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Synthesis and characterization of new mono-, bis-, and tris-oxamato proligands

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ABSTRACT

This communication presents the synthesis and the characterization of new organic molecules bearing up to three *N*-phenyl-oxalamic acid ethyl esters. The syntheses are based on Sonogashira-type cross-coupling reactions with preformed oxalamic ester intermediate building blocks. The short synthetic pathways lead easily to valuable potential oxamato-bridging ligands with overall interesting yields.

During the last decades, a growing interest for polymeric coordination networks motivated the scientific community. Applications of three-dimensional metal-organic frameworks (MOFs) are numerous. For example, gas storage materials[1] or molecule-based magnets[2] have been reported. Coordination polymers of lower dimentionality are also of interest.[3] The controlled design of new scaffolds is the focus of many research.[4]

Up to now, thousands of coordination polymers have been reported. Nevertheless, the design and synthesis of new bridging organic molecules remain a challenging task for the improvement of the final materials. Various ditopic ligands have been prepared. Their coordination chemistry has been well documented in the literature.[5] Stepwise introduction of different metals, a so called 'complex as ligand' or 'expanded ligand' approach, is probably a key step for the construction of heterometallic scaffolds.[6] This opportunity is interesting for magnetic properties regarding the ability of ligands to propagate spin alignment.[7]

Magnetic exchange interactions can be strong with ligands having one or two bridging atoms, as shown for example in cyano-bridged frameworks.[8] However, the structural variety is rather limited. A much larger diversity is offered by conjugated systems having three or more bridging atoms. This higher modulation is profitable for structure–property correlations.[9] Furthermore, additional variations allow the design of unique polydentate/polytopic ligands. Among several interesting diamagnetic-bridging ligands, the oxamato group attracted our attention. As reported in the literature, it combines several advantages for building multidimensional scaffolds with magnetic properties, like the easy synthesis and the good solubility of the corresponding precursor.[10]

Herein, we report the synthesis and characterization of new organic building blocks containing up to three *N*-phenyl-oxalamic acid ethyl ester groups (Fig. 1). Such ethyl esters of oxalamic acids can be used in situ for the preparation of oxamato-bridged metal complexes.

We present in this communication the use of iodo- and ethynyl-functionalized phenyl-oxalamic esters as reactants in a Sonogashira-type cross-coupling reaction. This enables the direct synthesis

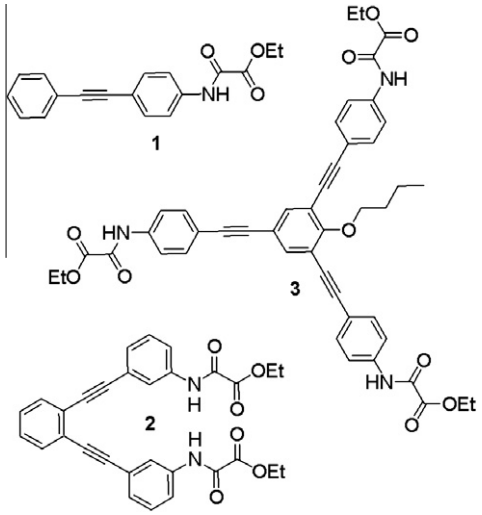

Figure 1. Drawing of the target mono-, bis- and tris-ditopic proligands.

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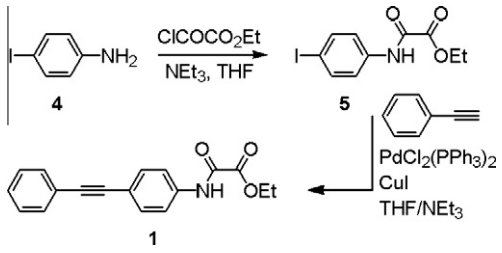


Scheme 1. Synthesis of the mono oxalamic acid ethyl ester **1**.

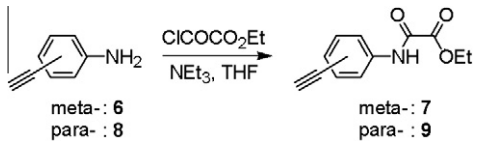
of the target molecule without the handling of amine intermediates, and/or additional protection–deprotection steps often required for the synthesis of larger molecules.

In a first step, we focused on the target compound *N*-(4-phenylethynyl-phenyl)-oxalamic acid ethyl ester **1**. The synthesis of the *N*-(4-iodo-phenyl)-oxalamic acid ethyl ester intermediate **5** in 88% yield was adapted from the literature (Scheme 1).[11] This iodo-derivative has already been synthesized in a different way, but no full characterization has been reported.[12] The second step could be performed in standard conditions using $PdCl_2(PPh_3)_2$ catalyst and CuI as co-catalyst. The compound **1** could be obtained in 76% yield after column chromatography.[13]

To prepare the bis- and tris-functionalized ligands **2**[14] and **3**[15], we used the intermediate building blocks bearing terminal triple bonds. In a first step, we synthesized the ethynyl-building blocks bearing an oxalamic ester group in *meta*-position (**7**) or *para*-position (**9**) in a standard way (Scheme 2). This reaction has been done in THF/NEt_3 at 50 °C or rt using the corresponding commercially available ethynyl–aniline derivatives **6** and **8**.[16]

The ammonium salt has been removed by filtration before the purification of the desired products by column chromatography on SiO_2. The ^1H and ^{13}C NMR spectra are in agreement with the connected amide and ester functional groups of the oxalamic ester for both compounds **7** and **9**. The IR spectra also show the presence of two bands attributed to the two different C=O bonds of such a motif.[17] Interestingly, the yields for the preparation of these precursors **7** and **9** are high (97% and 93%, respectively).

In a second step, a Sonogashira-type cross-coupling reaction between 2 equiv of the ethynyl compound **7** and 1,2-diiodobenzene **10** afforded the bis-*N*-phenyl-oxalamic acid ethyl ester **2** (Scheme 3).

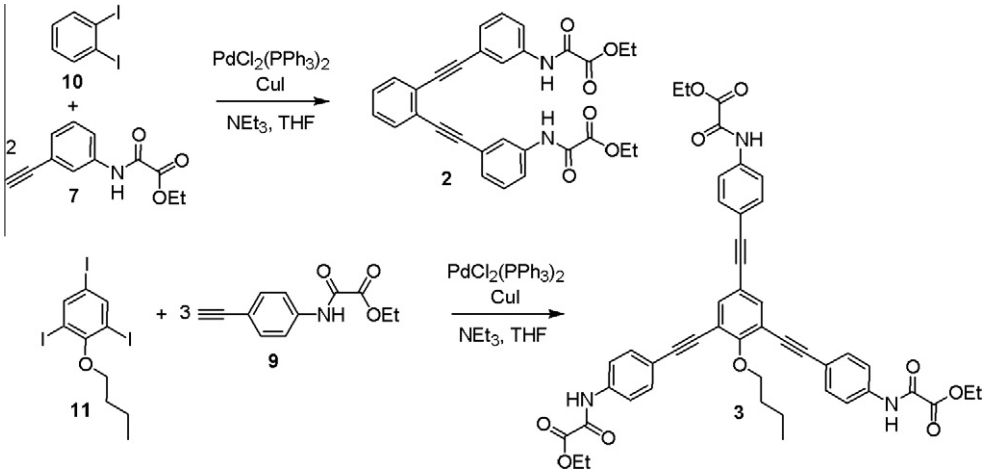


Scheme 2. General reaction scheme for the introduction of an oxamate functional group.

A careful purification by column chromatography on SiO_2 afforded this pincer-type proligand. *N*-(3-{2-[3-(ethoxyoxalyl-amino)-phenylethynyl]-phenylethynyl}-phenyl)-oxalamic acid ethyl ester **2** has been characterized by ^1H NMR, ^{13}C NMR, and IR spectroscopies, mass spectrometry, and elemental analysis.

A Sonogashira-type cross-coupling reaction between an excess of the ethynyl compound **9** and butoxy-2,4,6-triiodobenzene **11**[18] allowed the synthesis of *N*-(4-{4-butoxy-3,5-bis-[4-(ethoxyoxalyl-amino)-phenylethynyl]-phenylethynyl}-phenyl)-oxalamic acid ethyl ester **3**. The good solubility of the compound provided by the butoxyl group allowed purification by column chromatography. While the ^1H NMR spectrum is easily analyzed, the ^{13}C NMR is more complex due to the butoxyl fragment, and the C2 symmetry along the 1,4-carbon atoms of the central phenyl ring. As a consequence of the presence of this butoxyl fragment, two sets of ethynyl-phenyl-oxalamic esters are distinguished. For instance, four signals ranging between 85.0 and 93.7 ppm are attributed to the 2 equiv ethynyl fragments in *ortho*-position of the butoxyl and to the non-equivalent *para*-ethynyl fragment. The aromatic rings and the splittings of some signals are in keeping with the structure. Two carbonyl signals of the amide groups are clearly observed but only a broad peak for the ester carbon atoms is seen. This can be reasonably attributed to the overlapping of two close signals. Our interpretation is supported by the ^1H NMR spectrum, where the chemical shifts for the two non-equivalent amide protons are different for the same reason. The identity of the molecule is further confirmed by mass spectrometry and its purity by elemental analysis.

In conclusion, using a standard Sonogashira-type cross-coupling reaction, we could easily synthesize various scaffolds with up to three oxalamic ester groups as potential proligands. While the yields for the final steps are moderate, the short synthetic pathways to get the desired ligand precursors are attractive. The synthesis of poly-functionalized organic scaffolds is now under way.



Scheme 3. Synthesis of compounds **2** and **3**.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.117.

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13. Compound **1**: Phenylacetylene (200 mg, 1.77 mmol) and compound **5** (378 mg, 1.18 mmol) were added to dry THF/NEt_3 (20 mL, 3:1) under Ar. $Pd(PPh_3)_2Cl_2$ (42 mg, 0.060 mmol) and CuI (11 mg, 0.060 mmol) were added, and the mixture was stirred at rt overnight. The solvents were evaporated, and the crude was purified by column chromatography (CH_2Cl_2/hexane 9:1–1:0) to give 265 mg of the desired compound **1** (76%).
R_f (SiO_2, CH_2Cl_2/hexane 1:2): 0.46; ^1H NMR ($CDCl_3$): δ (ppm) = 1.43 (t, J = 7.2 Hz, 3H), 4.42 (q, J = 7.2 Hz, 2H), 7.32–7.37 (m, 3H), 7.50–7.56 (m, 4H), 7.63–7.66 (m, 2H), 8.94 (s, 1H); ^{13}C NMR ($CDCl_3$): δ (ppm) = 14.1, 64.0, 88.9, 89.9, 119.7, 120.5, 123.3, 128.5, 128.5, 131.7, 132.7, 136.3, 153.9, 161.0; ^{13}C-DEPT135 NMR ($CDCl_3$): δ (ppm) = 14.0, 63.9, 119.6, 128.3, 128.4, 131.6, 132.6; selected IR (KBr pellet, cm^{-1}): 3339, 1729, 1703, 1582, 1527, 1472, 1443, 1367, 1292, 1240, 1170, 1111, 1024, 1017, 843, 832, 760, 755, 687, 519; positive ion ESI (%), MeCN: m/z = 316.12 (100) $[M+Na]^+$, 609.25 (20) $[2M+Na]^+$; Anal. Calcd for $C_{18}H_{15}NO_3$ (M_r = 293.32): C, 73.71; H, 5.15; N, 4.78. Found: C, 73.58; H, 5.12; N, 4.76.
14. *Compound* **2**: 1,2-Diiodobenzene (375 mg, 0.669 mmol) and compound **7** (741 mg, 3.41 mmol) were dissolved in THF/NEt_3 (30 mL, 1:1). $Pd(PPh_3)_2Cl_2$ (80.0 mg, 0.114 mmol) and CuI (22.0 mg, 0.114 mmol) were added under N_2. After stirring overnight at rt, the solvents were removed. The residue was purified by chromatography (SiO_2, hexane/CH_2Cl_2 1:1–0:1 followed by SiO_2, CH_2Cl_2/MeCN 9:1) to afford the pure product **2** (339 mg, 59%) as a white powder.
R_f (SiO_2, CH_2Cl_2/MeCN 94:6): 0.61; mp 178 °C; ^1H NMR (CD_2Cl_2): δ (ppm) = 1.37 (t, J = 7.2 Hz, 6H), 4.33 (q, J = 7.2 Hz, 4H), 7.35–7.43 (m, 6H), 7.56–7.64 (m, 4H), 8.00 (s, 2H), 9.13 (s, 2H); ^{13}C NMR (CD_2Cl_2): δ (ppm) = 14.0, 63.6, 88.6, 92.9, 120.5, 123.2, 124.1, 125.5, 128.5, 128.7, 129.4, 132.0, 136.9, 154.6, 160.7; ^{13}C-DEPT135 NMR (CD_2Cl_2): δ (ppm) = 13.7, 63.6, 120.4, 123.1, 128.4, 128.6, 129.3, 132.0; selected IR (KBr pellet, cm^{-1}): 3334, 2205, 1703, 1604, 1587, 1545, 1478, 1443, 1428, 1368, 1300, 1280, 1265, 1217, 1181, 1166, 1019, 786, 769, 703, 686; positive ion ESI (%), MeCN: m/z = 531.1 (100) $[M+Na]^+$, 547.1 (30) $[M+K]^+$; UV–vis (MeCN) λ, nm (ε, $M^{-1}\,cm^{-1}$): 335 sh (10,940), 313 sh (22,460), 274 (73,900); 260 (54,090), 221 (40,790); Anal. Calcd for $C_{30}H_{24}N_2O_6$ (M_r = 508.52): C, 70.86; H, 4.76; N, 5.51. Found: C, 70.74; H, 4.82; N, 5.48.
15. *Compound* **3**: Butoxy-2,4,6-triiodobenzene **11** (353 mg, 0.669 mmol), and compound **9** (581 mg, 2.67 mmol) were dissolved in dry THF/NEt_3 (30 mL, 1:1). $Pd(PPh_3)_2Cl_2$ (70.5 mg, 0.10 mmol) and CuI (19.0 mg, 0.10 mmol) were added under N_2. After stirring for 5 h at rt, the solvents were removed and the residue was purified by chromatography (SiO_2, hexane/AcOEt 1:1 followed by SiO_2, hexane/CH_2Cl_2 2:1). The pure product **1** (70 mg, 13%) was obtained as a white powder.
R_f (SiO_2, CH_2Cl_2/AcOEt 1:1): 0.40; mp 91 °C dec; ^1H NMR (CD_2Cl_2): δ (ppm) = 0.97 (t, J = 7.2 Hz, 3H), 1.39 (t, J = 7.2 Hz, 9H), 1.57–1.65 (m, 2H), 1.84–1.89 (m, 2H), 4.34–4.41 (m, 8H), 7.50–7.56 (m, 6H), 7.61 (s, 2H), 7.63–7.69 (m, 6H), 8.99–9.00 (m, 3H); ^{13}C NMR (CD_2Cl_2): δ (ppm) = 13.8, 13.8, 19.5, 32.6, 63.9, 74.5, 85.0, 87.7, 89.7, 93.7, 118.1, 118.6, 119.7, 119.7, 119.8, 119.8, 132.5, 132.5, 136.3, 136.7, 136.9, 154.0, 154.0, 160.7, 161.0; ^{13}C-DEPT135 NMR (CD_2Cl_2): δ (ppm) = 13.7, 13.8, 19.4, 32.6, 63.8, 74.4, 119.6, 119.7, 132.4, 132.5, 136.3; selected IR (KBr pellet, cm^{-1}): 3337, 2959, 2935, 2210, 1708, 1605, 1584, 1526, 1471, 1444, 1407, 1370, 1294, 1237, 1179, 1157, 1111, 1015, 837, 525; positive ion ESI (%), MeCN: m/z = 818.2 (100) $[M+Na]^+$, 818.7 (33) $[2M+2Na]^{2+}$; 1216.4 (60) $[3M+2Na]^{2+}$; 1614.6 (20) $[4M+2Na]^{2+}$; UV–vis (MeCN) λ, nm (ε, $M^{-1}\,cm^{-1}$): 321 (114,000), 221 (39,660); Anal. Calcd for $C_{46}H_{41}N_3O_{10}$ (M_r = 795.83): C, 69.42; H, 5.19; N, 5.28. Found: C, 69.23; H, 5.06; N, 5.25.
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