WEAKENING OF AMIDE CONJUGATION WITH A NITROGEN ATOM INCLUDED IN A FOUR-MEMBERED RING

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The barriers to amide rotation about the N–N bond in 1-nitrosoazetidine, dimethylnitrosamine, 1-formylazetidine, 1,1'-carbonylbisazetidine, 1-dimethylcarbamoylazetidine, and dimethylformamide were measured by dynamic NMR spectroscopy. 1,1'-Carbonylbisazetidine and 1-dimethylcarbamoylazetidine, the structures of which were confirmed by data from the PMR and ^{13}C NMR spectra, were obtained.

A rule regarding weakening of amide conjugation with a nitrogen atom included in a strained three-membered ring [1, 2], which is general for N-acyl derivatives of aziridines [1-7], diaziridines [8, 9], and oxaziridines [8], has been previously formulated. One also might have expected weakening of conjugation with the nitrogen atom of a strained four-membered ring. However, the data on this question are extremely contradictory. According to the UV spectra, differences between 1-phenylazetidine, higher homologs, and N,N-dimethylanilines are not observed [10]. Ambiguous results were obtained by dynamic NMR spectroscopy for substituted vinylogs of azetidine urethanes as compared with higher homologs and N,N-dialkyl analogs [11]. A decrease in the barrier to rotation about the N–N bond was noted only for 1-nitrosoazetidines as compared with higher homologs and dimethylnitrosamine [12, 13].

In the present research data on 1-nitrosoazetidine (I) [12] were confirmed, and for the first time we demonstrated weakening of amide conjugation with the nitrogen atom of a four-membered ring on the basis of the decrease in the barrier to amide rotation ($\Delta G^{\neq}$) in 1-formylazetidine (II) as compared with DMF and the increase in $\Delta G^{\neq}$ in 1,1'-carbonylbisazetidine (III) as compared with tetramethylurea (singlet at −120°C) and N,N-dimethyl-N'-isopropylurea ($\Delta G^{\neq}$ = 9.7 kcal/mole) [14] and by internal comparison of the barriers to amide rotation in 1-dimethylcarbamoylazetidine (IV) (Table 1).

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were measured with Brucker WM-400 (^1H, 400.13 MHz; ^{13}C, 100.61 MHz) and WP-80-SY (^1H, 80.13 MHz; ^{13}C, 20.15 MHz) spectrometers.

The rate constants of retarded rotation were determined at the temperature of coalescence (T_c) of the signals of the exchange groups: $K = \pi \cdot \Delta\nu\sqrt{2}$. The $\Delta\nu$ values were extrapolated to the temperature of coalescence (T_c) of the signals. The change in the free energy of activation $\Delta G^{\neq}$ was found from the formula [15]

$$\Delta G^{\neq}_{T_c} = 4{,}57 \cdot T_c (10{,}32 + \lg T_c - \lg K).$$

The error in the determination of $\Delta G^{\neq} \leq 0.3$ kcal/mole with allowance for the accuracy in the measurement of $\Delta\nu$ (±2 Hz) and T_c (±1-2°C). It was assumed that $\Delta S^{\neq} = 0$ in analogy with retarded rotation processes [15]. The change in the free energy of activation at 25°C was determined from the formula [15]

$$\Delta G^{\neq}_{25^\circ} = \Delta G^{\neq}_{T_c} + R(T_c - 298).$$

N-Nitrosoazetidine (I). A mixture of 0.3 g (5.3 mmole) of azetidine and 1.1 g (12 mmole) of isopropyl nitrite in 3 ml of chloroform was reflexed for 3 h, after which the solvent was removed in vacuo, and the residue was fractionated to give 0.23 g (50%) of N-nitrosoazetidine with bp 56°C (1.33 hPa) (see [12]). PMR spectrum (80.13 MHz, $CDCl_3$): 2.39 (2H, p, ^3J = 7.5

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TABLE 1. Barriers to Amide Rotation*

Compound	Solvent	Observed group	T_c, °C	$\Delta\nu$, Hz	K, sec^{-1}	$\Delta G^{\neq}_{T_c} \pm 0.3$,** kcal/mole	$\Delta G^{\neq}_{25°}$,** kcal/mole
N-Nitrosoazetidine (I)	p-Dichloro-d_4-benzene	$CH_2N\{CCH_2C\}$	123	51,5	114,3	19,6	19,8
Dimethylnitrosamine (Ia)	p-Dichloro-d_4-benzene	Me_2N	183	60,0	133,2	22,6	22,9
N-Formylazetidine (II)	d_6-DMSO	$CH_2N\{CCH_2C\}$	73	20,0	44,4	17,7	17,8
DMF (IIa)	d_6-DMSO	Me_2N	120	14,3	31,7	20,5	20,7
III	d_8-Toluene	$CH_2N\{CCH_2C\}$	−55	64,0	142,1	10,5	10,3
IV	d_8-Toluene	$CH_2N\{CCH_2C\}$	−91	69,0	153,2	8,7	8,4
	CS_2+$CDCl_3$	Me_2N	−77	46,5	103,2	9,5	9,3
		$^{13}CH_2N$	−66	92,0	204,2	9,8	9,6
		$(^{13}CH_3)_2N$	−69	18,0	40,0	10,3	10,1

*Measured by dynamic ^1H (80.13 MHz) and ^{13}C (20.15 MHz) NMR spectroscopy: for I-IV, from coalescence of the signals of the MeN and CH_2N groups under conditions of decoupling of the $C-CH_2-C$ protons; for IV, in addition, from coalescence of the ^{13}C signals of the CH_2N and CH_3N groups under conditions of complete decoupling of the protons.
**Calculated as in [15]; see the experimental section.

Hz, CCH_2C); 4.11 and 4.82 ppm (2H, t, CH_2N). ^{13}C NMR spectrum (100.61 MHz, $CDCl_3$): 14.64 (^1J = 142.8 Hz, ^2J = 3.7 Hz, CCH_2C); 52.03 and 54.54 ppm (^1J = 150.8 Hz, ^2J = 3.7 Hz, CH_2N).

1-Formylazetidine (II). This compound was obtained from azetidine and ethyl formate by the method in [16].

1,1'-Carbonylbisazetidine (III). Excess phosgene was passed through a solution of 0.77 g (13.5 mmole) of azetidine and 1.5 g (15 mmole) of triethylamine in 7 ml of absolute ether at −70°C, after which the precipitated triethylamine hydrochloride was washed repeatedly with absolute ether, the filtrate was evaporated in vacuo, and the residue was fractionated to give 95 mg (6%) of N-chlorocarbonylazetidine with bp 48-50°C (1.33 hPa). PMR spectrum ($CdCl_3$, 80.13 MHz); 2.22 (2H, p, ^3J = 7.7 Hz, CCH_2C); 4.06 and 4.14 ppm (2H, t, CH_2N).

A solution of 90 mg (0.75 mmole) of N-chlorocarbonylazetidine was added with cooling (−70°C) and stirring to a solution of 43 mg (0.755 mole) of azetidine and 76 mg (0.76 mmole) of triethylamine, and the mixture was maintained at 20°C for 3 days. The precipitated triethylamine hydrochloride was removed by filtration, and the solvent was removed in vacuo to give 79 mg (75%) of the substance in the form of a colorless oil. PMR spectrum (80.13 MHz, d_8-toluene): 1.90 (2H, p, ^3J = 7.7 Hz, CCH_2C); 3.81 ppm (4H, t, CH_2N). ^{13}C NMR spectrum (100.61 MHz, d_8-toluene): 15.96 (^1J = 139.2 Hz, ^2J = 3.7 Hz, CCH_2C); 50.01 ppm (^1J = 147.3 Hz, ^2J = 3.5 Hz, CH_2N).

1-Dimethylcarbamoylazetidine (IV). A solution of 0.6 g (0.01 mole) of azetidine and 1 g (0.01 mole) of triethylamine in 5 ml of absolute ether was added with cooling (−20°C) and stirring to a solution of 1 g (0.01 mole) of dimethylcarbamoyl chloride in 5 ml of absolute ether. At the end of the exothermic reaction the mixture was maintained at 20°C for 1 h. The precipitated triethylamine hydrochloride was removed by filtration, the solvent was removed in vacuo, and the residue was fractionated to give 0.5 g (42%) of a substance with bp 62-63°C (1.33 hPa). PMR spectrum (400.13 MHz, d_6-toluene): 1.85 (2H, p, ^3J = 7.8 Hz, CCH_2C), 2.72 (6H, s, Me_2N), 3.84 ppm (4H, t, CH_2N). ^{13}C NMR spectrum (100.61, d_6-toluene) {^1H}: 15.79 (CCH_2C), 36.44 (Me_2N), 50.98 (CH_2N), 163.25 ppm (CO). Found: C 56.2, H 9.4, N 21.7%. Molecular weight 128. $C_6H_{12}N_2O$. Calculated: C 56.3, H 9.4, N 21.9%.

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ACETYLENIC FRAGMENTATION OF ACYL DERIVATIVES OF THE FISCHER BASE

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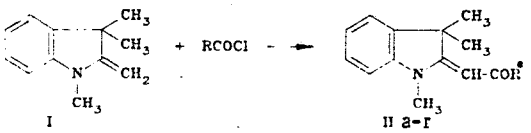
Indolenium salts, which readily undergo cleavage in aqueous alkali to give a monosubstituted acetylene and 1,3,3-trimethyl-2-oxindole, are formed when acyl derivatives of the Fischer base are heated with phosphorus oxychloride. Various aryl- and hetarylacetylenes can be conveniently obtained by this method.

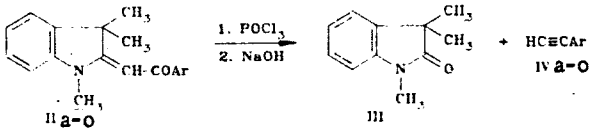
Enamino ketones of the indoline series (II), which are readily obtained by acylation of 1,3,3-trimethyl-2-methylene-indoline (I) — called the Fischer base in the literature — are characterized by high reactivities. They are used as intermediates for the synthesis of cyanine dyes [1] and thermochromic compounds [2] and for other purposes [3].



I II a-r

R= alkyl, aryl, hetaryl

We recently established [4] that acyl derivatives (II) of the Fischer base are convenient starting compounds for the synthesis of aromatic derivatives of acetylene. The new method for obtaining arylacetylenes consists in heating 1,3,3-trimethyl-2-phenacylideneindolines II with phosphorus oxychloride in dioxane and subsequent treatment with aqueous alkali; this leads to the formation of 1,3,3-trimethyl-2-oxindole (III) and a monoarylacetylene (IV):



II a-o III IV a-o

To determine the limits of applicability of the new method for introducing an ethynyl group into organic compounds we obtained various indoline enamino ketones IIa-r, which contain acyl groups of aliphatic, aliphatic-aromatic, aromatic, and heterocyclic acids (Table 1); IIa-r were then used for the synthesis of the corresponding monosubstituted acetylenes IVa-o (Table 2).

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