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An efficient synthesis of conjugated 5-aryl-1,3,4-oxadiazoles from 3-heteroarylacrylohydrazides and acid chlorides

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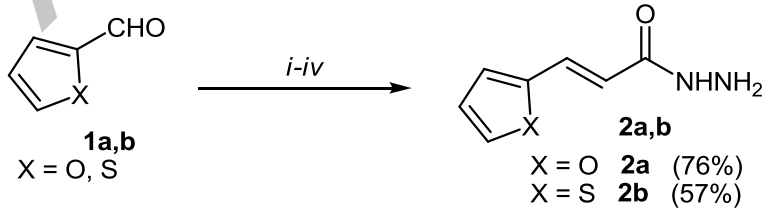
Abstract – New derivatives of 5-aryl-2-[2-(2-furyl)ethenyl]-1,3,4-oxadiazoles and 5-aryl-2-[2-(2-thienyl)ethenyl]-1,3,4-oxadiazoles are synthesized in a stepwise procedure through intermediate acyclic *N′*-arylcarbonyl-*N*-[2-(2-heteroaryl)acryloyl]hydrazines, starting from 3-(2-heteroaryl)acrylic acid hydrazides and acid chlorides. A facile one-pot methodology leading to the final 1,3,4-oxadiazoles is also described.

Keywords: cyclization; heterocycles; 1,3,4-oxadiazoles; 3-heteroarylacryloylhydrazide

Non-naturally occurring five-membered 1,3,4-oxadiazoles have been the subject of significant interest.[1] Many 1,3,4-oxadiazole-containing arrangements exhibit a broad spectrum of biological activity including antibacterial,[2] anti-inflammatory,[3] anticonvulsant,[4] antitumor[5] and antihypertensive.[6] Apart from in medicine, biological interactions of this class are also utilized in agriculture in crop protection (herbicides, fungicides, insecticides).[7] Symmetrically substituted derivatives of 2,5-diphenyl-1,3,4-oxadiazole are also known for their corrosion inhibitory effects.[8] 1,3,4-Oxadiazoles are also studied intensely due to their important electronic properties, which make them potentially useful targets for materials science. Many are used in organic light-emitting diodes (OLEDs), optical brighteners, and laser dyes.[9] Of particular interest are systems based on extended 1,3,4-oxadiazole π-conjugated hybrids, connected directly or indirectly to other electron-deficient systems such as pyridines, furans, thiophenes, phenoxazines and naphthalenes.[10] Such potential luminophores are able to electropolymerize with the formation of linear conducting polymers showing strong electroluminescence.

In continuation of our studies on the application of acid hydrazides in the synthesis of selected heterocyclic arrangements, we have elaborated methodologies for the synthesis of 1,3,4-oxadiazoles conjugated *via* an ethenyl linker to benzene, thiophene and furan rings.[11] These were obtained by cyclocondensation of the appropriate α,β-unsaturated acid hydrazides with triethyl orthoesters, both by conventional heating and under microwave irradiation. However, due to the limited number of commercially available orthoesters (R = Me, Et, Ph), the range of final conjugated products was reduced. Furthermore, compounds substituted with alkyl groups did not show interesting electronic properties and did not undergo electropolymerization. Bearing in mind all these facts, we decided to focus on the synthesis of novel 1,3,4-oxadiazoles containing aryl substituents at position 5, and to investigate another reaction path making use of the same α,β-unsaturated acid hydrazides and aryl chlorides instead of orthoesters. To the best of our knowledge, this stepwise methodology proceeds *via N,N′*-diacylhydrazines and needs the presence of a cyclodehydrating agent such as polyphosphoric acid, boron trifluoride-diethyl etherate, thionyl chloride, phosphorus oxychloride or the Burgess reagent.[12] These fragment hybrids, not described in literature, are promising monomers for optoelectronic applications because they combine different electron-deficient rings featuring excellent electron-transporting properties with high luminous efficiencies.

The key materials for the synthesis of 1,3,4-oxadiazole hybrids are generally two classes of compounds: hydrazides of α,β-unsaturated carboxylic acids (**2**) and aromatic acid chlorides (**3**). The first group of starting materials – acid hydrazides (**2**) – was obtained in a four-step procedure from commercially available aldehydes: 2-furancarboxaldehyde (**1a**) and 2-thiophenecarboxaldehyde (**1b**), according to the methodology described by us earlier.[11b]



Scheme 1. Synthesis of 3-(2-heteroaryl)acrylic acid hydrazides **2a,b**. Reagents and conditions: (*i*) $CH_2(COOH)_2$, pyridine, piperidine, reflux, 2 h; (*ii*) KOH, H_2O; (*iii*) $ClCOOC_2H_5$, CH_3CN, pyridine, reflux, 2 h; *iv*) $N_2H_4 \cdot H_2O$, CH_3CN, 0 °C, 24 h.

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