α-hydrogens, usually N-methyl hydrogens, in the diastereomers. Further, stereochemical assignments have often been based on the relative frequencies of these exo-α-hydrogen bands. Although aqueous solutions of diastereomeric quaternary salts have been most commonly used to obtain their NMR spectra, other solvents, chloroform in particular, have also been used. Surprisingly, there appears to have been little consideration given to the possibility that the relative resonance frequencies of exo-α-hydrogen bands of diastereomeric quaternary salts might be dependent on solvent.

In the course of our studies on the stereochemistry of quaternizations, we have recorded NMR spectra of several pairs of diastereomeric N-methyl- and N-benzylpiperidinium salts in deuteriochloroform and deuterium oxide. Examination of the data summarized in Table I reveals that for every pair of diastereomeric N,N-dialkylpiperidinium halides, change of

TABLE I

Resonance Frequencies of exo-α-Hydrogen Bands in NMR Spectra of Diastereomeric 4-Substituted-N,N-Dialkylpiperidinium Salts[a]

R_4N^+	X^-	Solvent	NCH_3 and/or $NCH_2\varphi$ Resonance Frequencies, τ-Scale, ppm [b,c]	
			eq	ax
	I^-	$DCCl_3$	6.62	6.70
		D_2O	6.93	
	φSO_3^-	$DCCl_3$	6.94	7.02
		D_2O	6.98	7.04
	I^-	$DCCl_3$	6.62	6.78
		D_2O	6.95	7.00
	φSO_3^-	$DCCl_3$	6.98	7.11
		D_2O	7.14	7.25
	Cl^-	$DCCl_3$	4.95	5.12
		D_2O	5.49	
	Cl^-	$DCCl_3$	4.72[d]	5.10[d]
		$DCCl_3$	6.67	6.79
		D_2O	5.45[d]	5.50[d]
		D_2O	7.04	6.99

[a] See the accompanying communication [A. T. Bottini and M. K. O'Rell, Tetrahedron Letters, (1966)] for the basis of the stereochemical assignments. [b] NMR spectra were determined of 10-20% solutions of diastereomeric mixtures with a Varian Associates A-60A system. Chemical shifts, which are considered accurate to ±0.02 ppm, were determined relative to internal tetramethylsilane (τ 10.00) or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (τ 10.00). See Ref. 4. Chemical shift differences are considered accurate to ±0.01 ppm. [c] Anion-dependent chemical shifts similar to those recorded here have been recorded by others. See ref. 3a. [d] N-Benzyl resonance.

solvent from deuteriochloroform to deuterium oxide causes the band due to equatorial α-hydrogens to undergo a greater upfield shift than that of the similar axial hydrogens. Note that for the diastereomeric 4-t-butyl-N-benzyl-N-methylpiperidinium chlorides, the equatorial methyl band appears at higher field (τ 7.04 ppm) than the axial methyl band (τ 6.99 ppm) in the spectrum of the deuterium oxide solution; in the spectrum of the deuteriochloroform solution, the equatorial methyl band appears at lower field (τ 6.67 ppm) than the axial methyl band (τ6.79 ppm). Not incidentally, the chemical shifts between exo-α-hydrogen bands useful for determination of piperidinium halide product ratios are greater in deuteriochloroform than in deuterium oxide. Indeed, no chemical shift is discernible between the N-methyl or N-benzyl resonances in the NMR spectra of deuterium oxide solutions of two pairs of the diastereomeric halides. Interestingly, although the exo-α-hydrogen bands of the diastereomeric piperidinium benzenesulfonates are shifted to higher field when the solvent is changed from deuteriochloroform to deuterium oxide, the difference in chemical shifts is nearly the same in both solvents.

Our data provide a strong argument for why product ratios from quaternization reactions should, if possible, be based on spectra taken in chloroform (or $DCCl_3$) as well as water (or D_2O). The degree of solvent dependence shown by the various exo-α-hydrogen bands may also prove useful in assignments of stereochemistry.

References

1. This research was supported in part by Grant No. CA-05528 from the National Cancer Institute of the Public Health Service.
2. G. L. Closs, J. Amer. Chem. Soc., 81, 5456 (1959).
3. Examples include: (a) H. O. House and C. G. Pitt, J. Org. Chem., 31, 1062 (1966) and references 13-16 cited therein; (b) H. O. House and B. A. Tefertiller, ibid., 31, 1068 (1966); (c) H. O. House, B. A. Tefertiller, and C. G. Pitt, ibid., 31, 1073 (1966); (d) J.-L. Imbach, A. R. Katritzky, and R. A. Kolinski, J. Chem. Soc., B, Phys. Org., 556 (1966); (e) A. T. Bottini, B. F. Dowden, and L. Sousa, J. Amer. Chem. Soc., 88, 3249 (1966); (f) A. T. Bottini, B. F. Dowden, and R. L. VanEtten, ibid., 88, 3250 (1966).
4. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, High Resolution Nuclear Magnetic Resonance Spectroscopy, Vol. I, pp. 264-266. Pergamon Press, London (1965).