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DERIVATIVES OF DIAZIRINE-3,3-DICARBOXYLIC ACID*

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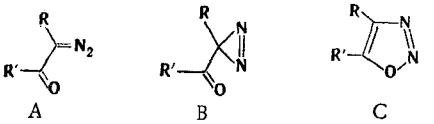
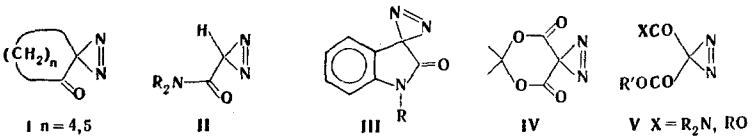
UDC 547.717

The amidation and alkaline hydrolysis of diazirine-3,3-dicarboxylic acid esters, which proceed with retention of the diazirine ring, were studied. The higher stability of diazirine-3,3-dicarboxylic acid esters as compared with their spirocyclic analogs is explained by the conformational lability of the C=O groups. The UV and mass spectra of the diazirines are discussed.

The synthesis and properties of α-diazo carbonyl compounds A have been studied extensively [2], while their valence isomers, viz., diazirines B, are represented by only a few examples.† These representatives are α-cyclodiazo ketones I, which were obtained by oxidation of the corresponding alcohols [4, 5], and products of photoisomerization of linear α-diazo carbonyl compounds, viz., cyclodiazoacetic acid amides II [6, 7], 3-cyclodiazo-2,3-dihydroindol-2-ones III [8], and isopropylidene cyclodiazomalonate (IV) [9].





However, the photochemical synthesis of diazirines is not of preparative value, since the yields in this case are 20-30% [6, 7, 9], and attempts to realize the photocyclization of the diester and amidoester of diazomalonic acid were unsuccessful; this was explained by the spontaneous retrotransformation of diazirines V because of the steric effect of two carbonyl substituents [6, 7], in analogy with 3,3-diphenyldiazirine [10].

We have previously shown that cyclodiazomalonic esters (diazirine-3,3-dicarboxylic acid esters) VIIa, b are readily obtained from O-tosyloximes VIa, b and alkoxyamines or by oxidation of diaziridine-3,3-dicarboxylic acid ester VIII [1, 11]:

*See [1] for our preliminary communication.
†A third valence isomer, viz., 1,2,3-oxadiazole C, has been found only in the gas phase by FES in the case of o-quinone diazide [3].

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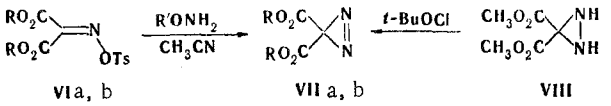


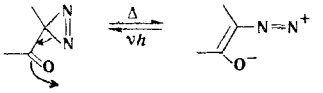
(1)

VIa, b VII a, b VIII

VI, VII a R = CH_3; b R = C_2H_5

Esters VIIa, b are colorless substances that are stable at 0°C. Thus the explanation for the unsuccessful attempts to synthesize diazirines V by means of purely steric reasons [6, 7] can be regarded as erroneous.

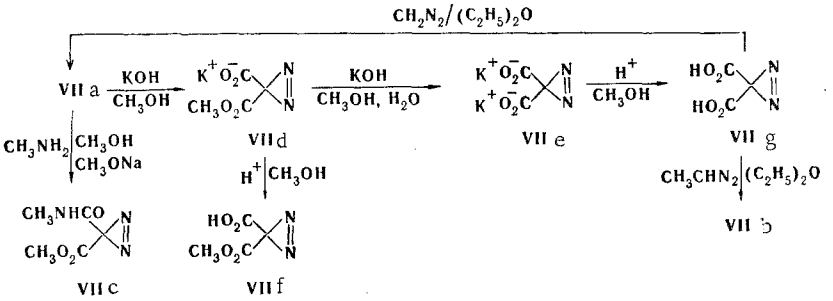
In contrast to linear isomers A [2, pp. 34, 64], the presence of an α-carbonyl group in diazirines B should lead to a decrease in stability because of the possibility of π,σ "pseudoconjugation" [8]:



(2)

According to molecular models, the most effective interaction of the antibonding π* orbitals of the C=O group with the bonding σ orbital of the C–N bond of the diazirine ring is observed in spirocyclic diazirines I, III, and IV with restricted conformational mobility of the C=O group (Fig. 1) (compare with the sprio activation in [12, 13]). In addition, distortion of the C–C(N_2)–C bond angle promotes destabilization of spirans, since, according to the data from microwave spectroscopy [14], the exocyclic bond angle in diazirines is ∿117°, while the corresponding angle in, for example, cyclohexanone [15] is ∿109°.

In fact, spirocyclic diazirines III and IV are considerably less stable than their analogs II and VIIa, b with conformationally labile C=O groups. Thus ester VIIa in the crystalline state remains unchanged for 1 month at 20°C, cycloacylal IV under the same conditions undergoes isomerization after a few weeks with opening of the diazirine ring [9], amides II [6, 7] undergo distillation at temperatures ⩾100°C, and spiran III is converted to a linear isomer at 20°C ($\tau_{1/2}$ ∿ 7 h) [8].



(3)

The low stability ($\tau_{1/2}$ = 1 h at 20°C) and the high sensitivity to acids of spirocyclic diazirine I (n = 4) can be explained by the unfavorable stereoelectronic situation (Fig. 1) [4, 5]. In the latter case an interaction of the σ_{C-N} orbital of the diazirine ring with the vacant p orbital of the carbonium ion formed by protonation of the carbonyl group is realized. At the same time, the conformational lability of the C=O groups and the possibility of competitive conjugation with the unshared electron pair of the oxygen atom of the MeO group ensures the stability of esters VIIa, b in a strongly acidic medium. For example, ester VIIa does not undergo appreciable decomposition in CF_3COOH after 2 h at 20°C (monitoring by PMR spectroscopy). We were therefore able to realize the transformations of ester VIIa presented in Scheme (3), including the liberation of free diazirine-3,3-dicarboxylic acid (VIIg).

The amidation and alkaline hydrolysis of ester VIIa under mild conditions (from 0 to −5°C) lead to monoamide VIIc and salts VIId, e (Table 1). Amide VIIc is stable at 0°C, and the dipotassium salt in the crystalline state remains unchanged after 2 months at 20°C, while the monopotassium salt undergoes decomposition after a few hours at 0°C. Both salts VIId, e explode when they are ground.

Acids VIIf, g (Table 1) are colorless crystalline substances that are stable at 0°C, and monoacid VIIf is readily sublimed *in vacuo* at 20°C (1 mm). The structure of diazirine-3,3-dicarboxylic acid (VIIg) was confirmed by conversion to esters VIIa, b via reactions with diazoalkanes (Scheme 3).

TABLE 1. Derivatives of Diazirine-3,3-dicarboxylic Acid

Compound	mp, °C	IR spectrum ν C=O, cm^{-1}	PMR spectrum δ, ppm (J, Hz)	PMR spectrum solvent	Mass spectrum (30 eV), m/e (relative intensity, %)	Yield, %
VII a	50—51 (dec.)	1730, 1750	3,21 s	C_6D_6	158 (M^+, 0,24), 130 (2), 127 (1), 99 (4), 59 (63), 28 (33), 15 (100)	98[a]
VII b	—[b]	1740, 1760	0,78 t, 3,75 q (7,0)	C_6D_6	186 (M^+, 0,21), 158 (6), 141 (5), 113 (5), 29 (100), 28 (27)	98[c]
VII c	25—27	1740, 1680	2,37 d (4,5) 2,95 s	C_6D_6	157 (M^+, 40), 99 (3), 98 (1), 58 (31), 42 (100), 28 (50), 15 (33)	92
VII d	104[d]	—	4,02 s	D_2O	—	90
VII e	195[d]	1610	—		—	79
VII f	49—51 (dec.)	1720	3,19 s, 10,49 s	C_6D_6	144 (M^+, 0,02), 127 (1), 116 (2), 113 (1), 99 (1), 85 (5), 59 (8), 45 (100), 28 (18), 15 (25)	73
VII g	76[d]	—	9,37 s	$(CD_3)_2CO$	—	90

[a]From diacid VIIg and CH_2N_2. [b]From diacid VIIg and $MeCHN_2$. [c]This compound had n_D^{20} 1.4248. [d]Decomposition temperature.

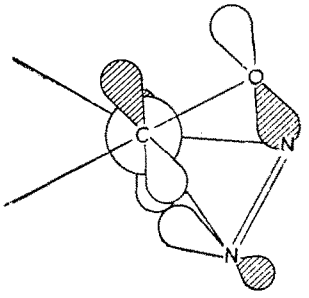


Fig. 1

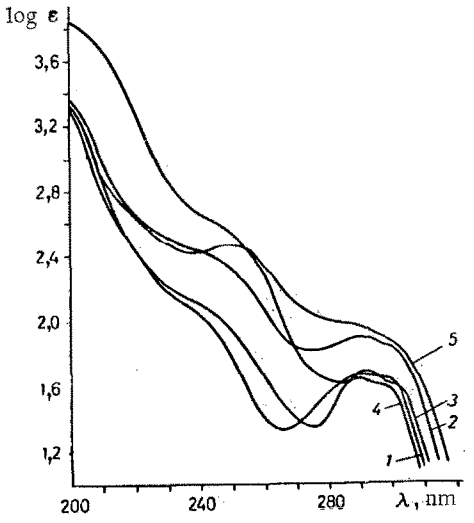


Fig. 2

Fig. 1. Overlapping of the σ_{C-N} and $\pi^*_{C=O}$ orbitals in spirocyclic diazirines.

Fig. 2. UV spectra of dimethyl ester VIa (1), diethyl ester VIIb (2), monoamide VIIc (3), monoacid VIIf (4), and diacid VIIg (5) in methanol.

A shoulder at 240-250 nm and a pronounced absorption band at 290-300 nm (Fig. 2), which, in contrast to the long-wave band of 3-alkyldiazirines (for example, see [16, 17]), does not have a fine structure and is shifted to the short-wave region, evidently because of the effect of electronegative substituents, since in the case of monoamide VIIc the hypsochromic shift is somewhat weaker (Fig. 2 and Table 2), are observed in the UV spectra of diazirines VIIa-c, f, g. There is no unified opinion with respect to the problem of the assignment of the long-wave band in the UV spectra of diazirines. According to calculations by the extended Hückel method, the $\pi \rightarrow \pi^*$ and $\sigma \rightarrow \pi^*$ transitions and one of the two $n \rightarrow \pi^*$ transitions are allowed for diazirine [18]. On the basis of this, the observed absorption at 320-360 nm was assigned to the $\sigma \rightarrow \pi^*$ transition. However, according to *ab initio* [19, 20] and MINDO2 [20, 21] calculations, the upper occupied orbital in the diazirine molecule is the antisymmetrical nonbonding p orbital. The data from the photoelectronic spectra are in

TABLE 2. UV Spectra of Diazirines and cis-Azoalkane

R	R′	Solvent	λmax of the long-wave band, nm	log ε	Literature
$(CH_2)_5$		Pentane	350	—	[16]
		$CHCl_3$	355	—	
		MeOH	355	—	
		H_2O	357	—	
$(CH_2)_5$		Hexane	366	2,18	[17]
		MeCN	352		
		MeOH	352		
		H_2O	352		
MeNHCO	H	EtOH	311	1,97	[6]
MeO_2C	MeO_2C	Pentane	289	1,63	This paper
		MeCN	289	1,83	
		MeOH	289	1,66	
		H_2O	288	1,94	
EtO_2C	EtO_2C	Pentane	289	1,89	This paper
		MeOH	289	1,89	
MeNHCO	MeO_2C	MeOH	292	1,67	„ „
$CO_2^-K^+$	MeO_2C	MeOH	300[a]	1,59	„ „
$CO_2^-K^+$	$CO_2^-K^+$	H_2O	298[a]	1,94	„ „
HO_2C	MeO_2C	MeOH	289	1,63	„ „
HO_2C	HO_2C	MeOH	286[a]	1,93	„ „
		Hexane	327	2,28	[17]
		MeCN	327		
		MeOH	323		
		H_2O	320		

[a]Shoulder.

agreement with the latter [20, 22]. The results of studies of the UV spectra of diazirines are contradictory. A red shift of the band at 350 nm when a nonpolar solvent (pentane) is replaced by a polar aprotic ($CHCl_3$) or protic (MeOH) solvent was observed for 3,3-pentamethylenediazirine and 3,3-dimethyldiazirine [16] (Table 2), and this band was assigned to a $\pi \rightarrow \pi^*$ transition in conformity with the principle in [23]. For 3,3-pentamethylenediazirine, on the other hand, a blue shift was observed [17] when hexane was replaced by acetonitrile or methanol (Table 2), and, in conformity with [23], it was concluded that it was due to an $n \rightarrow \pi^*$ transition. Moreover, different λ_{max} values have been presented for the same compound [16, 17] (Table 2). The conclusion from the experimental data [17] seems less correct. If one makes a comparison with cis-azoalkane (Table 2), for which there is no doubt regarding the long-wave $n \rightarrow \pi^*$ transition, in conformity with [23], a greater change in the position of the $n \rightarrow \pi^*$ band should be expected when an aprotic solvent is replaced by a protic solvent than when a nonpolar solvent is replaced by a polar solvent. The instability of 3-alkyldiazirines in an acidic medium [4, 5] does not make it possible to make measurements in an acidic solvent that give the most reliable criterion for the difference in the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions [23].

In the case of diazirines VIIa-c, f, g, which are stable in acidic media, the positions of the bands at 290-300 nm virtually coincide for esters VIIa, b and acids VIIf, g, do not depend on the polarity of the solvent (Table 2 and Fig. 2), and do not undergo a blue shift even in the case of the addition of $HClO_4$ to a solution of ester VIIa in MeOH, and this constitutes evidence in favor of a $\pi \rightarrow \pi^*$ transition. However, if the results of the calculations in [19, 20], which show that the p_- orbital is delocalized to a considerable extent by mixing with the σ orbitals of the diazirine ring and, consequently, that its interaction with proton-donor solvents will be slight, it may turn out that the criterion in [23] is inapplicable for diazirines.

The mass spectra of diazirine-3,3-dicarboxylic acid derivatives VIIa-c, f are characterized by low intensities of the M^+ peaks and considerable intensity of the ion with m/e 28 ($N_2^{\cdot +}$), and the maximum peaks correspond to the substituents attached to the carbon atom of

the diazirine ring and the hydrocarbon fragments with m/e 15 and m/e 29 (Table 1). The low intensities of the peaks of the $(M - N_2)^+$ ion and of diazirine cation D as compared with the corresponding peaks in the mass spectra of diazirines IXa-d (for example, see [24, 25]) are evidently due to destabilization of these ions by the electronegative COOR groups.

D

IXa-d

IXa R=R′=H; b R=H, R′=CH_3; c R=CH_3, R′=Cl; d R=CH_3, R′=Br

The same principle as in the case of diazirine IXa and diazomethane, i.e., high intensity of the M^+ peak of the linear isomer, which is explained by stabilization of the ion due to the removal of an electron from the antibonding orbital of the diazo compound [25], is observed when one compares the mass spectra of diazirine-3,3-dicarboxylic acid esters VIIa, b and the isomeric diazomalonic acid esters [26].

EXPERIMENTAL

The PMR spectra were obtained with a Tesla BS-487C spectrometer (80 MHz) with hexamethyldisiloxane as the internal standard. The IR and UV spectra were obtained with a UR-10 spectrometer and a Specord UV-vis spectrophotometer, respectively. The mass spectra were obtained with an MKh-1303 spectrometer with direct introduction of the samples into the ion source.

Diazirine-3,3-dicarboxylic Acid Methyl Ester N-Methylamide (VIIc). A solution of 0.34 g (11 mmole) of methylamine in 2 ml of absolute methanol was added dropwise with stirring and cooling (to 0°C) to a solution of 1.42 g (9 mmole) of diazirine VIIa [11] in 10 ml of absolute methanol containing traces of sodium methoxide, and the mixture was maintained at 0°C for 48 h. The solvent was evaporated *in vacuo* and the residue was sublimed at 24°C (1 mm) to give 1.30 g of amide VIIc (Table 1). Found: C 38.6; H 4.6; N 26.8%. $C_5H_7N_3O_3$. Calculated: C 38.2; H 4.5; N 26.7%.

Diazirine-3,3-dicarboxylic Acid Methyl Ester Potassium Salt (VIId). A solution of 0.42 g (7.50 mmole) of KOH in 5 ml of absolute methanol was added dropwise with stirring and cooling (to −10°C) to a solution of 1.26 g (7.86 mmole) of diazirine VIIa in 8 ml of absolute methanol, and the mixture was allowed to stand overnight at −10°C. Precipitated salt VIId (1.60 g; Table 1) was removed by filtration, washed with ether, and dried *in vacuo*.

Dipotassium Diazirine-3,3-dicarboxylate (VIIe). Water (10 ml) and a solution of 0.38 g (6.8 mmole) of KOH in 3.5 ml of methanol were added at 10°C to a suspension of 0.81 g (4.7 mmole) of monopotassium salt VIId in 12 ml of methanol, after which the mixture was maintained at 0°C for 12 h, and the crystals of salt VIIe (0.77 g; Table 1) were removed by filtration, washed with absolute methanol, and dried *in vacuo*. Found: C 17.8; N 13.9%. $C_3K_2N_2O_4$. Calculated: C 17.5; N 13.6%.

Methyl Diazirine-3,3-dicarboxylic Acid Methyl Ester (VIIf). A suspension of 0.25 g (1.4 mmole) of salt VIId and 1.0 g of Dowex 50W 12 (H^+) cation-exchange resin in 5 ml of absolute methanol was stirred at 0°C for 1 h, after which the cation exchange resin was removed, and the solvent was evaporated *in vacuo*. The residue was sublimed at 20° (1 mm) to give 0.15 g of monoacid VIIf (Table 1). Found: C 33.7; H 3.1; N 19.2%. $C_4H_4N_2O_4$. (0.34 g, Table 1). Calculated: C 33.4; H 2.8; N 19.4%.

Diazirine-3,3-dicarboxylic Acid (VIIg). This compound was obtained by the preceding method from 0.60 g (2.9 mmole) of salt VIIe and 3.0 g of cation-exchange resin with exclusion of the sublimation step.

Reaction of Diacid VIIg with Diazoalkanes. An ether solution of the diazoalkane was added dropwise at −10 to −15°C to a solution of 0.13 g (1 mmole) of acid VIIg in 2 ml of ether until a permanent yellow coloration developed. The ether was then removed, and the residue was sublimed *in vacuo* (1 mm) at 20°C (in the case of diazirine VIIb on a surface cooled to −70 to −60°C). Diesters VIIa, b (Table 1), which were identical to genuine samples [11], were obtained.

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