**Supplementary material**

# Development of conditions for the asymmetric alkylation of 3-halooxindoles with α-arylated malonate esters

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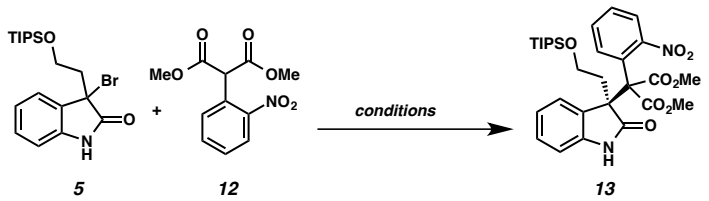
## *1. Initial screening results*

To an oven dried vials equipped with stirbar was charged with copper source (20 mol %), BINAP (20 mol %) and 3 Å molecular sieve in THF. The heterogeneous solution was agitated at ambient temperature for 10-20 min until clear homogeneous solution was generated. To the reaction mixture was charged additive (20 mol % unless specified in table) Reaction mixture was allowed to stir for 5 min and concentrated under reduced pressure. Mixture of bromooxindole **5** (10 mg, 0.024 mmol) and malonate **12** (18.5 mg, 0.073 mmol) in reaction solvent (0.15 ml, 0.2 M) was added to the mixture and allowed to stir for 10 minutes. After setting reaction temperature, base (2 equiv) was added to initiate the reaction. Upon completion of the reaction, saturated aqueous ammonium chloride solution (0.1 mL) was added, and the mixture was filtered through silica gel. Each filtrate was diluted by 1 mL of solvent (ethyl acetate or isopropanol) and analyzed by chiral SFC. The mixture was separated by an AD-H column with 20% isopropanol as eluent.




*5* *12* *13*

**Table 1.**

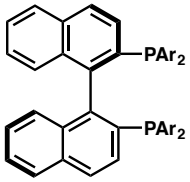
| Entry | Metal | Ligand | Solvent | Additives | Base | Temp. | Time | ee |
|---|---|---|---|---|---|---|---|---|
| 1 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Et_3N$ | 23 ºC | 24 h | 25% |
| 2 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 3 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | *i*-$Pr_2NH$ | 23 ºC | 24 h | – |
| 4 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | Pyridine | 23 ºC | 24 h | – |
| 5 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | DBU | 23 ºC | 24 h | 10% |
| 6 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | TMEDA | 23 ºC | 24 h | – |
| 7 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | KOAc | 23 ºC | 24 h | Mix |
| 8 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Na_2CO_3$ | 23 ºC | 24 h | Mix |
| 9 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Cs_2CO_3$ | 23 ºC | 24 h | Mix |
| 10 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | DBU | –20 ºC | 24 h | 7% |
| 11 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | KOAc | –20 ºC | 24 h | Mix |
| 12 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Na_2CO_3$ | –20 ºC | 24 h | trace |
| 13 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Cs_2CO_3$ | –20 ºC | 24 h | Mix |
| 14 | $Cu(OTf)_2$ | *(R)*-BINAP | $C_6H_6$ | | DBU | –20 ºC | 24 h | – |
| 15 | $Cu(OTf)_2$ | *(R)*-BINAP | $C_6H_6$ | | KOAc | 23 ºC | 24 h | trace |
| 16 | $Cu(OTf)_2$ | *(R)*-BINAP | $C_6H_6$ | | $Na_2CO_3$ | 23 ºC | 24 h | trace |
| 17 | $Cu(OTf)_2$ | *(R)*-BINAP | $C_6H_6$ | | $Cs_2CO_3$ | 23 ºC | 24 h | 15% |
| 18 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | DBU | 23 ºC | 24 h | 5% |
| 19 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | KOAc | 23 ºC | 24 h | Mix |
| 20 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | $Na_2CO_3$ | 23 ºC | 24 h | Mix |
| 21 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | $Cs_2CO_3$ | 23 ºC | 24 h | Mix |
| 22 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | $Et_3N$ | 23 ºC | 24 h | – |
| 23 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 24 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | *i*-$Pr_2NH$ | 23 ºC | 24 h | – |
| 25 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | Pyridine | 23 ºC | 24 h | trace |
| 26 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | DBU | –30 ºC | 24 h | – |
| 27 | $CuCl_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgSbF_6$ | $Cs_2CO_3$ | –30 ºC | 24 h | 20% |
| 28 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | $Et_3N$ | 23 ºC | 24 h | trace |
| 29 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 30% |
| 30 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Cs_2CO_3$ | –50 ºC | 24 h | trace |
| 31 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | DBU | –50 ºC | 24 h | – |
| 32 | $Cu(OTf)_2$ | *(R)*-BINAP | THF | | $Cs_2CO_3$ | –50 ºC | 24 h | Mix |
| 33 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$[a] | $Cs_2CO_3$ | –50 ºC | 24 h | Mix |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 34 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | DBU | –50 ºC | 24 h | – |
| 35 | $Cu(OTf)_2$ | *(R)*-BINAP | THF | $AgNO_3$ | DBU | –50 ºC | 24 h | – |
| 36 | $Cu(OTf)_2$ | *(R)*-BINAP | THF | $AgNO_3$ | $Et_3N$ | 23 ºC | 24 h | 10% |
| 37 | $Cu(OTf)_2$ | *(R)*-BINAP | THF | $AgNO_3$ | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 10% |
| 38 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | $Et_3N$ | 23 ºC | 24 h | 6% |
| 39 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 20% |
| 40 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | $Cs_2CO_3$ | –30 ºC | 24 h | 25% |
| 41 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | KOAc | 23 ºC | 24 h | trace |
| 42 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | $Na_2CO_3$ | 23 ºC | 24 h | Mix |
| 43 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | $Et_3N$ | 23 ºC | 24 h | 10% |
| 44 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 7% |
| 45 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | $Et_3N$ | –30 ºC | 24 h | 18% |
| 46 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | *i*-$Pr_2NEt$ | –30 ºC | 24 h | 10% |
| 47 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | –45 ºC | 24 h | 8% |
| 48 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | $Et_3N$ | –45 ºC | 24 h | 10% |
| 49 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | *i*-$Pr_2NEt$ | –45 ºC | 24 h | 20% |
| 50 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | $Et_3N$ | –45 ºC | 24 h | 20% |
| 51 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 52 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | $Et_3N$ | 23 ºC | 24 h | – |
| 53 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | $Cs_2CO_3$ | –45 ºC | 24 h | Mix |
| 54 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $C_6H_6$ | LiO*t*-Bu | $Cs_2CO_3$ | 23 ºC | 24 h | – |
| 55 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $C_6H_6$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | trace |
| 56 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $C_6H_6$ | $AgNO_3$, LiO*t*-Bu | $Cs_2CO_3$ | 23 ºC | 24 h | racemic |
| 57 | $Cu(OTf)_2$ | *(R)*-BINAP | Dioxane | $AgNO_3$ | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 7% |
| 58 | $Cu(OTf)_2$ | *(R)*-BINAP | Dioxane | $AgNO_3$ | $Et_3N$ | 23 ºC | 24 h | 15% |
| 59 | $Cu(OTf)_2$ | *(R)*-BINAP | Dioxane | | $Cs_2CO_3$ | –30 ºC | 24 h | Mix |
| 60 | $Cu(OTf)_2$ | *(R)*-BINAP | Dioxane | | $Na_2CO_3$ | 23 ºC | 24 h | 10% |
| 61 | $Cu(OTf)_2$ | *(R)*-BINAP | Dioxane | | KOAc | 23 ºC | 24 h | Mix |
| 62 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_3CN$ | $AgNO_3$ | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 15% |
| 63 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_3CN$ | $AgNO_3$ | $Et_3N$ | 23 ºC | 24 h | 15% |
| 64 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_3CN$ | | $Cs_2CO_3$ | –30 ºC | 24 h | trace |
| 65 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_3CN$ | | $Na_2CO_3$ | 23 ºC | 24 h | Mix |
| 66 | $Cu(OTf)_2$ | *(R)*-BINAP | $CH_3CN$ | | KOAc | 23 ºC | 24 h | Mix |
| 67 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | THF | LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | – |
| 68 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 20% |
| 69 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | $Cs_2CO_3$ | –50 ºC | 24 h | trace |
| 70 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | $Cs_2CO_3$ | 23 ºC | 24 h | trace |
| 71 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | $Cs_2CO_3$ | –50 ºC | 24 h | mix |
| 72 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu (1 mol %) | *i*-$Pr_2NEt$ | –50 ºC | 24 h | mix |
| 73 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu (2 mol %) | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 17% |
| 74 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu (4 mol %) | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 19% |
| 75 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu (8 mol %) | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 20% |
| 76 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu, NaEH | *i*-$Pr_2NEt$ | –50 ºC | 24 h | mix |
| 77 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, NaEH (ex) | | 23 ºC | 24 h | racemic |
| 78 | $Cu(isobutyrate)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | $Cs_2CO_3$ | –50 ºC | 24 h | mix |
| 79 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 9% |
| 80 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Et_3N$ | –50 ºC | 24 h | – |
| 81 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Cs_2CO_3$ | –50 ºC | 24 h | – |
| 82 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 20% |
| 83 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | $Et_3N$ | –50 ºC | 24 h | 15% |
| 84 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$ | $Cs_2CO_3$ | –50 ºC | 24 h | – |
| 85 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 10% |
| 86 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | $AgNO_3$, LiO*t*-Bu | $Et_3N$ | –50 ºC | 24 h | – |
| 87 | $Cu(EH)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | LiO*t*-Bu | NaEH | 23 ºC | 24 h | – |
| 88 | $Cu(tfacac)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Et_3N$ | –50 ºC | 24 h | – |
| 89 | $Cu(tfacac)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | *i*-$Pr_2NEt$ | –50 ºC | 24 h | – |
| 90 | $Cu(tfacac)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | $Cs_2CO_3$ | –50 ºC | 24 h | – |
| 91 | $Cu(tfacac)_2$ | *(R)*-BINAP | $CH_2Cl_2$ | | NaEH | –50 ºC | 24 h | – |
| 92 | $Cu(tfacac)_2$ | *(R)*-BINAP | THF | | $Et_3N$ | –50 ºC | 24 h | 7% |
| 93 | $Cu(tfacac)_2$ | *(R)*-BINAP | THF | | *i*-$Pr_2NEt$ | –50 ºC | 24 h | – |

$Cu(hfacac)_2$: copper(II) hexafluoroacetylacetonate, EH: ethylhexanoate, –: Desired product was not observed. [b] 44 mol % of ligand was used. Mix: complex mixtures

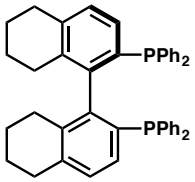
*2. Ligand screenings*

*2.1. Ligand list*

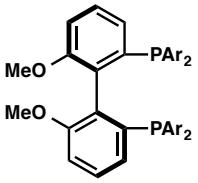



A1 : Ar = Ph
A2 : = Tol
A3 : = Xyl

***BINAP***

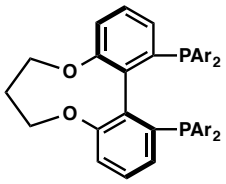



**A4**



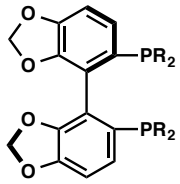

B1 : Ar = Xyl
B2 : = 3,5-*t*BuPh
B3: = 3,5-*t*Bu-4-MeOPh
B4 : = 3,5-*i*Pr-4-Me$_2$NPh

***MEOBIPHEP***



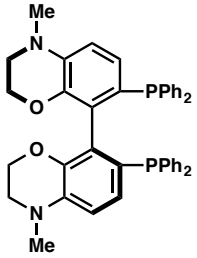

**C1**

***TUNEPHOS***



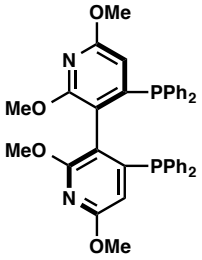

D1 : R = Ph
D2 : = 3,5-Me$_2$Ph
D3 : = 3.5-*t*Bu$_2$-4-MeOPh
D4 : = *i*Pr

***SEGPHOS***



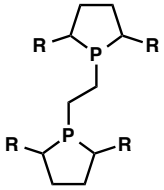

**E1**

***SOLOPHOS***



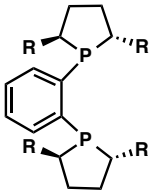

**F1**

***P-Phos***



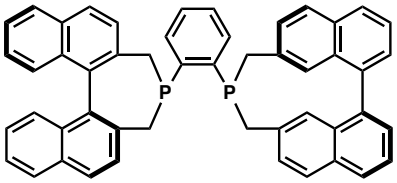

G1 : R = (*S,S*)-Me
G2 : = (*R,R*)-Et
G3 : = (*R,R*)-*i*Pr

***BPE***



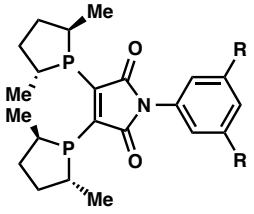

H1 : R = Me
H2 : = Et
H3 : = *i*Pr

***DUPHOS***

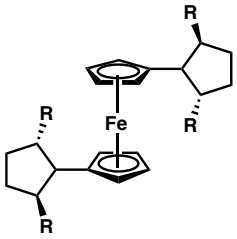



**I1**

***BINAPHANE***

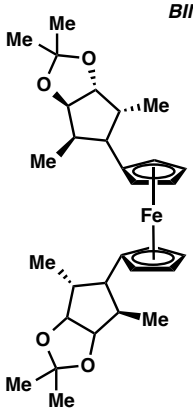



J1 : R = Me
J2 : = $CF_3$



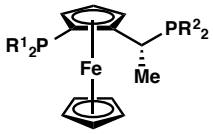

K1 : R = Me
K2 : = Et
K3 : = *i*Pr

***Ferrocelane***



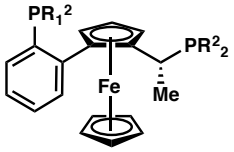

**L1**

***KetalPhos***



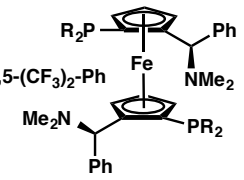

***JOSIPHOS***

M1 : $R^1$,$R^2$ = Ph, Cy
M2 : = Ph, *t*Bu
M3 : = Ph, Xyl
M4 : = aNp, *t*Bu
M5 : = aNp, Cy
M6 : = 3,5-$(CF_3)_2$-Ph, Cy
M7 : = 3,5-$(CF_3)_2$-Ph, Xyl
M8 : = 3,5-Me$_2$-4-MeOPh, Cy
M9 : = 3,5-Me$_2$-4-MeOPh, *t*Bu
M10 : = 3,5-Me$_2$-4-MeOPh, Xyl
M11 : = 2-Furyl, *t*Bu
M12 : = 2-Furyl, Xyl
M13 : = Cy, Cy
M14 : = Cy, *t*Bu
M15 : = Cy, Ph
M16 : = *t*Bu, Ph
M17 : = *t*Bu, 2-Tol



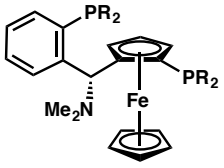

***WALPHOS***

**N1 : $R^1$,$R^2$ = Ph, Ph**
**N2 : = Ph, Xyl**
**N3 : = Ph, 3,5-$(CF_3)_2$-Ph**
**N4 : = 3,5-$Me_2$-4-MeOPh, 3,5-$(CF_3)_2$-Ph**
**N5 : = Ph, Cy**
**N6 : = Cy, 3,5-$(CF_3)_2$-Ph**
**N7 : = Xyl, Xyl**
**N8 : = Ph, Norbornyl**

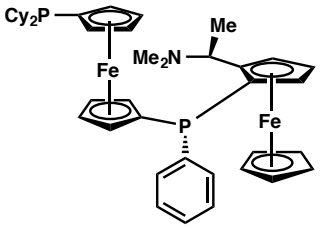



***MANDYPHOS***

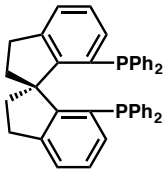
**O1 : R = Ph**
**O2 : = 2-Tol**
**O3 : = Xyl**
**O4 : = 3,5-$(CF_3)_2$-Ph**
**O5 : = 3,5-$Me_2$-4-MeOPh**
**O6 : = Cy (opposite stereochemistry)**



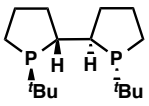

**P1 : R = Ph**
**P2 : = Cy**
***TANIAPHOS***



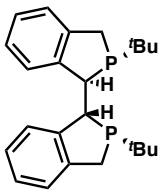

**Q1**
***CHENPHOS***



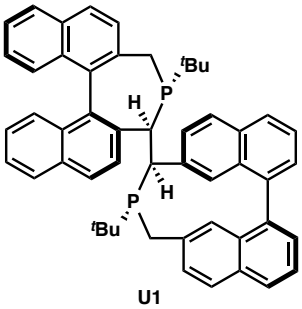

**S1**
***R*-SDP**



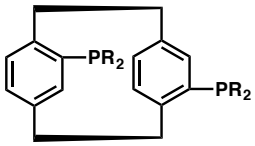

**S1**
***TANGPHOS***



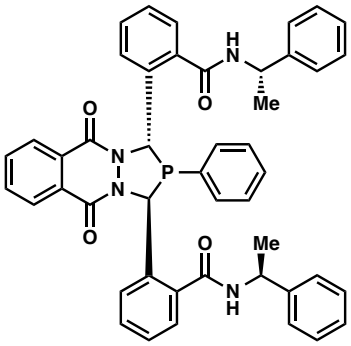

**T1**
***DUANPHOS***



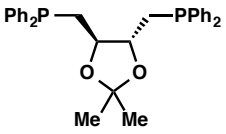

**U1**
***Binapine***



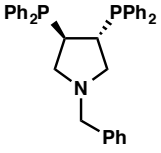

**V1 : R = Ph**
**V2 : R = Xyl**
***PHANEPHOS***



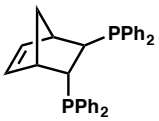

**W1 : *(S,S,S)*-DiazaPHOS-PPE**
**W2 : *(R,R,S)*-DiazaPHOS-PPE**
**W3 : Bis[*(R,R,S)*-DiazaPHOS-SPE]**
**W4 : Bis[*(S,S,S)*-DiazaPHOS-SPE]**




**X1**
***DIOP***



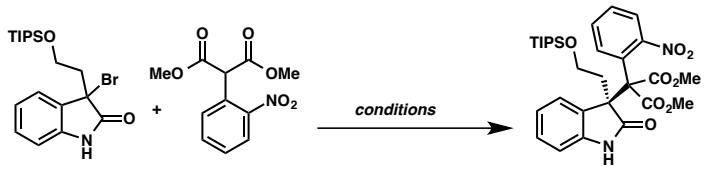

**Y1**




**Z1**
***NORPHOS***

### *2.2. Ligand screening results*

Every step was performed in a nitrogen-filled glove box. Solutions of copper(II) isoburtyrate (8 mg, 0.034 mmol) in THF (3.5 mL), lithium *tert*-butoxide (2.72 mg, 0.034 mmol) in THF (3.5 mL), bromooxindole **5** (70 mg, 0.17 mmol) and malonate **12** (129 mg, 0.51 mmol) in $CH_2Cl_2$ (1.75 mL), *i*-$Pr_2NEt$ (0.1 ml, 0.57 mmol) in $CH_2Cl_2$ (2 mL) were prepared in 2 dram vials prior to reaction setup. To 1 dram vials equipped with stirbars, and ligand (1.1 $\mu$mol, 22 mol %) were distributed copper(II) isobutyrate in THF (0.1 mL, 0.97 $\mu$mol, 20 mol %). The heterogeneous solution was agitated at room temperature for 10-20 min until a clear homogeneous solution was generated. The reaction mixtures were charged with lithium *tert*-butoxide in THF (0.1 mL, 0.97 $\mu$mol, 20 mol %). Reaction mixtures were allowed to stir for 5 min and concentrated under reduced pressure. A mixture of bromooxindole **5** and malonate **12** in $CH_2Cl_2$ (0.05 mL, 4.85 $\mu$mol, 14.55 $\mu$mol) was dispensed to each vial and allowed to stir for 10 min. After setting the reaction temperature, *i*-$Pr_2NEt$ in $CH_2Cl_2$ (0.05 mL, 14.55 $\mu$mol, 3 equiv) was added to the reaction vials and allowed to stir for 48 h. Upon completion, sat. aq. ammonium chloride solution (0.1 mL) was added, and the mixture was filtered through silica gel. Each filtrate was diluted by 1 mL of solvent (ethyl acetate or isopropanol) and analyzed by chiral SFC. The mixture was separated by an AD-H column with 20% isopropanol as eluent. See supplementary material for more details.

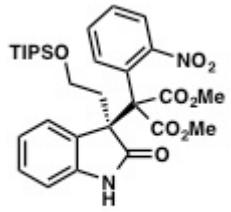



*5* *12* *13*

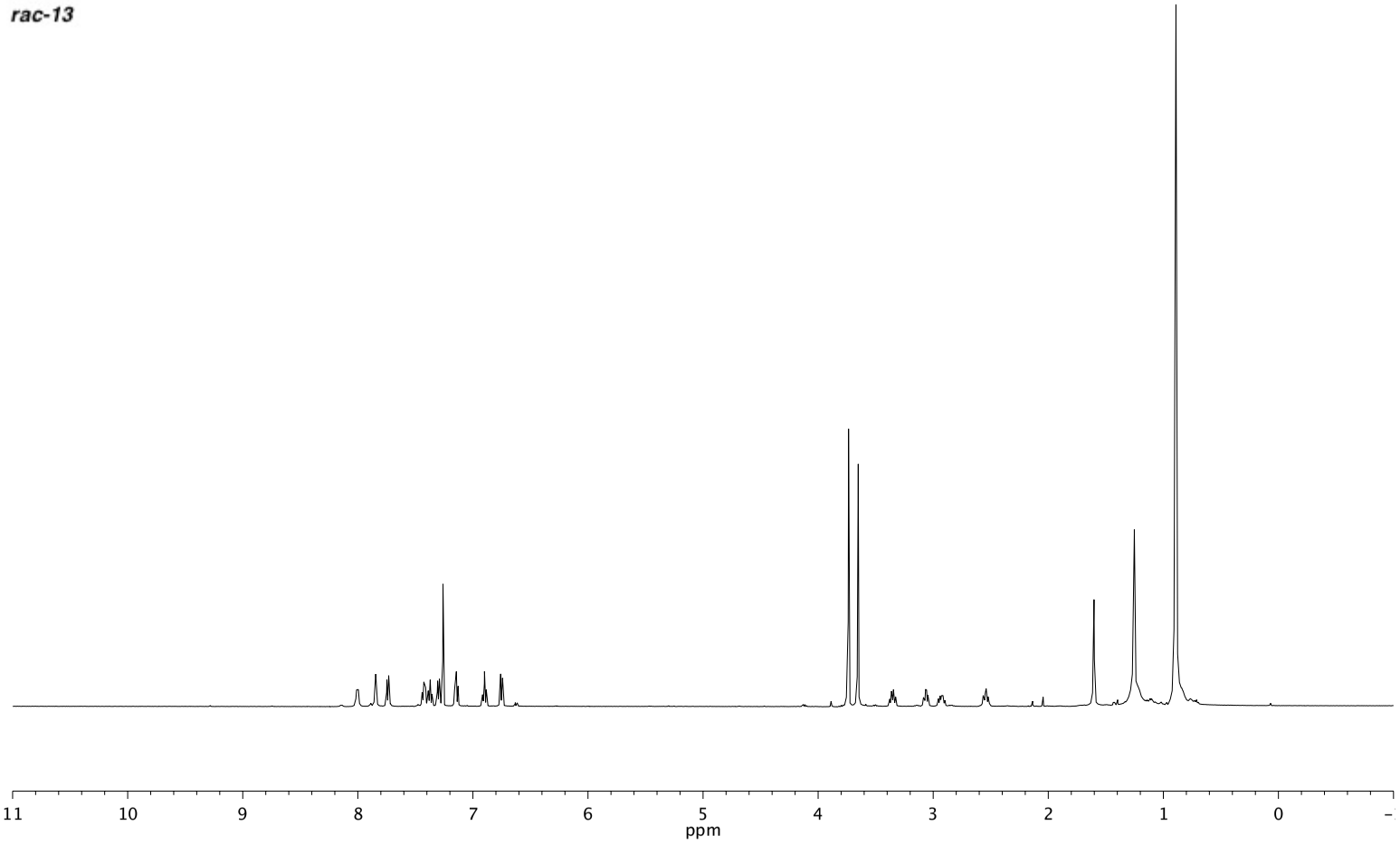
**Table 2.**

| Entry | Metal | Ligand | Solvent | Additives | Base | Temp. | Time | ee |
|---|---|---|---|---|---|---|---|---|
| 1 | Cu(isobutyrate)$_2$ | A1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 10% |
| 2 | Cu(isobutyrate)$_2$ | A2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 14% |
| 3 | Cu(isobutyrate)$_2$ | A3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NH$ | 0 ºC | 24 h | 20% |
| 4 | Cu(isobutyrate)$_2$ | A4 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | – |
| 5 | Cu(isobutyrate)$_2$ | B1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 11% |
| 6 | Cu(isobutyrate)$_2$ | B2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 10% |
| 7 | Cu(isobutyrate)$_2$ | B3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 9% |
| 8 | Cu(isobutyrate)$_2$ | B4 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 12% |
| 9 | Cu(isobutyrate)$_2$ | C1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | – |
| 10 | Cu(isobutyrate)$_2$ | D1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 17% |
| 11 | Cu(isobutyrate)$_2$ | D2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 10% |
| 12 | Cu(isobutyrate)$_2$ | D3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | racemic |
| 13 | Cu(isobutyrate)$_2$ | D4 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 8% |
| 14 | Cu(isobutyrate)$_2$ | E1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | NR |
| 15 | Cu(isobutyrate)$_2$ | F1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 10% |
| 16 | Cu(isobutyrate)$_2$ | G1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 16% |
| 17 | Cu(isobutyrate)$_2$ | G2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | racemic |
| 18 | Cu(isobutyrate)$_2$ | G3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 8% |
| 19 | Cu(isobutyrate)$_2$ | H1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 14% |
| 20 | Cu(isobutyrate)$_2$ | H2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 0 ºC | 24 h | 10% |
| 21 | Cu(isobutyrate)$_2$ | H3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 22 | Cu(isobutyrate)$_2$ | J2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 27% |
| 23 | Cu(isobutyrate)$_2$ | K1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 17% |
| 24 | Cu(isobutyrate)$_2$ | K2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 22% |
| 25 | Cu(isobutyrate)$_2$ | K3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 26 | Cu(isobutyrate)$_2$ | M1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 27 | Cu(isobutyrate)$_2$ | M2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | trace |
| 28 | Cu(isobutyrate)$_2$ | M3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | mix |
| 29 | Cu(isobutyrate)$_2$ | M4 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | – |
| 30 | Cu(isobutyrate)$_2$ | M5 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 6% |
| 31 | Cu(isobutyrate)$_2$ | M6 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 32 | Cu(isobutyrate)$_2$ | M7 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 16% |
| 33 | Cu(isobutyrate)$_2$ | M8 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 34 | Cu(isobutyrate)$_2$ | M10 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 14% |
| 35 | Cu(isobutyrate)$_2$ | M11 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | –50 ºC | 24 h | 10% |
| 36 | Cu(isobutyrate)$_2$ | M12 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 20% |
| 37 | Cu(isobutyrate)$_2$ | M13 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | mix |
| 38 | Cu(isobutyrate)$_2$ | M14 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | –10% |
| 39 | Cu(isobutyrate)$_2$ | M15 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | – |
| 40 | Cu(isobutyrate)$_2$ | M16 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-$Pr_2NEt$ | 23 ºC | 24 h | 10% |

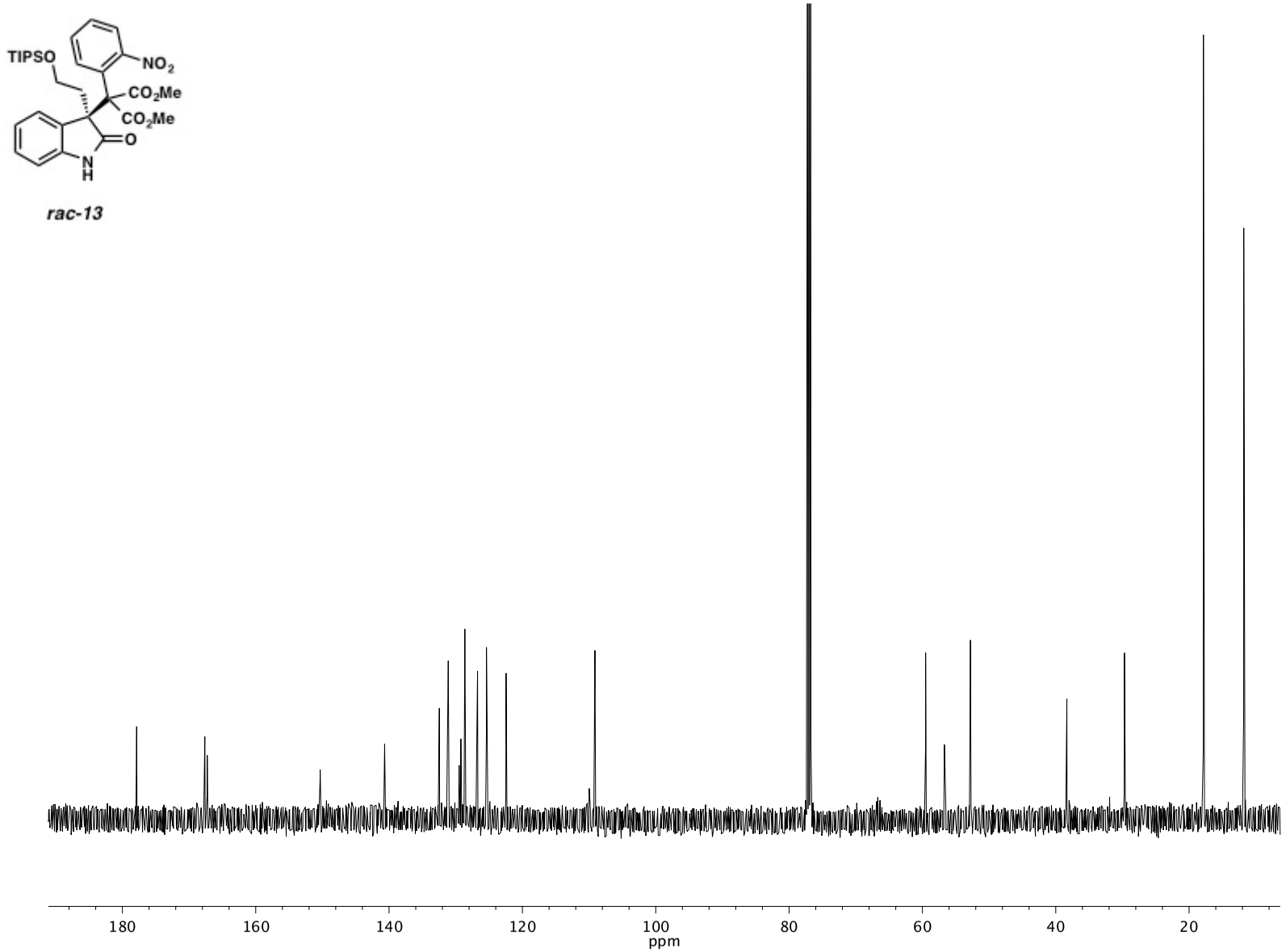
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 41 | Cu(isobutyrate)$_2$ | M17 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | racemic |
| 42 | Cu(isobutyrate)$_2$ | N1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 27% |
| 43 | Cu(isobutyrate)$_2$ | N2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 27% |
| 44 | Cu(isobutyrate)$_2$ | N3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | racemic |
| 45 | Cu(isobutyrate)$_2$ | N4 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | trace |
| 46 | Cu(isobutyrate)$_2$ | N5 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 47 | Cu(isobutyrate)$_2$ | N6 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | trace |
| 48 | Cu(isobutyrate)$_2$ | N7 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 49 | Cu(isobutyrate)$_2$ | N8 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 50 | Cu(isobutyrate)$_2$ | O1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 51 | Cu(isobutyrate)$_2$ | O2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 52 | Cu(isobutyrate)$_2$ | O3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 20% |
| 53 | Cu(isobutyrate)$_2$ | O4 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 10% |
| 54 | Cu(isobutyrate)$_2$ | O5 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 20% |
| 55 | Cu(isobutyrate)$_2$ | O6 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 56 | Cu(isobutyrate)$_2$ | P1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 10% |
| 57 | Cu(isobutyrate)$_2$ | P2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | –5% |
| 58 | Cu(isobutyrate)$_2$ | Q1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 59 | Cu(isobutyrate)$_2$ | R1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 60 | Cu(isobutyrate)$_2$ | S1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 61 | Cu(isobutyrate)$_2$ | T1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 62 | Cu(isobutyrate)$_2$ | V1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 63 | Cu(isobutyrate)$_2$ | V2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 64 | Cu(isobutyrate)$_2$ | W1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 40% |
| 65 | Cu(isobutyrate)$_2$ | W2 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | –50% |
| 66 | Cu(isobutyrate)$_2$ | W3 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | 10% |
| 67 | Cu(isobutyrate)$_2$ | X1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 68 | Cu(isobutyrate)$_2$ | Y1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |
| 69 | Cu(isobutyrate)$_2$ | Z1 | $CH_2Cl_2$ | LiO*t*-Bu | *i*-Pr$_2$NEt | 23 ºC | 24 h | – |




*rac-13*




$^{1}H$ NMR (500 MHz, $CDCl_3$) of compound ***rac*–13**.




$^{13}$C NMR (126 MHz, $CDCl_3$) of compound ***rac***–**13**.