6. V. A. Palm, Fundamentals of the Quantitative Theory of Organic Reactions [in Russian], Khimiya, Moscow (1977).
7. G. I. Kagan, I. N. Fundyler, and G. M. Kagan, Teor. Éksp. Khim., 2, No. 5, 589 (1966).
8. R. Phan-Tan-Luu, L. Bouscasse, E. J. Vincent, and J. Metzger, Bull. Soc. Chim. Fr., No. 9, 3283 (1967).

CONVERSION OF 2-AMINO-5-R-PHENYL-1,3,4-OXADIAZOLES INTO 3-R-PHENYL-5-ALKOXY-1,2,4-TRIAZOLES

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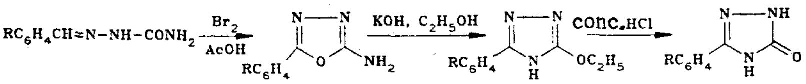
2-Amino-5-R-phenyl-1,3,4-oxadiazoles have been shown to isomerize in alcoholic potassium hydroxide solution to 3-R-phenyl-5-alkoxy-1,2,4-triazoles. The dissociative ionization of 3-R-phenyl-5-alkoxy-1,2,4-triazoles and 3-R-phenyl-1,2,4-triazolin-5-ones has been examined. The mass spectra of the oxadiazoles have been compared with those of the triazoles.

Some 1,3,4-oxadiazoles have been found to possess valuable biological properties [1]. It has previously been shown that 2-amino-1,3,4-oxadiazoles are converted into 1,2,4-triazoles on treatment with alcoholic potassium hydroxide [2].

The aim of this investigation was to study the isomerization of 2-amino-5-R-phenyl-1,3,4-oxadiazoles to 3-R-phenyl-5-ethoxy-1,2,4-triazoles, and to examine the dissociative ionization of 3-R-phenyl-5-ethoxy-1,2,4-triazoles and 3-R-phenyl-1,2,4-triazolin-5-ones under electron impact.



I-VI VII-XI XII-XVI

I, VII, XII R=H; II, VIII, XIII R=4-F; III, IX, XIV R=4-Cl; IV, X, XV R=4-Br, V R=4-NO$_2$; VI, XI, XVI R=4-CH$_3$O

Compounds (VII-XI) were obtained by the alcoholysis of 2-amino-5-R-phenyl-1,3,4-oxadiazoles in alcoholic potassium hydroxide at the boil for several hours. Subsequent acid hydrolysis with concentrated hydrochloric acid gave the triazolones (XII-XVI). Crystalline products were obtained (Table 1), the structures of which were confirmed by their elemental analyses, UV, IR, and mass spectra.

The UV spectra of the oxadiazoles (I-VI) were similar to those of known 2-amino-3-R-phenyl-1,3,4-oxadiazoles [3], absorption having a maximum at 270-280 nm and a minimum at 230 nm. In the spectra of the triazoles, the maximum underwent a hypsochromic shift at 250-260 nm.

In the IR spectra of the oxadiazoles, absorption was present corresponding to deformational (970 cm^{-1}) and stretching 1000 cm^{-1} vibrations of the —C—O—C— group. The strong doublet at 3450 cm^{-1} was due to stretching vibrations of the amino-group. The spectrum contained absorption for stretching vibrations of the C═N group at 1650 cm^{-1}. In the IR spectra of the 1,2,4-triazol-5-ones, a typical feature is carbonyl stretching absorption at 1750-1650 cm^{-1}.

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TABLE 1. Properties of 2-Amino-5-R-phenyl-1,3,4-oxadiazoles, 3-R-Phenyl-5-ethoxy-1,2,4-triazoles, and 3-R-Phenyl-1,2,4-triazolin-5-ones

Compound	mp, °C*	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
I	240—241	59,5	4,5	26,0	$C_8H_7N_3O$	59,6	4,4	26,1	60,3
II	235	53,7	3,4	23,6	$C_8H_6FN_3O$	53,6	3,4	23,5	80,0
III	273	49,1	3,2	21,6	$C_8H_6ClN_3O$	49,1	3,1	21,5	82,5
IV	280	40,0	2,4	17,6	$C_8H_6BrN_3O$	40,0	2,5	17,5	50,1
V	270	46,6	2,9	27,3	$C_8H_6N_4O_3$	46,6	2,9	27,2	60,0
VI	255	56,5	4,9	21,8	$C_9H_9N_3O_2$	56,5	4,8	21,9	70,9
VII	110	63,4	5,9	22,3	$C_{10}H_{11}N_3O$	63,4	5,9	22,2	80,0
VIII	140	57,8	4,8	20,3	$C_{10}H_{10}FN_3O$	57,9	4,9	20,3	75,3
IX	150	53,7	4,6	18,7	$C_{10}H_{10}ClN_3O$	53,7	4,5	18,7	91,2
X	145	44,6	3,7	15,6	$C_{10}H_{10}BrN_3O$	44,7	3,8	15,7	35,7
XI	142	65,1	6,3	20,6	$C_{11}H_{13}N_3O$	65,0	6,4	20,7	72,3
XII	332—333	59,5	4,5	26,0	$C_8H_7N_3O$	59,6	4,4	26,1	71,6
XIII	390—391	53,7	3,5	23,4	$C_8H_6FN_3O$	53,6	3,4	23,5	50,3
XIV	410—412	49,1	3,0	21,4	$C_8H_6ClN_3O$	49,1	3,1	21,5	75,9
XV	420—422	40,1	2,4	17,5	$C_8H_6BrN_3O$	40,0	2,5	17,5	63,7
XVI	347—349	46,6	2,8	27,3	$C_9H_9N_3O_2$	46,6	2,9	27,2	70,1

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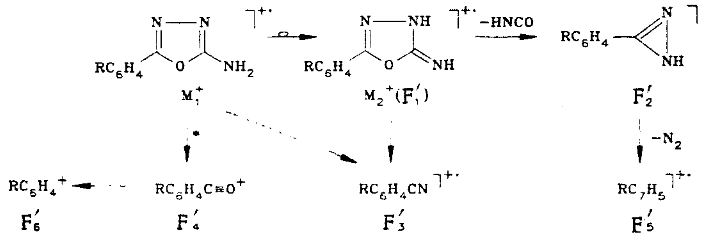
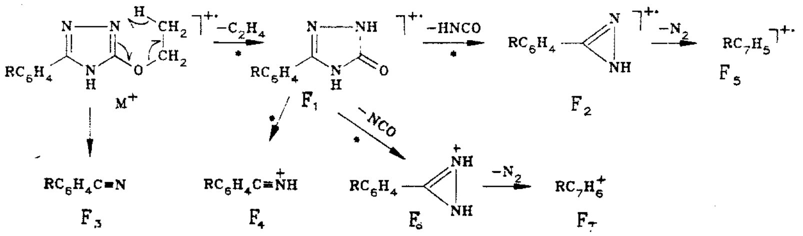
*Compounds (XII) and (XIV-XVI) melted with decomposition.

The mass spectra of the 1,3,4-oxadiazoles were in general accordance with those of known compounds [4], their breakdown being shown as follows:



The first event in the dissociative ionization of the molecular ions (M^+) of 5-ethoxy-1,2,4-triazoles is breakdown with MacLafferty rearrangement and loss of a molecule of ethylene to give ions F_1, which are heteroanalogs of oxadiazoles M^+_2 (F_1).



The peaks for the ions F_1 are maximal in the spectra. If breakdown with successive elimination of a molecule of isocyanate and nitrogen to give ions F_2 (F_2') and F_5 (F_5') is common to both heterocycles, and the formation of ions $RC_6H_4C\overset{+}{N}H$ (F_4) may be regarded as analogous to the formation of R-benzoyl cations (F_4'), then breakdown of ions F_1 with successive ejection of the NCO radical and a molecule of nitrogen (fragments F_6 and F_7) is specific and enables these heterocyclic analogs to be differentiated from their mass spectra. Apart from metastable transitions, this route is confirmed by high-resolution mass spectrometry (Table 3).

The routes of fragmentation of M^+ of 3-R-phenyl-1,2,4-triazolin-5-ones are the same as for ions F_1 of 3-R-phenyl-5-ethoxy-1,2,4-triazoles, small differences in the relative intensities of the fragment peaks of isomeric pairs apparently being due to the existence of 3-R-phenyl-1,2,4-triazolin-5-ones in the enol form, such as has been shown on more than one occasion in the condensed and liquid phases [5]. The electronic structure of the substituent in the benzene ring affects the dissociative ionization of (VII-XVI). For example,

TABLE 2. Intensities of Peaks of Characteristic Ions (%, Σ_{50}) at Ionization Energy 70 eV

Compound	M^+	F_1	F_2	F_3	F_4	F_5	F_6	F_7
VII	17,9	26,8	14,3	4,1	3,0	1,4	1,4	2,9
VIII	16,0	20,0	1,3	5,2	7,7	0,8	1,3	0,4
IX	10,4	18,8	9,6	6,7	6,3	—	1,1	2,1
X	3,8	11,8	4,7	0,7	1,3	0,4	0,4	0,5
XI	9,3	10,0	2,4	3,1	3,8	0,7	2,5	1,0
XII	32,4	—	18,9	2,0	2,6	0,6	1,4	8,0
XIII	34,7	—	17,9	3,3	3,3	0,8	1,7	9,9
XIV	15,8	—	13,2	0,5	3,2	0,6	1,3	6,8
XV	18,2	—	6,6	0,8	1,1	—	0,8	1,8
XVI	19,5	—	3,3	6,9	2,1	—	0,8	0,9

TABLE 3. Elemental Composition of Principal Ions Found in the Mass Spectrum of 3-R-Phenyl-5-ethoxy-1,2,4-triazole (VII)

Compound	m/z Value	Probable route of formation of ion	Elemental composition of ion	Exact mass	
				found	calculated
VII	161	$M^+ - C_2H_4$ (F_1)	$C_8H_7N_3O$	161,0537	161,0587
	119	F_1 $-NCO^{\cdot}$ (F_6)	$C_7H_7N_2$	119,0664	119,0607
	118	F_1 $-NCOH$ (F_2)	$C_7H_6N_2$	118,0499	118,0529

TABLE 4. Mass Spectra of 3-R-Phenyl-5-ethoxy-1,2,4-triazoles and 3-R-Phenyl-1,2,4-triazolin-5-ones at Ionization Energy 70 eV

Compound*	m/z value† (relative intensity as % of maximum peak)
VII	189 (67), 188 (5), 161 (100), 119 (5), 118 (53), 104 (30), 103 (15), 91 (10), 90 (5), 77 (27), 50 (11)
VIII	207 (80), 206 (5), 179 (100), 137 (9), 136 (7), 122 (38), 121 (26), 109 (2), 108 (4), 102 (3), 95 (20)
IX	223 (56), 222 (4), 195 (100), 153 (5), 152 (51), 138 (33), 137 (35), 125 (11), 111 (15), 102 (27), 75 (22)
X	267 (70), 266 (5), 239 (100), 197 (6), 196 (45), 182 (20), 181 (11), 169 (7), 168 (6), 155 (14), 102 (50)
XI	219 (93), 218 (5), 191 (100), 176 (27), 149 (25), 148 (24), 134 (38), 133 (31), 121 (10), 120 (7), 107 (8)
XII	161 (100), 119 (5), 118 (56), 104 (8), 103 (6), 91 (25), 90 (2), 89 (3), 77 (23), 75 (3), 51 (14)
XIII	179 (100), 137 (5), 136 (52), 122 (10), 121 (10), 109 (29), 108 (2), 107 (3), 95 (3), 75 (9), 50 (4)
XIV	195 (100), 153 (8), 152 (83), 138 (23), 137 (17), 125 (43), 123 (7), 111 (23), 102 (23), 90 (20), 89 (3)
XV	239 (100), 197 (5), 196 (33), 182 (8), 181 (5), 169 (10), 155 (8), 117 (14), 102 (14), 90 (3), 75 (22)
XVI	191 (100), 176 (3), 149 (4), 148 (17), 134 (10), 133 (35), 119 (3), 105 (7), 91 (5), 77 (4), 51 (67)

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*For compounds (IX) and (XIV) the ions shown are those containing the isotope (^{35}Cl), and for (X) and (XV), those containing the isotope (^{79}Br).

†The peak for the molecular ion ($M^{+\cdot}$) is given, together with the ten strongest peaks.

the stability of M^+ is highly dependent on the ability of the halogen to stabilize the charge on the cation, i.e., to show a +M effect. The intensities of the molecular ions decrease from 3-fluorophenyl-1,2,4-triazole to 3-bromophenyl-5-ethoxy-1,2,4-triazole. The intensities of the peaks for the ions F_1 vary similarly (Table 4). In contrast to oxadiazoles, in which the relative intensities of the ion peaks for F_2' and F_4' depend on the substituents in the benzene ring (electron donor substituents favor the formation of the benzoyl cation, but electron-acceptor substituents, on the other hand, facilitate rupture of the $O-C_{(5)}$ bond), in triazoles no such dependence is seen. This appears to be due to the absence of effective delocalization of the charge in the heterocyclic ring of oxadiazole, unlike the triazole ring.

The formation of ions F_6, F_2, and F_4 is confirmed by metastable transition. Ions F_5 and F_7 are then formed from ions F_6 and F_2 by elimination of a molecule of nitrogen.

It has thus been shown that mass spectrometry may be used to differentiate between the oxadiazoles (I-VI) and the isomeric triazolones (XII-XVI).

EXPERIMENTAL

Mass spectra were obtained on an LKB-2091 with direct introduction of the sample, ionizing electron energy 70 and 20 eV, the spectra being recorded using a vibratory oscillograph. High-resolution mass spectra were obtained on an MX-1320 with direct introduction. The resolving ability of the apparatus was 10,000-12,000 at an accelerating voltage of 2.5 kV and energy of ionizing electrons 70 eV. IR spectra were obtained on an IKS-29 instrument in KBr disks, and UV spectra on an SF-26 spectrophotometer in ethanol.

2-Amino-5-R-phenyl-1,3,4-oxadiazoles (I-VI). To a solution of 100 mmole of anhydrous sodium acetate and 20 mmole of the aldehyde semicarbazone was added with stirring 20 mmole of bromine. The mixture was stirred with heating for 1 h, poured into cold water, and the solid which separated filtered off and recrystallized from alcohol.

3-R-Phenyl-5-ethoxy-1,2,4-triazoles (VII-XI). A solution of 6 mmole of the 2-amino-5-R-phenyl-1,3,4-oxadiazole and 20 mmole of potassium hydroxide in 30 ml of ethanol was boiled for 5 h. After cooling, the mixture was acidified with acetic acid, and concentrated. Water was added to the reaction mixture, and the solid which separated was filtered off, washed, and recrystallized from aqueous alcohol.

3-R-Phenyl-1,2,4-triazolin-5-ones (XII-XVI). The 3-R-phenyl-5-ethoxy-1,2,4-triazole was boiled in 25 ml of conc. hydrochloric acid for 5 h. The mixture was then cooled, and the solid filtered off and recrystallized from alcohol.

LITERATURE CITED

1. Advances in Heterocyclic Chemistry (A. R. Katritzky, ed.), Vol. 7, Academic Press, Interscience, New York—London (1966), p. 183.
2. H. Gehlen and G. Blankenstein, Ann. Chem., 651, 128 (1962).
3. N. Najer, J. Minin, and J.-F. Giudicelly, Compt. Rend., 258, 4579 (1964).
4. R. Kraft, P. Nenklein, and G. Etrold, Org. Mass Spectrom., 11, 304 (1976).
5. Comprehensive Heterocyclic Chemistry (A. R. Katritzky, ed.), Vol. 7, Academic Press, Inter-p. 134.