STRUCTURE AND PROPERTIES OF 1-ACYLPYRAZOLINES

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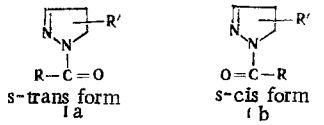
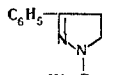
Proton magnetic resonance spectroscopy and the method of dipole moments demonstrated that 1-acylpyrazolines exist primarily in the s-trans form, which is stabilized by the repulsion of like-charged nitrogen and oxygen atoms. Simultaneous reduction of the C=O and C=N bonds was observed during the action of lithium aluminum hydride on 1-formyl- and 1-trifluoroacetylpyrazolines, which is explained by the relatively high polarity of the C=N bond.

We have previously reported [1] that 1-acylpyrazolines are converted smoothly to 1-alkylpyrazolines without involvement of the C=N bond on reaction with lithium aluminum hydride. In the case of 1-formyl derivatives, however, reduction of the pyrazoline ring occurs simultaneously. It has been assumed that this anomaly is associated with the stereochemistry [2].

A number of studies that make it possible to assume that Δ^2-pyrazolines have an almost planar structure have been published in recent years. In fact, the strong fluorescence of diarylpyrazolines has been explained by the ability of the carbon and nitrogen atoms of the pyrazoline ring to become coplanar (see [3,4], for example). The probability of the coplanarity of both the ring and acyl group for 1-acylpyrazolines is increased in view of the stabilization of the system through conjugation. If this is so, the possibility of considerable limitation of free rotation about the N–COR bond and predominant existence of the stable s-trans isomers [6] should be assumed on the basis of studies of the stereochemistry of acyl derivatives of the azole series [5], where the heterocyclic portion is known to be planar. This possibility, which is associated with the different orientation of the N_2 atom of the pyrazoline ring with respect to the oxygen atom of the carbonyl group, is due to an increase in the order of the N–COR bond as a result of conjugation of the p electrons of the nitrogen atom with the π electrons of the double bond of the C=O group.



The PMR spectrum of 3-phenylpyrazoline (IVa) contains a broad multiplet of the 5-H protons at 3.2-3.55 ppm. The multiplet is shifted to 3.7-4.1 and 3.75-4.0 ppm, respectively, on passing to IV and IVb. This shift on acylation of IVa confirms the probability of the existence of a stable trans form for both IV and IVb. The signal of the formyl proton in IV is seen as a distinct singlet (8.6 ppm). It could, of course, be assumed that this is a consequence of averaging of the spectrum due to rapid rotation about the C–N bond, but changing the temperature in the range 0-70° did not lead to a substantial change in the character



IV R = CHO;
IVa R = H;
IVb R = $COCH_3$

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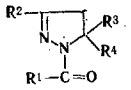
TABLE 1. Physical Constants and Dipole Moments of 1-Acyl-Δ^2-pyrazolines



Comp.	R¹	R²	R³	R⁴	bp, °C (mm)	mp, °C	R_f	Empirical formula
II	H	CH_3	C_6H_5	H	200—203 (17)	84—85	0,48	$C_{11}H_{12}N_2O$
III	H	CH_3	CH_3	CH_3	110—112 (20)[12]	—	0,58	
IV	H	C_6H_5	H	H	—	98	0,76	$C_{10}H_{10}N_2O$
V	CH_3	CH_3	CH_3	CH_3	92 (8)[12]	43	0,69	
VI	C_2H_5	CH_3	CH_3	CH_3	120—121 (8)	—	0,76	$C_9H_{16}N_2O$
VII	C_6H_5	CH_3	CH_3	CH_3		135[13]	0,56	

Table 1 (continued)

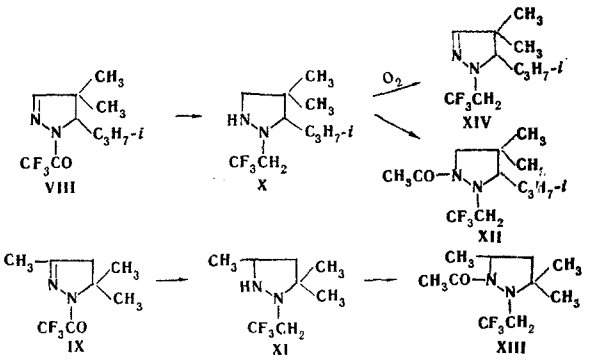
Comp.	Found, %		Calc., %		α_{av}	β_{av}	P_∞	R_D	μ_{exp}, D
	C	H	C	H					
II	70,1	6,5	70,2	6,4	14,211	0,197	533,51	55,03	4,81
III	70,3	6,5			12,061	0,240	440,08	34,15	4,45
IV	68,5	5,8	69,0	5,7	11,436	0,738	368,17	50,38	3,91
V	68,7	5,9			10,160	0,598	371,14	38,80	4,01
VI	64,4	9,5	64,2	9,9	8,942	0,211	299,74	49,40	3,46
VII	64,5	9,5			10,206	1,289	380,22	64,32	3,89

of the spectrum. From these results, it could be concluded that 1-formyl- and 1-acetylpyrazolines exist in the trans form or primarily in the trans form in inert solvents.

We measured the dipole moments of six 1-acylpyrazolines (see Table 1) and compared them with the values computed by the fragmentary calculation method [7, 8] starting from the dipole moments of 1,5-diphenylpyrazoline (2.92 D) and 1-(p-chlorophenyl)-5-phenylpyrazoline (4.34 D). For this, the moment of the $C_{arom}-Cl$ bond was assumed to be 1.59 D [6]. The results obtained by means of this path (μ_{trans} 3.92 D, μ_{cis} 5.35 D) also speak in favor of the predominant existence of 1-acylpyrazolines in the s-trans form, stabilized by repulsion of like-charged nitrogen and oxygen atoms, as was previously found for acyltriazoles [9]. The experimental μ value is closer to the calculated μ_{cis} value only in the case of 5-phenylpyrazoline. A phenyl group in the 5 position (adjacent to the acyl group) apparently increases the noncoplanarity of the pyrazoline ring or, by restricting conjugation of the carbonyl group, permits the appearance of the s-cis conformation. The μ values of 1-formylpyrazolines do not differ fundamentally from those for other 1-acylpyrazolines of the same model.

The reduction of 1-acylpyrazoline with lithium aluminum hydride can proceed through a step involving a complex, which, depending on the structure of the starting substance, includes one or two reactive groups of the molecule. Complexing can lead to facile trans-cis isomerization, but the hypothesis regarding the occurrence of the process through this sort of complex, where both reaction centers of the 1-acylpyrazoline are sterically regulated, does not make it possible to explain the anomalous behavior of the formyl derivatives.

This anomaly apparently is a consequence of the difference in the degree of polarization of the C=N bond, which, in view of the field effect created by the aliphatic portion of the ring, is considerably less reactive in pyrazolines than in open structures. If this is so, the introduction of strong electron-acceptor substituents into the acetyl group may give the same effect as the formyl group. In fact, the strong −I effect of three fluorine atoms in the reduction of 1-trifluoroacetylpyrazolines VIII and IX caused the reaction to proceed as for formylpyrazolines; i.e., the reduction of both the carbonyl group and the C=N bond to form



the corresponding 1-trifluoroethylpyrazolidines (X and XI), which are isolated as acetyl derivatives XII and XIII, proceeded to give high yields.

We have previously arrived at the erroneous conclusion that the C=N bond is stable in these models, since X is autooxidized to pyrazoline XIV after several minutes (we identified XIV in [2]). In addition, the data available in the literature [10] regarding the facile elimination of fluorine atoms in the reduction of trifluoroacetamides were not confirmed in our case.

EXPERIMENTAL

All of the 1-acylpyrazolines were chromatographed on a thin layer of activity II aluminum oxide with methyl ethyl ketone–benzene (1 : 6) and development by iodine vapors. The dipole moments of benzene solutions at 25 ± 0.1° were determined with an IDM-2-dipole meter for mole fractions from 0.002 to 0.005 via the method in [11]. The IR spectra were recorded with a UR-10 spectrometer.

1-Trifluoroacetyl-4,4-dimethyl-5-isopropylpyrazoline (VIII). This compound was obtained in 75% yield by acylation of 8.7 g (0.05 mole) of 4,4-dimethyl-5-isopropylpyrazoline by the action of 37.8 g (0.15 mole) of trifluoroacetic anhydride. The product had bp 105-1. 0° (18 mm), mp 33°, and R_f 0.79. IR spectrum: 1602 (C=N), 1700 cm^{-1} (C=O) [2].

1-Trifluoroacetyl-3,5,5-trimethylpyrazoline (IX). This compound was similarly obtained in 80% yield and had bp 105-110° (20 mm), n_D^{20} 1.4320, mp 38°, and R_f 0.83. IR spectrum: 1590 (C=N), 1690 cm^{-1} (C=O). Found: C 45.1; H 5.4; N 13.4%. $C_8H_{11}F_3N_2O$. Calculated: C 45.3; H 5.3; N 13.4%.

2-Acetyl-4,4-dimethyl-1-(2,2,2-trifluoroethyl)-5-isopropylpyrazolidine (XII). A solution of 9 g (0.075 mole) of pyrazoline VIII in 20 ml of absolute tetrahydrofuran was added slowly to a suspension of 8 g (0.15 mole) of lithium aluminum hydride in 200 ml of absolute tetrahydrofuran, and the reaction mixture was refluxed for 2 h and cooled. The unchanged aluminum hydride was decomposed by the action of 15 ml of moist ether followed by the same amount of water. The precipitated lithium hydroxide was removed by filtration and washed thoroughly on the filter with ether. Then, without isolating base X, excess acetic anhydride was added, and the mixture was refluxed for 3 h. The acetic anhydride was removed by distillation, and the residue was distilled to give 6 g (60%) of XII with bp 128-130° (15 mm), n_D^{20} 1.4355, and Rf 0.65. IR spectrum: 1680 cm^{-1} (C=O); no band was present at 1580-1620 cm^{-1} (C=N). Found: C 54.2; H 7.7; F 21.1%. $C_{12}H_{21}F_3N_2O$. Calculated: C 54.1; H 8.00; F 21.4%.

2-Acetyl-3,5,5-trimethyl-1-(2,2,2-trifluoroethyl)pyrazolidine (XIII). This compound was similarly obtained in 55% yield and had bp 134-138° (20 mm), n_D^{20} 1.4370 and R_f 0.61. IR spectrum: 1670 cm^{-1} (C=O). Found: C 52.4; H 7.7; N 12.4%. $C_{10}H_{17}F_3N_2O$. Calculated: C 52.4; H 7.1; N 11.8%.

Some time after the present paper had been submitted to press, we obtained a paper by French chemists [14] that confirms our conclusions regarding the predominant s-trans conformation of 1-acylpyrazolines.

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