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Editor's Choice paper

# Supporting multiple organometallic catalysts on poly(norbornene) for cyanide addition to α,β-unsaturated imides

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ABSTRACT

A two-catalyst system comprising of salen(AlCl) and pybox($ErCl_3$) complexes supported onto poly(norbornene) has been developed. As a proof of concept the activity of the two-catalyst system was gauged for the addition of cyanide to α,β-unsaturated imides which has been shown to follow a bimetallic mechanism. The activity of the supported two-catalyst system was significantly higher than catalytic systems derived from mixtures of the two catalysts. In addition, the co-polymer could be readily recovered and reused up to 3 cycles without significant loss in conversions and yields. Nevertheless, a decrease in enantioselectivity of the cyanide adduct was observed with each subsequent cycle indicating some loss in catalytic selectivity. The reported strategy opens up avenues for supporting multiple catalysts on the same polymer backbone for catalyst-based one-pot cascade reactions.



## 1. Introduction

A rapidly emerging area in salen catalysis involves the immobilization of salen catalysts onto polymers [1–4]. Supported catalysts can be removed readily from reaction mixtures and often recycled resulting in higher turn over numbers as well as lower metallic waste disposal for these catalysts as compared to their unsupported analogs. We have demonstrated that a flexible polymer backbone enhances the activity of salen catalysts for reactions involving a bimetallic transition state such as the hydrolytic kinetic resolution of epoxides or the cyanide addition to α,β-unsaturated imides [1,5–9]. We hypothesize that the flexible backbone enhances the local catalyst concentration thereby improving the catalytic activity of transformations that have bimetallic transition state. There are, however, no examples where multiple catalysts that work together in a bimetallic transition state have been supported onto the same polymer backbone. In this contribution, we realize such a goal by extending our expertise in supported salen catalysis and norbornene chemistry by immobilizing two catalysts onto poly(norbornene) using highly functional group tolerant ring-opening metathesis polymerization (ROMP) [10,11]. Furthermore, we investigate the catalytic activity of the resulting catalyst system and compare it to its non-supported analogues.

An ideal reaction to evaluate our multiple supported catalyst system is the conjugate addition of cyanide to α,β-unsaturated imides since it has been reported that a combination of salen(AlCl) and pybox($ErCl_3$) complexes works superior to each individual complex for the reaction catalysis [12,13]. Poly(norbornene) was chosen as the support since norbornene monomers can be polymerized in a highly controlled and often living fashion using functional group tolerant ring-opening metathesis polymerization (ROMP). Furthermore, we have demonstrated that poly(norbornene) enhances the catalytic activity of salen(AlCl) for the cyanide addition reaction making poly(norbornene)-supported salen (AlCl) catalysts ideal candidates for our study [8]. The basic target copolymer **1** consisting of poly(norbornene) that supports salen(AlCl) and pybox($ErCl_3$) complexes is shown in Fig. 1.

## 2. Experimental

### 2.1. General

All starting materials were obtained from commercial suppliers and used without further purification unless otherwise stated. All air- or moisture-sensitive reactions were performed using oven-dried or flame-dried glassware under an inert atmosphere of dry argon or nitrogen. Air- or moisture-sensitive liquids and solutions were transferred *via* syringe or cannula. Dichloromethane and acetonitrile were distilled from calcium hydride, acetone from potassium carbonate, toluene from sodium, and 2-propanol from calcium sulfate. Thionyl chloride was distilled prior to use. *Caution*: Trimethylsilyl cyanide and hydrogen cyanide are highly toxic

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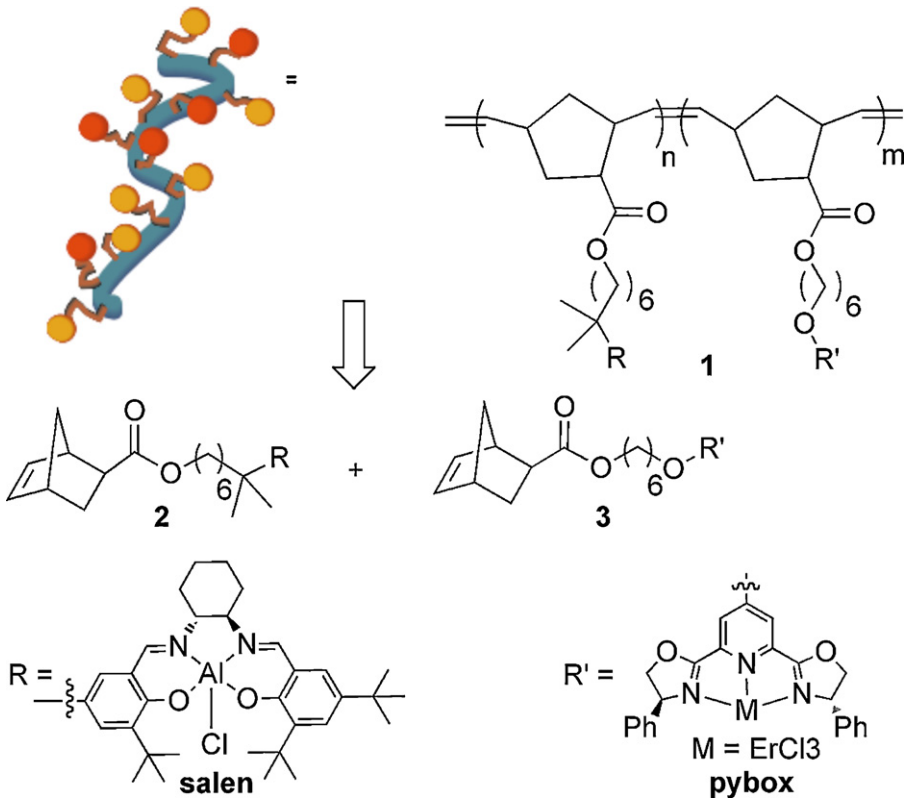



**Fig. 1.** Representation of the poly(norbornene) supported salen(AlCl) and pybox($ErCl_3$) catalyst.

and should be handled extremely carefully in a fume hood as per the experimental protocol mentioned below. Analytical thin layer chromatography (TLC) was performed using Silica XHL pre-coated (250 μm thickness) glass backed TLC plates from Sorbent Technologies. Eluting solvents are reported as volume ratios or volume percents. Compounds were visualized using UV light, potassium permanganate, *p*-anisaldehyde or iodine stains. Flash column chromatography was performed using silica gel 60 Å (230–400 mesh). All $^1H$ and $^{13}C$ NMR spectra were recorded on Varian Mercury Vx 300 or Varian Mercury Vx 400 spectrometers using $CDCl_3$ as the solvent. Chemical shifts are expressed in parts per million ($\delta$), coupling constants ($J$) are reported in Hertz (Hz), and splitting patterns are reported as singlet (s), doublet (d), triplet (t), quartet (q), unresolved multiplet (m), and apparent (app). All NMR spectra are referenced to residual solvent peaks as the standard with $\delta$ values of 7.26 ppm for $CDCl_3$. High-resolution mass spectra were obtained from the Georgia Institute of Technology mass spectrometry lab. Chiral HPLC analyses were performed on a Shimadzu-10A system, using Pirkle-L-Leucine column from Regis Technologies, Inc.

### 2.2. Pyridyl benzyl ether 5 [14]

Pyridyl diester **4** [15] (2.62 g, 0.012 mol, 1 equiv.) and acetone (50 mL) were added to a flame dried 100 mL Schlenk flask equipped with a stir bar and a reflux condenser under an atmosphere of Ar. Subsequently, benzyl bromide (4.28 g, 0.025 mol, 2.1 equiv.) and potassium carbonate (3.40 g, 0.025 mol, 2.1 equiv.) were added to the flask. The reaction mixture was heated under reflux for 19 h under an atmosphere of Ar, following which the reaction mixture was cooled and filtered. The filtrate was concentrated *in vacuo* to afford a yellow oil, which was dissolved in $CH_2Cl_2$ (200 mL). The resultant solution was washed with water (2 × 100 mL), saturated NaCl solution (100 mL), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo* to afford an oily residue. The residue was recrystallized with ethyl acetate (8 mL) to afford 3.54 g (90%) of ether **5** as a white solid. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ = 7.85 (s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (m, 5H, $H_{Ar(Bn)}$), 5.20 (s, 2H, $CH_{2(Bn)}$), 4.45 (q, 4H, $J$ = 7.2 Hz, $OCH_2CH_3$); 1.44 (t, 6H, $J$ = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ = 166.8, 164.9, 150.5, 134.9, 129.1, 129.0, 128.0, 114.8, 71.0, 62.6, 14.4; HRMS (FAB) calcd. for $C_{18}H_{20}NO_5$ ($MH^+$) 330.1342, found 330.1352.

### 2.3. Diacid chloride 6 [14]

Pyridyl benzyl ether **5** (2.35 g, 0.007 mol, 1 equiv.), ethanol (56 mL) and potassium hydroxide (1.40 g, 0.03 mol, 3.5 equiv.) were added to a 100 mL round-bottomed flask equipped with a stir bar. The reaction mixture was heated to 50 °C and allowed to stir for 45 min. Subsequently, the reaction mixture was cooled to room temperature and filtered. The precipitate was washed with cold ethanol to afford 2.40 g (98%) of the pyridyl dicarboxylic dipotassium salt as a white solid. The dipotassium salt (2.50 g, 7.1 mmol, 1 equiv.) was then added in portions over 1 h to a solution of thionyl chloride (7.80 mL, 105 mmol, 14.8 equiv.) in toluene (16 mL) in a 100 mL Schlenk flask. After the addition of the salt was complete, the reaction mixture was heated under reflux for 4.5 h under an atmosphere of Ar, following which the reaction was concentrated under vacuum to afford a white residue. To the residue $CH_2Cl_2$ (300 mL) was added and the resultant solution was filtered. The filtrate was concentrated *in vacuo* to afford a white residue which was recrystallized from hexane (30 mL) to afford 1.60 g (73%) of the diacid chloride **6** as a white solid. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ = 7.87 (s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (m, 5H, $H_{Ar(Bn)}$), 5.26 (s, 2H, $CH_{2(Bn)}$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ = 169.8, 167.4, 150.8, 134.1, 129.4, 129.3, 128.01, 115.9, 71.7.

### 2.4. Pyridyl diamide 7

*R*-phenyl glycinol (1.10 g, 7.8 mmol, 2.2 equiv.), $CH_2Cl_2$ (10 mL) and triethylamine (2.90 mL, 21 mmol, 6 equiv.) were added to a 100 mL Schlenk flask equipped with a magnetic stir bar under an atmosphere of Ar. The solution was cooled to 0 °C and a solution of the diacid chloride **6** (1.10 g, 3.5 mmol, 1 equiv.) in $CH_2Cl_2$ (13 mL) was slowly added to it over a period of 30 min. After the addition was complete, the reaction mixture was warmed to room temperature and allowed to stir for 24 h, following which thionyl chloride (2.60 mL, 35 mmol, 10 equiv.) was added to the solution. The reaction mixture was heated under reflux for 3 h and subsequently poured into ice water (100 mL). The organic layer was separated and washed with saturated NaCl solution (100 mL), 0.1 M aqueous potassium carbonate (300 mL), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo* to afford an oily residue. The residue was subjected to flash column chromatography ($CH_2Cl_2$) to afford 980 mg of the hydrochloride salt of the product as an off-white solid. The solid was stirred with 5% aqueous NaOH (9 mL) in methanol (27 mL) for 24 h, following which $CH_2Cl_2$ was added. The organic layer was separated, dried over magnesium sulfate, filtered and concentrated to afford 883 mg (46%) of the neutralized product **7**. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 8.64 (d, 2H, $J$ = 8.2 Hz, CONH), 7.92 (s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (m, 15H, $H_{Ar(Bn)}$, $H_{Ar(Ph)}$), 5.55–5.45 (m, 2H, NHCHPh), 5.15 (d, 2H, $J$ = 4 Hz, $CH_{2(Bn)}$), 4.05–3.88 (m, 4H, $CH_2Cl$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 168.0, 163.1, 150.6, 138.5, 135.0, 129.1, 129.0, 128.9, 128.5, 127.9, 126.8, 112.2, 70.9, 53.8, 48.6; HRMS (FAB) calcd. for $C_{30}H_{28}N_3O_3Cl_2$ ($MH^+$) 548.1508, found 548.1467.

### 2.5. Pyridyl diamide OH 8

A solution of benzylated diamide **7** (320 mg, 0.583 mmol, 1 equiv.) in ethyl acetate (45 mL) and methanol (15 mL) and 10% palladium on carbon (ca. 100 mg) were added to a 100 mL round-bottomed flask equipped with a magnetic stir bar. A hydrogen balloon was added to the flask and the reaction mixture was stirred for 18 h in an atmosphere of hydrogen. Subsequently, the reaction mixture was filtered through a pad of celite. The celite was rinsed with ethyl acetate (50 mL) and the combined filtrates were concentrated *in vacuo* to afford 265 mg (99%) of the pure product as a white solid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 9.34 (br s, 1H, OH), 8.64 (d, 2H, $J$ = 8.2 Hz, CONH), 7.99 (s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (m, 10H, $H_{Ar(Ph)}$), 5.55–5.45 (m, 2H, NHCHPh), 4.05–3.88 (m, 4 H, $CH_2Cl$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 167.2, 163.5, 150.2, 138.2, 129.2, 128.6, 126.8, 113.7, 54.0, 48.7; HRMS ($ESI^+$) calcd. for $C_{23}H_{22}N_3O_3Cl_2$ ($MH^+$) 458.1033, found 458.1075.

### 2.6. Norbornene ester 9 [11]

Norbornene exo-acid (500 mg, 3.62 mmol, 1 equiv.) and $CH_2Cl_2$ (30 mL) were added to a 100 mL round-bottomed flask equipped with a magnetic stir bar and a reflux condenser. To the solution, DCC (747 mg, 3.62 mmol, 1 equiv.), 6-bromo hexanol (474 μL, 3.62 mmol, 1 equiv.), and DMAP (catalytic) were added. The reaction mixture was heated under reflux for 16 h under an atmosphere of Ar, following which the reaction mixture was diluted with $CH_2Cl_2$ and filtered. The filtrate was dried over magnesium sulfate, filtered and concentrated *in vacuo* to afford an oil. The crude mixture was purified by flash column chromatography (20:1, hexane/EtOAc) to afford 880 mg (81%) of the ester **9** as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 6.15–6.05 (m, 2H, $CH=CH_{(nb)}$), 4.08 (t, 2H, $J$ = 6.6 Hz, $OCOCH_2$), 3.40 (t, 2H, $J$ = 7.1 Hz, $CH_2Br$), 3.10 (br s, 1H, $CH_{(nb)}$), 2.91 (br s, 1H, $CH_{(nb)}$), 2.21 (m, 1H, $CH_{(nb)}$), 1.95–1.80 (m, 3H, $CH_{2(alk)}$, $CH_{(nb)}$), 1.65 (m, 2 H, $CH_{2(alk)}$), 1.54–1.33 (m, 7H, $CH_{2(alk)}$, $CH_{(nb)}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 176.5, 138.2, 136.0, 64.5, 46.8, 46.6, 43.4, 41.9, 33.9, 32.8, 30.5, 28.7, 28.0, 25.4; HRMS (FAB) calcd. for $C_{14}H_{22}O_2Br$ ($MH^+$) 301.0803, found 301.0825.

### 2.7. Non-metallated pybox monomer 10

Norbornene ester **9** (477 mg, 1.58 mmol, 2.5 equiv.), potassium carbonate (218 mg, 1.58 mmol, 2.5 equiv.) and anhydrous DMF (5 mL) were added to a Schlenk flask (25 mL) equipped with a magnetic stir bar and an addition funnel. A solution of **8** (290 mg, 0.633 mmol, 1 equiv.) in anhydrous DMF (3 mL) was added slowly to the reaction mixture at room temperature *via* the addition funnel over 1 h. Upon completion of the addition, the reaction mixture was heated to 60 °C and allowed to stir for 48 h, following which DMF was removed *in vacuo* to give a yellow oily residue. $CH_2Cl_2$ (20 mL) and water (20 mL) were added to the residue and the organic layer was separated. The aqueous layer was subjected to extractions with $CH_2Cl_2$ (2 × 50 mL) and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo* to afford an oily residue. The crude mixture was purified by flash column chromatography (Gradient elution: $CH_2Cl_2$ → 3:1 $CH_2Cl_2$/EtOAc) to afford 247 mg (64%) of the monomer **10** as an oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 7.99 (s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (m, 10H, $H_{Ar(Ph)}$), 6.15–6.05 (m, 2H, $CH=CH_{(nb)}$), 5.44 (dd, 2H, $J$ = 10.5, 2 Hz, CHPh), 4.92 (t, 2H, $J$ = 8.7 Hz, $CH_{2(linker)}$), 4.41 (t, 2H, $J$ = 8.8 Hz, $CH_{2(linker)}$), 4.15–4.04 (m, 6H, $CH_{2(linker)}$, $CH_{2(pybox)}$), 3.00 (br s, 1H, $CH_{(nb)}$), 2.91 (br s, 1H, $CH_{(nb)}$), 2.24–2.17 (m, 1H, $CH_{(nb)}$), 1.90–1.70 (m, 3H, $CH_{2(linker)}$, $CH_{(nb)}$), 1.72–1.60 (m, 2H, $CH_{2(linker)}$), 1.54–1.30 (m, 7H, $CH_{2(linker)}$, $CH_{(nb)}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 176.7, 166.4, 163.8, 148.4, 142.0, 138.3, 136.1, 129.1, 128.2, 126.8, 113.1, 75.7, 70.5, 68.8, 64.7, 62.9, 47.0, 46.8, 43.6, 42.1, 33.1, 30.7, 29.3, 25.9; HRMS ($ESI^+$) calcd. for $C_{37}H_{40}N_3O_5$ ($MH^+$) 606.2962, found 606.2982.

### 2.8. Metallated pybox monomer 3

Monomer **10** (200 mg, 0.330 mmol, 1 equiv.), erbium chloride (90 mg, 0.33 mmol, 1 equiv.) and acetonitrile (15 mL) were added to a Schlenk flask (25 mL) equipped with a magnetic stir-bar. The reaction mixture was stirred at room temperature under an atmosphere of Ar for 2.5 h. The solvent was removed *in vacuo* to afford 286 mg (99%) of the metallated monomer **3** as an off-white solid. Since Er is paramagnetic the complex could not be characterized by NMR spectroscopy. Anal. calcd. for $C_{37}H_{39}N_3O_5ErCl_3$: C, 50.54; H, 4.47; N, 4.78; Er, 19.02; found: C, 46.48; H, 4.83; N, 4.67; Er, 18.9.

### 2.9. Catalyst 1

A solution of pybox monomer **3** (40 mg, 0.045 mmol, 10 equiv.) and salen monomer **2** [8] (37 mg, 0.045 mmol, 10 equiv.) in deoxygenated $CH_2Cl_2$ (2 mL) was added to a scintillation vial (20 mL). Subsequently, a solution of Grubbs 3rd generation initiator (4 mg, 0.005 mmol, 1 equiv.) in deoxygenated $CH_2Cl_2$ (1.5 mL) was added to the vial. The reaction mixture was stirred for 1 h at room temperature, following which 5 drops of ethyl vinyl ether was added to quench the polymerization. The reaction mixture was concentrated to 2 mL, the polymer was precipitated using diethyl ether and isolated *via* centrifugation. The process of precipitation and centrifugation was repeated three times to afford 71 mg (92%) of catalyst **1** as an off-white solid. Anal. calcd. for $C_{86}H_{109}N_5O_9ErAlCl_4$: C, 61.02; H, 6.49; N, 4.14; Er, 9.88; Al, 1.59; found: C, 56.43; H, 6.37; N, 4.91; Er, 9.93; Al, 1.9.

### 2.10. Catalyst precursor 11

A solution of pybox monomer **10** (70 mg, 0.116 mmol, 25 equiv.) and salen monomer **2** [8] (94 mg, 0.116 mmol, 25 equiv.) in deoxy-

genated $CH_2Cl_2$ (6 mL) was added to a scintillation vial (20 mL). Subsequently, a solution of Grubbs 3rd generation initiator (4 mg, 0.005 mmol, 1 equiv.) in deoxygenated $CH_2Cl_2$ (3 mL) was added to the vial. The reaction mixture was stirred for 1 h at room temperature, following which 5 drops of ethyl vinyl ether was added to quench the polymerization. The reaction mixture was concentrated to 3 mL, the polymer was precipitated using diethyl ether and isolated *via* centrifugation. The process of precipitation and centrifugation was repeated three times to afford 114 mg (70%) of catalyst precursor **11** as a pale yellow solid. The precursor is insoluble in most organic solvents and could not be characterized by NMR spectroscopy.

### 2.11. Small molecule pybox 16

Tetrahydrofuran (10 mL) and 60% sodium hydride in oil (187 mg, 4.68 mmol, 2.7 equiv.) were added to a Schlenk flask (50 mL) immersed in an ice bath at 0 °C. A solution of benzylated dimide **7** (950 mg, 1.73 mmol, 1 equiv.) in THF (12 mL) was added slowly to the reaction mixture. The reaction mixture was stirred at 0 °C for 1.5 h, following which the insoluble residue was removed by filtration. The filtrate was concentrated *in vacuo* to afford a residue to which diethyl ether (9 × 100 mL) was added. The suspension was triturated and filtered. The combined filtrates were concentrated *in vacuo* to afford a mixture of pybox **16** and diimide **7** (1:0.2). Since the crude mixture decomposed in the presence of silica or alumina, the mixture was resubjected to the reaction conditions to ensure complete conversion of diimide **7** to pybox **16**. After reaction work-up as described above 600 mg (73%) of pybox **16** was obtained as an off-white solid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 7.95 (s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (m, 15H, $H_{Ar(Bn)}$, $H_{Ar(Ph)}$), 5.45 (dd, 2H, $J$ = 10.5, 1.7 Hz C*H*Ph), 5.15 (s, 2H, $J$ = 4 Hz, $CH_{2(Bn)}$), 4.92 (dd, 2H, $J$ = 10.6, 1.7 Hz, C*H*H$_{(pybox)}$), 4.41 (app t, 2H, $J$ = 8.7 Hz, C*H*H$_{(pybox)}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 166.0, 163.8, 148.5, 141.9, 135.3, 129.1, 129.0, 128.7, 128.1, 127.8, 127.1, 113.3, 75.8, 70.8, 70.5; HRMS (ESI$^+$) calcd. for $C_{30}H_{26}N_3O_3$ ($MH^+$) 476.1969, found 476.1924.

### 2.12. Homopolymer pybox 12

A solution of pybox monomer **10** (70 mg, 0.116 mmol, 50 equiv.) in deoxygenated $CH_2Cl_2$ (2.5 mL) was added to a scintillation vial (20 mL). Subsequently, a solution of Grubbs 3rd generation initiator (2 mg, 0.002 mmol, 1 equiv.) in deoxygenated $CH_2Cl_2$ (2 mL) was added to the vial. The reaction mixture was stirred for 1.5 h at room temperature, following which 5 drops of ethyl vinyl ether was added to quench the polymerization. The reaction mixture was concentrated to 1 mL, the polymer was precipitated using diethyl ether and isolated *via* centrifugation. The process of precipitation and centrifugation was repeated three times to afford 64 mg (91%) of pybox homopolymer **12** as an off-white solid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 7.8 (br s, 2H, $H_{Ar(pyr)}$), 7.50–7.30 (br m, 10H, $H_{Ar(Ph)}$), 5.41 (br t, 2H, $J$ = 9.52 Hz, C*H*Ph), 5.40–5.10 (br m, 2H, C*H* = C*H*$_{(pnb)}$), 4.88 (br t, 2H, $J$ = 8.9 Hz, $CH_{2(linker)}$), 4.37 (br t, 2H, $J$ = 8.2 Hz, $CH_{2(linker)}$), 4.15–4.04 (br m, 6H, $CH_{2(linker)}$, $CH_{2(pybox)}$), 3.10–2.90 (overlapping br s, 2H, $CH_{(pnb)}$), 2.7–1.7 (br m, 6H, $CH_{2(linker)}$, $CH_{(pnb)}$), 1.60–1.20 (br m, 7H, $CH_{2(linker)}$, $CH_{(nb)}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 176.7, 166.4, 163.8, 148.3, 141.9, 129.1, 128.7, 128.0, 127.1, 126.6, 113.0, 75.8, 70.4, 68.9, 66.1, 64.5, 42 (overlapping signals), 37 (overlapping signals), 32.4, 28.9, 28.5, 25.9, 25.8, 25.7.

### 2.13. General procedure for catalytic studies with $ErCl_3$ complex generated in situ (Table 1)

The appropriate quantity of pybox precursor (**16**, **12** or **11**), $ErCl_3$ (1 equiv. with respect to pybox) and acetonitrile (250 μL) were added to a Schlenk tube (50 mL) equipped with a magnetic stir-bar. The suspension was stirred at room temperature in an atmosphere of Ar for 1.5 h, following which the solvent was removed *in vacuo* to afford the pybox/$ErCl_3$ catalyst. An appropriate amount of the salen catalyst (if required) was added to the Schlenk tube. The catalyst mixture was dried azeotropically with toluene (2 × 50 μL). Subsequently, the imide **13** (50 mg, 0.26 mmol, 1 equiv.), toluene (80 μL) and TMSCN (132 μL, 1.06 mmol, 4 equiv.) were added to the tube. The reaction mixture was heated gently with a heat gun, immersed in an oil bath at 45 °C and isopropanol was added (81 μL, 1.06 mmol, 4 equiv.). The flask was sealed and allowed to stir for 18 h, following which the reaction mixture was vented into a $FeSO_4$ solution to quench any un-reacted hydrogen cyanide. After allowing the HCN to bubble out for 10–15 min, the solvent was removed *in vacuo* to afford the crude cyanide adduct **14** which was purified by flash column chromatography.

### 2.14. General procedure for cyanide addition reaction using catalyst 1 (Table 2) and recycling studies

Catalyst **1** (22.4 mg, 0.013 mmol, 0.05 equiv.) was added to a Schlenk tube (50 mL) equipped with a magnetic stir bar. The catalyst was dried azeotropically with toluene (2 × 50 μL). Subsequently, the imide **13** (50 mg, 0.26 mmol, 1 equiv.), toluene (80 μL) and TMSCN (132 μL, 1.06 mmol, 4 equiv.) were added to the tube. The reaction mixture was heated gently with a heat gun, immersed in an oil bath at 45 °C and isopropanol was added (81 μL, 1.06 mmol, 4 equiv.). The flask was sealed and allowed to stir for 18 h, following which the reaction mixture was vented into a $FeSO_4$ solution to quench any un-reacted hydrogen cyanide. After allowing the HCN to bubble out for 10–15 min, the solvent was removed *in vacuo*. Ethyl acetate (4 × 20 mL) was added to extract the crude cyanide adduct **14**, while the catalyst **1** precipitated from the solution. The combined supernatant solutions were concentrated to afford the crude cyanide adduct **14** which was purified by flash column chromatography. The residue comprised catalyst **1** which was dried under vacuum and used for subsequent catalytic cycles.

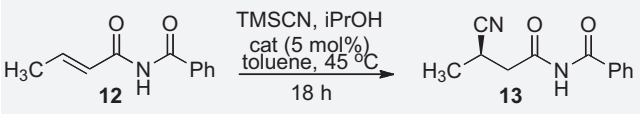
### 2.15. N-[3-(S)-cyano-butyryl]-benzamide 14

[$^1$H] NMR (300 MHz, $CDCl_3$) $\delta$ = 8.88 (s, 1H, N*H*), 7.89 (dd, 2H, $J$ = 8.0 Hz, $J$ = 1.5 Hz, $H_{Ar}$), 7.64 (t, 1H, $J$ = 7 Hz, $H_{Ar}$), 7.54 (t, 2H, $J$ = 6.3 Hz, $H_{Ar}$), 3.47 (dd, 1H, $J$ = 17.2 Hz, $J$ = 7 Hz, C*H*CN), 3.31 (m, 1H CNCHCH*H*); 3.2 (m, 1H, NCCHC*H*H), 1.45 (d, 3H, $J$ = 7.3 Hz, $CH_3$). Enantioselectivities were determined using HPLC with a chiral Pirkle-L-Leucine column with 5% ethanol in hexane as the eluant (0.7 mL min$^{-1}$) and the detector set at 254 nm.

### 2.16. Procedure for the kinetics studies with 5 mol% loading of catalyst 1

The addition reaction was divided into four NMR tubes. In each tube the catalyst (3 mg, 0.002 mmol, 0.05 equiv.), imide substrate 13 (7.6 mg. 0.04 mmol, 1 equiv.) and toluene (4 μL) were added. The NMR tube was sealed with a septum and TMSCN (20 μL, 0.16 mmol, 4 equiv.) and 2-propanol (12 μL, 0.16 mmol, 4 equiv.) were added. The reaction was heated to 45 °C and quenched at the appropriate time by adding $CDCl_3$ (200 μL). 1,1,2,2-Tetrachloroethane (0.0075 mmol) in $CDCl_3$ (100 μL) was added to the NMR tube as an internal standard. The NMR tube was agitated in an ultrasound bath and filtered through a pad of silica to remove the catalyst. The silica was rinsed with (400 μL) of $CDCl_3$ and the combined filtrates were analyzed by $^1$H NMR to determine the amount of product 13 found (data shown in Fig. S1 in supporting information).

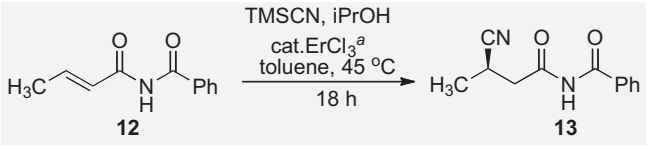
**Table 1**
Comparison of the activity of catalyst **11**-$ErCl_3$ with other salen(AlCl) and pybox($ErCl_3$) mixtures for cyanide addition.




| No. | Cat. | Conversion[a] (yield)[b] | ee[c] |
|---|---|---|---|
| 1 | **1** | 98 (88) | 80 |
| 2 | Cycle 2 | 98 (86) | 57 |
| 3 | Cycle 3 | 95 (80) | 51 |

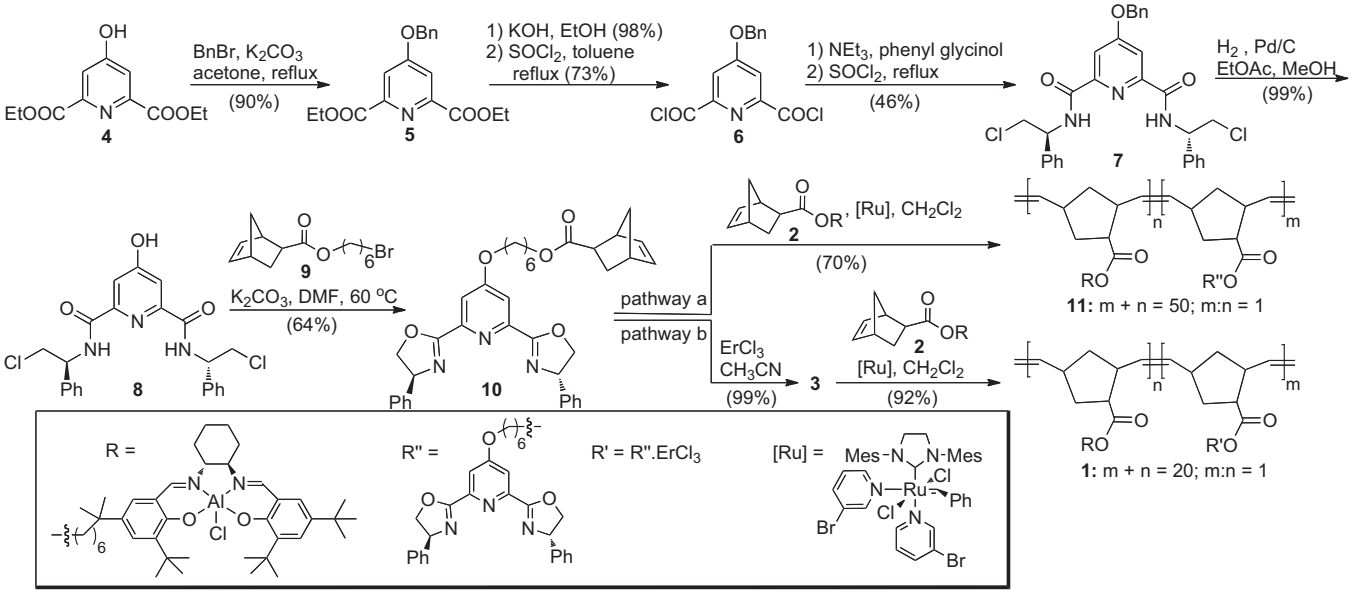
[a] Complex generated *in situ*.
[b] Isolated yield.
[c] Determined by HPLC analyses using a chiral Pirkle-L-leucine column.

**Table 2**
Catalysis and reusability studies of catalyst **1**.




| No. | Cat. (conc.) | Yield[b] (ee)[c] |
|---|---|---|
| 1 | **14** (2 mol%) + **15** (3 mol%) | 25 (59) |
| 2 | **14** (2 mol%) + **16** (3 mol%) | 7 (72) |
| 3 | **11** (5 mol%) | 70 (84) |

[a] Determined by NMR.
[b] Isolated.
[c] Determined by HPLC analysis using a Chiral Pirkle-L-Leucine column.




**Scheme 1.** Synthesis of poly(norbornene)-supported salen(AlCl) and pybox($ErCl_3$) catalysts.

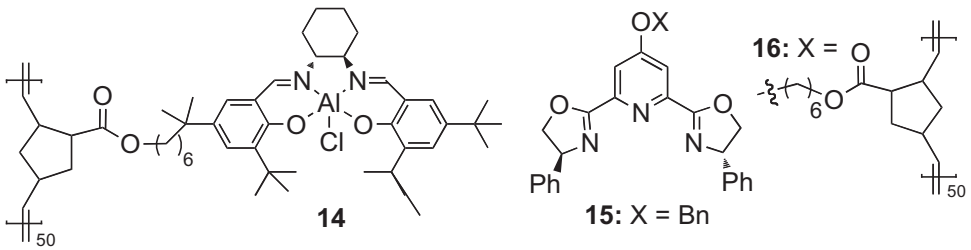



**Fig. 2.** Catalysts used for the cyanide addition.

## 3. Results and discussion

The synthesis of catalyst **1** can be envisioned by copolymerizing the *R*-salen monomer **2** and the *R*-pybox monomer **3**. Linkers comprised of seven carbon atoms were chosen for both monomers as we have demonstrated before that this is the preferred length for facilitating bimetallic reactions using poly(norbornene)-supported salen catalysts [5,9]. The *R*-salen monomer **2** was synthesized as described earlier [8]. The pybox monomer **3** was synthesized in several steps from the diester **4** as described in Scheme 1 [15]. The hydroxyl group of **4** is reacted with benzyl bromide and potassium carbonate to afford the ether **5** in 90% yield. The diesters in **5** are then hydrolyzed using potassium hydroxide and ethanol and subsequently treated under reflux with thionyl chloride to form the diacid chloride **6** in 73% yield [14]. Acid chloride **6** is then treated with *R*-phenyl glycinol and triethyl amine at room temperature for 24 h, followed by the reaction with thionyl chloride to afford the open form **7** of pybox in 46% yield [16]. The benzyl group is removed *via* hydrogenation using palladium on carbon to afford **8** in 99% yield. Treating **8** with norbornene bromide **9** and potassium carbonate leads to etherification of the hydroxyl position as well as the ring-closing of the pybox in one-pot to yield the non-metallated monomer **10** in 64% yield. Since, the Er-pybox complex was generated *in situ* during the catalytic reaction in an earlier report [12], the non-metallated pybox monomer **10** was polymerized with salen monomer **2** using Grubbs' 3rd generation initiator to provide random co-polymer **11** in 70% yield (Scheme 1, pathway a). The resulting co-polymer was not fully soluble in organic solvents presumably due to the co-ordination of Al from the salen to some of the free pybox ligands resulting potentially in crosslinks [17]. Crosslinking of the polymer through co-ordination of Ru from the initiator to multiple pybox ligands was ruled out since the homopolymerization of **10** gave the highly soluble pybox homopolymer **12** which could be readily characterized by NMR spectroscopy. The insolubility of the co-polymer **11** prevented its characterization by NMR spectroscopy as well as gel-permeation chromatography. Therefore, the polymer composition ($m+n$ and $m$:$n$) is based approximately on the monomer/initiator ratios used during polymerization. Despite the limited solubility of the copolymer **11** and the incapability to completely characterize **11** we were interested in examining its catalytic activity before optimizing the synthesis of the catalytic system. Hence, the catalytic activity of **11** was studied for the cyanide addition to α,β-unsaturated imide **13** for the synthesis of cyanide adduct **14**. The erbium complex was generated in the reaction flask by stirring **11** with $ErCl_3$ in acetonitrile and removing the solvents prior to addition of the reagents [12]. The catalytic reaction was carried out in toluene at 45 °C with 5 mol% of the catalyst and the cyanide was generated *in situ* from trimethyl silyl cyanide and isopropanol [18]. The substrate was added and the reaction flask was sealed to prevent cyanide leakage which prevented monitoring of the reaction by thin layer chromatography. Hence, the reaction was carried out for 18 h to ensure completion. In order to gauge the effect of having the two catalysts on the same polymer backbone on catalysis a comparison was made with dual catalyst systems obtained by combining salen homopolymer **15** either with the small molecule pybox **16** or the pybox homopolymer **12**, respectively (Fig. 2).

The catalyst studies (Table 1) indicated that the dual catalyst systems in entries 1 and 2, afforded lower yields and enantioselectivities for the cyanide adduct **14**. The best yield of 70% with an enantioselectivity of 84% was obtained when both catalysts were supported on the same polymer backbone (entry 3). The transition state for the reaction is hypothesized to be bimetallic with the imide co-ordinated to the salen(AlCl) and the cyanide co-ordinated to the pybox [12]. Hence, having the salen(AlCl) on a polymer backbone (entry 1) might lower the accessibility of pybox **16** thereby lowering its interaction with the Al-center in the transition. The effect worsened when the pybox is also supported on a polymer and is alleviated in entry 3 where both catalysts are on the same polymer backbone. This result was intriguing from a mechanistic point of view despite the fact that the catalytic system derived from polymer **11** was less active than our previously reported salen(AlCl) homopolymer [8]. Therefore, we wished to optimize the performance of the dual catalyst system by synthesizing a more soluble variant of polymer **11**.

Since we attributed the lower solubility of polymer **11** to the presence of free pybox, we metallated the ligand prior to polymerization (Scheme 1, pathway b). The metallated monomer **3** was copolymerized with **2** in a 9:9:1 ratio (**3**:**2**:initiator) to afford polymer **1** which was soluble in organic solvents such as dichloromethane. Characterization by GPC was not possible since the highly charged, metal complex-containing polymers did not elute from the GPC columns. Unfortunately, the paramagnetism of Er prevented characterization by NMR spectroscopy. Therefore, elemental analysis was used to characterize polymer **1**. As before the polymer composition was approximately calculated based on the monomer/initiator ratio used for the polymerization.

The catalytic activity of polymer **1** was studied for the above described cyanide addition using the reaction conditions described above and the results are shown in Table 2. A significant improvement in activity was observed with 98% conversion (88% isolated yield) for the formation of **14** (entry 1) with comparable enantioselectivities to **11**. Furthermore, the product could be isolated by extraction into ethyl acetate and decantation. The catalyst remained in the reaction flask and could be used for 3 cycles with no significant losses in conversion (entries 2 and 3). A drop in ee was observed indicating a loss in catalytic selectivity with each subsequent cycle. Since this loss in enantioselectivity was not observed with the salen(AlCl) homopolymer reported earlier by our group, the loss in enantioselectivity might be attributed to the degradation of the chiral pybox ligand [8]. Despite the loss in enantioselectivity the fact that we were able to synthesize a reusable complex two-catalyst system supported onto poly(norbornene) which efficiently catalyzed the cyanide addition reaction is extremely encouraging [19].

## 4. Conclusions

In summary, we have supported salen(AlCl) and pybox($ErCl_3$) onto a single poly(norbornene) backbone in a random fashion. The resulting catalyst system was able to efficiently catalyze the addition of cyanide to α,β-unsaturated imides. Supporting both catalysts on the same polymer backbone enhanced the formation of the cyanide adduct as compared to catalyst systems derived from a mixture of the two catalysts. Furthermore, the random co-polymer **1** could be used for 3 cycles without significant loss in conversions and yields. A loss in enantioselectivity of the cyanide adduct was observed indicating a decrease in the catalytic selectivity over multiple cycles. The fact that we were able to readily support two catalysts onto the same polymer backbone and demonstrate its utility for catalysis paves the way for developing more efficient two catalyst systems or multiple catalyst systems that can be utilized for catalyzing multiple reactions or tandem reactions in a one-pot setting.

## Acknowledgement

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2010.10.023.

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[17] The insolubility of the catalyst made it extremely difficult to characterize it by NMR spectroscopy or Mass spectrometry.
[18] Trimethyl silyl cyanide and hydrogen cyanide are extremely toxic and should be handled carefully in a well-ventilated fume hood.
[19] The kinetics for the cyanide addition catalyzed by **1** was studied using NMR spectroscopy. Data shown in the supplemental information.