SYNTHESIS AND STUDY OF THE STRUCTURE OF o-HYDROXYARYL-1,2,4-OXADIAZOLES

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The reaction of 4-oxo-1,3-benz- and -naphthoxazinium perchlorates with hydroxylamine leads to 5-(o-hydroxyaryl)-1,2,4-oxadiazoles rather than to 3-(o-hydroxyaryl)-1,2,4-oxadiazoles, as was previously assumed. The structure of the compounds obtained was proved by alternative synthesis, as well as by mass spectrometry and comparison of the experimentally found and calculated dipole moments and Kerr constants of the possible structures of the o-hydroxyaryl-1,2,4-oxadiazoles.

In a continuation of research to ascertain the possibilities of the conversion of oxazinonium salts to various heterocycles [1], in the present research we developed a preparative method for obtaining o-hydroxyaryl-1,2,4-oxadiazoles by the reaction of readily accessible 4-oxo-1,3-benz- and -naphthoxazinium salts I [2, 3] with hydroxylamine, which proceeds via the ANRORC scheme. Oxadiazoles are formed in 68-98% yields (Table 1, method A) when perchlorates I are heated to boiling point with twofold amounts of hydroxylamine hydrochloride and sodium acetate in glacial acetic acid or triethylamine in benzene.

A group of bands of medium intensity at 1500-1660 cm^{-1} that are related to the vibrations of oxadiazole and aromatic rings is present in the IR spectra of the compounds obtained (see Table 1). The presence of a phenol or naphthol hydroxy group is indicated by absorption bands of stretching vibrations of an OH group at 3160-3250 cm^{-1}, which, however, are not observed for all of compounds because of their low intensity. In tetrachloromethane the absorption of an OH group shows up at 3170-3270 cm^{-1} in the form of bands of medium strength, the locations and intensities of which do not depend on the concentration. This, together with the shift of the signal of the OH group in the ^1H NMR spectra of the oxadiazoles from the 4.0-7.5 ppm region that is characteristic for free phenols [4] to weak field (9.85-12.10 ppm, see Table 1), indicates the presence of an intramolecular hydrogen bond (IHB) [5] between the nitrogen atom of the oxadiazole ring and the hydroxy group in the compounds. The presence of an OH group is also confirmed by the formation of O-acetyl and O-methyl derivatives, which, as shown below, have VII and VIII structures.

According to the results of quantum-chemical calculations [6], the most active center for nucleophilic attack is the 2 position of the I cation; the formation of intermediates II also is not excluded in the reaction with hydroxylamine of 4-oxo-1,3-benzoxazines III, which are capable of developing under the reaction conditions by deprotonation of salts I by hydroxylamine. Another reaction pathway could have included the intermediate formation of oximes IV. As a result of subsequent recyclization of intermediates II or IV one should have expected the formation of one of the isomeric oxadiazoles V or VI. (See scheme at the top of the next page.)

Structure VI was previously assigned to the synthesized oxadiazoles on the basis of a comparison of the experimental and calculated dipole moments and Kerr constants [7, 8]. However, the fact of the production from salt Ie of an oxadiazole with mp 154°C, which differs from oxadiazole VIe (mp 128°C) previously obtained [9] from O-benzoylsalicylamidoxime Xb, contradicted this. The agreement between the melting points of the oxadiazoles obtained from salt Ia and by the reaction of salicylamidoxime IX with acetic anhydride [9] via a modified method [10] proved to be coincidental. These compounds gave a melting-point depression when they were mixed, had different IR spectra, and, consequently, were isomers. In addition, the melting point of methylated derivative VIIIa differed from that of its isomer [11]. Since the conclusions in [7] contradicted these results, it was necessary to ascertain which isomer (V or VI) is formed from salts I, especially since the literature data

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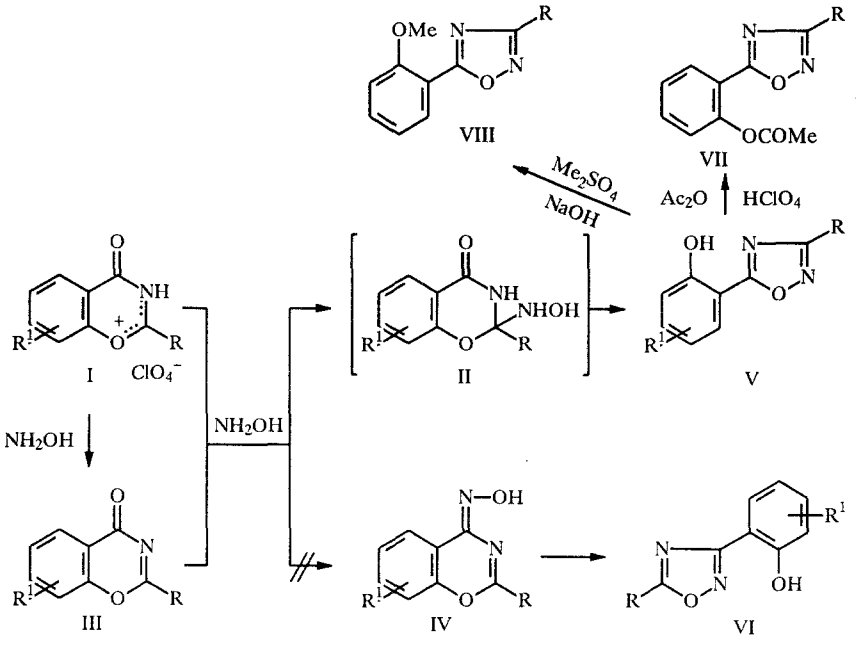
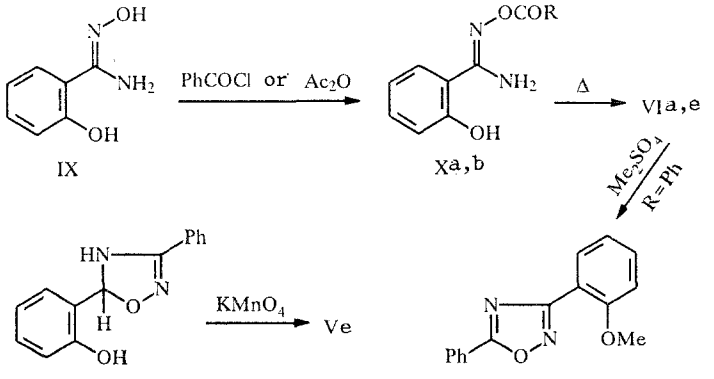


I, V a-g R^1 = H, a R = Me; b R = 4-$NMe_2C_6H_4$; c R = 4-$MeOC_6H_4$; d R = 4-MeC_6H_4; e R = Ph; f R = 4-ClC_6H_4; g R = CH=CHPh; I, V h-j R = Me; h R^1 = 3,4-benzo; i R^1 = 4,5-benzo; R^1 = 5,6-benzo
VIa, e R^1 = H; a R = Me; e R = Ph; VII, VIII a R = Me; b R = Ph

on the structure of oxadiazole VIe are also questionable. Thus it has been reported that the same compound (VIe) is formed in the cyclization of O-benzoylsalicylamidoxime Xb [9] and in the oxidation of dihydro compound XII — the product of condensation of salicylaldehyde and benzamidoxime [12] — although a priori isomeric oxadiazoles Ve and VIe should be obtained in these transformations.



X a R = Me; X b R = Ph

The possibility of rearrangement in one of these reactions was therefore assumed in a review article [13]. However, we obtained both isomers Ve and VIe when we reproduced the described methods. Despite [12], the substance obtained from XII had mp 154°C rather than 128°C and was identical to the oxadiazole synthesized from salt Ie. In addition, oxadiazole VIe, with mp 128°C, was converted by methylation to the known XI [11], which confirmed the structure of the latter, since it was heretofore in questionable.

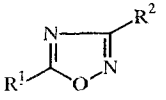
Thus it was established that rearrangement does not occur in the production of oxadiazoles Ve and VIe through XII and X, and the oxadiazole synthesized from salt Ie should have structure Ve rather than VIe, as indicated in [7].

The structures of Ve and VIe, as well as the other oxadiazoles, were confirmed by mass spectrometry (Table 2). The dominating processes in the fragmentation of the molecular ions of o-hydroxyphenyl-1,2,4-oxadiazoles and their O-methyl derivatives are similar to the processes observed for other oxadiazoles [14] and include the formation of fragments F-2 and F-3.

TABLE 1. 5-(o-Hydroxyaryl)-1,2,4-oxadiazoles Va-k

Compound	Yield, %		Tmp, °C	Recrystallization solvent	IR spectrum in mineral oil (in CCl_4) cm^{-1}		^1H NMR spectrum, ppm				
	method A	method B			OH	C=C arom and C=N	C—CH_3 (3H, s)	Ar—H (m)	OH (1H, s)	other groups	solvent
Va	89	23	77	Ethanol	3186 (3240)	1627 (1640), 1587, 1553	2,37	6,75...8,00(4H)	10,12		CCl_4
Vb	40		180...183	"		1626, 1613, 1596, 1553					
Vc	92		148...149	2-Propanol	3188	1623, 1607, 1589, 1549		6,95...8,20(8H)	10,37	3,8(3H, s OCH_3)	Acetone
Vd	87		157...158	"	3160	1634, 1599, 1563					
Ve	98	55	154	Ethanol	3180 (3250)	1629 (1642), 1594, 1554, 1530		6,65...8,10(9H)	10,25		CCl_4
Vf	96	92	150	Water—2-propanol	3200	1636, 1608, 1598, 1564					
Vg	95		143...144	Benzene	3180	1650, 1629, 1593, 1559		6,80...7,70(4H)	10,37	7,30 & 7,72 (1H, dd $J_{CH=CH}$=8 Hz)	Acetone
Vh	68		104	Water—propanol	(3170)	1648 (1648), 1613, 1592, 1510	2,40	7,18...8,55(6H)	11,25		CCl_4
Vi	89		123	" "	3250 (3270)	1660 (1661), 1624, 1588, 1564	2,40	7,05...8,42(6H)	9,85		CCl_4
Vj	71	39	119...120	Ethanol		1620, 1593, 1560	2,30	6,90...8,60(6H)	12,10		$CDCl_3$
Vk		77	243...244	Acetonitrile		1613, 1571, 1520, 1503					

TABLE 2. Characteristics of the Most Typical Ions in the Mass Spectra of the 1,2,4-Oxadiazoles



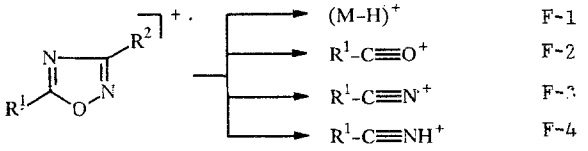
Compound	R^1	R^2	M^+		F-1		F-2		F-3		F-4		F-5		F-6	
			m/z	I_{rel}, %	m/z	I_{rel}, %	m/z	I_{rel}, %	m/z	I_{rel}, %	m/z	I_{rel}, %	m/z	I_{rel}, %	m/z	I_{rel}, %
Va	2-HOC_6H_4	CH_3	176	46	—	—	121	70	—	—	120	19	—	—	—	—
VIIIa	2-$CH_3OC_6H_4$	CH_3	190	34	189	12	135	10	133	48	—	—	161	22	133	48
Ve	2-HOC_6H_4	C_6H_5	238	22	—	—	121	100	119	12	120	14	—	—	—	—
VIIIb	2-$CH_3OC_6H_4$	C_6H_5	252	84	251	22	135	40	133	40	—	—	223	33	195	13
XIV*	2-HOC_6H_4	2-HOC_6H_4	254	19	—	—	121	100	119	17	—	—	—	—	—	—
VIe	C_6H_5	2-HOC_6H_4	238	4	237	24	105	100	103	3	104	3	—	—	—	—
XI	C_6H_5	2-$CH_3OC_6H_4$	252	14	251	11	105	100	103	12	—	—	223	18	195	5

*Compound XIV was described by Yu. I. Ryabukhin, L. N. Faleeva, and V. G. Korobkova in *Khim. Geterotsikl. Soedin.*, No. 3, 406 (1983).

TABLE 3. Kerr Constants and Dipole Moments of o-Hydroxyaryl-1,2,4-oxadiazoles Obtained from Salts I in Comparison with the Calculated Values for the Probable Structures (λ = 633 nm, 298°K, Determined in Dioxane)

Compound	Exptl. Kerr const 10^{12} cgs un.	μ_{exp}, D	Probable structure	Calc. Kerr constant, $\cdot 10^{12}$, cgs units	μexp, D
			VA	116	0,87
			VB	44	0,68
Va	88	0,66			
			VIA	553	2,43
			VB	214	2,83
			VA	138	1,42
			VB	222	1,57
Vc	266	1,45			
			VIA	1021	3,01
			VB	730	3,45
			VA	155	0,87
			VB	73	0,68
Ve	101	0,81			
			VIA	1031*	2,43
			VB	816*	2,83
			VA	928	2,13
			VB	220	1,20
Vf	519	1,18			
			VIA	101	1,55
			VB	240	1,30

*The exaltation of the polarizability was taken into account as the difference between the calculated spur of the polarizability tensor of the molecule calculated via an additive scheme and the spur found from experimental refraction of VIe (R_D = 76.9 cm^3). The exaltation is distributed uniformly in the plane of the o-hydroxyphenyloxadiazole.

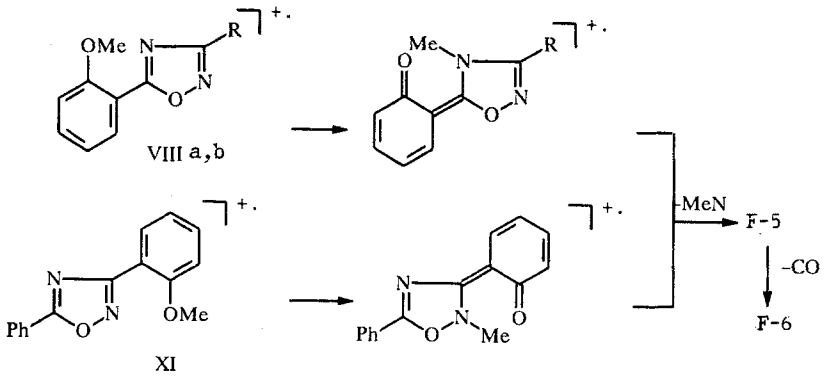


It is apparent from Table 2 that the locations of the substituents in the oxadiazoles can be judged from the m/z values for the F-2 ion (as the indicator fragment). This ion is characterized by high intensity and corresponds to an o-hydroxybenzoyl fragment for Va, e and XIV and to a benzoyl fragment for VIe and XI. In the case of 5-(o-methoxyphenyl) derivatives VIIIa, b, however, the intensity of the F-2 ion is 60% lower than for the corresponding o-hydroxy compounds Va, e.

In addition, another fragmentation pathway that includes a rearrangement — O → N migration of a methyl group in the molecular ion, as indicated by the development of fragments F-5 and F-6 — is also realized in o-methoxyphenyl derivatives VIIIa, b, as well as XI. (See scheme at the top of the next page.)

In the case of O-acetoxy derivative VIIb ketene (CH_2CO) is initially split out from the molecular ion, and the subsequent fragmentation is similar to the fragmentation of oxadiazole Ve.

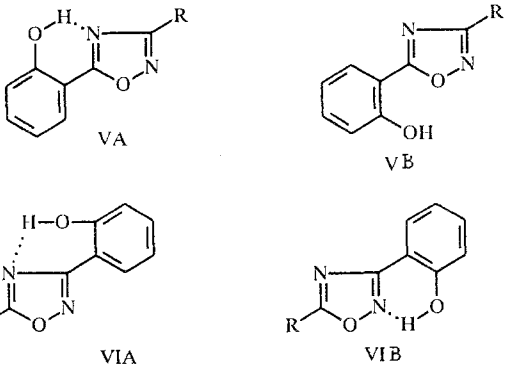
Since the data on the synthesis and the mass-spectral data show that oxadiazoles V are formed from salts I, we reviewed the additive calculation of their Kerr constants and dipole moments that was carried out in [7], in which isomeric structure VI was assigned to these compounds. In [7] the basis of the vector calculation of the dipole moments of the probable structures of o-hydroxyaryloxadiazoles V and VI was the orientation of the dipole moment of the isoxazole in accordance with a



previously proposed additive scheme [15, 16]. In this calculation the direction of the dipole moment of the N→O bond was adopted in conformity with the electronegativities of the atoms in a direction from the nitrogen atom to the oxygen atom with $\mu(N\rightarrow O) = 0.96$ D.

However, another solution in which the dipole moment of the N→O bond has the opposite direction — from the oxygen atom to the nitrogen atom — and its magnitude will be 1.61 D when one uses a dipole moment of isoxazole of, according to microwave-spectroscopic data [17], 2.9 D, as well as the moments of the other bonds [15, 16] and the geometry of a regular pentagon for the isoxazole ring (the approximation used in [7]), is also possible. This direction, although it does not correspond to the electronegativities of the atoms, does, however, convey the ability of an oxygen atom of the "furan" type to donate π electrons to an adjacent π-acceptor nitrogen atom of the "pyridine" type [18, 19].

Taking this into account, in the present study we calculated the theoretical Kerr constants and dipole moments of the oxadiazoles for probable structures VA, B and VIA, B.



It was assumed that the o-hydroxyphenyl substituent in these structures is coplanar with the heteroring, while the OH group is oriented differently with respect to the heteroring to give conformers VA, B and VIA, B. The geometry of a regular pentagon was assumed in the calculation of the Kerr constants and dipole moments of the molecules for the oxadiazole ring, while the standard values corresponding to hybridization of the atoms were assumed for the remaining bond angles. The formation of a ring due to an IHB in structures VA and VIA, B (excluding conformer VB, the formation of an IHB in which is impossible) was taken into account by introduction of the anisotropic-polarizability parameters determined for the same ring in salicylalaniline in accordance with the scheme presented in [7]. The polarizability tensors of the remaining fragments, groups, and bonds were taken from the publications cited in [7]. The magnitude and orientation of the moment of the OH group and the polarities of substituents R were adopted in accordance with the scheme of group dipole moments [20].

The Kerr constants for structures V and VIe, f were calculated for conformations in which the aryl substituent (R) is turned 30° relative to the plane of the heteroring. In structures V and VIc the p-anisyl fragment, taking into account the π-donor properties of the methoxy group and its planarizing effect on the aryl substituent, which is capable of rotating around a single bond [21], was assumed to be coplanar with respect to the heteroring. The two possible orientations of the methoxy group, which was assumed to be coplanar with respect to the benzene ring, were assumed to be equally likely. The calculated Kerr constants and dipole moments for the probable structures of the o-hydroxyaryloxadiazoles in comparison with the experimental values of the Kerr constants and dipole moments determined in [7] are presented in Table 3. It should be noted

that the calculated values of the Kerr constants for the versions of coplanarity of aryl substituent R and its free rotation relative to the oxadiazole ring differ by 10-30% from those presented in Table 3 to the larger or smaller side but do not change the qualitative picture; however, the dipole moments do not change.

It is apparent from Table 3 that the reaction of benzoxazinonium salts I with hydroxylamine proceeds with the formation of isomers V. This is in agreement with the above-presented mass-spectrometric data and data on the synthesis of the oxadiazoles but completely contradicts the conclusion regarding the structure of the oxadiazoles drawn in [7]. The reasons for this disparity stem from the different selection of the direction and magnitude of the moment of the N⋯O bond. The correctness of our calculation is confirmed by the good agreement between the calculated (see Table 3) and experimental values of the Kerr constants and dipole moments for oxadiazole and structure VIe proposed in [9] and confirmed by us [$_{\infty}(_{M}K_2)$ = $1007 \cdot 10^{-12}$ cgs units, μ = 2.68 D].

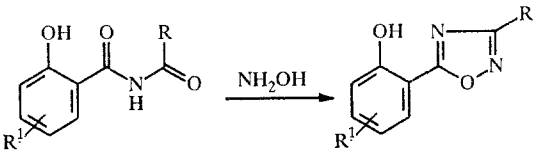
The observed difference between the calculated and experimental values (see Table 3) should be ascribed to the errors in the additive approximation and the assumptions adopted in the geometry and conformations of the molecules.

In solution, oxadiazole VIe evidently exists in the form of two conformers with preponderance of conformer A, in which chelation by a hydrogen bond is realized at the more nucleophilic nitrogen atom. In the case of oxadiazoles V, however, only conformer A actually exists, since the IHB detected by the IR spectra recorded in solution cannot be realized in conformer B.

The formation of oxadiazoles V rather than VI from salt I constitutes evidence that the reaction proceeds through intermediate II and repudiates the assumption of an alternative pathway through oximes IV. The production from benzoxazinone III (R = C_6H_5, R^1 = H) of oxime IV, the conclusion regarding the structure of which was drawn only on the basis of the absence of a qualitative reaction for a phenol hydroxy group with an alcohol solution of $FeCl_3$, has been reported [22]. However, the synthesized aryl-substituted oxadiazoles actually do not color an alcohol solution of $FeCl_3$, in contrast to the alkyl and styryl analogs, which give, respectively, a violet or brown coloration. However, in reproducing the described method for obtaining this oxime in order to subsequently convert it to oxadiazole VIe we obtained a compound with mp 154°C rather than 135°C, as in [22]. This compound was not hydrolyzed by refluxing in 10% HCl and was found to be oxadiazole Ve.

Thus the reaction of benzoxazinones III with hydroxylamine takes place in the 2 position rather than at the carbonyl group, which indicates the reality of the synthesis of oxadiazoles V from salts I through their deprotonation, although it does not repudiate the possibility of direct nucleophilic attack at the 2 position of salts I.

Considering the reality of the recyclization of benzoxazinones III and salts I, one should also take into account the possibility of their hydrolytic opening under the reaction conditions with subsequent reaction of the resulting N-acylsalicylamides XIII with hydroxylamine. In fact, oxadiazoles Va, e, f, j, k, respectively, were obtained from the genuinely synthesized XIIIa-e.



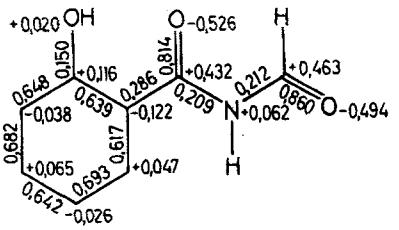
XIII V

XIII a-dR^1 = H, a R = Me, b R = Ph, c R = 4-ClC_6H_4, d R = 4-$NO_2C_6H_4$; XIII e R^1 = 5,6-benzo R = Me; Va, e, f, k; R^1 = H, a R = Me, e R = Ph, f R = 4-ClC_6H_4, k R = 4-$NO_2C_6H_4$; V j R^1 = 5,6-benzo R = Me

However, the lower yields of the products of this reaction (see Table 1, method B) indicate the realization of the ANRORC scheme in the conversion of salts I to oxadiazoles.

The reaction of various N-acylamides [23] with hydroxylamine may become a convenient method for the synthesis of oxadiazoles similar to the Einhorn—Brunner reaction for obtaining 1,2,4-triazoles [24]. However, the formation of mixtures of isomers because of the participation of any of the carbonyl groups of the N-acylamides in the first step is possible in this reaction.

The regioselectivity of the process in the case of N-acylsalicylamides XIII (only isomers V were isolated) is explained by the results of quantum-chemical calculations made by the Pariser—Parr—Pople (PPP) method for model compound N-formylsalicylamide in the Z,E form, which is realized for XIII in solution [25].



It is apparent from the molecular diagram that the highest positive charge is concentrated on the carbonyl carbon atom that is not bonded to the electron-donor o-hydroxyphenyl substituent. This atom is therefore the first atom to undergo nucleophilic attack as in the case of both alkyl and aryl substituents R of N-acylsalicylamides XIII.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil or solutions in CCl_4 (10^{-4}-10^{-3} mole/liter) were recorded with Specord IR-75 and UR-20 spectrometers. The ^1H NMR spectra were recorded with a Tesla BS-487C spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The mass spectra were recorded with Finnigan 4021 and MAT-212 spectrometers at an ionization energy of 70 eV with direct introduction of the samples into the ion source.

The Kerr effect was observed with the apparatus described in [26]. The dielcometric measurements were made with an E-7-5A capacitance meter with calculation of the $_\infty P_2$ polarizabilities by means of the Fujita formula [27]. The densities were measured by a hydrostatic method, and the refractive indexes were measured with an IRF-23 refractometer.

The characteristics of the synthesized compounds are presented in Tables 1-3. The results of elementary analysis for C, H, and N were in agreement with the calculated values.

5-(o-Hydroxyaryl)-1,2,4-oxadiazoles (V). A. A 1.41-g (0.02 mole) sample of hydroxylamine hydrochloride was added to 1.64 g (0.02 mole) of anhydrous sodium acetate in 10 ml of glacial acetic acid, 10 min after which 0.01 mole of 4-oxo-1,3-arenoxazinium perchlorate Ia-j was added, and the reaction mixture was heated to the boiling point and allowed to cool. It was then diluted with 30 ml of water, and the resulting precipitate was removed by filtration. This procedure was used to obtain oxadiazoles Va-j.

When the sodium acetate was replaced by an equimolar or twofold amount of triethylamine (with respect to the hydroxylamine hydrochloride), the yields of oxadiazole Va were, respectively, 80% and 74%.

B. A 0.8-g (0.01 mole) sample of hydroxylamine hydrochloride was added to a suspension of 0.01 mole of N-acylsalicylamide XIIIa-e in 6 ml of pyridine, after which the mixture was refluxed for 6 h. It was then cooled, diluted with 20 ml of water, and filtered. This method was used to obtain oxadiazoles Va, e, f, j, k.

3-(o-Hydroxyphenyl)-5-methyl-1,2,4-oxadiazole (VIa). A mixture of 0.5 g (3.3 mmole) of salicylamidoxime IX, 1 ml of glacial acetic acid, and 0.63 ml (6.6 mmole) of acetic anhydride was refluxed for 15 min, after which it was cooled and poured over ice. The resulting precipitate was removed by filtration to give a product with mp 77°C (from aqueous ethanol) (mp 77°C [9]). IR spectrum: 3147 (OH); 1613, 1593, 1573, 1527 cm^{-1} (C=C and C=N). The yield was 0.5 g (88%).

3-Methyl-5-(o-methoxyphenyl)-1,2,4-oxadiazole (VIIIa). A 5.28-g (30 mmole) sample of oxadiazole Va and 2.85 ml (30 mmole) of dimethyl sulfate were added to a solution of 1.5 g (37.5 mmole) of NaOH in 5 ml of water, and the mixture was stirred on a boiling-water bath for 30 min. It was then cooled and extracted with ether, and the extract was dried with anhydrous Na_2SO_4 and evaporated to give a product with mp 68-69°C (from petroleum ether). IR spectrum: 1618, 1570 cm^{-1} (C=C and C=N). ^1H NMR spectrum (CCl_4): 2.35 (3H, s, 3-CH_3), 3.88 (3H, s, OCH_3), 6.80-8.00 ppm (4H, m, C_6H_4). The aqueous layer was acidified and extracted with ether to give 0.5 g of the starting oxadiazole. The yield was 4.15 g (72%).

5-(o-Methoxyphenyl)-3-phenyl-1,2,4-oxadiazole (VIIIb). A 0.6-g (2.5 mmole) sample of oxadiazole Ve was added to 2 ml of 50% NaOH solution, the reaction mixture was stirred for 5 min, 0.35 ml (3.7 mmole) of dimethyl sulfate was added, and the mixture was refluxed for 3 h. The resulting precipitate was removed by filtration to give a product with mp 94-95°C (from 2-propanol). IR spectrum: 1613, 1587 cm^{-1} (C=C, C=N). ^1H NMR spectrum (d_7-DMF): 3.92 (3H, s, OCH_3), 7.02-8.12 ppm (9H, m, Ar—H). The yield was 0.2 g (32%).

3-(o-Methoxyphenyl)-5-phenyl-1,2,4-oxadiazole (XI). A 0.2-g (3.6 mmole) sample of powdered KOH and 0.2 ml (2.1 mmole) of dimethyl sulfate were added successively to a solution of 0.24 g (1 mmole) of oxadiazole VIe in 4 ml of

DMSO, and the reaction mixture was stirred for 20 min. Water (20 ml) was added to the resulting suspension, and the mixture was extracted with ether. The extract was dried with anhydrous Na_2SO_4 and evaporated to give a product with mp 117°C [2-propanol—hexane (2:1)] [mp 117°C (ethanol)]. IR spectrum: 1593, 1576, 1553 cm^{-1} (C=C and C=N). The yield was 0.1 g (40%).

5-(o-Acetoxyphenyl)-3-methyl-1,2,4-oxadiazole (VIIa). Three drops of 70% $HClO_4$ were added to a suspension of 0.88 g (5 mmole) of oxadiazole Va in 3 ml of acetic anhydride, and the mixture was heated until the solid dissolved and then allowed to stand overnight. Water (10 ml) was added, and the colorless precipitate was removed by filtration to give a product with mp 61-62°C (from petroleum ether). IR spectrum: 1768 ($OCOCH_3$); 1620, 1595, 1574 cm^{-1} (C=C and C=N). The yield was 0.9 g (82%).

5-(o-Acetoxyphenyl)-3-phenyl-1,2,4-oxadiazole (VIIb). This compound was similarly obtained from oxadiazole Va and had mp 115-116°C (from hexane). IR spectrum: 1767 ($OCOCH_3$); 1611, 1600, 1565 cm^{-1} (C=C and C=N). The yield was 85%.

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THE 3,4-DIHYDRO-N-OXO-3-ETHYL-2,1-BENZOXAZINIUM CATION IN THE SYNTHESIS OF β- AND γ-SUBSTITUTED ARYLBUTANES AND 1-ARYL-2-BUTENES

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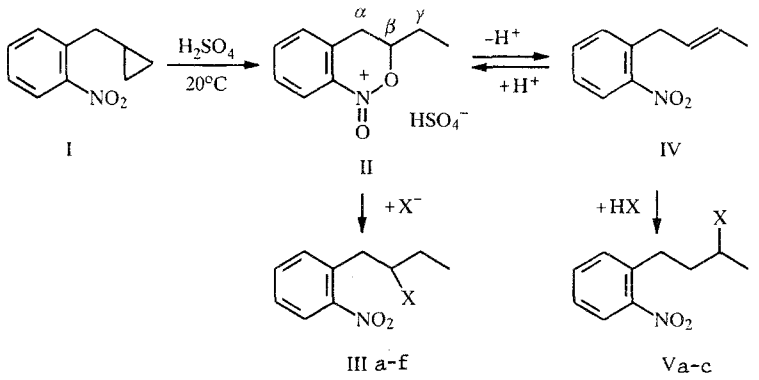
The reaction of 3,4-dihydro-N-oxo-3-ethyl-2,1-benzoxazinium salts with reagents with nucleophilic and basic character can be used to obtain β- or γ-substituted arylbutanes and trans-1-aryl-2-butenes. The reactions proceed regiospecifically and are regulated by the nature of the reagents used.

It is known that certain difficulties are encountered in the synthesis of β- or γ-substituted alkylbenzenes and unconjugated alkenylbenzenes.

In the present research we were able to show that 3,4-dihydro-N-oxo-3-ethyl-2,1-benzoxazinium salts II, which are readily formed, for example, from 2-nitrobenzylcyclopropane (I) [1], can serve as convenient synthones for obtaining either β- or γ-substituted butylbenzenes or trans-1-(2-nitrophenyl)-2-butenes.

For example, treatment of a sulfuric acid solution of heterocyclic ion II with nucleophilic reagents such as the bromide ion, methanol, or acetonitrile leads to β-substituted 1-arylbutanes — the corresponding bromide IIIa, ether IIIb, and acetamidobutylbenzene IIIc* — in virtually quantitative yields. The reaction of cyclic ion II with acetonitrile essentially models the Ritter reaction [2].



III aX=B , bX=OMe, c X=NHCOMe, dX=OC_3H_7, eX=OCOMe, f X=OH; V aX=NHCOMe, bX=OC_3H_7-*i*, c X=OH

*In this case, a small amount (≈5%) of γ-substituted isomer Va is formed in addition to the chief reaction product, viz., IIIc.

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