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Several new 2,5-disubstituted 1,3,4-oxadiazoles have been synthesized in good yields by reaction of aromatic acids with hydrazine dihydrochloride in a mixture of orthophosphoric acid, phosphorus pentoxide and, in general, with addition of phosphorus oxychloride to the reaction mixture. The structures of new oxadiazoles derivatives were confirmed by analytical and spectral data.

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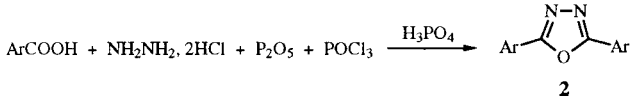
Introduction.

The synthesis of 2,5-disubstituted 1,3,4-oxadiazoles can be performed by several methods under anhydrous conditions [1]. One of them [2] involves the reaction between an aromatic acid and hydrazine derivative in polyphosphoric acid or phosphorus oxychloride. This reaction, however, needs a large quantity of polyphosphoric acid. Moreover, the high viscosity of the latter makes the isolation of the final product quite difficult. Here we report on an attractive method for the preparation of symmetrical 2,5-diaryl-1,3,4-oxadiazoles. The synthesis of oxadiazoles **2a-o** has been carried out in an easier fashion by treatment of aromatic acids with hydrazine dihydrochloride in the molar ratio 2:1 in a mixture of orthophosphoric acid, phosphorus pentoxide and phosphorus oxychloride (Scheme 1). This synthetic approach was based on the assumption that the aromatic acid could lead to 1,2-diaroylhydrazine. The latter reacts then with phosphorus oxychloride and/or phosphorus pentoxide affording 1,3,4-oxadiazoles as shown in Scheme 2. Analytically pure oxadiazoles **2a-o** were obtained in excellent yields (Table 1). Phosphorus oxychloride proved not to be suitable for synthesis of oxadiazoles starting from salicylic acid (**1p**), 3- and 4-hydroxybenzoic acids (**1q** and **1r**). Better yields have been accomplished in the absence of phosphorus oxychloride.

Scheme 1



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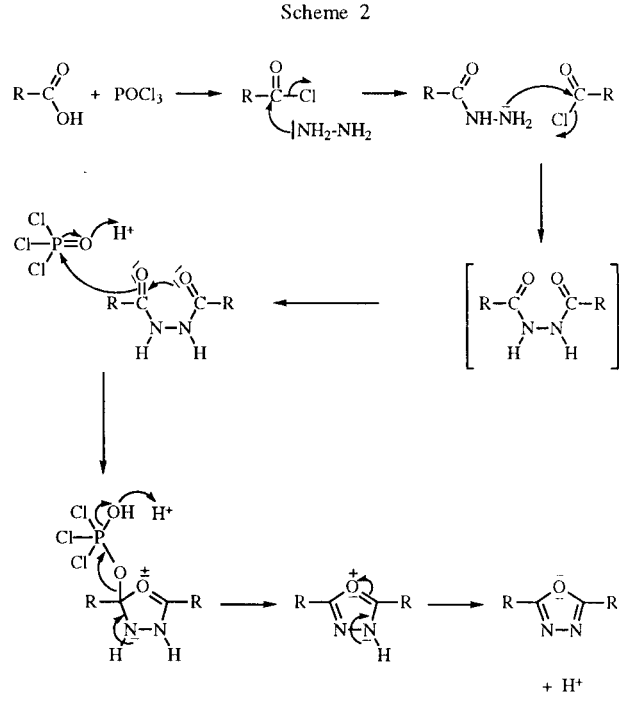
1,2a	Ar = C_6H_5	**1,2j**	Ar = 4-ClC_6H_4
b	Ar = 2-$CH_3C_6H_4$	**k**	Ar = 4-$NO_2C_6H_4$
c	Ar = 3-$CH_3C_6H_4$	**l**	Ar = 2-$CH_3OC_6H_4$
d	Ar = 4-$CH_3C_6H_4$	**m**	Ar = 3-$CH_3OC_6H_4$
e	Ar = 2-pyridyl	**n**	Ar = 4-$CH_3OC_6H_4$
f	Ar = 3-pyridyl	**o**	Ar = 2-thienyl
g	Ar = 4-pyridyl	**p**	Ar = 2-HOC_6H_4
h	Ar = 2-$H_2NC_6H_4$	**q**	Ar = 3-HOC_6H_4
i	Ar = 2-ClC_6H_4	**r**	Ar = 4-HOC_6H_4

A suggested mechanism is given in Scheme 2.

Scheme 2



The use of these compounds as corrosion inhibitors is under investigation, now.

Results and Discussion.

The synthesis of oxadiazoles is performed as shown in Scheme 1. We suppose that phosphorus oxychloride reacts with the carboxylic acid to give the acyl chloride, which consequently is successively attacked by two nucleophilic amino groups of the hydrazine derivative. As a result, the non-isolated 1,2-diaroylhydrazine arises, which is further converted into final 2,5-diaryl-1,3,4-oxadiazole. In all cases the corresponding oxadiazoles have been isolated in better yields than those reported in the literature where the classical reaction with polyphosphoric acid as cyclizing reagent (Table 1) was exploited. Addition of phosphorus oxychloride to the reaction mix-

Table 1

2,5-Diaryl-1,3,4-oxadiazoles **a-r**

Compound No.	Ar	Yield %	Lit Yield %	Mp °C	Lit Mp °C	References
a	C_6H_5	99	92	138	138-139	[2b]
b	2-$CH_3C_6H_4$	97	96.4	121.5	121	[3]
c	3-$CH_3C_6H_4$	99.8	94.8	72	72	[3]
d	4-$CH_3C_6H_4$	98.7	100	175	173.8-175.2	[2c]
e	2-pyridyl	60	25	154	153-154	[2b]
f	3-pyridyl	67	60	188	188-189	[2b]
g	4-pyridyl	70		189		
h	2-$H_2NC_6H_4$	70	25	200.5	200-201	[2b]
i	2-ClC_6H_4	99.2	96	95	94-94.5	[2a]
j	4-ClC_6H_4	98.6	98	242	241-242	[2a]
k	4-$NO_2C_6H_4$	99	92	314	314.5-316.5	[2a]
l	2-$CH_3OC_6H_4$	88.5	47	99.5	98-99	[2a]
m	3-$CH_3OC_6H_4$	90.3		87.5		
n	4-$CH_3OC_6H_4$	93.3	69.1	161.5	162	[2c]
o	2-thienyl	81.7		116.8	117-118	[1e]
p	2-HOC_6H_4	64	30	209	209-210	[2b]
q	3-HOC_6H_4	32		204		
r	4-HOC_6H_4	25		350		

ture does not improve the yields when started from hydrobenzoic acids **1p-r**. The elemental analyses (Table 2) and mass spectra are in accordance with the structure proposed for compounds **2a-r**. The melting points of the known oxadiazoles are in good agreement with those reported elsewhere (Table 1). The ^1H and ^{13}C nmr data are given in Tables 3 and 4. The number of signals in ^1H nmr spectra of compounds **2a-r** indicates the presence of the plane of symmetry perpendicular to the plane of oxadiazole ring going through the oxygen atom and the middle point of the N-N bond. The aromatic protons give a multiplet at δ 6.9-8.9 ppm. Chemical shifts for other signals are all in accordance with the structure proposed. Note that the signal characteristic for the oxadiazole carbon atom in the ^{13}C nmr spectra in displayed at δ 162-171 ppm.

Table 2

Elemental Analyses of **a-r**

Compound No.	Molecular Formula	Calcd.			Found		
		C	H	N	C	H	N
a	$C_{14}H_{10}N_2O$	75.67	4.50	12.61	75.51	4.63	12.72
b	$C_{16}H_{14}N_2O$	76.80	5.60	11.20	76.89	5.43	11.18
c	$C_{16}H_{14}N_2O$	76.80	5.60	11.20	76.78	5.65	11.15
d	$C_{16}H_{14}N_2O$	76.80	5.60	11.20	76.84	5.52	11.21
e	$C_{12}H_8N_4O$	64.28	3.57	25.00	64.3	3.55	25.08
f	$C_{12}H_8N_4O$	64.28	3.57	25.00	64.35	3.56	24.92
g	$C_{12}H_8N_4O$	64.28	3.57	25.00	64.27	3.58	24.96
h	$C_{14}H_{12}N_4O$	66.67	4.76	22.22	66.71	4.68	22.18
i	$C_{14}H_8N_2OCl_2$	57.75	2.75	9.62	57.73	2.72	9.67
j	$C_{14}H_8N_2OCl_2$	57.75	2.75	9.62	57.78	2.69	9.65
k	$C_{14}H_8N_4O_5$	53.85	2.56	17.95	53.87	2.51	18.01
l	$C_{16}H_{14}N_2O_3$	68.08	4.96	9.93	68.19	4.87	9.95
m	$C_{16}H_{14}N_2O_3$	68.08	4.96	9.93	68.23	4.85	9.92
n	$C_{16}H_{14}N_2O_3$	68.08	4.96	9.93	68.15	4.91	9.90
o	$C_{10}H_6N_2S_2O$	51.25	2.56	11.96	51.81	2.70	11.32
p	$C_{14}H_{10}N_2O_3$	66.14	3.94	11.02	66.3	3.87	11.1
q	$C_{14}H_{10}N_2O_3$	66.14	3.94	11.02	66.25	3.91	11.23
r	$C_{14}H_{10}N_2O_3$	66.14	3.94	11.02	66.19	3.96	11.15

Table 3

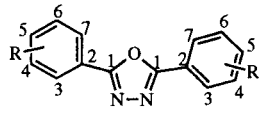
^{1}H NMR Data (δ Values, Dimethyl-d_6 Sulfoxide) for 2,5-Diaryl-1,3,4-oxadiazoles **a-r**

Compound No.	Aromatic Signals	Substituent
a	7.65 (6H, m), 8.17 (4H, m)	
b	7.48 (6H, m), 8.10 (2H, d)	2.70 (6H, *s*) CH_3
c	7.5 (6H, m), 8.00 (2H, d)	2.45 (6H, *s*) CH_3
d	7.43 (4H, d), 7.99 (4H, d)	2.41 (6H, *s*) CH_3
e	7.68 (2H, d); 8.08 (2H, t), 8.29 (2H, d); 8.82 (2H, d)	
f	7.69 (2H, t); 8.52 (2H, d); 8.84 (2H, d); 9.34 (2H, *s*)	
g	8.11 (2H, dd), 8.88 (2H, dd)	
h	6.49 (2H, t); 6.73 (2H, d); 7.21 (2H, t); 7.73 (2H, d)	8.82 (4H, *s*) NH_2
i	7.55-7.79 (6H, m), 8.19 (2H, dd)	
j	8.14 (4H, d); 8.58 (4H, d)	
k	8.41-8.56 (8H, m)	
l	7.15 (2H, t), 7.31 (2H, d), 7.64 (2H, t), 7.92 (2H, d)	3.91 (6H, *s*) OCH_3
m	7.23 (2H, d), 7.55 (2H, t), 7.65 (2H, *s*), 7.73 (2H, d)	3.90 (6H, *s*) OCH_3
n	7.19 (4H, d), 8.08 (4H, d)	3.88 (6H, *s*) OCH_3
o	7.31 (2H, t), 7.92 (2H, dd), 8.06 (2H, d)	
p	7.44 (2H, t), 7.69 (2H, d), 7.85 (2H, t); 8.27 (2H, d)	10.40 (2H, *s*) OH
q	6.92 (4H, m), 7.54 (2H, t), 7.85 (2H, dd)	10.35 (2H, *s*) OH
r	6.95 (4H, d), 7.91 (4H, d)	10.27 (2H, *s*) OH

Table 4

^{13}C NMR. Data (δ Values, Dimethyl-d_6 Sulfoxide) for 2,5-Diary-1,3,4-oxadiazoles **a-r**

The general formula of the parent oxadiazoles with corresponding numbering scheme is given below:



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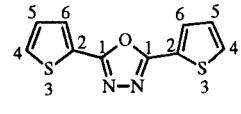

Compound No.	C_1	C_2	C_3	C_4	C_5	C_6	C_7	Substituent
a	164.0	132.0	123.3	126.7	129.4	126.7	123.3	—
b	163.9	131.8	137.6	131.5	128.9	126.5	122.5	21.5
c	164.0	123.3	128.4	138.9	133.4	130.7	123.8	20.8
d	163.8	126.6	120.6	129.9	142.1	129.9	120.6	21.1
e	163.9	148.3	—	150.1	126.3	137.7	123.0	—
f	162.6	123.6	147.5	—	152.7	124.4	134.4	—
g	163.9	130.2	120.4	150.9	—	150.9	120.4	—
h	170.9	115.6	144.4	117.9	130.4	122.9	131.1	—
i	162.7	122.5	133.6	131.6	131.4	128.1	132.1	—
j	162.9	127.7	121.3	128.8	136.0	128.8	121.3	—
k	164.5	138.0	124.6	128.3	149.4	128.3	124.6	—
l	163.2	112.9	157.9	113.3	133.9	121.3	130.7	56.5
m	164.0	124.5	111.6	159.7	118.0	130.7	119.1	55.5
n	163.5	128.4	114.8	115.8	162.0	115.8	114.8	55.5
o	159.8	142.1	—	128.8	131.7	135.0	—	—
p	162.8	109.4	156.5	117.1	133.4	119.7	128.8	—
q	164.3	124.7	113.3	158.4	119.5	131.0	117.6	—
r	163.5	128.4	116.1	114.2	160.6	114.2	116.1	—

EXPERIMENTAL

Melting points were determined with a Digital melting point apparatus of IA 9000 series and are uncorrected. Elemental analyses of C, H and N were performed at the Elemental Analysis service of CNRS, Vernaison, France. The ^{1}H and ^{13}C nmr spectra were recorded with a Bruker F.T. AC 200 spectrometer in dimethyl-d_6 sulfoxide with tetramethylsilane as internal standard. Mass spectra were obtained using a Finnigun MAT Vision 2000 MALDI-TOF spectrometer (Laser desorption). All starting materials were of reagent grade and used as purchased.

2,5-Diaryl-1,3,4-oxadiazoles **2a-o**.

To a stirred aromatic acid **1a-o** (0.1 mole), hydrazine dihydrochloride (0.05 mole) in an aqueous solution of orthophosphoric acid 85% (27 ml), phosphorus pentoxide (0.3 mole) was slowly added followed by phosphorus oxychloride (0.1 mole). The viscous liquid was heated at 140° under stirring for 2 hours. After cooling, the reaction mixture was poured over crushed ice with stirring to yield a solid product which was filtered off, washed with a 5% solution of sodium hydrogencarbonate and water, dried in air and recrystallized from ethanol. Yields are given in Table 1.

2,5-Diaryl-1,3,4-oxadiazoles **2p-r**.

To a stirred mixture of aromatic acid **1p-r** (0.1 mole) and hydrazine dihydrochloride (0.1 mole) in an aqueous solution of orthophosphoric acid 85% (27 ml), phosphorus pentoxide (0.3 mole) was slowly added under stirring. Then the conditions and workup employed for compounds **2a-o** were used.

REFERENCES AND NOTES

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