An Improved Synthesis of 1,3- and 1,4-Bis[5-aryl-1,3,4-oxadiazol-2-yl]benzenes via Oxidation of Bis-aroylhydrazones of Iso- and Terephthalaldehyde with Lead(IV) Acetate[1]

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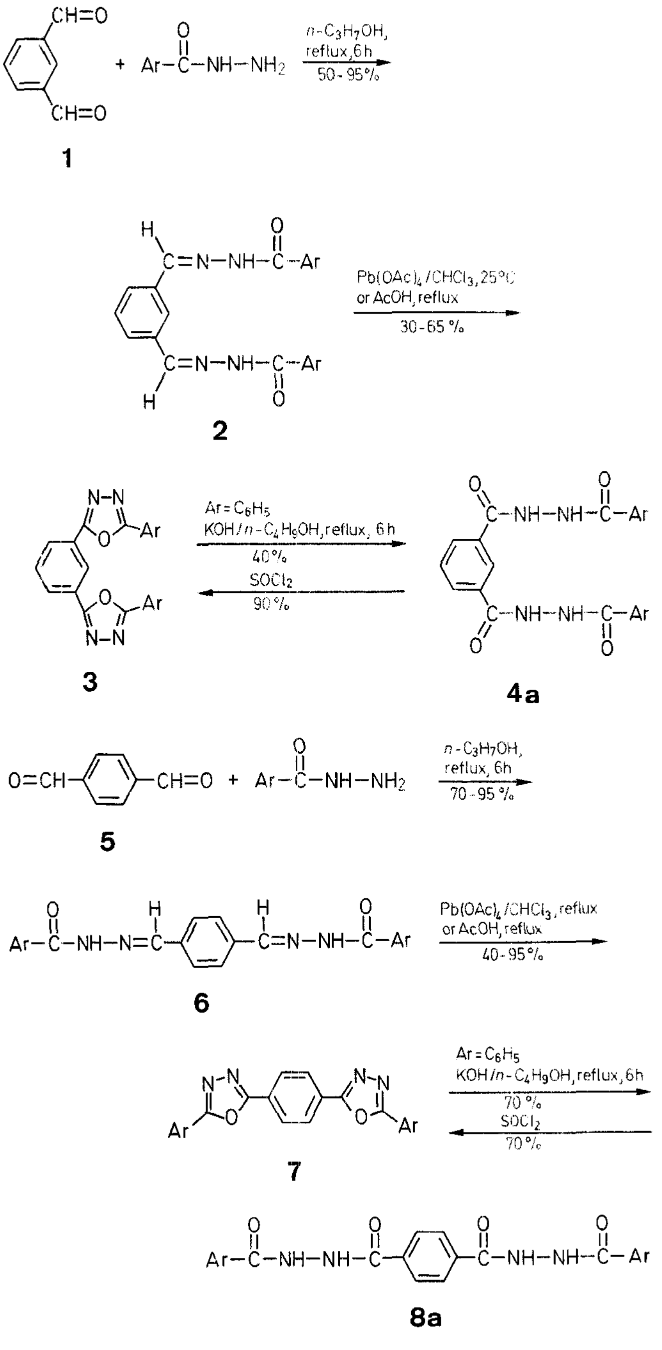
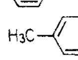
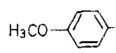
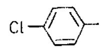
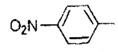
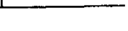
The oxidation of bis-aroylhydrazones of iso- and terephthalaldehyde with lead(IV) acetate leading to 1,3- and 1,4-bis[5-aryl-1,3,4-oxadiazol-2-yl]benzenes is described.

The fluorescence and scintillation properties of 2,5-diaryloxazoles and 1,3,4-oxadiazoles, the most common being known as POPOP and PDPDP[2,3], led to the development of many methods for their preparation. In respect to the synthesis of 1,4-bis[5-aryl-1,3,4-oxadiazol-2-yl]benzenes, the most suitable methods are the cyclization of 1,2-diaroylhydrazines by phosphoryl chloride or by the sulfur trioxide/dimethylformamide complex[4], and the more recent benzoylation of 5-aryltetrazoles[2,5,6]. Of these methods the former have the disadvantage of rather difficult purifications of the reaction products[3,4] and the later the very long reaction times (up to seven days heating) for the synthesis of the tetrazole derivatives[2,5,6].

In connection with our previous work on the lead(IV) acetate oxidation of phthalaldehyde bis-aroylhydrazones[7], we have undertaken the synthesis and oxidation of bis-aroylhydrazones of iso- and terephthalaldehyde in an attempt to prepare the title compounds by a simpler way. The present method is characterized by a simplicity in the synthesis of starting materials (**2**, **6**), good overall yields, and by an easy separation and purification of the reaction products.

The hydrazones **2** and **6** were prepared from iso- and terephthalaldehyde (**1** and **5**) by refluxing with aroic acid hydrazides in propanol and they are generally insoluble in the most common solvents. In the I.R. spectra (Nujol), the bis-aroylhydrazones **2** and **6** exhibit absorptions at $\nu = 3200-3260\ cm^{-1}$ (NH) and $\nu = 1640-1660\ cm^{-1}$ (CO), whereas in the mass spectra they show peaks for molecular ion with very low intensity. Compounds **2a–b** in the ^1H-N.M.R. spectra (DMSO-d_6) gave, besides the aromatic protons, two peaks at $\delta = 8.7$ (CH=) and $\delta = 12.1$ (NHCO) ppm, exchangeable with D_2O.



2–4, 6–8	Ar
a	
b	
c	
d	
e	

The oxidation of **2** and **6** with lead(IV) acetate takes place in a chloroform or glacial acetic acid suspension, via a nitrilimine intermediate[8] which cyclizes to oxadiazoles **3** and **7**, in 30–95% yield. It is of interest to note that lead(IV) acetate cyclizations of some other aldehyde *N*-acylhydrazones leading to the 1,3,4-oxadiazole ring system have been described previously[9,10,11].

The structural assignment of the oxidation products **3** and **7** was based on their spectral and chemical data. In the I.R. spectra they absorb at $1600-1620\ cm^{-1}$ (C=N), with no absorptions for NH and CO groups. In the mass spectra they show low intensity peaks for molecular ions. Other prominent ion peaks are those corresponding to $[M-ArCNO]^{+\cdot}$ and $[M-ArCN]^{+\cdot}$ as well as peaks corresponding to the ions $[ArCON]^{+\cdot}$, $[ArCO]^+$ and $[ArCN]^{+\cdot}$. These products show very low solubility in all common solvents and it was not possible to run N.M.R. spectra.

The compounds **3** and **7** are very stable to acid hydrolysis, but on heating with a base they give the corresponding iso- and terephthalic acid bis[*N'*-aroylhydrazides] (**4**) and (**8**) in 40–70% yield. These products upon treatment with thionyl chloride give again the oxadiazole derivatives **3** and **7** in good yield (70–90%).

Iso- and Terephthalaldehyde Bis-aroylhydrazones (2) and (6); General Procedure: A mixture of iso- or terephthalaldehyde (**1** or **5**, respectively; 1 molar equivalent) and aroylhydrazine (2.1 molar equivalent) in propanol (25 ml per mmol **1** and **5**) is refluxed under stirring for 6 h. The pecipitated hydrazone **3** or **6**, respectively, is isolated by suction and washed with methanol (20 ml) and diethyl ether. This product is pure enough for the oxidation with lead(IV) acetate, whereas for elemental analysis it is recrystallized from methanol (Table).

1,3- and 1,4-Bis[5-aryl-1,3,4-oxadiazol-2-yl]benzenes (3) and (7); General Procedure:

Method A, (for compounds **3a–c**): A suspension of hydrazone **2a–c** (1 mmol) and lead(IV) acetate (2.1 mmol) in chloroform

Table. Compounds **2**, **3**, **6**, and **7** prepared

Product	Yield [%]	m.p. [°C]	Molecular Formula[a] or Lit. m.p. [°C]
2a	95	256–258°	$C_{22}H_{18}N_4O_2$ (370.4)
2b	88	250–252°	$C_{24}H_{22}N_4O_2$ (398.5)
2c	50	240–242°	$C_{24}H_{22}N_4O_4$ (430.5)
2d	90	293–295°	$C_{22}H_{16}Cl_2N_4O_2$ (439.3)
2e	92	312–313°	$C_{22}H_{16}N_6O_6$ (460.4)
3a	65	249–251°	243–244°[6]
3b	60	245–247°	$C_{24}H_{18}N_4O_2$ (394.4)
3c	30	272–274°	$C_{24}H_{18}N_4O_4$ (426.4)
3d	30	290–292°	$C_{22}H_{12}Cl_2N_4O_2$ (435.3)
3e	55	> 370°	$C_{22}H_{12}N_6O_6$ (456.4)
6a	95	287–289°	$C_{22}H_{18}N_4O_2$ (370.4)
6b	70	354–356°	$C_{24}H_{22}N_4O_2$ (398.5)
6c	95	329–331°	$C_{24}H_{22}N_4O_4$ (430.6)
6d	95	352–354°	$C_{22}H_{16}Cl_2N_4O_2$ (439.3)
6e	86	364–365°	$C_{22}H_{16}N_6O_6$ (460.4)
7a	95	323–324°	322°[2,5]; 308–309°[3]
7b	62	362–364°	361°[2]
7c	52	327–329°	311°[2]
7d	40	370–372°	$C_{22}H_{12}Cl_2N_4O_2$ (435.3)
7e	45	> 370°	405°[2]

[a] Satisfactory microanalyses obtained: C ±0.28, H ±0.18, N ±0.27; exceptions: **2c**, H −0.37; **3e**, C −0.34.

(50 ml), free from ethanol, is stirred at 25 °C for 4 h and then the mixture is poured into water (150 ml). The organic layer is washed with aqueous 10% sodium carbonate (50 ml) and water (100 ml), dried with sodium sulfate, and evaporated in vacuo. By addition of diethyl ether (10 ml) to the residue and leaving the mixture at 25 °C compounds **3a–c** separate as solids, which are recrystallized from ethanol.

Method B, (for compounds **7a–c**): A suspension of hydrazone **6a–c** (1 mmol) and lead(IV) acetate (2.1 mmol) in chloroform (50 ml), free from ethanol, is refluxed under stirring for 4 h. After cooling the precipitated solid is isolated by suction, washed with 4 normal hydrochloric acid (100 ml) to remove any lead compounds hot water (100 ml), methanol (20 ml) and recrystallized from ethanol.

Method C, (for compounds **3d–e, 7d–e**): A suspension of hydrazone **2d–e, 6d–e** (1 mmol) and lead(IV) acetate (2.1 mmol) in glacial acetic acid (50 ml) is refluxed for 4 h. After cooling the mixture is poured into water (100 ml). The precipitated solid is isolated by suction and treated as in Method B.

Hydrolysis of Oxadiazoles 3a and 7a:

A suspension of compound **3a** or **7a**, (1 mmol) in 20% potassium hydroxide in *n*-butanol (50 ml) is refluxed for 30 min. After cooling the mixture is diluted with water (100 ml) and acidified with 4 normal hydrochloric acid (pH 5.5). The remaining solid is washed with hot water (50 ml) and recrystallized from methanol to give iso- and terephthalic acid bis[N'-aroylhydrazides]; **4a**; m. p. 295–297 °C; I.R. $\nu = 3200\ \mathrm{cm}^{-1}$ (NHNH), $\nu = 1645\ \mathrm{cm}^{-1}$ (CO) and **8a**: m.p. 327–329 °C; I.R. $\nu = 3210\ \mathrm{cm}^{-1}$ (NHNH), $\nu = 1620\ \mathrm{cm}^{-1}$ (CO). These compounds gave correct (C -0.27, H -0.06, N $+0.21$) elemental analysis. The hydrazides **4a** and **8a** (0.25 mmol) on refluxing with an excess of thionyl chloride (5 ml) for 30 min gave the corresponding oxadiazoles **3a** and **7a**, identical with those previously prepared.

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