DIAZOCARBONYL DERIVATIVES OF HETEROCYCLES.
7.* DIAZOACETYLOXIRANES FROM THE INTERACTION OF HALOALKYLDIAZOKETONES WITH ARYLALDEHYDES

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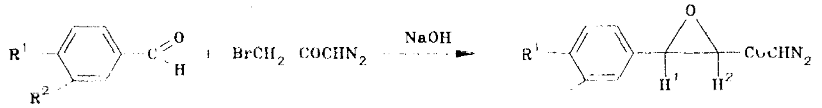
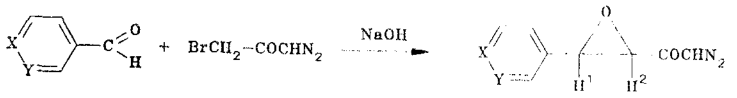
By the interaction of substituted benzaldehydes or pyridylaldehydes with 3-bromo-1-diazopropanone, a number of 1-aryl- and 1-pyridyl-2-diazoacetyloxiranes have been obtained. The IR, UV, and PMR spectra of these compounds are reported here, along with data from x-ray structure analysis.

It is known that haloalkyl-α-diazoketones enter into conversions of the aldol type while preserving the structure of the diazocarbonyl fragment; in these reactions, mobility of the methylene group proton is realized (for example, the Darzens reaction) [2, 3]. Under conditions analogous to those described in [4], we have synthesized new 1-aryl-2-diazoacetyloxiranes Ia-c (see Table 1) by the interaction of 3-bromo-1-diazo-2-propanone with substituted benzaldehydes in accordance with the scheme



Ia R=R¹=OCH_3;Ib R=H, R¹=CH_3;Ic R=H, R¹=Cl

Starting with nicotinaldehyde under analogous conditions, we have obtained for the first time the representatives of pyridine-containing diazoacetyloxiranes IIa, b:



IIa) X=N, Y=CH;IIb X=CH, Y=N

The increase in yield of the diazoketones I and II with increasing acceptor properties of the substituents is in good agreement with the known aldol mechanism of this reaction [4, 5]. The yields of type I compounds described in [4] (30% with R^2 = H and R^1 = OCH_3, 65% with R^1 = H, and 90% with R^1 = NO_2) are also consistent with this relationship.

The PMR spectra of the oxiranes I and II are in accord with the proposed structure; and the SSCC of the methine protons of the epoxy group (J = 1.5 Hz) corresponds to their transoid position relative to the epoxide ring, by analogy with the data of [6, 7]. The electronic spectra of compounds I and II (Table 1) have the same character as the spectra obtained for this class of compounds in [4].

For compound IIa, an x-ray structure analysis was performed. The structure was established through the ELLIDS program [8] with 50% probability ellipsoids of thermal oscillations. The molecule has the *trans* conformation, which is sterically the most favorable. The planes of the pyridine ring and the diazocarbonyl fragment pass through the bisectrices of the corresponding angles of the epoxy group triangle. The planes of the substituents are almost perpendicular to the plane of the epoxide fragment (about 80°). The bond lengths $O_{(1)}$—$C_{(8)}$ 1.44, $O_{(1)}$—$C_{(9)}$ 1.42, and $C_{(8)}$—$C_{(9)}$ 1.49 Å, as well as the bond angles in the epoxide ring, are in good agreement with

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*For Communication 6, see [1].

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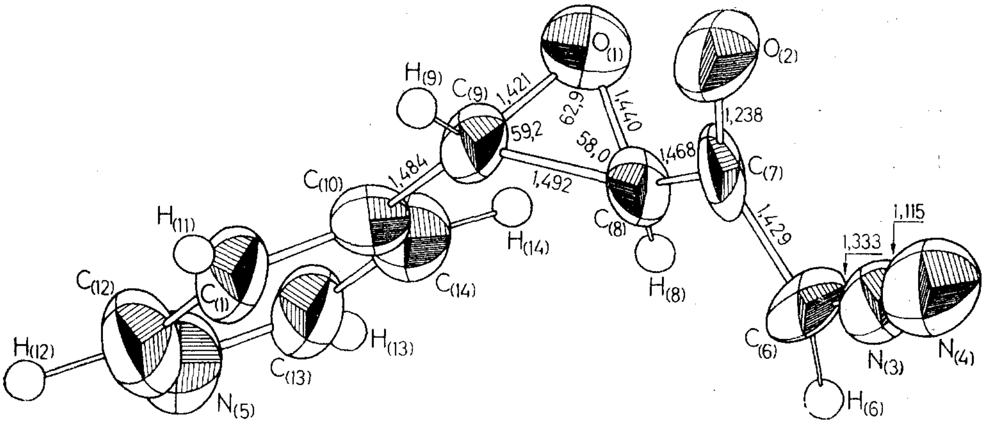

Fig. 1. Molecular structure of compound IIa.

TABLE 1. Characteristics of Diazoacetyloxiranes I and II

Compound	Empirical formula	R_f*	mp , °C	IR spectrum $\nu_{C=O}$, cm^{-1}**	UV spectrum λ_{max}, nm ($\lg \varepsilon$)	PMR spectrum ($CDCl_3$), δ, ppm			Yield, %
						1-H (d, J = 1.5 Hz, 1H)	2H (d, J = 1.5, Hz, 1H)	CHN_2 (s, 1H)	
Ia	$C_{12}H_{12}N_2O_4$	0,69	105...107	1590	274 (4,10), 252 (4,24)	3,40	3,75	5,60	32
Ib	$C_{11}H_{10}N_2O_2$	0,82	113	1615	273 (4,00), 248 (4,18)	3,35	3.8	5,60	40
Ic	$C_{10}H_7ClN_2O_2$	0,79	115...116	1620	273 (4,15), 244 (4,22)	3,45	4,1	5,72	75
IIa	$C_9H_7N_3O_2$	0,50	93	1620	273 (4,18), 250 (4,22)	3,45	3,90	5,80	68
IIb	$C_9H_7N_3O_2$	0,58	67	1620	273 (4,21), 230 (4,05)	3,55	3,95	5,75	79

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*Compounds Ia-c in 3:1 benzene—ethyl acetate mixture, IIa,b in 1:10 benzene—ethyl acetate mixture.

**Ia-c and IIa, b: ν 2100 cm^{-1} (N=N).

TABLE 2. Coordinates of Atoms (×10^4, or ×10^3 for H)

Atom	x	y	z	B_{iso}, Å^2	Atom	x	y	z	B_{iso}, Å^2
$O_{(1)}$	900(0)	931(4)	3251(8)	3,83	$C_{(12)}$	−671(5)	−2103(8)	308(13)	4,07
$O_{(2)}$	1601(3)	1659(5)	7501(9)	4,22	$C_{(13)}$	−1474(5)	−1524(9)	3266(16)	4,64
$N_{(3)}$	2240(4)	−493(6)	10248(13)	3,16	$C_{(14)}$	−954(5)	−646(8)	4443(12)	3,54
$N_{(4)}$	2538(4)	−82(7)	11853(14)	4,81	$H_{(6)}$	199(4)	−197(9)	737(15)	3,82
$N_{(5)}$	−1350(5)	−2251(7)	1271(13)	4,93	$H_{(8)}$	116(4)	−129(8)	407(14)	3,06
$C_{(6)}$	1856(5)	−891(7)	8328(14)	3,47	$H_{(9)}$	2(4)	113(9)	602(14)	3,38
$C_{(7)}$	1528(4)	307(7)	6993(11)	2,96	$H_{(11)}$	45(4)	−126(9)	54(15)	3,50
$C_{(8)}$	1064(5)	−199(6)	5013(12)	2,96	$H_{(12)}$	−55(4)	−277(11)	−137(16)	4,28
$C_{(9)}$	305(4)	401(7)	4660(12)	3,24	$H_{(13)}$	−206(5)	−157(10)	401(16)	4,77
$C_{(10)}$	−265(4)	−506(6)	3426(11)	2,72	$H_{(14)}$	−111(4)	2(9)	603(14)	3,51
$C_{(11)}$	−116(4)	−1259(7)	1340(12)	3,31					

the analogous values in [1]. The diazocarbonyl group is planar and has the *cis* conformation. The oxygen atoms of the carbonyl and epoxide groups are *cis*-oriented relative to each other. The bond lengths and angles in the diazocarbonyl fragment are extremely close to the corresponding values in other diazocarbonyl compounds for which the structure has been investigated [9-11]. Attention is directed to the significant shortening of the bond length $C_{(7)}—C_{(8)}$ 1.47 Å, which is 0.03 Å shorter than the $C_{(sp^2)}—C_{(sp^3)}$ bond. This is the shortest experimentally detected distance between carbon atoms of the C=O group and the "carrier" of the diazocarbonyl fragment. In ω-diazoacetophenone, where both carbon atoms are in the sp^2-hybridized state, the length of the C—C bond is 1.50 Å [9]; in diazane, $C_{(sp^2)}—C_{(sp^3)}$ 1.50 Å [10]; and in 3- and 4-[(4-chlorophenyl)sulfamoyl]-1-diazoalkan-2-ones, $C_{(sp^2)}—C_{(sp^3)}$ 1.53 and 1.54 Å [11]. We are not clear on the reason for the shortening of the $C_{(7)}—C_{(8)}$ bond. This question is all the more puzzling since the electronic structure of the diazocarbonyl fragment, judging by its geometric parameters, remains the same in all of the compounds that have been investigated.

The 1-aryl-2-diazoacetyloxiranes I and II that were obtained in the present work, since they have two alkylating centers that differ in reactivity, are of interest as models of bifunctional cytostatic agents; also, compounds IIa, b are readily soluble in water, thus offering considerably broader possibilities of application. The results obtained in screening these compounds on models of experimental solid (S-180) and ascitic (ARÉ) tumors and leucosis P-388 demonstrated moderate antitumor activity (up to 65% retardation of growth of the S-180 sarcoma and up to 40% for ARÉ, in the case of the IIa); the tests showed that the compounds had no antileukemic effect. Another feature of the molecules of compounds I and II is the presence of the oxirane group, which is active in reactions with nucleophiles, so that these compounds can be regarded as interesting synthons in obtaining new, functionally substituted diazocarbonyl compounds.

EXPERIMENTAL

The UV spectra were taken in a Specord UV-Vis instrument (in methanol), the IR spectra in a Specord IR-75 instrument (in white mineral oil in a liquid film, using NaCl plates). The NMR spectra were recorded in a Tesla 497 instrument (100 MHz) in $CDCl_3$ solution with TMS internal standard. Values of R_f were determined in Silufol UV-254 plates.

The crystals of compound IIa are orthorhombic; a = 18.187(4), b = 8.855(3), c = 5.626(3) Å, M = 189.09, d_{calc} = 1.40 g/cm^3, Z = 4. Of the two possible space groups, we selected the noncentrosymmetric $P2_1ab$ (= $Pca2_1$). In the centrosymmetric group P*cam*, with a total multiplicity of 8, the molecule must be located in the plane of symmetry m, which is a priori impossible. The determination of structure confirmed the correctness of selection of space group $P2_1ab$.

The intensities of 449 independent nonzero reflections of the hk0-hk5 type with $I \geq 2\sigma$ were measured in a DAR-UM automatic diffractometer on monochromatized CuK_α radiation, max $\sin\theta/\lambda = 0.5$. Absorption was not taken into account. The structure was solved by the direct statistical method. The hydrogen atoms were localized objectively from a difference synthesis. The LMS refinement was completed in the full-matrix anisotropic approximation (for the nonhydrogen atoms), with R = 0.038. All calculations were performed with the Rentgen-75 set of programs [12] in a BÉSM-6 computer. In Table 2 we have listed the coordinates of the atoms. Coefficients of the anisotropic thermal oscillations can be obtained from the authors.

1-Aryl-2-diazoacetyloxiranes Ia-c (General Method). To a solution of 4.5 mmole of the arylaldehyde in 20 ml of dry methanol, chilled to 0°C, 4.5 mmoles of 1-bromo-3-diazo-2-propanone and 4.5 mmole of 1 M NaOH were added while stirring. After 30-50 min of stirring at 0°C, the mixture was warmed to room temperature, and 50 ml of water, prechilled to 5°C, was added. The resulting precipitate was filtered off and recrystallized from a methanol—water mixture.

1-Pyridyl-2-diazoacetyloxiranes IIa, b (General Method). The synthesis of these compounds was analogous to the synthesis of compounds I. After 4 h of stirring at 0°C, the mixture was warmed to room temperature, the solvent was removed under reduced pressure, and the residue was separated chromatographically in a column with Al_2O_3 (Brockman activity rating II), sorbing fractions with R_f 0.45-0.55 for compound IIa and 0.55-0.60 for compound IIb. The solvent was removed under reduced pressure, and the residue was crystallized by chilling to —20°C, after which it was triturated with diethyl ether.

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