ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
http://web.icf.ro/rrch/

Rev. Roum. Chim.,
2015, *60*(4), 339-343

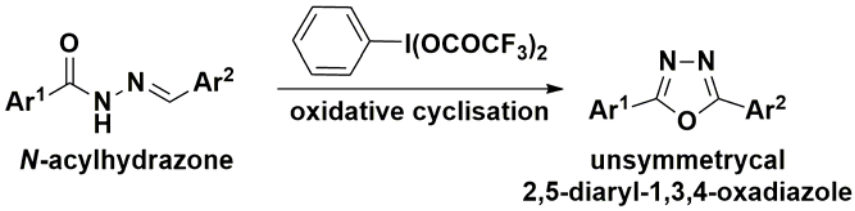
SYNTHESIS OF NEW 1,3,4-OXADIAZOLES BY OXIDATIVE CYCLISATION WITH BIS(TRIFLUOROACETOXY)IODOBENZENE

Codruta C. PARASCHIVESCU, Anca G. COMAN, Cătălin C. ANGHEL and Mihaela MATACHE*

University of Bucharest, Faculty of Chemistry, 90-92 Panduri Street, RO-050663-Bucharest, Roumania

Received January 12, 2015

2,5-Diaryl-1,3,4-oxadiazoles are valuable molecules mainly in the construction of Organic Light Emitting Diodes (OLEDs) due to their electron deficient character. More recently, unsymmetrical 2,5-disubstituted compounds found important applications as fluorescent sensor for various ions. We describe herein synthesis of new 2,5-diaryl-1,3,4-oxadiazoles having as intermediates *N*-acylhydrazones, readily available through the condensation reaction between aldehydes and hydrazides. The oxadiazole ring was formed by oxidative cyclisation using hypervalent iodine reagents, particularly, bis(trifluoroacetoxy)iodobenzene, which acts as a mild and convenient reagent for the synthesis of this type of unsymmetrical heterocyclic compounds. All synthesized compounds were fully characterized by NMR and MS measurements to confirm their purity and identity.



INTRODUCTION

Oxadiazoles[1] and, in particular, 1,3,4-oxadiazoles, have become an interesting target during the past decades due to their various applications. For instance, they were found to act as good anti-inflammatory, antimicrobial, anticonvulsant, analgesic, antitumor or antiviral agents[2] as well as to display useful properties as electron-transporting materials for the construction of Organic Light Emitting Diodes.[3] In addition, they are useful in the synthesis of polymers and copolymers with interesting optoelectronic properties[4] as well as for manufacture of sensors for various cations[5] or anions[6] and coordination polymers.[7] Metal complexes of 1,3,4-oxadiazoles have also recently gained attention as gelators of organic solvents,[8] molecular logic gates and fluorescent switches.[9]

The variety of the applications that were earlier foreseen for this class of heterocyclic compounds prompted the search for convenient synthetic procedures.[10] The main pathways currently encountered for the synthesis of 2,5-disubstituted-1,3,4-oxadiazoles start from different starting materials and involve: (*i*) dehydrative cyclisation of *N*,*N*-diacylhydrazines using dehydrative agents such as $POCl_3$[11] or $SOCl_2$[12]; (*ii*) oxidative cyclisation of *N*-acylhydrazones using milder reaction conditions and oxidative agents such as ceric ammonium nitrite[13] or hypervalent iodine reagents[14] and (*iii*) Huisgen reaction between tetrazoles and acyl chlorides.[15]

Enhancement of the photophysical properties of the 2,5-diaryl-1,3,4-oxadiazoles may be achieved by structural diversification either through variation of the functional groups on the aryl moieties or by increase in the number of the heterocyclic rings.[15] In continuation of our previous work on new methodology for the synthesis of such compounds,[14] we describe herein new 2,5-disubstituted-1,3,4

* Corresponding author: mihaaela.matache@g.unibuc.ro

oxadiazoles functionalized with groups able to confer interesting electronic properties or to allow further functionalization with applications, for example, in biolabelling.[16]

RESULTS AND DISCUSSION

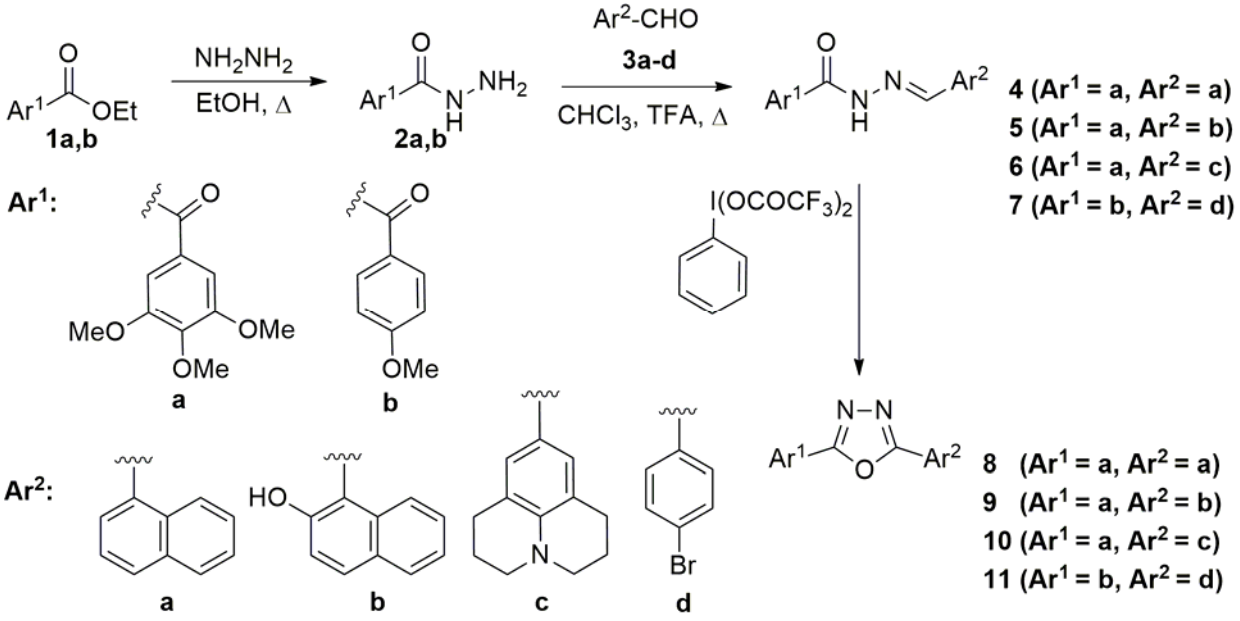
For the synthesis of the new unsymmetrical 2,5-disubtituted-1,3,4-oxadiazoles **8-11** we followed the synthetic approach shown in Scheme 1. The precursors *N*-acylhydrazones **4-7** are readily available from the condensation reaction between aryl hydrazides **2** and aldehydes **3** in chloroform using trifluoroacetic acid as acid catalyst. The reaction affords the hydrazone products in excellent yields and short reaction times (4 hours of reflux). The compounds are easily purified by repeated washings of the resulted solids with diethyl ether. The hydrazides **2** were commercially available raw materials (**2b**) or synthesized from the corresponding ethyl ester and hydrazine hydrate in ethanol (**2a**). The aldehydes **3** were also either commercially available, such as aldehydes **3a** and **3d** or synthesized by Vilsmeier-Haak[17] reaction of 2-naphtol (**3b**) or commercial julolidine (**3c**). For the heterocycle ring closure we chose the oxidative cyclisation of *N*-acyhydrazones **4-7** using bis(trifluoroacetoxy)iodobenzene in anhydrous dichloromethane, at room temperature. The choice was based on our previous work with hypervalent iodine reagents[14] as convenient mild agents for the oxadiazole ring formation, which avoids the harsh conditions used for the dehydration of *N*,*N*-diacylhydrazines with toxic and corrosive compounds, high temperatures and long reactions times. Thus, we obtained the new heterocyclic compounds **8-11**. The cyclisation reactions occurred in good yields, with complete conversion of the substrates, even in the case of the substrate **5**, having known the side reactions of phenols that may occur in presence of hypervalent iodine reagents.[18]

3,4,5-Trimetoxibenzhydrazide moiety has been extensively used in the synthesis of similar structures aimed to serve either as potent biologically active compounds[19] or may be efficient intermediates in the preparation of derivatives decorated with longer alkoxy chains with liquid crystals properties.[20] In addition, since the 1,3,4-oxadiazole core has a great electron deficient character, the methoxy groups may determine a certain behaviour in their electronic properties and for this reason we decided to preserve this moiety in compounds **8-10**. The design of compounds **8** and **9** was made in order to study the variability of the photophysical properties as a result of the hydroxy group, considering the general intrinsic fluorescence behaviour of the naphthyl group.[21] The julolidine core is known to provide dyeing properties to structures incorporating it[22] and therefore, we considered of interest to conjugate it to an oxadiazole ring (compound **10**) as a new potential fluorescent molecule. Compound **11**[23] was designed as an intermediate in the preparation of compound **14** (Scheme 2), which is functionalized at one aromatic ring with a carboxyl group able to further react, for example, with an amino group, and at the other aromatic ring with a bromine that may be used in cross-coupling reactions.

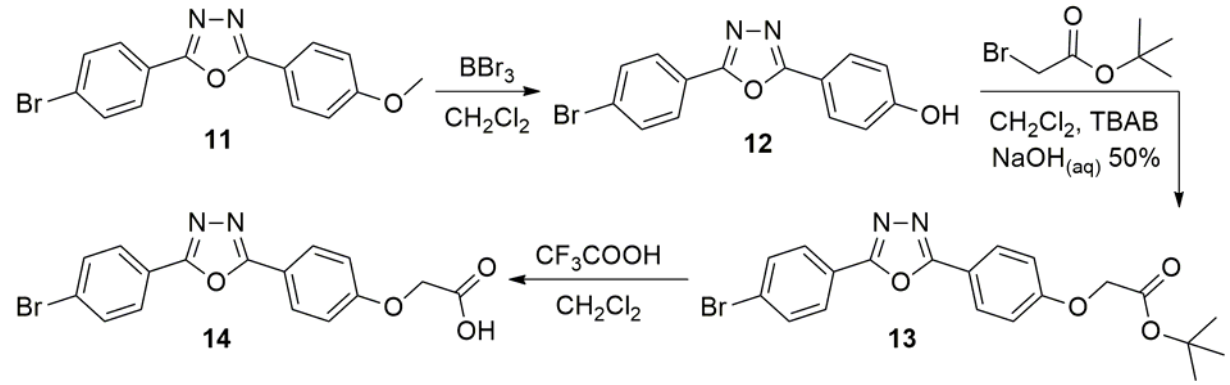
Once the oxadiazole **11** was synthesized the methoxy group was deprotected using a strong Lewis acid (boron tribromide) in anhydrous dichloromethane, under inert atmosphere (argon), at room temperature, following a previously described procedure.[24] A phase transfer catalysed reaction[25] of the resulted compound **12** with *tert*-butyl bromoacetate in presence of tetra-*n*-butylammonium bromide, in basic medium (aqueous solution of 50% NaOH) afforded compound **13** in 92% yield. Finally, deprotection of the *tert*-butyl ester was performed by simple stirring with a solution of 25% trifluoroacetic acid, yielding compound **14** in excellent (92%) yield. All compounds were characterised by Nuclear Magnetic Resonance and High Resolution Mass Spectrometry which confirmed their identity and purity.

EXPERIMENTAL

General information. The air and water sensitive reactions were performed in anhydrous solvents under argon. Dry dichloromethane was distilled from CaH_2. The NMR spectra were recorded on Bruker NMR spectrometers operating at 600, 400 and 300 MHz. Chemical shifts (δ) are reported in parts per million (ppm) using the residual solvent peak as an internal reference. High-resolution mass spectra were recorded using the positive mode atmospheric pressure chemical ionization (APCI) technique on a spectrometer equipped with an Orbital Ion Trap mass analyser. Reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F_{254} plates. All plates were visualized by UV irradiation at 254 nm. Preparative column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm. The melting points were determined in open capillaries using a STUART SMP3 electrical melting point apparatus and are uncorrected.



Scheme 1 – General synthetic pathway for the synthesis of 2,5-diaryl-1,3,4-oxadiazoles 8-11 by oxidative cyclisation of *N*-acylhydrazones 4-7 using bis(trifluoroacetoxy)iodobenzene (PIFA).



Scheme 2 – Synthetic scheme for the preparation of carboxyl-decorated compound **14**.

General procedure for the synthesis of *N*-acylhydrazones. Aldehyde **2** (1 mmol) and the corresponding hydrazide **3** (1 mmol) were dissolved in $CHCl_3$ (10 mL). Trifluoroacetic acid (a few drops) was added and the resulted solution heated to reflux for 4 h. After cooling, the solvent was removed in vacuum and the residue was washed with cold diethyl ether. The product was further used without any other purification.

3,4,5-Trimethoxy-N'-(naphthalen-1-ylmethylene)benzhydrazide **4**.[26] White solid, *m.p.* 240-243 °C, yield 75%, R_f=0.80 (silica gel, MeOH/DCM = 1:5). ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.75 (3H, s, OCH_3), 3.89 (6H, s, OCH_3), 7.30 (2H, s, H_{Ar}), 7.71-7.59 (3H, overlapped peaks, H_{Ar}), 7.95 (1H, d, J=4.4 Hz, H_{Ar}), 8.06-8.02 (2H, overlapped peaks, H_{Ar}), 8.90 (1H, d, J=8.4 Hz, H_{Ar}), 9.11 (1H, s, CH=N), 11.84 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 56.1 (OCH_3), 60.1 (OCH_3), 105.2, 124.2, 125.6, 126.3, 127.3, 127.7, 128.5, 128.8, 129.5, 130.1, 130.5, 133.5, 140.4, 147.5, 152.7, 162.5. HR-MS (APCI-Orbit trap) m/z calcd for $C_{21}H_{20}N_2O_4$ $[M+H]^+$, 365.1457; found, 365.1509.

N'-((2-hydroxynaphthalen-1-yl)methylene)-3,4,5-trimethoxybenzhydrazide **5.**[27] White solid, *m.p.* 237-239 °C, yield 85%, R_f=0.45 (silica gel, MeOH/DCM = 1:10). ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 3.75 (3H, s, OCH_3), 3.90 (6H, s, OCH_3), 7.25 (1H, d, J=8.92 Hz, H_{Ar}), 7.31 (2H, s, H_{Ar}), 7.42 (1H, t, J=7.6 Hz, H_{Ar}), 7.61 (1H, t, J=7.6 Hz, H_{Ar}), 7.91 (1H, d, J=8.0 Hz, H_{Ar}), 7.94 (1H, d, J=8.92 Hz, H_{Ar}), 8.92 (1H, d, J=8.92 Hz, H_{Ar}), 9.46 (1H, s, CH=N). ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 56.2, 60.2, 105.3, 108.6, 118.9, 120.8, 123.6, 127.7, 127.8, 129.0, 130.1, 131.6, 132.7, 140.7, 146.6, 152.8, 158.0, 162.1. HR-MS (APCI-Orbit trap) m/z calcd for $C_{21}H_{20}N_2O_5$ $[M+H]^+$, 381.1406; found, 381.1460.

N'-((1,2,3,5,6,7-hexahydropyrido[3,2,1-ij]quinolin-9-yl)methylene)-3,4,5-trimethoxybenzhydrazide **6.** White solid, *m.p.* 237-239 °C, yield 73%, R_f=0.65 (silica gel, MeOH/CH_2Cl_2 = 1:10). ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.87 (4H, quintet, J=6.0 Hz, $H_{aliphatic}$), 2.70 (4H, t, J=6.0 Hz, $H_{aliphatic}$), 3.19 (4H, t, J=6.0 Hz, $H_{aliphatic}$), 3.71 (3H, s, OCH_3), 3.85 (6H, s, OCH_3), 7.07 (2H, s, H_{Ar}), 7.20 (2H, s, H_{Ar}), 8.16 (1H, s, CH=N), 11.37 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 21.1, 27.0, 49.1, 56.0, 60.0, 87.1, 104.9, 120.5, 125.9, 128.9, 140.0, 144.2, 148.7, 152.6, 161.9. HR-MS (APCI-Orbit trap) m/z calcd for $C_{23}H_{27}N_3O_4$ $[M+H]^+$, 410.2035; found, 410.2090.

N'-(4-bromobenzylidene)-4-methoxybenzhydrazide **7.**[23] White solid, *m.p.* 208-210 °C, yield 96%, R_f=0.41 (silica gel, AcOEt/CH_2Cl_2 = 9:1). ^{1}H NMR (600 MHz, DMSO-d_6), δ (ppm): 3.81

(3H, s, CH_3), 7.03 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.68 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.75 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.85 (2H, d, *J*=8.4 Hz, H_{Ar}), 8.39 (1H, s, C*H*), 11.79 (1H, s, N*H*). ^{13}C NMR (150 MHz, DMSO-d_6), δ (ppm): 55.2, 111.0, 114.3, 126.7, 128.7, 129.6, 131.4, 137.1, 147.9, 180.8, 191.7. HR-MS (APCI-Orbit trap) m/z calcd for $C_{15}H_{14}BrN_2O_2$ $[M+H]^+$, 333.0160, 335,0073, found: 333.0248, 335.0226.

General procedure for the synthesis of the 2,5-diaryl-1,3,4-oxadiazoles. The corresponding *N*-acylhydrazone (0.5 mmol) and PIFA (1.1 equiv, 0.55 mmol) were dissolved in dry CH_2Cl_2 (10 mL) under argon and the solution was stirred overnight at *rt*. The solvent was removed *in vacuum*, the residue treated with ethyl acetate (30 mL) and washed with a solution of 5% $NaHCO_3$, water, brine, then dried over anhydrous $MgSO_4$ and evaporated. The residue was column chromatographed to afford the pure product.

2-(Naphthalen-1-yl)-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole **8**. White solid, *m.p.* 128-131 °C, yield 76%, R_f=0.70 (silica gel, AcOEt/CH_2Cl_2 = 1:4). ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.78 (3H, s, OCH_3), 3.94 (6H, s, OCH_3), 7.46 (2H, s, H_{Ar}), 7.82-7.67 (3H, overlapped peaks, H_{Ar}), 8.12 (1H, d, *J*=8.0 Hz, H_{Ar}), 8.25 (1H, d, *J*=8.0 Hz, H_{Ar}), 8.48 (1H, d, *J*=8.0 Hz, H_{Ar}), 9.22 (1H, d, *J*=8.0 Hz, H_{Ar}). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 56.2, 60.2, 104.2, 116.2, 117.2, 118.4, 125.4, 125.6, 126.8, 128.3, 128.9, 129.2, 132.7, 133.4, 140.6, 153.5, 163.4, 163.8. HR-MS (APCI-Orbit trap) m/z calcd for $C_{21}H_{18}N_2O_4$ $[M+H]^+$, 363.1300, found: 363.1355.

1-(5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazol-2-yl)naphthalen-2-ol **9**. White solid, *m.p.* 181-183 °C, yield 40%, R_f=0.64 (silica gel, AcOEt/petroleum ether = 1:2). ^{1}H-NMR (600 MHz, $CDCl_3$), δ (ppm): 3.97 (3H, s, OCH_3), 4.01 (6H, s, OCH_3), 7.36 (1H, d, *J*=8.94 Hz, H_{Ar}), 7.44 (2H, s, H_{Ar}), 7.46 (1H, t, *J*=7.4 Hz, H_{Ar}), 7.66 (1H, t, *J*=7.4 Hz, H_{Ar}), 8.74 (1H, d, *J*=7.98 Hz, H_{Ar}); 7.87 (1H, d, *J*=8.94 Hz, H_{Ar}), 7.98 (1H, d, *J*=8.94 Hz, H_{Ar}), 8.74 (1H, d, *J*=8.94 Hz, H_{Ar}). ^{13}C NMR (150 MHz, DMSO-d_6), δ (ppm): 56.5, 61.1, 100.2, 104.5, 118.4, 119.3, 123.2, 124.0, 128.5, 128.6, 129.4, 130.2, 134.9, 141.6, 141.7, 153.9, 159.6, 165.5. HR-MS (APCI-Orbit trap) m/z calcd. for $C_{21}H_{18}N_2O_5$ $[M+H]^+$, 379.1288, found: 379.1290.

2-(1,2,3,5,6,7-Hexahydropyrido[3,2,1-ij]quinolin-9-yl)-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole **10**. White solid, *m.p.* 161-165 °C, yield 25%, R_f=0.53 (silica gel, AcOEt/CH_2Cl_2 = 1:2). ^{1}H-NMR (600 MHz, $CDCl_3$), δ (ppm): 1.99 (4H, quintet, *J*=6.0 Hz, $H_{aliphatic}$), 2.81 (4H, t, *J*=6.0 Hz, $H_{aliphatic}$), 3.26 (4H, t, *J*=6.0 Hz, $H_{aliphatic}$), 3.92 (3H, s, OCH_3), 4.0 (6H, s, OCH_3), 7.32 (2H, s, H_{Ar}), 7.52 (2H, s, H_{Ar}). ^{13}C NMR (150 MHz, $CDCl_3$), δ (ppm): 21.5, 27.7, 49.9, 56.4, 61.0, 104.0, 109.5, 119.7, 120.9, 125.7, 140.7, 145.4, 153.6, 163.2, 165.5. HR-MS (APCI-Orbit trap) m/z calcd for $C_{23}H_{25}N_3O_4$ $[M+H]^+$, 408.1918, found: 408.1922.

2-(4-Bromophenyl)-5-(4-methoxyphenyl)-1,3,4-oxadiazole **11**.[23] White solid, *m.p.* 157-158 °C, yield 90%, R_f=0.41 (silica gel, AcOEt/CH_2Cl_2 = 9:1). ^{1}H NMR (600 MHz, DMSO-d_6), δ (ppm): 3.86 (3H, s, OCH_3), 7.16 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.82 (2H, d, *J*=8.4 Hz, H_{Ar}), 8.03 (2H, d, *J*=8.4 Hz, H_{Ar}), 8.05 (2H, d, *J*=8.4 Hz, H_{Ar}). ^{13}C-NMR (150 MHz, $CDCl_3$), δ (ppm): 55.5, 113.7, 114.8, 115.4, 122.6, 125.4, 128.4, 128.5, 131.2, 132.4, 162.1, 162.8, 164.0. HR-MS (APCI-Orbit trap) m/z calcd for $C_{15}H_{11}BrN_2O_2$ $[M+H]^+$, 331.0037, 333, 0017, found: 331.0094, 333.0071.

4-(5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl)phenol **12**. Compound **11** (0.317 mg, 1 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and BBr_3 (1.1 equiv, 1.1 mmol). The mixture was stirred at 0°C for 4 hours and overnight at room temperature. The solvent was removed *in vacuum*, the residue was dissolved in AcOEt (20 mL) and washed with a solution of 5% $NaHCO_3$ (3 × 10 mL), water, brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuum* and the crude product recrystallized from methanol. White solid, *m.p.* 269-271 °C, yield 92%, R_f=0.34 (silica gel, AcOEt/CH_2Cl_2 = 1:1). ^{1}H NMR (600 MHz, $CDCl_3$), δ (ppm): 6.92 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.60 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.90 (2H, d, *J*=8.4 Hz, H_{Ar}), 7.92 (2H, d, *J*=8.4 Hz, H_{Ar}). ^{13}C-NMR (150 MHz, $CDCl_3$), δ (ppm): 114.6, 116.1, 122.9, 125.8, 128.0, 128.7, 132.2, 160.1, 163.0, 164.9. HR-MS (APCI-Orbit trap) m/z calcd for $C_{15}H_9BrN_2O_2$ $[M+H]^+$, 316.9847, 318.9860 found: 316.9939, 318.9912.

tert-Butyl 2-(4-(5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl)phenoxy) acetate **13**. To a solution of compound **12** (0.1 g; 0.32 mmol) in CH_2Cl_2 (10 mL) cooled below 10°C was added an aqueous solution of 50% NaOH (0.153 g, 3.84 mmoli), tetra-*n*-butylammonium bromide (0.01 g, 0.035 mmoli) and the mixture was stirred for 30 minutes at this temperature. *tert*-Butyl bromoacetate (0.066 g, 0.34 mmol) was then added and the reaction stirred at room temperature overnight. The solution was diluted with CH_2Cl_2 (10 mL) and water (10 mL) and the two phases separated. The aqueous layer was further extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, the solvent was removed *in vacuum* and the crude product recrystallized from methanol. White solid, *m.p.* 185-187 °C, yield 92%, R_f=0.37 (silica gel, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$), δ (ppm): 1.49 (9H, s, *t*Bu), 4.60 (2H, s), 7.03 (2H, d, *J*=8.76 Hz, H_{Ar}), 7.67 (2H, d, *J*=8.46 Hz, H_{Ar}), 7.98 (2H, d, *J*=8.46 Hz, H_{Ar}), 8.07 (2H, d, *J*=8.76 Hz, H_{Ar}). ^{13}C-NMR (150 MHz, $CDCl_3$), δ (ppm): 27.8, 28.0, 65.5, 82.8, 115.2, 117.1, 123.0, 126.2, 128.2, 128.8, 132.4, 160.7, 164.5, 167.3. HR-MS (APCI-Orbit trap) m/z calcd for $C_{20}H_{19}BrN_2O_4$ $[M+H]^+$, 431.0528, 433.0541, found: 433.0584, 374.9975 $[M-t\text{Bu}]^+$.

2-(4-(5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl)phenoxy)acetic acid **14**. Compound **13** (0.1 g; 0.23 mmol) was treated with 25% trifluoroacetic acid in CH_2Cl_2 (10 mL) and stirred at *rt* for 4 h. The solution was diluted with water, the two phases separated and the aqueous solution was extracted with CH_2Cl_2. The organic layers were washed with water, brine, dried over anhydrous $MgSO_4$ and the solvent removed *in vacuum*. The crude product recrystallized from methanol. White solid, *m.p.* 260-262 °C, yield 92%, R_f=0.12 (silica gel, CH_2Cl_2). ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 4.83 (2H, s, CH_2), 7.16 (2H, d, *J*=8.82 Hz, H_{Ar}), 7.84 (2H, d, *J*=8.52 Hz, H_{Ar}), 8.05 (2H, d, *J*=8.52 Hz, H_{Ar}), 8.06 (2H, d, *J*=8.82 Hz, H_{Ar}), 13.15 (1H, s, COO*H*). ^{13}C-NMR (75 MHz, $CDCl_3$), δ (ppm): 64.5, 115.3, 115.9, 122.6, 125.4, 128.4, 128.5, 132.4, 160.6, 163.0, 164.0, 169.7. HR-MS (APCI-Orbit trap) m/z calcd for $C_{16}H_{11}BrN_2O_4$ $[M+H]^+$, 374.9902, found: 374.9975.

CONCLUSIONS

In conclusion, we described synthesis of new 2,5-diaryl-1,3,4-oxadiazoles **8-11** as potent fluorescent molecular structures as well as synthesis of compound **11** as intermediate in the preparation of carboxyl-derived oxadiazole **14** which may be also a valuable molecule either in terms of fluorescence behaviour or bearing two point of further functionalization: in cross coupling

reactions due to the presence of the bromine and as a biolabelling reagent due to the possibility of the carboxyl group to react with an amino group usually encountered in protein structures. Study of the photophysical properties and potential applications in conjunction with proteins are currently under way.

REFERENCES

1. V. Zhdankin, "Five-membered Rings – Triazoles, Oxadiazoles, Thiadiazoles and their Fused Carbocyclic Derivatives" Vol. 5 in "Comprehensive Heterocyclic Chemistry III", A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor (Eds.), Elsevier, 2008.
2. C.S. de Oliveira, B. Freitas Lira, J.M. Barbosa-Filho, J.G. Fernandez Lorenzo and P.F. de Athayde-Filho, *Molecules*, **2012**, *17*, 10192-10231.
3. G. Hughes and M.R. Bryce, *J. Mater. Chem.*, **2005**, *15*, 94-107.
4. See for example: a) B. Schulz, M. Bruma and L. Brehmer, *Adv. Mater.,* **1997**, *9*, 601-613; b) M. Bruma, M.D. Damaceanu and I.A. Ronova, *Rev. Roum. Chim.*, **2012**, *57*, 383-391; c) M.-D. Damaceanu, M. Bruma and B. Schulz, *Polymer*, **2012**, *53*, 5258-5267.
5. Selected examples: a) C. Zheng, A. Yuan, Z. Zhang, H. Shen, S. Bai and H. Wang, *J. Fluoresc.*, **2013**, *23*, 785-791; b) Q. Liu, W. Bian, H. Shi, L. Fan, S. Shuang, C. Dong and M.M.F. Choi, *Org. Biomol. Chem.*, **2013**, *11*, 503-508; c) S.H. Mashraqui, S. Sundaram and A.C. Bhasikuttan, *Tetrahedron,* **2007**, *63*, 1680-1688.
6. Selected examples: a) J. Ma, Z. Li, Y. Zong, Y. Men and G. Xing, *Tetrahedron Lett.*, **2013**, *54*, 1348-1351; b) C.K. Kwak, C.-H. Leeb and T.S. Lee, *Tetrahedron Lett.*, **2007**, *48*, 7788-7792; c) J. Chen, C.-P. Li, J. Shang and M. Du, *Inorg. Chem. Commun.*, **2012**, *15*, 172-175.
7. Z.-L. Fang, J.-G. He, Q.-S. Zhang, Q.-K. Zhang, X.-Y. Wu, R.-M. Yu and C.-Z. Lu, *Inorg. Chem.,* **2011**, *50*, 11403-11411.
8. a) C. Zhao, H. Wang, B. Bai, S. Qu, J. Song, X. Ran, Y. Zhanga and M. Li, *New J. Chem.*, **2013**, *37*, 1454-1460; b) C. Zhao, B. Bai, H. Wang, S. Qu, G. Xiao, T. Tian and M. Li, *J. Molec. Struct.*, **2013**, *1037*, 130-135.
9. A.-F. Li, Y.-B. Ruan, Q.-Q. Jiang, W.-B. He and Y.-B. Jiang, *Chem. Eur. J.*, **2010**, *16*, 5794-5802.
10. Z. Jakopin and M.S. Dolenc, *Curr. Org. Chem.*, **2008**, *12,* 850-898.
11. X.-B. Zhang, B.-C. Tang, P. Zhang, M. Li and W.-J. Tian, *J. Mol. Struct.*, **2007**, *846*, 55-64.
12. S. Borg, R.C. Vollinga, M. Labarre, K. Payza, L. Terenius and K.J. Luthman, *J. Med. Chem.,* **1999**, *42*, 4331-4342.
13. M. Dabiri, P. Salehi, M. Baghbanzadeh and M. Bahramnejad, *Tetrahedron Lett.*, **2006**, *47*, 6983-6986.
14. a) C. Dobrotă, C.C. Paraschivescu, I. Dumitru, M. Matache, I. Baciu and L.L. Ruță, *Tetrahedron Lett.,* **2009**, *50*, 1886-1888; b) C.C. Paraschivescu, M. Matache, C. Dobrotă, A. Nicolescu, C. Maxim, C. Deleanu, I.C. Fărcășanu and N.D. Hădade, *J. Org. Chem.*, **2013**, *78*, 2670-2679.
15. C.-C. Yang, C.-J. Hsu, P.-T. Chou, H.C. Cheng, Y.O. Su and M. Leung, *J. Phys. Chem. B*, **2010**, *114*, 756-768.
16. M. Sameiro and T. Gonçalves, *Chem. Rev.*, **2009**, *109*, 190-212.
17. O. Maior, A. Nicolae and S. Florea, "Reacții nominalizate în sinteza organică", Editura Briliant, Bucureşti, 1996.
18. a) Y. Kita, T. Takada, M. Ibaraki, M. Gyoten, S. Mihara, S. Fujita and H. Tohma, *J. Org. Chem.*, **1996**, *61*, 223-227; b) H. Liang and M.A.Ciufolini, *Tetrahedron*, **2010**, *66*, 5884-5892.
19. L. Jin, J. Chen, B. Song, Z. Chen, S. Yang, Q. Li, D. Hu and R. Xu, *Bioorg. Med. Chem. Lett.*, **2006**, *16*, 5036-5040.
20. S. Qu and M. Lin, *Tetrahedron*, **2007**, *63*, 12429-12436.
21. K. Kubo, S. Sakaguchi and T. Sakurai, *Talanta*, **1999**, *49*, 735-744.
22. A Srivastava, P.K. Singh, M. Kumbhakar, T. Mukherjee, S. Chattopadyay, H. Pal and S. Nath, *Chem. Eur. J.*, **2010**, *16*, 9257-9263.
23. Previously described by S. Zhenhua, *Synth. Commun.*, **2006**, *36*, 2927-2937.
24. S. Punna, S. Meunier and M. G. Finn, *Org. Lett.*, **2004**, *6*, 2777-2779.
25. N.D. Bogdan, M. Matache, V.M. Meier, C. Dobrotă, I. Dumitru, G.D. Roiban and D.P. Funeriu, *Chem. Eur. J.*, **2010**, *16*, 2170-2180.
26. D.M. Borchhardt, A. Mascarello, L.D. Chiaradia, R.J. Nunes, G.Y. Oliva, A. Rosendo and A.D. Andricopulo, *J. Braz. Chem. Soc.*, **2010**, *21*, 142-150.
27. K.K. Kim, T.S. Lange, R.K. Singh and L. Brard, *BMC Cancer*, **2010**, *10*, 72-90.