# Supplementary Material (ESI) for Dalton Transactions


Supporting Information

# Designing new ligands: asymmetric cyclopropanation by Cu(I) complexes based on functionalised pyridine-containing macrocyclic ligands

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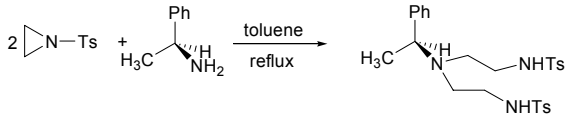
**General.** NMR spectra were recorded on Bruker Avance 300-DRX or Avance 400-DRX spectrometers. Chemical shifts (ppm) are reported relative to TMS. The $^{1}$H NMR signals of the compounds described in the following have been attributed by COSY and NOESY techniques. Assignments of the resonance in $^{13}$C NMR were made using the APT pulse sequence and HSQC and HMBC techniques. The $^{15}$N NMR signals of the compound described have been attributed by HMBC technique. Infrared spectra were recorded on a BIO-RAD FTS-7 spectrophotometer. Elemental

analyses and mass spectra were recorded in the analytical laboratories of Milan University. GC-MS analysis were performed on a Shimadzu GCMS-QP5050A instrument. $[\alpha]_D$ values are given in $10^{-1}$ deg $cm^2$ $g^{-1}$. Unless otherwise specified, all the reactions were carried out in a dinitrogen atmosphere employing standard Schlenk techniques and magnetic stirring. Solvents were dried prior use by standard procedures and stored under dinitrogen. α-Methylstyrene was distilled over $CaH_2$ and stored under dinitrogen. Copper(I) triflate benzene complex, copper(I) tetrakis-acetonitrile esafluorophosphate complex and copper(I) tetrakis-acetonitrile tetrafluoro borate complex were synthesized following literature methods.[1] All other starting materials were commercial products and were used as received.

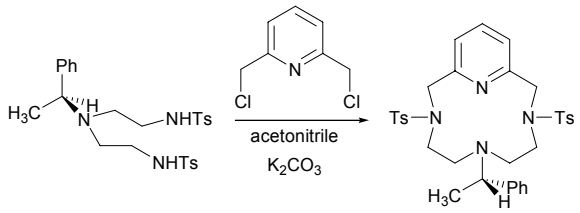
**Synthesis of 1,7-ditosyl-4-[(S)-1-phenylethyl]-1,4,7-triazaheptane**




This synthesis can be performed in the air. A solution of tosyl aziridine (4.707 g, 23.86 mmol) and (S)-α-methyl benzyl amine (1.360 g, 10.85 mmol) in toluene (13 ml) was stirred and heated under reflux for 4 hours. The mixture was dried and purified by chromatographic column on silica using ethyl acetate : hexane = 50:50 as eluant, obtaining a yellow oil (3.987 g, 70%).$^1$H NMR (400 MHz; $CDCl_3$; T = 300 K): $\delta$ 7.72 (4 H, d, $J$ = 8.4 Hz, Ar*H*), 7.34–7.28 (7 H, m, Ar*H*), 7.18–7.16 (2 H, m, Ar*H*), 4.85 (2H, br s, N*H*), 3.73 (1 H, q, $J$ = 6.9 Hz, C*H*), 2.88 (4 H, m, C$H_2$), 2.61 (2 H, m, C$H_2$), 2.43 (6 H, m, C$H_3$), 2.42 (2 H, m, C$H_2$), 1.30 (3 H, d, $J$ = 6.9 Hz, C$H_3$). $^{13}$C NMR (75 MHz; $CDCl_3$; T = 300 K): $\delta$ 143.9, 137.2, 136.7, 130.3, 128.8, 128.4, 127.8, 127.55, 58.8, 50.5, 41.6, 21.9, 21.5.

1,7-ditosyl-4-[(S)-1-phenylethyl]-1,4,7-triazaheptane was synthesized in the same way by employing (R)-α-methyl benzyl amine instead.

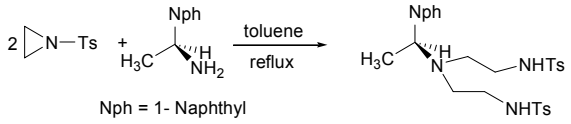
**Synthesis of 6-[(S)-1-phenylethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (1a)**




A solution of 1,7-ditosyl-4-[(S)-1-phenylethyl)]-1,4,7-triazaheptane (3.040 g, 5.505 mmol), bis-chloro methyl pyridine (0.969 g, 5.505 mmol) and micronized anhydrous potassium carbonate (3.043 g, 22.02 mmol) in distilled acetonitrile (30 ml) was stirred and heated under reflux for 11 hours. The mixture was washed with water end extracted with ethyl acetate. The product was then crystallized layering *n*-hexane on a warm solution in ethyl acetate, yielding a white solid (2,460 g, 72%).$^{1}$H NMR (400 MHz; $CDCl_3$; T = 300 K): $\delta$7.78 (1 H, t, *J* = 7.7 Hz, Ar*H*), 7.57 (4 H, d, *J* = 8.1 Hz, Ar*H*), 7.40 (2 H, d, *J* = 7.7 Hz, Ar*H*), 7.34–7.32 (3 H, m, Ar*H*), 7.26 (4 H, d, *J* = 8.1 Hz, Ar*H*), 7.20 (2 H, m, Ar*H*), 4.32 (4 H, m, C$H_2$), 3.58 (1 H, q, *J*= 6.6 Hz, C*H*), 3.13 (2 H, m, C$H_2$), 3.00–2.92 (2 H, m, C$H_2$), 2.44 (6 H, s, C$H_3$), 2.23–2.19 (4 H, m, C$H_2$), 1.24 (3 H, d, *J* = 6.6 Hz, C$H_3$). $^{13}$C NMR (75 MHz; $CDCl_3$; T = 300 K) $\delta$155.3, 145.4, 139.2, 136.2, 130.1, 128.7, 127.6, 127.5, 127.3, 124.6, 61.7, 54.8, 50.1, 45.7, 21.9, 20.5. One signal relative to an aromatic quaternary carbon was not detected. $^{15}$N NMR (40 MHz; $CDCl_3$; T = 300 K): $\delta$ 312 (*N*-Py), 95 (*N*-Ts), 41 (*N*C*). Elemental Analysis: Found: C, 64.0; H, 6.2; N, 9.1% Calc. for $C_{33}H_{38}N_4O_4S_2$: C, 64.05; H, 6.2; N, 9.05%. m/z 619 ($M^+$ 100%), 516 (45). IR $\nu$ ($cm^{-1}$) = 1743.6 (w), 1594.1 (w), 1492.0 (w), 1460.1 (w), 1344.6 (m), 1160.6 (s). $[\alpha]_D^{20}$ = -50 (*c* 1 in $CHCl_3$).

6-[(R)-1-phenylethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (**1a**) was synthesized in the same way. $[\alpha]_D^{20}$ = +50 (*c* 1 in $CHCl_3$).

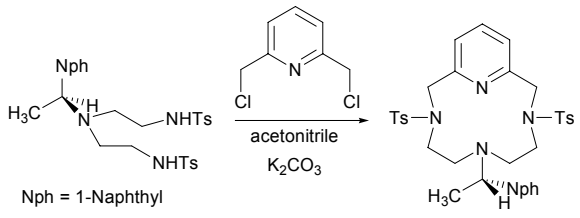
**Synthesis of 1,7-ditosyl-4-[(S)-1-(1-naphthyl)ethyl]-1,4,7-triazaheptane**




This synthesis can be performed in the air. A solution of tosyl aziridine (2.168 g, 10.334 mmol) and (S)-1-(1-naphthyl)ethyl amine (0.851 g, 4.971 mmol) in toluene (9 ml) was stirred and heated under reflux for 10 hours. The mixture was dried and purified by chromatographic column on silica using ethyl acetate : hexane 40:60 as eluant, obtaining a yellow oil (2.534 g, 88%). $^{1}$H NMR (400 MHz; $CDCl_3$; T = 300 K): $\delta$8.36 (1 H, d, *J* = 8.6 Hz, Ar*H*), 7.86 (1 H, d, *J* = 7.5 Hz, Ar*H*), 7.76 (1 H, m, Ar*H*), 7.67 (1 H, m, Ar*H*), 7.54 (1 H, m, Ar*H*), 7.50 (4 H, d, *J* = 8.0, Ar*H*), 7.41–7.40 (2 H, m, Ar*H*), 7.24 (4 H, d, *J* = 8.0, Ar*H*), 4.69 (1 H, q, *J* = 6.7, C*H*), 4.63 (2 H, br s, N*H*), 2.82–2.71 (2 H, m, C$H_2$), 2.69 (4 H, m, C$H_2$), 2.56 (2 H, m, C$H_2$), 2.42 (6 H, s, C$H_3$), 1.46 (3 H, d, *J* = 6.7 Hz, C$H_3$). $^{13}$C NMR (100 MHz; $CDCl_3$; T = 300 K) $\delta$143.2, 138.3, 136.7, 134.9, 133.9, 131.6, 129.7, 128.3, 126.6, 124.2, 57.1, 51.1, 41.8, 21.5, 12.7.

1,7-ditosyl-4-[(R)-1-(1-naphthyl)ethyl]-1,4,7-triazaheptane was synthesized in the same way by employing (R)-1-(1-naphthyl)ethyl amine instead.

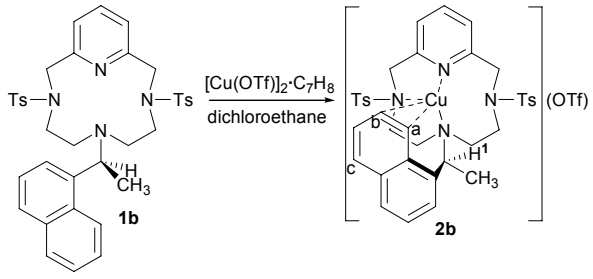
**Synthesis of 6-[(S)-1-(1-naphthyl)ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (1b)**



A solution of 1,7-ditosyl-4-[(S)-1-(1-naphthyl)-ethyl)]-1,4,7-triazaheptane (2.451 g, 4.231 mmol), bis-chloro methyl pyridine (0.745 g, 4.231 mmol) and micronized anhydrous potassium carbonate (2.339 g, 16.92 mmol) in distilled acetonitrile (25 ml) was stirred and heated under reflux for 10 hours. The mixture was washed with water and extracted with ethyl acetate. The product was then crystallized layering hexane over a warm solution in ethyl acetate, yielding a white solid (2.275 g, 80.4%). $^{1}$H NMR (300 MHz; $CDCl_3$; T = 300 K): $\delta$8.16 (1 H, d, *J* = 8.4 Hz, Ar*H*), 7.94 (1 H, d, *J* = 7.5 Hz, Ar*H*), 7.87-7.77 (2 H, m, Ar*H*), 7.56–7.54 (4 H, m, Ar*H*), 7.43 (2 H, d, *J* = 7.5 Hz, Ar*H*), 7.41 (4 H, d, *J* = 8.1 Hz, Ar*H*), 7.13 (4 H, d, *J* = 8.1, Ar*H*), 4.37 (1 H, q, *J* = 6.5 Hz, C*H*), 4.27 (4 H, m, C$H_2$), 3.09 (2 H, m, C$H_2$), 2.82-2.85 (2 H, m, C$H_2$), 2.37 (6 H, s, C$H_3$), 2.28-2.32 (4 H, m, C$H_2$), 1.34 (3 H, d, *J* = 6.5, C$H_3$). $^{13}$C NMR (75 MHz; $CDCl_3$; T = 300 K) $\delta$155.3, 143.6, 140.5, 139.2, 136.0, 134.4, 132.0, 130.0, 129.1, 127.9, 127.4, 126.1, 125.8, 125.7, 124.8, 124.6, 124.5, 58.2, 54.8, 50.2, 45.6, 21.8, 14.5. $^{15}$N NMR (40 MHz; $CDCl_3$; T = 300 K): $\delta$ 313 (*N*-Py), 39 (*N*C*). The signals relative to *N*(Ts) were not detected. Elemental Analysis: Found: C, 66.2; H, 6.2; N, 8.3% Calc. for $C_{37}H_{40}N_4O_4S_2$ : C, 66.4; H, 6.0; N, 8.4%. m/z 669 ($M^+$ 100%). IR ν ($cm^{-1}$) = 1595.1 (w), 1457.7 (w), 1357.0 (w), 1339.8 (s), 1253.4 (w), 1158.0 (s). $[\alpha]_D^{20}$ = -43 (*c* 1 in $CHCl_3$).

6-[(R)-1-(1-naphthyl)ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (**1b**) was synthesized in the same way. $[\alpha]_D^{20}$ = +43 (*c* 1 in $CHCl_3$).

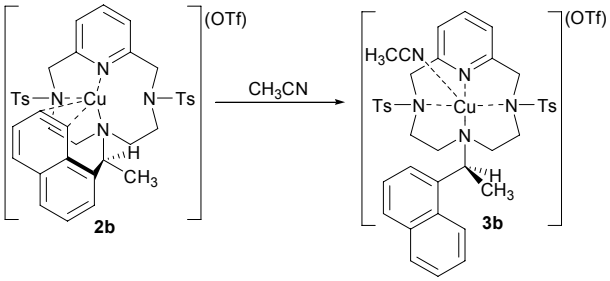
**Synthesis of Cu(OTf) complex of 6-[(S)-1-(1-naphthyl)-ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (2b)**



Copper (I) triflate toluene complex (0.077 g, 0.150 mmol) was added to a solution of **1b** (0.200 g, 0.299 mmol) in dichloroethane (5 ml). The solution was stirred at room temperature for one hour, concentrated at 5 ml and then 10 ml of benzene were layered. After standing at room temperature for 16 h the solid was filtered and dried *in vacuo* under nitrogen (0.259 g, 98%). $^{1}$H NMR (300 MHz; $CDCl_3$; T = 300 K): $\delta$ 8.93 (1 H, d, *J* = 8.1 Hz, Ar*H*$^{a}$), 8.07 (1 H, d, *J* = 8.3 Hz, Ar*H*$^{c}$), 7.92–7.88 (3 H, m, Ar*H*), 7.82–7.74 (2 H, m, Ar*H*), 7.69–7.62 (2 H, m, Ar*H*), 7.53–7.48 (3 H, m, Ar*H*), 7.39–7.36 (3 H, m, Ar*H*), 7.29 (2 H, m, Ar*H*), 7.05 (1 H, d, *J* = 7.5, Ar*H*), 5.59 (1 H, q, *J* = 6.5 Hz, C*H*$^{1}$), 5.31 (1 H, d, *J* = 16.4 Hz, C$H_2$), 4.69 (1 H, m, C$H_2$), 4.35 (1 H, m, C$H_2$), 3.94 (1 H, d, *J* = 16.6 Hz, C$H_2$), 3.18 (1 H, m, C$H_2$), 3.04 (1 H, d, *J* = 14.2 Hz, C$H_2$), 2.88–2.82 (3 H, m, C$H_2$), 2.56 (3 H, s, C$H_3$), 2.42 (3 H, s, $CH_3$), 2.34 (2 H, m, C$H_2$), 2.21 (1 H, d, *J* = 14.2 Hz, C$H_2$), 1.69 (3 H, d, *J* = 6.5 Hz, C$H_3$). $^{13}$C NMR (100 MHz; $CDCl_3$; T = 300 K) $\delta$ 156.2, 152.9, 146.2, 145.9, 140.0, 137.2, 134.1 (*C*$^{c}$), 131.9, 131.5, 130.6, 130.0, 129.2, 128.9, 128.3, 128.2, 126.7, 126.0, 125.2, 124.7, 124.6, 124.1, 118.2 (*C*$^{b}$), 94.2 (*C*$^{a}$), 56.5, 56.1, 53.1 (*C*H$^{1}$), 51.0, 48.9, 45.9, 21.7, 21.5, 12.9. $^{15}$N NMR (40 MHz; $CDCl_3$; T = 300 K): $\delta$ 245 (*N*-Py), 51 (*N*C*). The signal relative to *N*(Ts) were not detected. $^{19}$F NMR (376 MHz; $CDCl_3$; T = 300 K): $\delta$ -78.5. IR $\nu$ (cm$^{-1}$) = 1447.0 (w), 1343.5 (w), 1223.5 (w), 1260.9 (s), 1223.5 (m), 1165.4 (s), 1085.3 (w), 1029.5 (s), 802.6 (w), 759.7 (m), 720.4 (m), 710.0 (m), 660.5 (s), 637.6 (s). Elemental Analysis: Found: C, 51.6; H, 4.9; N, 6.7%; M$^{+}$, 881. Calc. for $C_{38}H_{40}CuF_3N_4O_7S_2$: C, 51.9; H, 4.6; N, 6.4%. $[\alpha]_D^{20}$ = -115 (*c* 0.5 in $CHCl_3$).

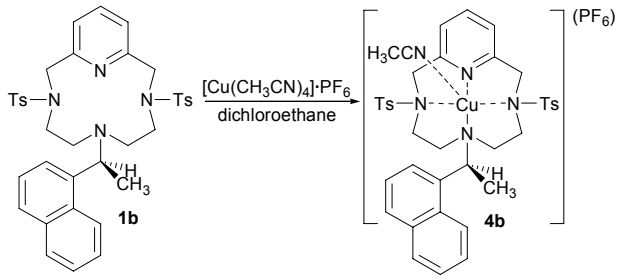
Cu(OTf) complex of 6-[(R)-1-(1-naphthyl)ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (**2b**) was synthesized in the same way. $[\alpha]_D^{20}$ = +115 (*c* 1 in $CHCl_3$)

**Synthesis of [Cu(CH$_3$CN)](OTf) complex of 6-[(S)-1-(1-naphthyl)-ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (3b)**



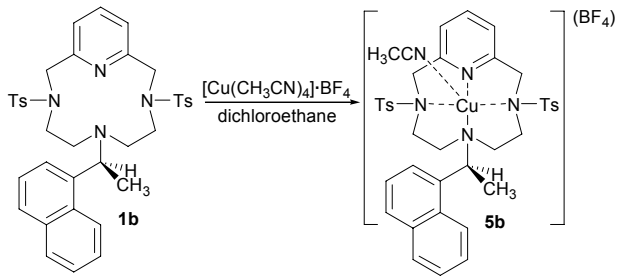

Complex **2b** (0.051 g, 0.0579 mmol) was dissolved in dichloroethane (3 ml). $CH_3CN$ (0.015 ml, 0.295 mmol) was added and the resulting solution was stirred at room temperature for 20 min. Solvent was removed *in vacuo* and the solid residue was kept under reduced pressure at 40 °C for 4 h. *n*-Hexane (3 ml) was added and complex **3b** was collected and dried *in vacuo* as a white powder (0.050 g, 94%). $^1$H NMR (300 MHz; $CDCl_3$; T = 300 K): $\delta$ 8.83 (1 H, d, *J* = 8.4 Hz, Ar*H*), 7.98 (1 H, d, *J* = 8.1 Hz, Ar*H*), 7.87 (2 H, d, *J* = 8.1 Hz, Ar*H*), 7.83–7.65 (6 H, m, H aromatics), 7.60–7.54 (2 H, m, Ar*H*), 7.52 (2 H, d, *J* = 8.1 Hz, Ar*H*), 7.38 (2 H, d, *J* = 8.1 Hz, Ar*H*), 7.25-7.20 (2 H, m, Ar*H*), 5.98 (1 H, br, C*H*), 5.17 (2 H, d, *J* = 14.7 Hz, C$H_2$), 4.62–4.49 (1 H, m, C$H_2$), 5.14–5.05 (1 H, m, C$H_2$), 4.23-3.95 (1 H, m, C$H_2$), 3.70 (2 H, d, *J* = 14.7 Hz, C$H_2$), 3.67 (1 H, m, C$H_2$), 3.54–3.34 (1 H, m, C$H_2$), 2.83–2.71 (2 H, m, C$H_2$), 2.56 (3 H, s, C$H_3$), 2.47 (3 H, s, C$H_3$) overlapping with 2.47 (1 H, m, C$H_2$), 2.28 (3 H, br s, C$H_3$CN), 2.04 (3 H, br, C$H_3$). $^{13}$C NMR (75 MHz; $CDCl_3$; T = 300 K) $\delta$ 155.0, 146.0, 145.6, 139.7, 136.6, 134.7, 132.4, 131.0, 130.8, 130.7, 130.4, 129.1, 128.3, 128.2, 127.9, 126.0, 125.9, 125.8, 124.9, 122.9, 122.2, 116.1 ($CH_3CN$), 57.0, 56.6, 54.5 (*C*H), 52.0, 51.7, 47.4, 43.8, 22.1, 21.9, 12.1 (*C*H$_3$), 3.3 (*C*H$_3$CN). $^{15}$N NMR (40 MHz; $CDCl_3$; T = 300 K): $\delta$ 251 (*N*-Py), 95 (*N*-Ts), 38 (*N*C*). $^{19}$F NMR (282 MHz; $CDCl_3$; T = 300 K): $\delta$ -78.7. IR ($CHCl_3$) $\nu$ (cm$^{-1}$) = 2250 (CN).

**Synthesis of [Cu(CH$_3$CN)](PF$_6$) complex of 6-[(S)-1-(1-naphthyl)-ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13-triene (4b)**




[Cu(CH$_3$CN)$_4$]·(PF$_6$) (0.112 g, 0.299 mmol) was added to a solution of **1b** (0.200 g, 0.299 mmol) in dichloroethane (5 ml). The solution was stirred at room temperature for one hour, then solvent was removed *in vacuo*. *n*-Hexane was added to the residue and **4b** was collected as a white powder under nitrogen (0.265 g, 97%). The same pattern reported for **3b** is found in the $^1$H NMR,$^{13}$C NMR and $^{15}$N NMR spectra. $^{19}$F NMR (282 MHz; CDCl$_3$; T = 300 K): $\delta$ -73.6 (d, $J_{F\text{-}P}$ = 711 Hz). $^{31}$P NMR (121 MHz; CDCl$_3$; T = 300 K): $\delta$ -144.2 (hept., $J_{P\text{-}F}$ = 711 Hz). IR (CHCl$_3$) $\nu$ (cm$^{-1}$) = 2250 (CN). Elemental Analysis: Found: C, 51.5; H, 4.4; N, 7.9%; M$^+$, 918. Calc. for $C_{39}H_{43}BcuF_6N_5O_4PS_2$ : C, 51.0; H, 4.7; N, 7.6%.

**Synthesis of [Cu(CH$_3$CN)](BF$_4$) complex of 6-[(S)-1-(1-naphthyl)-ethyl]-3,9-ditosyl-3,6,9,15-tetraazabicyclo[9,3,1]pentadeca-1(15),11,13.triene (5b)**




[Cu(CH$_3$CN)$_4$]·(BF$_4$) (0.094 g, 0.299 mmol) was added to a solution of **1b** (0.200 g, 0.299 mmol) in dichloroethane (5 ml). The solution was stirred at room temperature for one hour, then solvent was

removed *in vacuo*. *n*-Hexane (10 ml) was added to the residue and **5b** was collected as a white powder under dinitrogen (0.235 g, 91%). The same pattern reported for **3b** is found in the $^{1}H$ NMR,$^{13}C$ NMR and $^{15}N$ NMR spectra. $^{19}F$ NMR (282 MHz; $CDCl_3$; T = 300 K): $\delta$ -153.6. IR ($CHCl_3$ solution) $\nu$ ($cm^{-1}$) = 2250 (CN). Elemental Analysis: Found: C, 54.4; H, 5.4; N, 7.9%; $M^+$, 860. Calc. for $C_{39}H_{43}BCuF_4N_5O_4S_2$ : C, 54.5; H, 5.0; N, 8.1%.

**General procedure for the catalytic cyclopropanation reactions**

$[Cu(OTF)]_2 \cdot (C_6H_6)$ (0.0075 g, 0.015 mmol), the ligand (0.020 g (**1b**), 0.018 g for (**1a)**, 0.030 mmol) and α-Methyl styrene (0.650 ml, 5.0 mmol) were dissolved in distilled dichloroethane (5 ml) and the solution stirred for one hour at 0° C. Then a dichloroethane (2 ml) solution of EDA (0.114 g, 0.105 ml, 1 mmol) was slowly added by a syringe pump during 1.5 hours. The reaction was monitored by IR, following the disappearance of the band due to the stretching of $N_2$ moiety at 2114 $cm^{-1}$. After the complete conversion of EDA the mixture was evaporated to dryness *in vacuo* and the residue purified by chromatography on silica gel (eluant AcOEt / *n*-hexane = 0.7:10).

1. K. M. Gillespie, C. J. Sanders, P. O'Shaughnessy, I. Westmoreland, C. P. Thickitt and P. Scott, *J. Org. Chem.* , 2002, **67**, 3450-3458.