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SYNTHESIS AND PROPERTIES OF FURAN DERIVATIVES. 4.* SYNTHESIS OF 2,5-DISUBSTITUTED 1,3,4-OXADIAZOLES CONTAINING FURAN FRAGMENTS

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The condensation of hydrochloride salts of iminoesters of furan acids with hydrazides of carboxylic acids gives 2,5-disubstituted 1,3,4-oxadiazoles containing furan fragments. Such compounds are also formed in the condensation of hydrazides of 5-R-furan-2-carboxylic acids with hydrochloride salts of carboxylic acid iminoesters. The reaction of furan acids with hydrazine dihydrochloride in polyphosphoric acid gave symmetrically disubstituted 1,3,4-oxadiazoles containing furan fragments.

In a continuation of our work on the synthesis of furylazoles [1-3], we obtained 2,5-disubstituted 1,3,4-oxadiazoles containing furan fragments.

There have been only a few reports on the preparation and properties of 1,3,4-oxadiazoles containing 2-furyl or 5-nitro-2-furyl substituents [4-8] and there is no information on their β-furylvinyl analogs. On the other hand, some of these compounds have been found to possess high antibacterial activity [6], while others are organic luminophors with good fluorescent properties [7, 8].

Hydrochloride salts of iminoesters of carboxylic acids may serve as convenient synthones for the synthesis of 1,3,4-oxadiazoles [4, 9, 10]. In the present work, hydrochloride salts of ethyl iminoesters of 5-nitrofuran-2-carboxylic (Ia) and (*E*)-β-(5-R-2-furyl)acrylic acids (Ib) and (Ic) were used as the starting compounds. The condensation of Ia-Ic with carboxylic acid hydrazides IIa-IIf give 2-(5-nitro-2-furyl)-5-R^1- (IIIa)-(IIIe) and 2-[(*E*)-β-(5-R-2-furyl)-vinyl]-5-R^1-1,3,4-oxadiazoles (IIIf)-(III*l*), respectively (method A). The best yields of 1,3,4-oxadiazoles IIIa-III*l* (Table 1) were achieved upon heating the reagents at reflux in ethanol or dioxane for 4-5 h with 1.25:1 mole ratio. We should note that our attempts to synthesize 1,3,4-oxadiazoles containing 5-bromo-2-furyl or β-(5-bromo-2-furyl)vinyl substituents by this method starting with the corresponding iminoester hydrochlorides were unsuccessful. Heavy tar formation occurred and the desired products could not be isolated from the product mixture.

Oxadiazoles IIIa, IIIb, IIId, IIIe, and IIIm-IIIp were also obtained by the condensation of the ethyl iminoester hydrochlorides of carboxylic acids (IVa)-(IVe) with the hydrazides of furan-2-carboxylic (IIc) and 5-nitrofuran-2-carboxylic acids (IId), respectively (method B). These reactions were carried out upon heating these reagents (IV:II mole ratio = 1.25:1) at reflux in methanol for several hours. The corresponding 1,3,4-oxadiazoles IIIa, IIIb, IIId, IIIe, IIIm-IIIp in 60-76% yield (see Table 1).

Furthermore, in order to obtain IIIm, IIIn, and IIIp, we used the cyclodehydration of the corresponding N-acyl-N^1-furoyl-2)hydrazines (Va)-(Vc) by the action of $POCl_3$ (method C) [11]. N,N^1-diacylhydrazines Va-Vc are formed in 68-73% yield in the acylation of hydrazides IIa, IIb, and IIe by the acid chloride of furan-2-carboxylic acid in pyridine. Brief heating of Va-Vc with $POCl_3$ leads to heavy tar formation and 1,3,4-oxadiazoles IIIm, IIIn, and IIIp were isolated in 35-43% yield from the reaction mixtures along with unidentified compounds.

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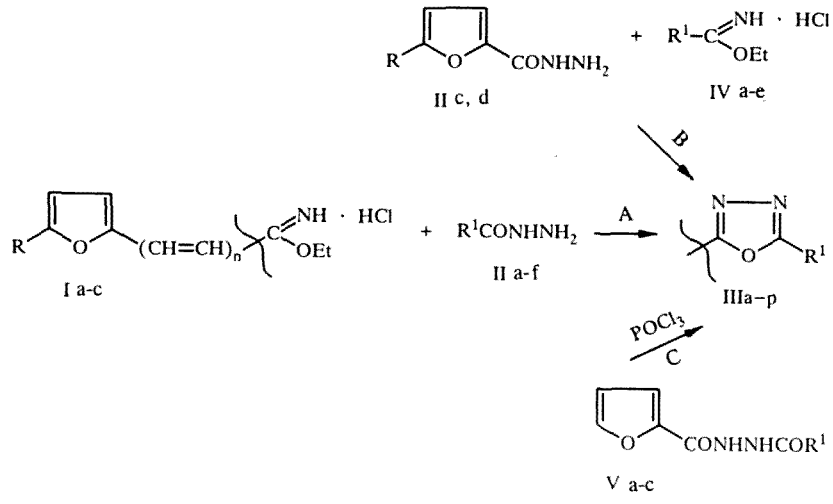
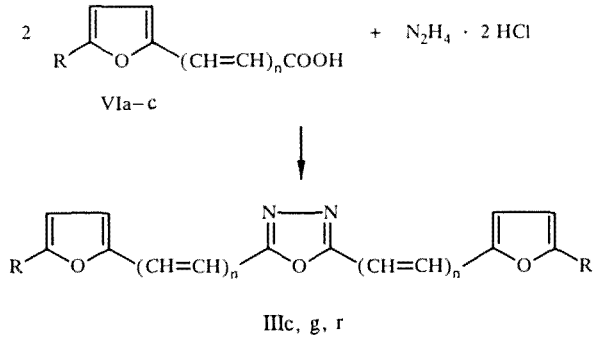


Ia, IIIa-e R = NO_2, n = 0; Ib, IIIf-h R = H, n = 1; Ic, IIIi-*l* R = NO_2, n = 1; IIIm-p R = H, n = 0; IIa, IIIa, i, m, IVa, Va R^1 = Me; IIb, IIIb,f,j,n, IVb,Vb R^1 = Ph; IIe, IIIg, R^1 = 2-furyl; IId, IIIc R^1 = 5-nitro-2-furyl; IIe, IIId,h,k,p, IVd, Vc R^1 = 3-indolyl; IIf, IIIe,*l*, IVe R^1 = indolyl-3-methyl; IIIo, IVc R^1 = $PhCH_2$

The reaction of carboxylic acids with hydrazine dihydrochloride in the presence of dehydrating agents such as $POCl_3$ and polyphosphoric acid leads to symmetrically disubstituted 1,3,4-oxadiazoles [12]. In the present work, we decided to use this method for preparing 1,3,4-oxadiazoles containing a furyl residue. Maintenance of furan acids with hydrazine dihydrochloride in polyphosphoric acid at 150-160°C for several hours leads to the corresponding disubstituted oxadiazoles IIIc, IIIq, and IIIr in 45-52% yield (method D).



IIIc, g, r

IIIc, VIa R = NO_2, n = 0; IIIq, VIb R = H, n = 0; IIIr, VIcR = H, n = 1

The indices for disubstituted 1,3,4-oxadiazoles IIIa-IIIr are given in Table 1. The structures for these compounds given above are in good accord with the elemental analysis data as well as the PMR, IR, and mass spectral parameters. Thus, the IR spectra display strong bands at 1615-1585 and 1490-1460 cm^{-1} characteristic for oxadiazole ring stretching vibrations [4, 13]. The existence of an oxadiazole ring is also indicated by the bands at 1250-1225 and 1045-1020 cm^{-1} characteristic for stretching bands of the =C–O–C= fragment in 1,3,4-oxadiazoles [14] and the bands in the vicinity of 970 cm^{-1} related to oxadiazole ring breathing modes [13].

The furan ring proton signals in the PMR spectra of furyl-1,3,4-oxadiazoles IIIf, IIIh, IIIm, IIIn, IIIp, and IIIq (Table 2) appear as three doublets of doublets at 6.18-6.34 ppm (3-H, J_{35} = 0.7-0.9 Hz), 6.40-6.62 ppm (4-H, J_{34} = 3.1-3.7 Hz) and 7.14-7.32 ppm (5-H, J_{45} = 1.7-1.9 Hz), which is characteristic for 2-substituted furans [13,15]. The signals for furan ring protons 3-H and 4-H in the spectra of oxadiazoles IIIa, IIIb, IIId, IIIe, IIIi, and IIIk, which contain 5-nitrofuryl

TABLE 1. Characteristics of Synthesized Compounds

Compound	Chemical formula	mp, °C*	R_f (solvent system)	Yield, % (preparation method)
IIIa	$C_7H_5N_3O_4$	132...134	0,42 (a)	63 (A), 61 (B),
IIIb	$C_{12}H_7N_3O_4$	155...156,5 (dec.)	0,28 (a)	82 (A), 73 (B)
IIIc	$C_{10}H_4N_4O_6$	194...195 (dec.)	0,53 (a)	73 (A), 45 (D)
IIId	$C_{14}H_8N_4O_4$	222...224 (dec.)	0,46 (b)	79 (A), 64 (B)
IIIe	$C_{15}H_{10}N_4O_4$	185...186	0,54 (b)	75 (A), 60 (B)
IIIf	$C_{14}H_{10}N_2O_2$	118...119	0,32 (a)	71 (A)
IIIg	$C_{12}H_8N_2O_3$	97...98,5	0,24 (a)	80 (A)
IIIh	$C_{16}H_{11}N_3O_2$	166...167,5	0,38 (b)	76 (A)
IIIi	$C_9H_7N_3O_4$	89...90	0,62 (a)	71 (A)
IIIj	$C_{14}H_9N_3O_4$	172...174	0,54 (a)	85 (A)
IIIл	$C_{16}H_{10}N_4O_4$	203...204 (dec.)	0,50 (b)	78 (A)
IIIl	$C_{17}H_{12}N_4O_4$	178...180	0,62 (b)	74 (A)
IIIm	$C_7H_6N_2O_2$	83...85	0,40 (b)	66 (B), 35 (C)
IIIn	$C_{12}H_8N_2O_2$	103...104*[2]	0,70 (b)	73 (B), 43 (C)
IIIo	$C_{13}H_{10}N_2O_2$	95...96	0,38 (a)	76 (B),
IIIp	$C_{14}H_9N_3O_2$	160...161	0,30 (b)	70 (B), 40 (C)
IIIq	$C_{10}H_6N_2O_3$	111...112	0,24 (a)	50 (D)
IIIr	$C_{14}H_{10}N_2O_3$	126...127	0,62 (b)	52 (D)

*Recrystallization solvents: IIIa,d,j-i,*l*p,r) aqueous ethanol, IIIb,j) aqueous dioxane, IIIc,k) 2-propanol, IIIe) 50% CH_3CO_2H, IIIf) 10:1 benzene–methanol, IIIi) 15:1 benzene–chloroform, IIIn,o) CCl_4, IIIq) chloroform.

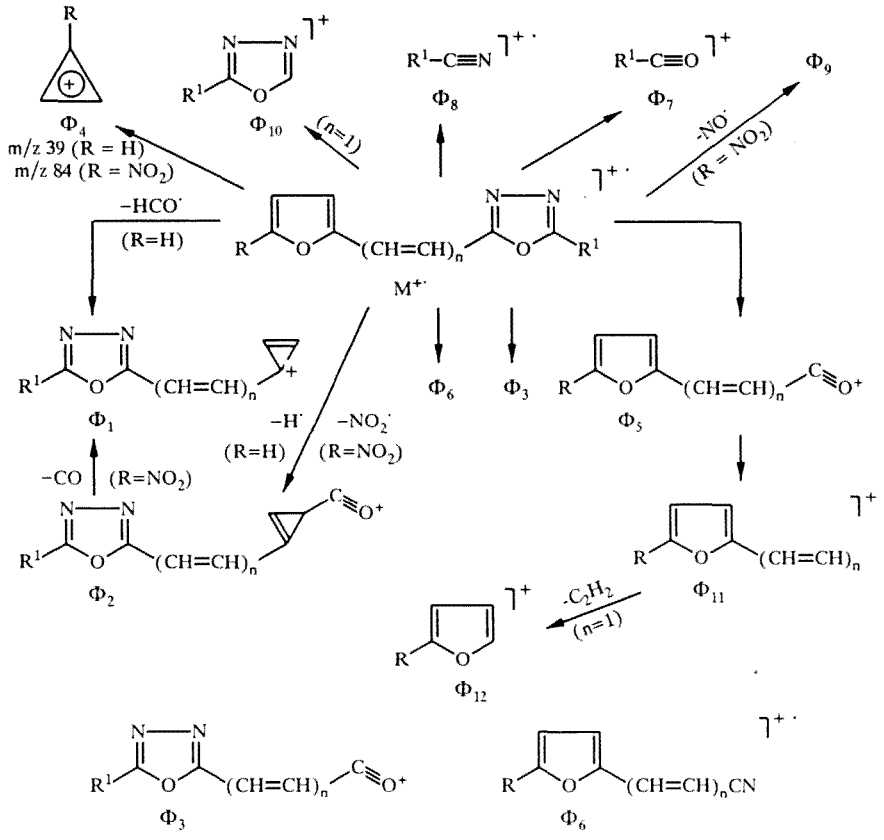
*[2]Lit. mp 102°C [7].

fragments, appear as doublets at 6.40-6.68 and 6.80-7.05 ppm, respectively, with J_{34} = 3.1-3.8 Hz. The vinyl group proton signals in the spectra of IIIf, IIIh, IIIi, and IIIk appear as doublets at 6.72-7.03 (α-H) and 7.20-7.56 ppm (β-H) with $J_{\alpha\beta}$ = 13.8-15.5 Hz, which indicates their *trans* arrangement. The data of Lukevits [15] and Gracza [17] on the PMR spectra of α,β-disubstituted vinyl furans indicate that the downfield doublets are related to the protons in the β-position to the furan ring.

The mass spectra of products III (Table 3) show rather strong peaks for the molecular ion $M^{+\cdot}$. The major fragmentation pathways involve competitive decomposition of the furan and 1,3,4-oxadiazole rings. We should note that the spectra of 2-(5-R-2-furyl)-5-R^1-1,3,4-oxadiazoles IIIa, IIIb, IIId, IIIe, IIIm, IIIn, IIIp, and IIIq lack ions, whose formation would have been expected as the result of cleavage of the bond between the furyl fragment and oxadiazole ring in $M^{+\cdot}$, which is characteristic for conjugated bisheteroaromatic compounds [18].

Fragmentation of the molecular ions $M^{+\cdot}$ of III with loss of the furan moiety proceeds with formation of ions Φ_1-Φ_4 through pathways typical for mono- and disubstituted furans [18, 19]. The data of Budzikewicz [19] and Krapivin [20] indicate that ions Φ_1, Φ_3, and Φ_4 contain a cyclopropene group.

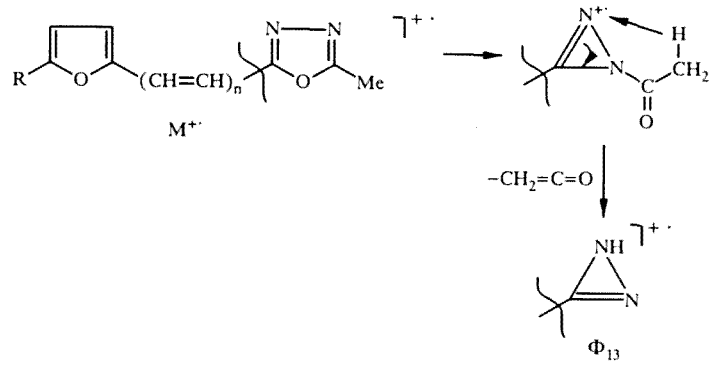
The decomposition of the oxadiazole rings in the molecular ions of these compounds occurs through several parallel pathways (see the work of Porter [18], Ushakova [21], and Nakano [22]) by cleavage of the $C_{(2)}-N_{(3)}$ and $O-C_{(5)}$ bonds as well as of the $O-C_{(2)}$ and N–N bonds, $O-C_{(2)}$ and $C_{(5)}-N_{(4)}$ bonds, and $O-C_{(5)}$ and N–N bonds with formation of fragmentation ions Φ_5-Φ_8. The predominant pathway for decomposition of the oxadiazole ring is mainly a factor of the nature of substituent R^1. For example, The Φ_5 ion peaks with *m/z* 95 (R = H) or with *m/z* 140 (R = NO_2) in the spectra of 2-(5-R-2-furyl)-5-R^1-1,3,4-oxadiazoles IIIa, IIIb, IIIm, IIIn, and IIIq (R = H, NO_2; R^1 = Me, Ph, $PhCH_2$, 5-nitro-2-furyl, and 2-furyl) are predominant, while the Φ_6 peaks with *m/z* 93 or *m/z* 138 have only 12-16% intensity. On the other hand, the Φ_7 ion peak with *m/z* 144 is predominant in the spectrum of IIId and IIIp (R^1 = 3-indolyl), which is characteristic for indolyloxadiazoles [21].



The fragmentation of $M^{+\cdot}$ in the case of 1,3,4-oxadiazoles IIIa, IIIb, IIId, IIIe, IIIi, and IIIk, which contain 5-nitrofuryl groups, is complicated by the elimination of NO· and NO_2· species at various steps, which is characteristic for heteroaromatic nitro compounds [18, 19]. The formation of fragmentation ion $[M - NO]^+$ (Φ_9) is the most significant of these processes. Ions Φ_1 and Φ_3 in the spectra of these compounds probably appear as the result of consecutive elimination of NO_2· and CO from $M^{+\cdot}$ [20].

Processes with cleavage of the bonds in the molecular ion between the furylvinyl fragment and the oxadiazole ring also are observed for 2-[β-(5-R-2-furyl)vinyl]-5-R^1-1,3,4-oxadiazoles IIf, IIIh, IIIi, and IIIk, leading to Φ_{10} ions (5-13%) with charge localization in the 1,3,4-oxadiazole fragment [22]. Φ_{12} ion peaks $[\Phi_5 - CO - C_2H_2]^+$ are also found in the spectra of IIIf and IIIi, while Φ_7 ion peaks are found in the spectra of IIIh and IIIk.

The mass spectra of 5-methyl-1,3,4-oxadiazoles IIIa, IIIi, and IIIm have Φ_{13} ion peaks (32-39%) with *m/z* 153 (IIIa), 179 (IIIi), and 108 (IIIm), whose formation may be attributed to cleavage of the $O-C_{(5)}$ bond in $M^{+\cdot}$, subsequent cyclization to an aziridine intermediate, and elimination of a ketene molecule [22].



The major pathway in the fragmentation of $M^{+\cdot}$ in the mass spectra of 5-(indolyl-3-methyl)-1,3,4-oxadiazole IIIe initially involves dissociation of the bond in the β-position relative to the indole ring ("benzylic" cleavage) [21] to give a quinolinium ion with *m/z* 130 [18, 23], which gives the predominant peak in this spectrum.

TABLE 2. PMR Spectral Parameters of Synthesized Compounds

Compound	Chemical shifts, δ, ppm,* coupling constants, J, Hz						
	furan ring protons						other protons
	3-H	4-H	5-H	J_{35}	J_{34}	J_{45}	
1	2	3	4	5	6	7	8
IIIa	6,52 (1H, d)	6,88 (1H, d)	–	–	3,5	–	2,55 (3H, s, Me)
IIIb	6,40(1H, d)	6,82 (1H, d)	–	–	3,7	–	6,94...7,12 (5H, m, Ph)
IIIc	6,68 (2H, d)	7,05 (2H, d)	–	–	3,2	–	–
IIId	6,48 (1H, d)	6,95 (1H, d)	–	–	3,4	–	7,10...7,52 (4H, m, H_{arom}), 7,70 (1H, d, 2-H indole, J = 4,0Hz), 8,14 (1H, b.s., NH)
IIIe	6,54 (1H, d)	6,84 (1H, d)	–	–	3,8	–	3,94 (2H, s, CH_2), 7,03...7,34 (4H, m, H arom), 7,45 (1H, d, 2-H indole, J = 2,5 Hz), 8,08 (1H, br.s, NH)
IIIf	6,28 (1H, d.d)	6,62 (1H, d.d)	7,14 (1H, d.d)	0,9	3,2	1,8	6,78 (1H, d, α-CH=, $J\alpha\beta$ = 14,5 Hz), 6,92...7,06 (5H, m, Ph), 7,44 (1H, d, β-CH=)
IIIh	6,18 (1H, d.d)	6,44 (1H, d.d)	7,25 (1H, d.d)	0,7	3,4	1,7	6,72 (1H, d, α-CH=, $J\alpha\beta$ = 13,8 Hz), 6,90...7,12 (4H, m, Harom), 7,36 (1H, d, β-CH=), 7,82 (1H, d, 2-H arom), J = 3,2 Гц), 8,05 (1H, br. s, NH)
IIIi	6,42 (1H, d)	6,84 (1H, d)	–	–	3,5	–	2,50 (3H, s, Me), 7,03 (1H, d, α-CH=, $J\alpha\beta$ = 15,5Hz), 7,56 (1H, d, β-CH=)
IIIj	6,55 (1H, d)	6,86 (1H, d)	–	–	3,8	–	6,72 (1H, d, α-CH=, $J\alpha\beta$ = 14,5Hz), 6,96...7,18 (5H, m, Ph), 7,42 (1H, d, β-CH=)

TABLE 2 (continued)

Compound	Chemical shifts, δ, ppm,* coupling constants, J, Hz						
	furan ring protons						other protons
	3-H	4-H	5-H	J_{35}	J_{34}	J_{45}	
1	2	3	4	5	6	7	8
III k	6,53 (1H, d)	6,98 (1H, d)	–	–	3,4	–	6,75 (1H, d, α-CH–, $J\alpha\beta$ = 15,0 Hz), 7,08...7,25 (4H, m, Harom), 7,34 (1H, d, β-CH–) 7,78 (1H, d, 2-H indole, J = 3,0 Hz), 8,10 (1H, br.s, NH)
III *l*	6,45 (1H, d)	6,92 (1H, d)	–	–	3,6	–	4,20 (2H, d, CH_2), 6,75 (1H, s, α-CH–, $J\alpha\beta$ = 14,8 Hz), 7,04...7,26 (4H, m, Harom), 7,45 (1H, d, 2-H indole, J = 2,8 Hz), 7,52 (1H, d, β-CH–), 8,12 (1H, br.s, NH)
III m,	6,18 (1H, d.d)	6,54 (1H, d.d)	7,28 (1H, d.d)	0,9	3,2	1,9	2,64 (3H, s, Me)
III n	6,30 (1H, d.d)	6,44 (1H, d.d)	7,20 (1H, d.d)	0,8	3,3	1,7	6,85...7,06 (5H, m, Ph)
III o	6,25 (1H, d.d)	6,42 (1H, d.d)	7,15 (1H, d.d)	0,8	3,4	1,7	3,54 (2H, s, CH_2), 6,78...7,04 (5H, m, Ph)
III p	6,28 (1H, d.d)	6,60 (1H, d.d)	7,32 (1H, d.d)	0,9	3,3	1,8	6,90...7,16 (4H, m, Harom), 7,70 (1H, 2-H indole, J = 3,6 Hz), 8,14 (1H, br.s, NH)
III q	6,20 (2H, d.d)	6,58 (2H, d.d)	7,37 (2H, d.d)	0,9	3,1	1,8	
III r	6,18 (2H, d.d)	6,41 (2H, d.d)	7,20 (2H, d.d)	0,7	3,2	1,7	6,94 (2H, d, α-CH–, $J\alpha\beta$ = 15,3 Hz), 7,56 (2H, d, β-CH–)

*The spectra of IIIa, IIIb, IIIi, and IIIq were taken in CD_3OD, the spectra of IIIb, IIId, IIIh, IIIj, IIIk, IIIp, and IIIr were taken in DMSO-D_6, while the spectra of IIIe, IIIf, III*l*, and IIIo were taken in acetone-D_6.

TABLE 3. Mass Spectra of 2,5-Disubstituted 1,3,4-Oxadiazoles Synthesized

Compound	m/z (relative intensity, % rel. to maximum peak)*										
	$M^{+\cdot}$	ions characteristic for major decomposition pathways									other ions
		Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6	Φ_7	Φ_8	Φ_9	
1	2	3	4	5	6	7	8	9	10	11	12
IIIa	195 (15)	121 (68)	149 (32)	111 (5)	84 (10)	140 (100)	138 (24)	43 (17)	41 (6)	165 (18)	Φ_{13} 153 (39), $[\Phi_{13}-N_2]^+$ 125 (74), 123 (9), 110 (5), 108 (11), $[\Phi_6-CO-NO]^+$ 80 (15), 64 (7) , 38 (46), 37 (10)
III b	257 (33)	183 (71)	211 (21)	173 (6)	84 (6)	140 (100)	138 (42)	105 (13)	103 (17)	227 (32)	171 (7), 170 (5), 155 (6), 154 (12), $[\Phi_6-CO-NO]^+$ 80 (12), 77 (32), 76 (5), 64 (6), 38 (30), 37 (22)
III d	296 (41)	222 (7)	250 (18)	218 (8)	84 (14)	140 (35)	138 (16)	144 (100)	142 (48)	266 (40)	295 (12),210 (5), 209 (9), 194 (6), 195 (7), 190 (15), $[\Phi_7-CO]^+$ 116 (36), 115 (6), 90 (14), 89 (7), $[\Phi_6-CO-NO]^+$ 80 (9), 64 (8), 38 (32), 37 (13)
III e	310 (54)	236 (62)	264 (20)	–	84 (6)	140 (21)	138 (13)	158 (14)	156 (9)	280 (42)	309 (14), 198 (6), $[Ind\ CH_2]^+$ 130 (100), 129 (5), 103 (54), 102 (8), $[\Phi_6-CO-NO]^+$ 80 (10), 77 (32), 64 (7), 38 (14), 37 (31)
III f	238 (17)	209 (5)	237 (8)	199 (7)	39 (21)	121 (17)	119 (10)	105 (13)	103 (6)	–	Φ_{10} 145 (5), Φ_{11} 93 (31), $[\Phi_6-HCN]^{+\cdot}$ 92 (54), 77 (67), 76 (38), Φ_{12} 67 (100), 65 (11), 64 (23), 29 (10)
III h	277 (38)	248 (7)	276 (10)	238 (5)	39 (17)	121 (6)	119 (15)	144 (100)	142 (51)	–	Φ_{10} 184 (13), $[\Phi_7-CO]^+$ 116 (30), 115 (8), Φ_{11} 93 (22), $[\Phi_6-HCN]^{+\cdot}$ 92 (50), 90 (14), 89 (6), Φ_{12} 67 (73), 65 (12), 64 (27), 63 (5), 29 (17)
III i	221 (30)	147 (5)	175 (7)	153 (9)	84 (18)	166 (17)	164 (10)	43 (7)	41 (15)	191 (57)	Φ_{13} 179 (32), $[\Phi_{13}-N_2]^+$ 151 (78), 149 (5), 139 (3), Φ_{11} 138 (25), $[\Phi_6-HCN]^{+\cdot}$ 137 (32), 125 (7), Φ_{12} 112 (100), 110 (21), 107 (6), Φ_{10} 86 (11), 74 (13), 64 (10)

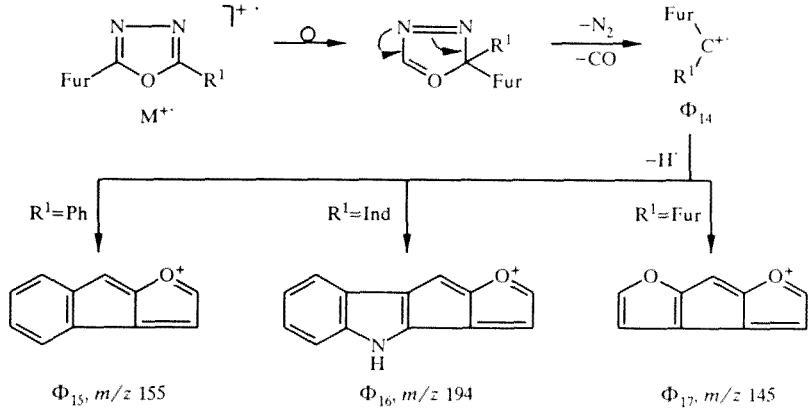
TABLE 3 (continued)

Compound	m/z (relative intensity, % rel. to maximum peak)*										
	$M^{+\cdot}$	ions characteristic for major decomposition pathways									other ions
		Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6	Φ_7	Φ_8	Φ_9	
1	2	3	4	5	6	7	8	9	10	11	12
III k	322 (12)	248 (15)	276 (5)	238 (10)	84 (12)	166 (54)	164 (21)	144 (100)	142 (62)	292 (62)	321 (5), 264 (10), Φ_{10} 184 (8), 147 (6), Φ_{11} 138 (25), $[\Phi_6\text{-HCN}]^{+\cdot}$ 137 (20), $[\Phi_7\text{-CO}]^{+}$ 116 (11), 115 (9), Φ_{12} 112 (17), 110 (17), 90 (10), 89 (6), 63 (5)
III m	150 (7)	121 (12)	149 (5)	111 (7)	39 (5)	95 (100)	93 (16)	43 (5)	41 (9)	–	Φ_{13} 108 (36), 83 (11), $[\Phi_{13}\text{-N}_2]^{+}$ 80 (77), 64 (40), 37 (20)
III n	212 (41)	183 (16)	211 (6)	173 (9)	39 (8)	95 (100)	93 (12)	105 (32)	103 (11)	–	Φ_{14} 156 (15), Φ_{15} 155 (10), 77 (34), 76 (48), 64 (43), 37 (22)
III p	251 (61)	222 (15)	250 (13)	212 (6)	39 (14)	95 (31)	93 (10)	144 (100)	142 (54)	–	Φ_{14} 195 (9), Φ_{16} 194 (14), $[\Phi_7\text{-CO}]^{+}$ 116 (36), 115 (9), 90 (10), 89 (5), 64 (25), 63 (6), 37 (18)
III q	202 (12)	173 (17)	–	163 (27)	39 (15)	95 (100)	93 (71)	–	–	–	Φ_{14} 146 (12), Φ_{17} 145 (8), 135 (12), 134 (5), 67 (15), 64 (41), 37 (7)

*$M^{+\cdot}$ ion peaks and ion peaks with intensity > 5% are given.

Interest is found in the pathway involving decomposition of the molecular ion in the mass spectrum of 2-(2-furyl)-5-R^1-1,3,4-oxadiazoles IIIn, IIIp, and IIIq (R^1 = Ph, 3-indolyl, 2-furyl) with formation of fragmentation ions with *m/z* 156 and 155 (IIIn), 195 and 194 (IIIp), and 146 and 145 (IIIq). The fragmentation of $M^{+\cdot}$ leading to these ions involves rearrangements with initial migration of the furyl substituent from $C_{(2)}$ to the carbon atom bearing the phenyl or heteryl groups and subsequent opening of the oxadiazole ring with simultaneous elimination of N_2 and CO molecules.

The formation of Φ_{14} ions and Φ_{15}-Φ_{17} ions has been noted in the fragmentation of the molecular ion of 2,5-diphenyl-1,3,4-oxadiazole [24]. Similar dissociative ionization pathways also occur for 5-nitrofuryl derivatives IIIb and IIId (R^1 = Ph, 3-indolyl). However, this process does not occur for the molecular ion in the case of these derivatives but rather in the $[M - NO]^+$ (Φ_9) and $[M - NO_2]^+$ (Φ_2) ions to give ion peaks with *m/z* 171, 170, 155, and 154 (IIIb) and with *m/z* 210, 209, 194, and 193 (IIId).



Fur = furyl-2 , Ind = indolyl-3

EXPERIMENTAL

The IR spectra were taken on a Bruker IFS-48 spectrometer for KBr pellets or vaseline mulls. The PMR spectra were taken on a Bruker WP-100 SY spectrometer with TMS as the internal standard. The mass spectra were taken on an LKB-2091 spectrometer with direct sample inlet into the ion source at 70 eV. The emission current was 25 μA and the temperature of the ion source was 200°C. The injection temperature was 130-150°C. The reaction course and purity of the products were monitored by thin-layer chromatography on Brockmann Grade-III alumina with 20:1 CCl_4–methanol (a) and 10:1 benzene–methanol (b). The plates were developed with iodine vapor.

The elemental analysis data for C, H, and N were in accord with the calculated values.

The starting ethyl iminoester hydrochlorides Ia-Ic [25], hydrazides IIc [26], IId and IIf [27], and IIe [28] and also ethyl iminoester hydrochlorides IVa and IVb [29], IVc [30], and IVd and IVe [31] were obtained according to reported procedures.

2-(5-Nitro-2-furyl)-5-phenyl-1,3,4-oxadiazole (IIIb). A mixture of 2.75 g (12.5 mmoles) iminoester hydrochloride Ia and 1.36 g (10 mmoles) hydrazide IIb in 25 ml absolute ethanol was heated at reflux with stirring for 4 h. The reaction mixture was cooled to 15°C and poured into 100 ml cold water. The precipitate of IIIb was filtered off, dried, and crystallized from aqueous dioxane.

Analogous procedures starting from iminoester hydrochlorides I and hydrazides II gave 1,3,4-oxadiazoles IIIa and IIIc-*l*.

2-(2-Furyl)-5-methyl-1,3,4-oxadiazole (IIIm). B. A mixture of 1.26 g (10 mmoles) hydrazide IIc and 1.37 g (12.5 mmoles) iminoester hydrochloride IVa in 20 ml absolute methanol was heated at reflux with stirring for 5-6 h until starting hydrazide IIc disappeared as indicated by thin-layer chromatography. The solvent was evaporated at reduced temperature and

the residue was treated with 30 ml cold water. The precipitate of IIIm was filtered off, dried, and crystallized from 15:1 benzene–chloroform.

Analogous procedures starting from the corresponding hydrazides II and iminoester hydrochlorides IV gave 1,3,4-oxadiazoles IIIa, IIIb, IIId, IIIe, and IIIn-IIIp.

N-Acetyl-N^1-(furoyl-2)hydrazine (Va, $C_7H_8N_2O_3$). A sample of 4.57 g (35 mmoles) acid chloride of furan-2-carboxylic acid was added dropwise to a stirred solution of 2.59 g (35 mmoles) hydrazine IIa in 30 ml anhydrous pyridine. The reaction mixture was heated at reflux with stirring for 2 h, cooled to 20°C, and poured into 200 ml cold water. The precipitate formed was filtered off, washed on the filter with water, dried, and crystallized from 2-propanol to give 4.0 g (68%) hydrazide Va, mp 143-144°C, R_f 0.22 (b). IR spectrum: 3310-3220 (νNH), 3080, 1645, 1630 (νC=O), 1560-1545 (δNH), 1140 (N–N), 750, 725 cm^{-1}.

N-Benzoyl-N^1-(furoyl-2)hydrazine (Vb, $C_{12}H_{10}N_2O_3$) was obtained analogously from hydrazide IIb in 73% yield, mp 169-170.5°C (from methanol), R_f 0.28 (b).

N-(3-Indolylcarbonyl)-N^1-(furoyl-2)hydrazine (Vc, $C_{14}H_{11}N_3O_3$) was obtained analogously from hydrazide IIe in 70% yield, mp 184-186°C (from ethanol), R_f 0.14 (b). IR spectrum: 3310-3200, 3180 (νNH), 1655, 1630 (νC=O), 1605-1590, 1555, 1540 (δNH), 1135 (N–N), 750, 725 cm^{-1}.

5-Phenyl-2-(2-furyl)-1,3,4-oxadiazole (IIIn). A mixture of 4.6 g (20 mmoles) hydrazine Vb and 25 ml $POCl_3$ was heated at reflux with stirring for 0.5 h. The reaction mixture was then cooled to 20°C, poured onto 200 g ice, and neutralized by adding ammonium hydroxide to pH 7.5. The dark precipitate formed was filtered off, dried, and extracted with three 20-ml portions of hot acetone. The extract was evaporated to dryness under reduced pressure and the residue was recrystallized from CCl_4.

1,3,4-Oxadiazoles IIIo and IIIp were analogously synthesized from N,N^1-diacylhydrazines Va and Ve, respectively.

2,5-bis-(2-Furyl)-1,3,4-oxadiazole (IIIq). D. A mixture of 2.46 g (22 mmoles) furan-2-carboxylic acid and 1.36 g (13 mmoles) hydrazine dihydrochloride in 30 ml polyphosphoric acid was stirred for 4 h at 150°C. The reaction mixture was cooled to 20°C, poured into 200 ml cold water, and neutralized by adding 5% aqueous $NaHCO_3$. The precipitate formed was filtered off, washed on the filter with water, dried, and crystallized from chloroform.

1,3,4-Oxadiazoles IIIc and IIIr were synthesized analogously from the corresponding acids.

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