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ASYMMETRICAL NONBRIDGEHEAD NITROGEN. VI[1]

NITROGEN PYRAMIDE IN AMIDES: N-ACYLDIAZIRIDINES AND N-ACYLOXAZIRIDINES

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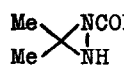
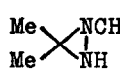
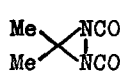
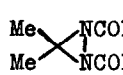
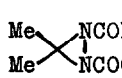
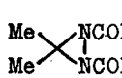
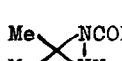
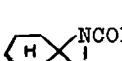
This work provides a proof of pyramidal configuration of nitrogen in N-acyldiaziridines I-IX and N-acyloxaziridine X (see Table 1)[2]. In respect to the NMR time scale the inversion of this configuration is fairly slow. The data presented here are in agreement with an earlier observation[3] that the amide conjugation diminishes when nitrogen is incorporated into a three-membered ring.

In the case of 1-acyl-2-alkyl-3,3-dimethyldiaziridines the presence of configurationally more stable alkyl-substituted nitrogen prevents the NMR-monitoring of the stereochemistry at the amide nitrogen by bringing about the non-equivalence of geminal methyl groups whatever the configuration of the amide nitrogen[4]. This obstacle could be avoided in the case of monoacyldiaziridines I, II and III as well as the vinylog of the latter (IV) by rapid exchange between NH and CD_3COOD (δ_{NH-OH} 8-9ppm). Such an exchange is equivalent to the effective flattening of configuration at this centre and thus facilitates the determination of stereochemistry at the amide nitrogen. The pyramidal configuration of the latter becomes less stable in II and III in comparison with I; this must be due to the weakening of the competitive conjugation between the substituent and the carbonyl group and, consequently, to the strengthening of the amide conjugation with the ring nitrogen. A similar effect was observed earlier for some aziridine analogs[5]. A slow inversion at the substituted nitrogen can also be observed in the case of vinylog IV (upon rapid exchange between NH and CD_3COOD), while this was not possible for the aziridine analogs[6]. The parameters of inversion for III and its vinylog IV differ but slightly[7].

Competitive amide conjugation with a substituent at the carbonyl group is

TABLE 1

N	Compound	Solvent	The signal monitored	$\Delta\nu$ d) in cps	T_c °C	$\Delta G^{\neq}$ kcal/mole
I		CH_2Cl_2 CD_3COOD	Me_2C	9.8	+2	14.3
II	 a)b)	$CDCl_3$ CD_3COOD	Me_2C	8.8	-6	14.0
III		CCl_4 CD_3COOD	Me_2C	10.4	-34	12.4
IV		$CDCl_3$ CD_3COOD	Me_2C	14.0	-32	11.3
V		CD_3OD	Me_2C	16.0	+13	15.3
VI		$CDCl_3$	Me_2C	7.7	-14	13.6
VII		$CDCl_3$	Me_2C	11.0	-17	13.3
VIII	 c)	$CDCl_3$	MeCH	4.2	+33	16.6
IX		$CDCl_3$				
X		CCl_4	MeCH	2.4	+74	19.3
			Ph	1.9	+70	19.3

a) In $CDCl_3$ at -40°C the ratio trans/cis is 4/3. b) For rotation about CO-NMe_2 bond $\Delta\nu$ =5.5cps, Tc +46°C and $\Delta G^{\neq}$=17.1kcal/mole. c) The ratio of diastereomers is 1:1.05 at +20° and 1:1.25 at -20°. d)The values derived from the temperature dependence of $\Delta\nu$ by extrapolation to the coalescence temperature.

palpably revealed in compound II where the rotation about the CO-NMe_2 bond is more restricted than the inversion at the acylated nitrogen (see Table 1). In the absence of CD_3COOD the NMR spectrum II at -50°C (see Fig.1) corresponds to the mixture of cis- and trans-isomers in a ratio close to 3/4. In this case the cis-form is stabilized by the hydrogen bonding between NH and carbonyl group (5-membered ring). The addition of acid transforms the low-temperature spectrum of II into one corresponding to an apparently individual compound with a virtually flat NH-centre (as the resalt of rapid exchange with CD_3COOD) and with a pyramidal acylated nitrogen.

In the case of the unsymmetrical 1,2-diacyldiaziridines V-VII the coalescen-

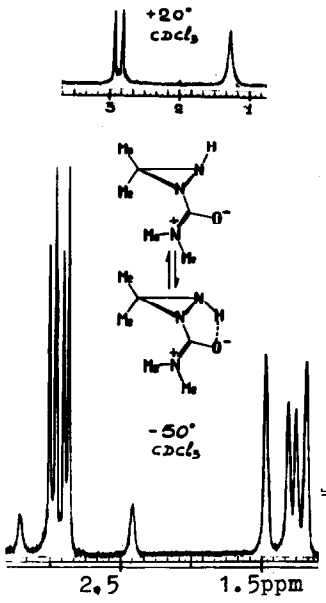


Fig. 1

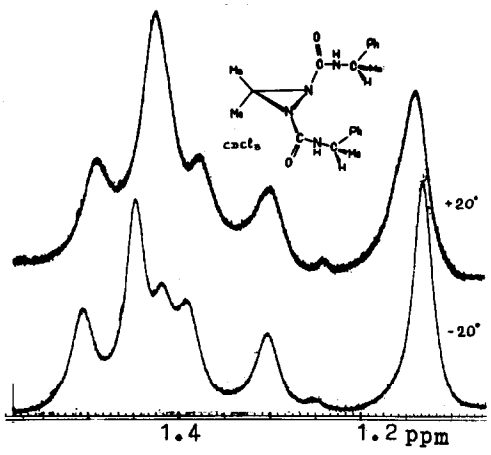


Fig. 2

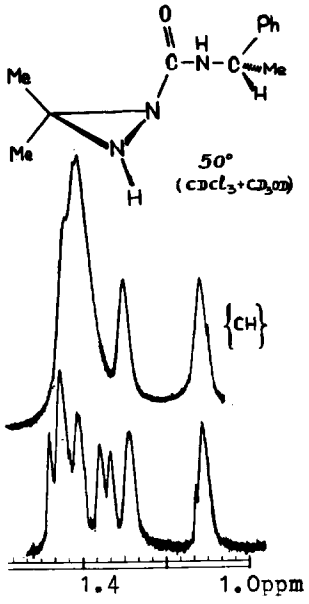


Fig. 3

ce of signals belonging to the non-equivalent methyl groups in ring was used to estimate the inversion barrier for the slower inverting nitrogen (see Table 1).

In symmetrical 1,2-diacyl-3,3-dimethyldiaziridines it is possible to monitor the configurational changes at both nitrogens if the acyl substituents contain additional asymmetrical centres with established configuration. If the amide nitrogens are pyramidal, two diastereomers should be observed in such situation. The spectrum of compound VIII shows it to be actually the case since it displays two sets of signals belonging to two energetically non-equivalent diastereomers (see Table 1 and Fig 2)[8].

The spectrum of the monocarbamoyl derivative IX also reveals the presence of two diastereomers (see Fig 3)[8]. However, in this case the parameters of inversion could not be determined since compound IX decomposes in presence of CD_3COOD, while in CD_3OD the exchange at NH is slower than the inversion at the acylated nitrogen. The signal of the CH-proton appears as a superposition of a quartet with a quintiplet due to the partial substution of NH-proton by deuterium, while the signals of methyl groups remain unaltered even at +50°C.

The parameters of inversion at the amide nitrogen in N-acyloxaziridine X can be estimated from the coalescence of signals belonging to the MeCH and phenyl

protons in the diastereomers with asymmetrical amide nitrogen. On recrystallization from hexane the content of one of diastereomers in the mixture is somewhat increased. The ratio thus obtained is not altered when the crystalline material is stored at 20°C for 24 hrs.

As can be seen from this evidence, the pyramidal stability of the amide nitrogen increases on passage from N-acyldiaziridines to N-acyloxaziridines in accordance with the changes in the values of inversion barriers of nitrogen in the corresponding amines[9].

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REFERENCE AND NOTES

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2. The synthesis of these compounds will be described elsewhere (R.G.Kostyanovsky, K.S.Zakharov, M.Zaripova, V.F.Rudtchenko, Izvest.Akad.Nauk SSSR, Ser.Khim., 1974, in press).
3. T.Z.Papoyan, I.I.Tchervin, R.G.Kostyanovsky, Izvest.Akad.Nauk SSSR, Ser.Khim., 1968, 1530.
4. For instance, the geminal methyl groups in PhNHCONCMe$_2$NMe remain non-equivalent both at 36°C ($\Delta\nu$ =2.4cps) and at 100°C ($\Delta\nu$ =1.2cps) when Ph_2O is used as solvent (A.Mannschreck, R.Radeglia, E.Gründemann, R.Ohme, Chem.Ber., 100, 1778 (1967).
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6. The signals of the aziridine ring protons and methyl groups show no splitting or widening in the spectra of CH$_2$CH$_2$NCH=CHCOOMe(cis/trans=1) and cis-Me$_2$CCH$_2$NCH=CHCN even at -50°C(in CH_2Cl_2).
7. Similar parameters of inversion(T_c 148°C, $\Delta G^{\neq}$ 24kcal/mole) were found by the same procedure for phosphorus in acetyl-di-iso-propylphosphine (R.G.Kostyanovsky, A.A.Fomitchov, L.M.Zagurskaya, K.S.Zakharov, Izvest.Akad.Nauk SSSR, Ser. Khim., 1973, 1915). For phosphorus in trans-MeO$_2$C-CH=CHP(i-Pr)$_2$ $\Delta\nu$=4.5cps, T_c 144°C and $\Delta G^{\neq}$=23kcal/mole (R.G.Kostyanovsky, Yu.I.Elnatanov, L.M.Zagurskaya, K.S.Zakharov, Izvest.Akad.Nauk SSSR, Ser.Khim., 1972, 1893). In both cases Ph_2O was used as solvent.
8. The possibility that the double sets of signals in the proton spectra of I, VI, VIII and IX might be due to the rotation about the substituent amide bond is ruled out on the following grounds: (i) Such isomerism could not be observed in the case of 2-methyl analog of I (see ref.4); (ii) The spectra of N-acylaziridines such as PhNHCONCH$_2$CMe$_2$ or Ph(Me)CHNHCONCH$_2$CR$_2$ (R=H,Me) in $CHCl_3$ display only single sets of signals at -50°C.
9. M.Jautelat, J.D.Roberts, J.Am.Chem.Soc., 91, 642(1969); A.Mannschreck, W.Seitz, Ang. Chem., 81, 224 (1969); R.G.Kostyanovsky, A.E.Polyakov, V.I.Markov, Izvest.Akad. Nauk SSSR, Ser.Khim., 1974, 1671; Bjørgo, D.R.Boyd, J.Chem.Soc., Perkin Trans.II, 1973, 1575.