Nuclear Magnetic Resonance Spectroscopy. A Reinvestigation of the Kinetic Parameters for Inversion of 1,2,2-Trimethylaziridine[1]

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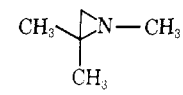
Abstract: Kinetic parameters for inversion of 1,2,2-trimethylaziridine have been evaluated by the line-shape method for the temperature-dependent nmr spectra of the neat liquid and solutions in acetone, benzene, and chloroform. The previously reported activation energy for inversion of this substance is substantially too low. There appears to be a striking difference in activation energy, but not in rate, for inversion in acetone and in chloroform.

The stereochemical stability of trivalent nitrogen compounds has been of special interest for several decades. The rapid nitrogen inversion of ordinary tertiary amines at room temperature has prevented separation of such substances into optical antipodes, and considerable attention has been focussed on aziridines[2] because the possibility for successful resolution of the optical forms of such substances has been predicted to be enhanced by a slowing of inversion because of strain in the three-membered ring. This idea received strong support by an approximate activation energy of 25 kcal/mol calculated by Kincaid and Henriques[3] for 1-methylaziridine. Nonetheless, all attempts to resolve appropriately substituted aziridines have so far failed.[4] For those aziridines which have been studied (other than N-chloroaziridines[4b]), the rates of inversion very often fall in the range which can be determined by nmr line-separation and line-shape techniques at convenient temperatures.[5] The temperature dependence of the spectra can be used to obtain activation parameters for inversion but there seems to be rather considerable discrepancies in the values obtained even for similar structures. For example, Heeschen and Gutowsky[5b,c] report an activation energy for 1-methylaziridine of 19 kcal/mol while for 1,2,2-trimethylaziridine (**1**), Loewenstein, Neumer, and Roberts[6] obtained an activation energy of 10 kcal/mol by measuring the changes in the line shapes of the *gem*-methyl resonances as a function of temperature. The latter energy barrier seems rather too small in view of the approximately 12 kcal/mol obtained for the inversion of N-methoxy-N-methyl-N-benzylamine[7a] and 4,4-difluoropiperidine,[7b] as well as



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results obtained with other aziridines.[8-11]

The history of activation-energy determinations by nmr has not always been happy. A range of 7–26 kcal/mol has been reported for barrier to rotation about the C–N bond in N,N-dimethylformamide with the highest value being currently favored.[12] Some of the reasons for the difficulties which have been encountered have been discussed recently,[13,14] and with the improvements in methods of calculating line shapes even for rather complex spectra,[15] it seemed desirable to reinvestigate the kinetic parameters for inversion of 1,2,2-trimethylaziridine (**1**).

Results

The nmr spectrum of neat **1** at 35° shows five resonances with the N-methyl at δ 2.27 (line width 0.8 Hz), the methylene protons at 0.85 and 1.56 (line width 2.5 Hz), and the *gem*-methyl groups at 1.05 and 1.16 (line width 1.9 Hz[16]), all relative to internal tetramethylsilane (line width 0.5 Hz). In other solvents,[17] such as acetone, benzene, and chloroform, the spectra are generally similar although there are chemical-shift and line-width changes. As the temperature is increased the methyl and methylene signals broaden and at about 60° the methyl signals coalesce. The methyl-

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(15) See, for example, J. T. Gerig and J. D. Roberts, *ibid.*, **88**, 2791 (1966), and S. L. Spassov, D. L. Griffith, E. S. Glazer, K. Nagarajan, and J. D. Roberts, *ibid.*, **89**, 88 (1967).

(16) The line width of the methyls is partly due to exchange resulting from inversion because, at lower temperature, the width decreases to 1.6 Hz.

(17) In carbon disulfide, **1** appears to be converted to $(CH_3)_2CCH_2N(CH_3)C(=S)S$ which in $CDCl_3$ gives proton resonances at δ 1.42 (s, 6 H), 3.14 (s, 3 H), and 3.16 (s, 2 H). In methanol, the high-field resonances of the *gem*-methyl groups overlap with those of the methylene protons, and it was not possible to carry out an accurate line-shape analysis.

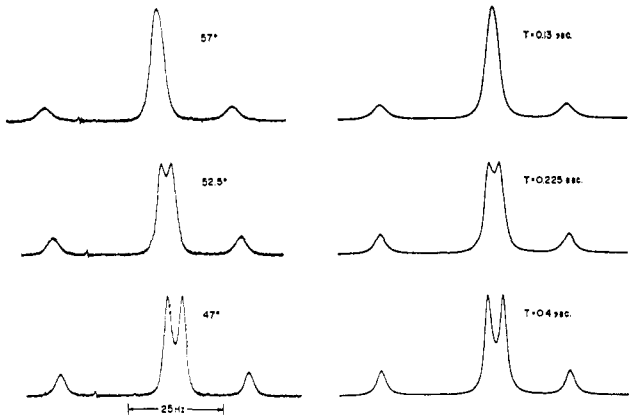

Figure 1. Experimental and calculated spectra of 1,2,2-trimethylaziridine in benzene at various temperatures.

ene protons, because of their larger chemical-shift difference, do not coalesce until about 100°. For determination of the inversion rates, primary reliance was placed on the changes in the methyl resonances because the substantial line widths of the methylene protons appeared to reflect either a geminal proton–proton coupling of unknown magnitude or H–C–N couplings which could be profoundly influenced by changes in the quadrupole relaxation rates as a function of temperature. However, the changes in the line shapes of the methylene protons with τ, the mean lifetime before inversion as deduced from the changes in methyl line shapes, were calculated and compared with the observed line-shape changes as a secondary check on the procedure. In these calculations, the possibility of a geminal coupling was ignored.

The theoretical spectra calculated as a function of τ were calculated by two different programs written for IBM 7094 computers. One program (GMW)[18] is based on the equations of Sack[19] while the other (INAB)[20] follows the density-matrix treatment of Alexander.[21] These programs gave identical theoretical spectra with the same input of chemical shifts, line widths, and τ values. Illustrative experimental and theoretical spectra for solutions of **1** in benzene are shown in Figure 1, the theoretical spectra in this case being composite spectra obtained by summing individual theoretical spectra for the methyl and methylene protons with the same τ values. In none of the cases investigated was it possible to obtain a good fit of the theoretical to experimental nmr curves by assuming the chemical shift between the methyl and methylene protons to be invariant with temperature. Similar behavior has been frequently noted previously.[13–15,22] For this reason both the chemical shift and τ values were adjusted until the calculated spectra were as close to being superimposable on the experimental spectra as possible. In general the fit was good except for the methylene resonances at low temperature. Interestingly, while the "infinity chemical-shift difference"[13]

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Table I. Chemical-Shift Differences, $\Delta\nu$, and τ Values for 1,2,2-Trimethylaziridine at Different Temperatures

Solvent	Temp, °C[a]	$\Delta\nu$, Hz Methylene	$\Delta\nu$, Hz Methyl	τ, sec
Neat	45.5	41.8	6.2	0.345
	49.0	42.2	6.2	0.235
	51.0	42.3	6.2	0.175
	53.0	42.3	6.2	0.142
	55.0	42.0	6.0	0.108
	56.0	42.4	6.0	0.102
	57.0	42.4	6.0	0.09
	60.0	42.8	5.9	0.064
	63.5	42.5	5.9	0.047
	0.0	39.6	7.1	
(Line width	0.0	2.5	1.6)	
Neat (100 MHz)	47.0		10.8	0.24
	50.0		10.7	0.184
	52.0		10.7	0.126
	55.0		10.6	0.095
	56.0		10.5	0.084
	59.0		10.4	0.061
	61.0		10.2	0.052
	63.5		10.2	0.040
	69.0		10.0	0.022
	25.0		11.0	
(Line width	25.0		2.2)	
Benzene	47.0	51.0	4.4	0.40
	49.5	51.2	4.2	0.30
	51.5	51.0	4.0	0.25
	52.5	51.0	3.8	0.225
	53.5	51.0	3.7	0.205
	54.5	51.0	3.7	0.17
	56.0	50.8	3.5	0.15
	57.0	50.8	3.4	0.13
	−10.0	51.7	7.3	
(Line width	−10.0	2.2	1.5)	
Chloroform-*d*	56.0	43.3	4.0	0.84
	59.0	43.6	4.0	0.46
	61.0	43.7	3.9	0.35
	63.5	43.5	3.9	0.25
	65.5	43.7	3.8	0.215
	66.5	44.0	3.8	0.18
	67.5	43.7	3.8	0.15
	70.5	43.9	3.7	0.09
	0.0	42.3	4.6	
(Line width	0.0	1.8	1.4)	
Acetone-d_6	55.5	38.2	7.1	0.265
	57.5	38.2	7.0	0.20
	60.0	38.3	7.0	0.16
	62.0	38.3	6.9	0.126
	63.0	38.4	6.8	0.115
	64.0	38.4	6.8	0.106
	65.0	38.6	6.8	0.095
	66.0	38.8	6.7	0.085
	67.0	38.8	6.7	0.077
	70.0	39.0	6.6	0.052
	−24.0	35.2	8.3	
(Line width	−24.0	2.2	1.5)	

[a] Temperatures are considered to be no more accurate than ±0.5°.

of the methyl groups decreased rather markedly with increasing temperature, that of the methylene groups was less sensitive and if anything increased with increasing temperature (Table I). Apparently, there is no appreciable contribution of methyl–methyl proton coupling to the line width of the C-methyl protons at low temperature because the same line width (1.6 Hz) is observed above 90°, when the methyl groups are exchanging environments rapidly, as at 0°, when they are exchanging slowly. That the line width of the methyl protons is substantially greater than that of TMS may be the result of small unresolvable couplings either with the ^{14}N or the methylene protons. Similar

Table II. Chemical-Shift Differences, Coalescence Temperatures, and Rate Constants for Inversion of 1,2,2-Trimethylaziridine in Different Solvents

Solvent	$\Delta\nu$,[a] Hz		T_c,[b] °C	k_c,[c] sec^{-1}	k,[d] sec^{-1}	k,[e] sec^{-1}
	Low temp	T_c				
Neat	7.1	6.0	57.0	11.1	11.4	13.3
Neat (100 MHz)	11.0	10.2	61.0	19.2	20.0	22.6
Benzene	7.3	3.5	56.0	6.7	6.0	7.8
Chloroform-*d*	4.6	3.8	67.5	6.7	6.8	8.4
Acetone-d_6	8.3	6.7	67.0	13.0	13.1	14.9

[a] Chemical-shift difference of the *gem*-methyl group. [b] Coalescence temperature. [c] Rate constant at T_c, obtained from the line-shape analysis. [d] Rate constant at T_c, calculated as in ref 25. [e] Rate constant at T_c, calculated from the Gutowsky–Holm equation.[24]

problems have been described by Gutowsky and coworkers[23] in studies of the temperature dependence of the nmr spectra of N-methyl-N-benzylformamide and hexahydro-1,3,5-trimethyltriazine. The coalescence temperatures (T_c) of the methyl signals of **1** and the chemical shifts and rates for these temperatures as a function of solvent are shown in Table II. Included for comparison purposes are the rate constants at T_c calculated by the Gutowsky–Holm equations[24] and an equation used by Schmid and coworkers.[25] Arrhenius parameters were calculated by standard procedures[26] and a typical example is shown in Figure 2. The Arrhenius parameters and the corresponding ΔF^* and ΔS^* values are collected in Table III.

Table III. Arrhenius Parameters for 1,2,2-Trimethylaziridine in Different Solvents

Solvent	E_a, kcal/mol[a]	Log A[a]	ΔF^*, kcal/mol[b]	ΔS^*, eu[b]
Neat	24.06 ± 0.45	16.96 ± 0.96	17.9	17
Neat (100 MHz)	23.52 ± 0.58	16.67 ± 0.82	17.7	16
Benzene	23.37 ± 0.75	16.33 ± 0.67	18.2	14
Chloroform-*d*	32.50 ± 1.39	21.67 ± 1.51	18.9	38
Acetone-d_6	24.15 ± 0.53	16.63 ± 0.71	18.3	15

[a] The uncertainties are root-mean-square deviations. [b] Average value for the temperature range employed.

The sizable difference in the activation parameters obtained in this and earlier work[6] on **1** is not because of the method used previously for extracting the kinetic data from the line widths (the τ values so obtained correspond to τ values derived by the total line-shape procedure) but from too poor resolution and possibly from inadequate temperature control.

Discussion

The rates of inversion of **1** as measured by the line-shape technique were reasonably reproducible. Different samples of neat **1** gave E_a values which checked within 1 kcal/mol. In chloroform, separate determinations of E_a checked to within 2 kcal/mol and deviation, in ΔF^* were always small. As would be expected the

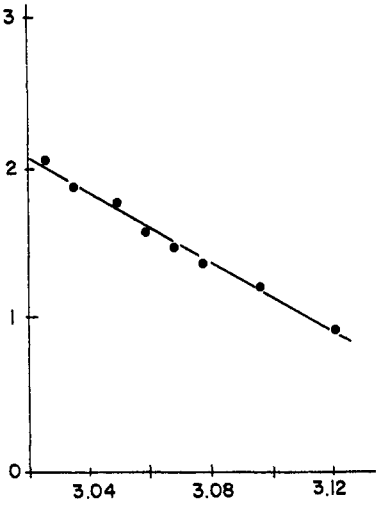

Figure 2. Arrhenius plot of the inversion rate of **1** in benzene as obtained by the complete line-shape analysis.

ΔS^* values were most difficult to reproduce and deviations as large as 5 eu were observed for neat **1** and as large as 10 eu for solutions in chloroform.

In view of the wide discrepancies reported for determinations of activation parameters by nmr methods, it seems well to examine the proposition that, while the line-shape procedure[18–21] seems to have considerable validity for situations in which the chemical shifts are large compared to the line widths of the peaks under conditions of slow exchange, the approximations made in the derivations of the line-shape equation (especially as regards the phenomenological T_2) might in fact give incorrect line shapes when the chemical shifts are not much larger than the line widths. The simplest way to check this seemed to be by comparing the rates and activation parameters obtained at 60 MHz, with those at 100 MHz where the shifts are 67% larger. The agreement between the τ and activation-parameter values is quite satisfactory considering the differences between the instruments used, there being a trend toward greater discrepancy between the rates at the lower temperatures.

The ΔF^* values for **1** (Table III) appear to be generally larger than those reported for other aziridines except the N-haloaziridines.[4] This is as would be expected for such substances as phenylaziridine (ΔF^* = 12.8 kcal/mol[9]) and 1-methanesulfonylaziridine (ΔF^* = 14.0 kcal/mol[9]) which like 1-ethyl-2-methyleneaziridine[5a] are expected to have especially facile inversion through resonance stabilization of the transition state. Not many E_a values for aziridine inversion have been pub-

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(25) H. G. Schmid, H. Friebolin, S. Kabuss, and R. Mecke, *Spectrochim. Acta*, **22**, 623 (1966), wherein $1/k = \tau = \sqrt{2}(\pi\Delta\nu)^{-1}[1 + (3\sqrt{2}/8)\cdot(b_E/\Delta\nu) + (21/64)(b_E/\Delta\nu)^2]$.

(26) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, New York, N. Y., 1963, p 71.

lished. The reported E_a for 1-methylaziridine[5b,c] of 19 kcal/mol is smaller than the 24 kcal/mol obtained here for **1** and may warrant further investigation for the same reasons that prompted this work. The much smaller E_a of 11.4 kcal/mol obtained for 1-phenylsulfonylaziridine[9b] is expected on the basis of the electrical character of the sulfonyl groups.

The large positive ΔS^* values found for inversion of **1** seem consistent enough to warrant comment. That the transition state is less constrained than the ground state could be the result of inversion by way of homolytic breaking and re-forming the C–C bond across the, ring from the nitrogen, but this mechanism seems unlikely in view of the known C–C bond strengths in three-membered rings. More reasonably, there could be some measure of constraint associated with interactions between the N-methyl and *gem*-methyls which would be absent in the transition state or perhaps the aziridine molecules are substantially associated in the ground state and become unassociated in the transition state. In the latter connection, evidence has been presented recently for association of N-alkylaziridines in the pure liquid as well as in carbon tetrachloride solutions.[27]

The barrier to inversion of **1** seems very much less sensitive to solvent variations (except for the special case of chloroform) than the barrier for inversion of N-methoxy-N-methyl-N-benzylamine which decreases with increasing dielectric constant.[7a] A similar solvent insensitivity has been found for 1-phenylsulfonylaziridine.[9b] Chloroform seems to produce a remarkable effect on the activation parameters without, however, much changing the coalescence point of the methyl resonances (see Table III). Assuming that the data for chloroform solutions are correct (as mentioned earlier, they seem reproducible), the effect of chloroform on the activation parameters is consistent with the known[27,28] substantial hydrogen bonding involving the imine nitrogen and the solvent, provided that the degree of hydrogen bonding is reduced in the transition state. Greater hydrogen bonding in the ground state than in the transition state would lead to both a larger E_a and a more positive ΔS^*.

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Experimental Section

1,2,2-Trimethylaziridine was synthesized from 2-amino-2-methyl-1-propanol by the following sequence:[29] formylation of the amino group by ethyl formate, reduction of the formylamino group by lithium aluminum hydride to 2-methylamino-2-methyl-1-propanol, formation of the sulfate with sulfuric acid, and ring closure to 1,2,2-trimethylaziridine by treatment with base.[30] The aziridine was purified after distillation (bp 66–68°) by preparative vpc through a 20-ft SE-30 column at 85°.

For determination of the nmr spectra, the samples of neat aziridine and solutions (about 25 wt %) in acetone-d_6 and deuteriochloroform each contained about 5% TMS. However, TMS was not used for the benzene solutions because it was found that TMS strongly reduced the chemical-shift difference between the methyl signals of **1**.

The nmr spectra were taken on Varian A-56/60 and HA-100 spectrometers equipped with V-6040 variable-temperature accessories. The temperature readings of the probe were calibrated by measuring the hydroxyl-shift difference of ethylene glycol for temperatures above 40° and of methanol for temperatures below 40°. The temperatures are believed to be more accurate than ±2°. The samples were allowed to equilibrate for a minimum of 10 min with each change in temperature.

Acknowledgment. We are indebted to Dr. K. L. Servis and Mr. S. Surface of the University of Southern California for the variable-temperature spectra of **1** at 100 MHz.

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The Optical Rotatory Power of 2-Methylenebenznorbornene[1]

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Abstract: (+)-2-Methylenebenznorbornene, a simple prototype of a conformationally rigid, chiral homoconjugated styrene, was prepared from (+)-2-benznorbornenone by the Wittig reaction. The compound exhibits an intense Cotton effect centered near 224 mμ which is attributed to a transition arising from mixing of ethylenic and benzenoid electronic states. The ORD of 2-methylenebenznorbornene correlates satisfactorily with the position and intensity of the CD bands in the instrumentally accessible region.

Earlier theoretical and experimental work[3] has established that, with respect to its optical activity, (+)-(1*R*)-5-methylenebicyclo[2.2.1]hept-2-ene (**1**) may be conveniently treated as an extended chiral π system. Similar considerations also serve to account for the high rotation observed for pimara-8(14),15-diene[4] (**2**). However, due to instrumental limitations, only plain curves were measured in the optical rotatory dispersion (ORD) of **1** and **2**. The present paper describes the observation of complete Cotton effects in (+)-2-methyl-

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.
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