

A SIMPLE LARGE SCALE SYNTHESIS OF 1,3-BIS-(4,4-DIMETHYL-2- OXAZOLINYL)BENZENE*

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ABSTRACT

A simple “one-pot” procedure for the large scale and high yield synthesis of the title ligand (**1**) is presented which involves Lewis acid catalysed formation of **1** from 1,3-dicyanobenzene followed by a simple recrystallisation step.

INTRODUCTION

Ligands of the so-called “pincer” class (**A**: figure) have been receiving considerable attention in recent years due to their ability to stabilise unusual

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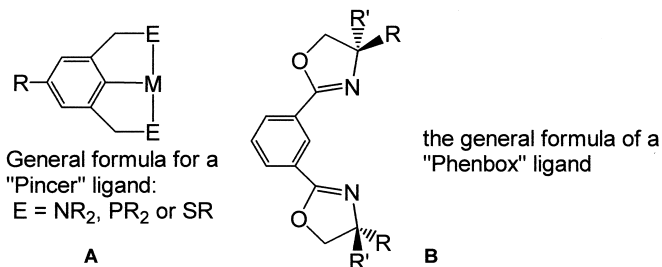


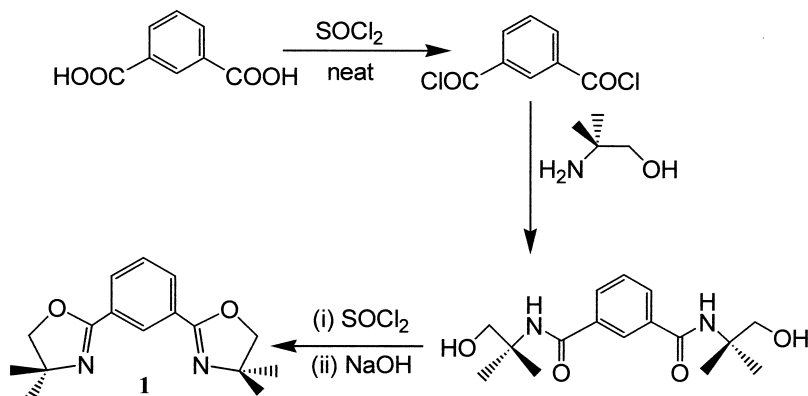
Figure.

metal oxidation states and/or novel ligand bonding motifs.^{1,2} In addition, a variety of organometallic pincer complexes have demonstrated potent reactivity in both regio-^{3,4} and enantio-selective⁵ organic transformations (i.e., catalysis), in addition to applications in materials science.⁶ Oxazoline compounds constitute an important area of natural products chemistry⁷ and in the development of synthetic methodologies,⁸ in addition to their recent applications in crystal engineering^{9a} and functionalised polymers.^{9b} We have been interested in the study of the achiral ligand 1,3-bis-(4,4-dimethyl-2-oxazolinyl)benzene (**1**) as a model for more complex chiral pincer systems containing fragments derived from, for example, Phenbox (ⁱPr) (**B**: R=ⁱPr, R'=H; figure). Specifically, we are investigating the direct metallation^{10,11} and the (organometallic) coordination chemistry of **1**. Complexes incorporating the Phenbox class of ligands, including **1**, have recently found application in coordination chemistry¹² and metal-mediated catalysis.¹³

The original synthesis of **1** involves a four-step procedure and the use of large quantities of thionyl chloride.¹⁰ For environmental, financial and safety reasons, we have designed a "one-pot" procedure that avoids the use of this toxic reagent and can produce large quantities of the desired product (>50 g) in a single-step procedure from cheap commercially available materials.

RESULTS AND DISCUSSION

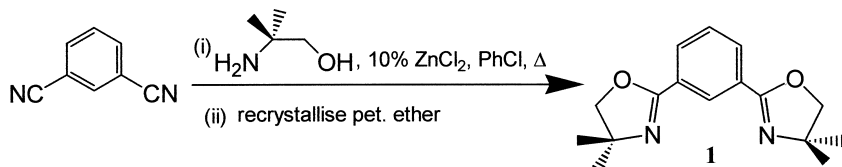
The earlier synthetic protocol for the synthesis of **1** is detailed in Scheme 1. Although this is an effective synthetic method to produce this bis(oxazoline), we desired an alternative method that avoids the use of large quantities of thionyl chloride but at the same time gives high yields of **1** without the need for chromatographic purification nor complicated work-up procedures. In addition, we have found that the method outlined



Scheme 1.

in Scheme 1 makes for a difficult and tedious isolation of the final *solid* product, probably due to the resulting oil retaining some SOCl_2 following the cyclisation step.

Using the methodology¹⁴ described by Peer et al., we have found that anhydrous zinc dichloride^{14,15} is an effective Lewis acid catalyst for the large-scale production of **1** starting from commercially available 1,3-dicyanobenzene and 2-methyl-2-amino-1-propanol (Scheme 2). In a typical procedure, 38.5 g of 1,3-dicyanobenzene (0.30 mol; Sigma-Aldrich, 97%) and 2-methyl-2-amino-1-propanol (59.0 g; 0.63 mol; 2.1 equiv., Sigma-Aldrich) was placed in a round-bottomed flask and dissolved in chlorobenzene (350 mL; pre-dried by storage over 4 Å molecular sieves). To this mixture was added anhydrous ZnCl_2 (5.0 g, 10 mol%; Fisher, melted thrice under vacuum [15 mmHg] and cooled under Ar). The resulting suspension was heated at reflux for a period of 48 h under an atmosphere of dry Ar, during which time a pink colouration was noted in the reaction vessel. The flask was cooled to room temperature and all volatile components



Scheme 2.

were removed *in vacuo* (25 mmHg; -75°C). The residue was extracted with 150 mL of dichloromethane and 150 mL of distilled water. The two layers were then separated and the inorganic portion was then extracted with further dichloromethane (2×100 mL). The organic fractions were then combined, dried with excess anhydrous Na_2SO_4 , filtered and the solvent removed by rotary evaporation. The resulting viscous oil was dissolved in approximately 100 mL of hot petroleum ether (bp $65\text{--}70^{\circ}\text{C}$) and the mixture cooled to -30°C for 14 h. A copious quantity of an off-white solid precipitated from the solution. This material was removed by filtration, washed with cold petroleum ether (-20 mL) and the *product* was then dried *in vacuo* (yield: 65.4 g, 81%). The compound isolated in this way is suitable for further synthetic use (purity $> 97\%$: NMR) and has virtually identical properties to a sample obtained by the previously reported method.^{13,16} In conclusion, we have presented an effective synthesis of 1,3-bis-(4,4-dimethyl-2-oxazoliny)benzene that can be performed easily and on a large scale without the use of hazardous thionyl chloride nor chromatographic separation.

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16. Analytical and spectroscopic data for **1**: mp (uncorrected): 75–78°C; IR (NaCl): 1650 cm⁻¹ [$\nu(\text{C}=\text{N})$]; ¹H NMR (300 MHz, CDCl₃/TMS, ppm): δ = 8.45 (s, 1H, ArH), 8.02 (d, J = 9.5 Hz, 2H, ArH), 7.40 (t, 1H, ArH), 4.07 (s, 4H), 1.34 (s, 12H) [lit.¹³ mp 78–80°C; IR (CHCl₃): 1650 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ = 8.47 (s), 8.02 (d, J = 7 Hz), 7.40 (t), 4.07 (s), 1.33 (s)].

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