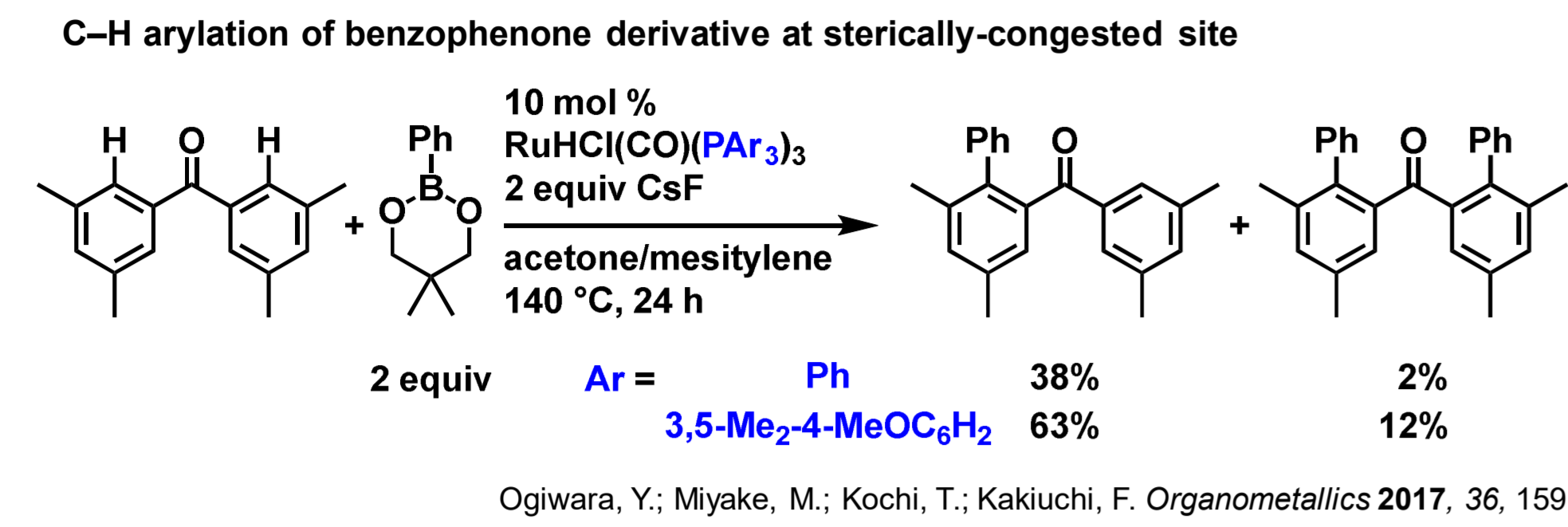


A01-7 In-Situ Generation of Ruthenium Phosphine Catalysts: Their Use for Selective C-O Arylation and Asymmetric Synthesis

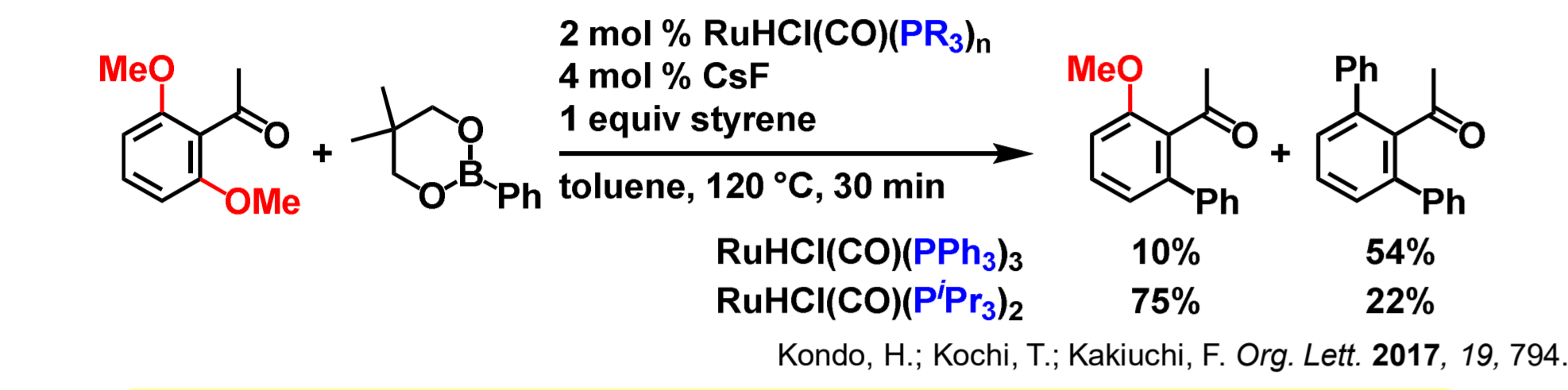
Fumitoshi KAKIUCHI (Department of Chemistry, Keio University)



The Use of Various RuHCl(CO)(PR₃)_n for C-H and C-O Arylations

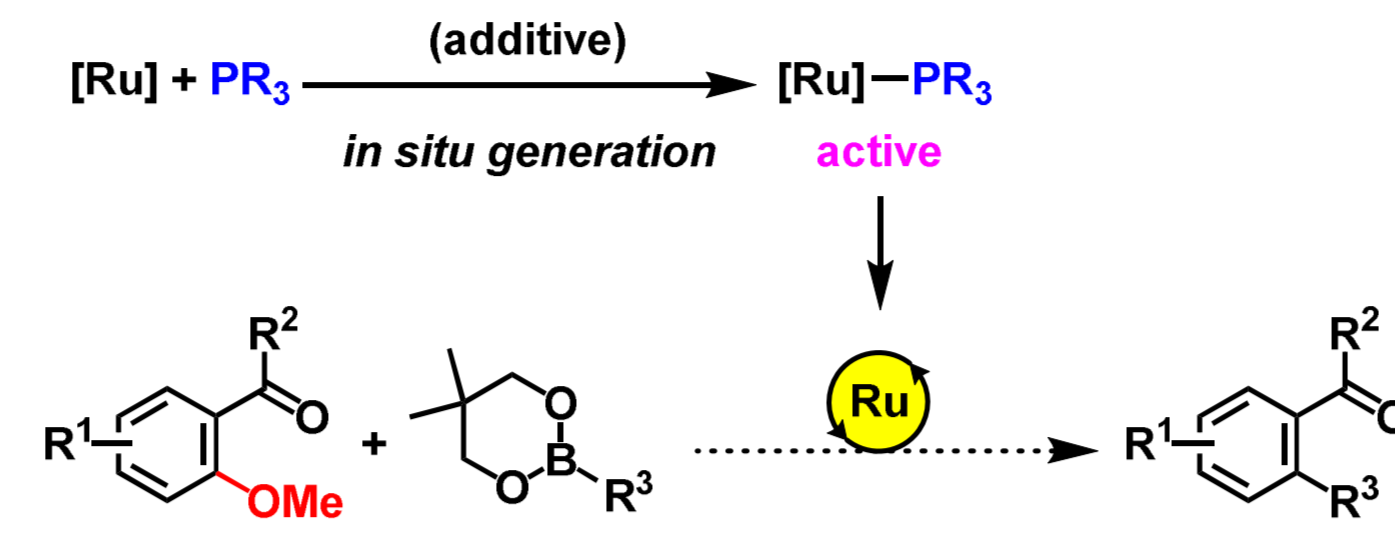


C-O arylation of 2',6'-dimethoxyacetophenone



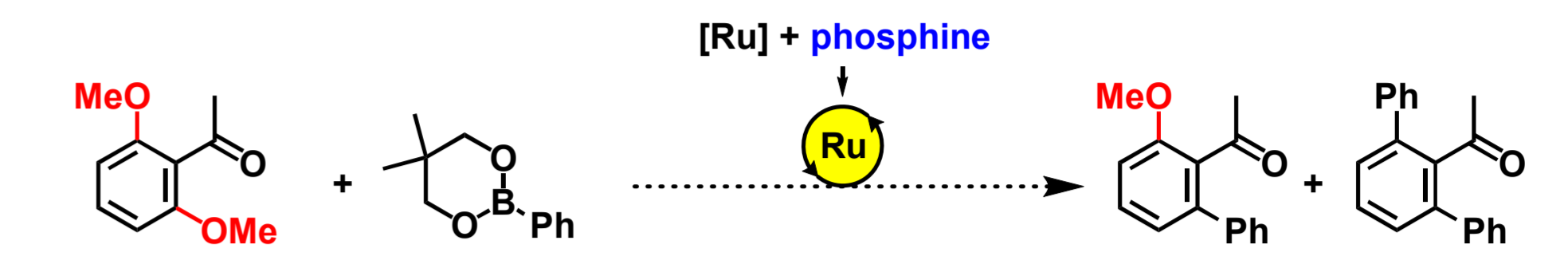
To find appropriate phosphine ligand, it is necessary to prepare each (phosphine)Ru complexes before evaluation.

In Situ Generation of Ruthenium Phosphine Catalysts for Convenient Screening

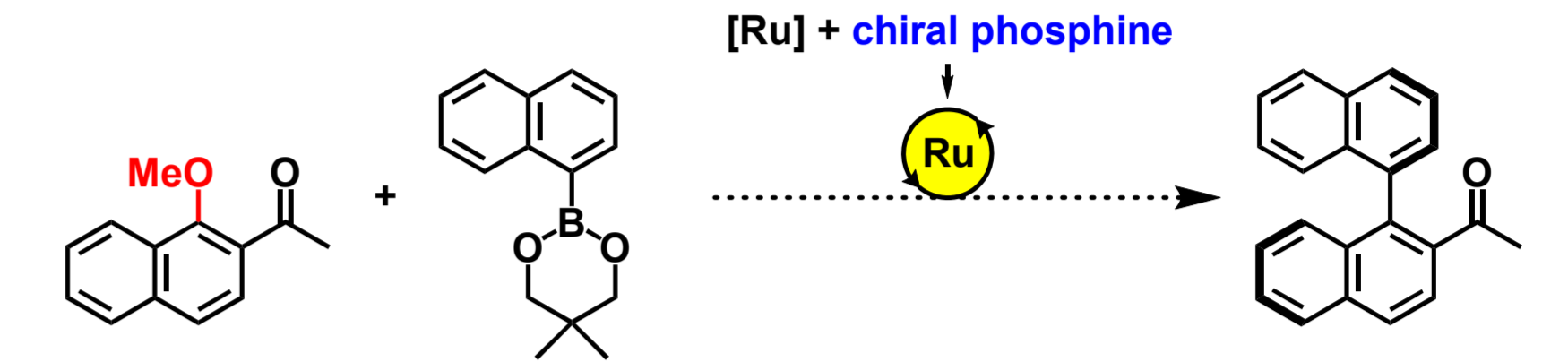


This Work

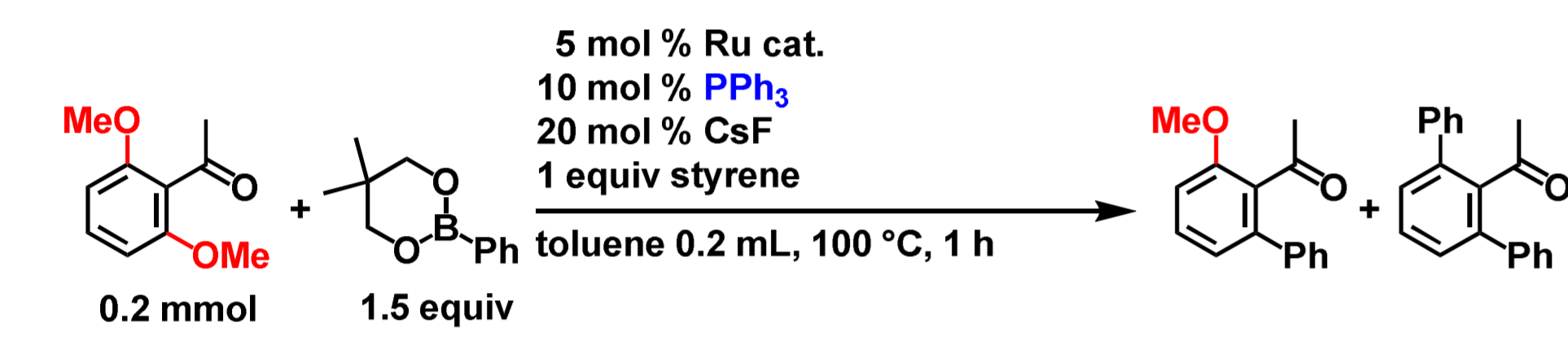
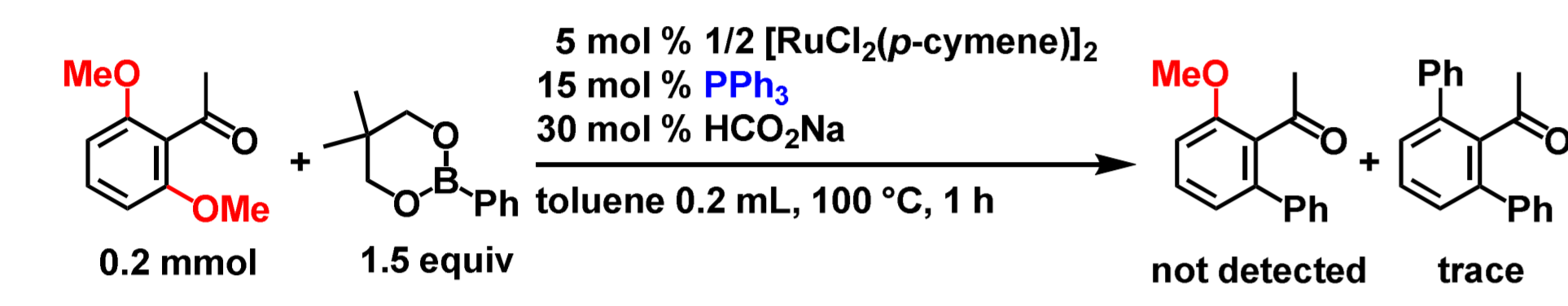
use of in situ generated ruthenium phosphine catalyst for C-O arylation



application to atropo-enantioselective arylation

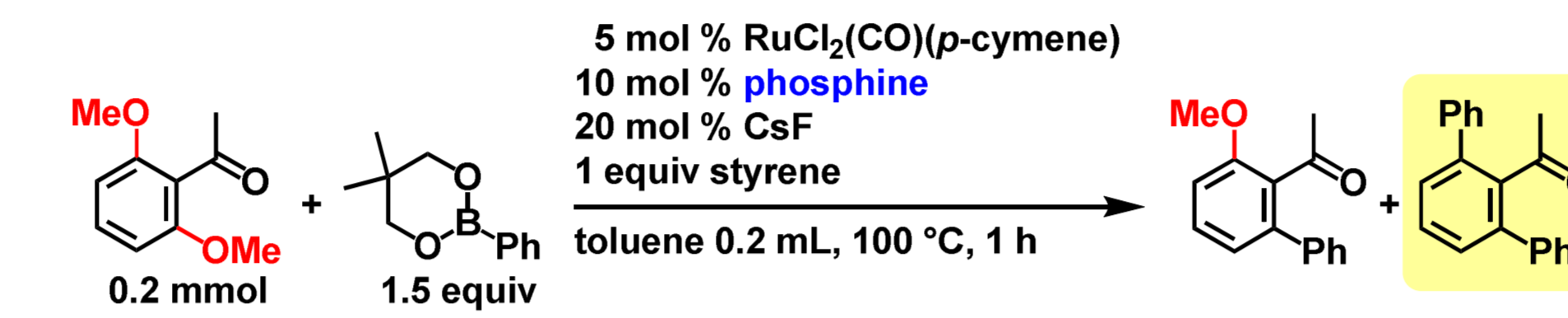


Initial Attempts for In Situ Generation of Ruthenium Phosphine Catalyst



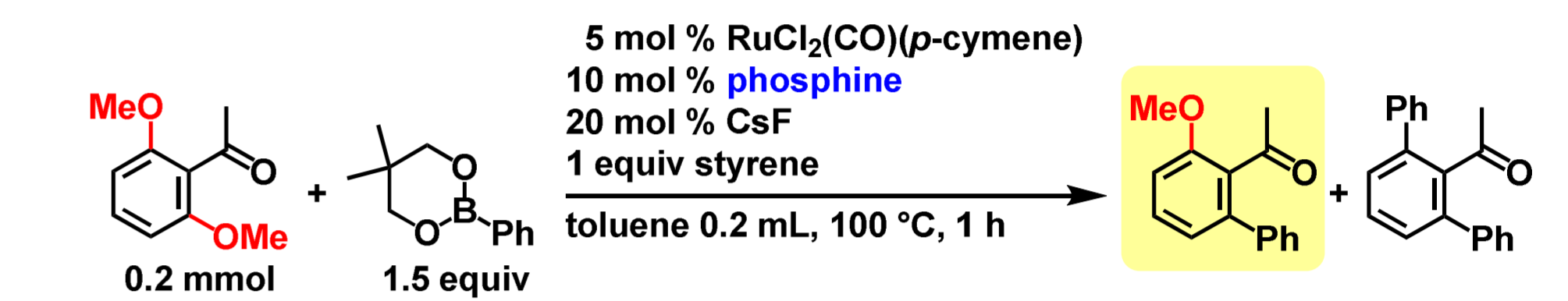
| entry | Ru cat. | conv. | GC yields | |
|-------|---|-------|----------------|--------------|
| | | | mono-arylation | di-arylation |
| 1 | 1/2 [RuCl ₂ (p-cymene)] ₂ | 18% | 2% | 13% |
| 2 | RuCl ₂ (CO)(p-cymene) | 62% | 7% | 53% |

Screening of Triarylphosphines for C-O Arylation



| entry | phosphine | conv. | GC yields | |
|-------|--|-------|----------------|--------------|
| | | | mono-arylation | di-arylation |
| 1 | none | 2% | 2% | not detected |
| 2 | PPh ₃ | 62% | 7% | 53% |
| 3 | P(2-MeC ₆ H ₄) ₃ | <1% | trace | not detected |
| 4 | P(3-MeC ₆ H ₄) ₃ | 79% | 8% | 63% |
| 5 | P(4-MeC ₆ H ₄) ₃ | 42% | 7% | 35% |
| 6 | P(4-MeOC ₆ H ₄) ₃ | 12% | 2% | 5% |
| 7 | P(4-F ₃ CC ₆ H ₄) ₃ | 78% | 17% | 61% |

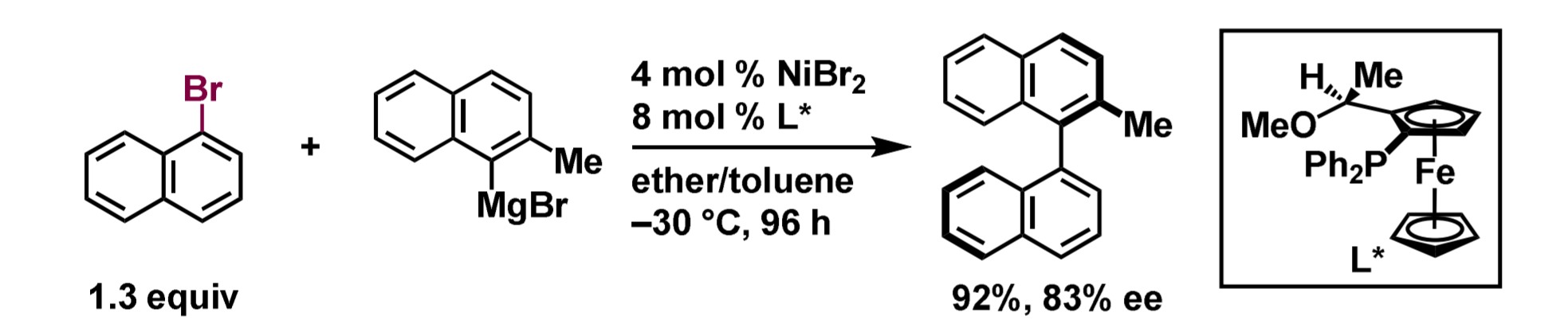
Screening of Alkylphosphines for C-O Arylation



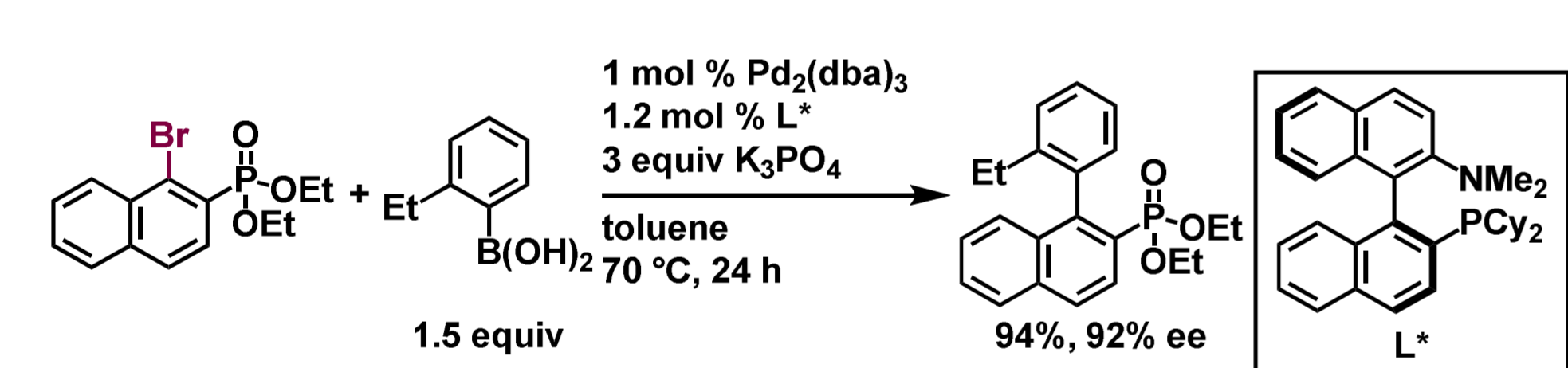
| entry | phosphine | conv. | GC yields | |
|-------|-----------------------------------|-------|----------------|--------------|
| | | | mono-arylation | di-arylation |
| 1 | PPh ₂ Cy | 11% | 5% | 4% |
| 2 | PPhCy ₂ | 2% | 2% | trace |
| 3 | PCy ₃ | 81% | 66% | 9% |
| 4 | P ^t Bu ₃ | 13% | 7% | not detected |
| 5 | P ⁱ Bu ₂ Me | 90% | 76% | 13% |
| 6 | P ⁿ Bu ₃ | 96% | 78% | 17% |
| 7 | P ^o Bu ₃ | <1% | trace | not detected |
| 8 | PMe ₃ | 1% | 1% | not detected |

Syntheses of Axially Chiral Biaryls Using Chiral Transition-Metal-Catalyst

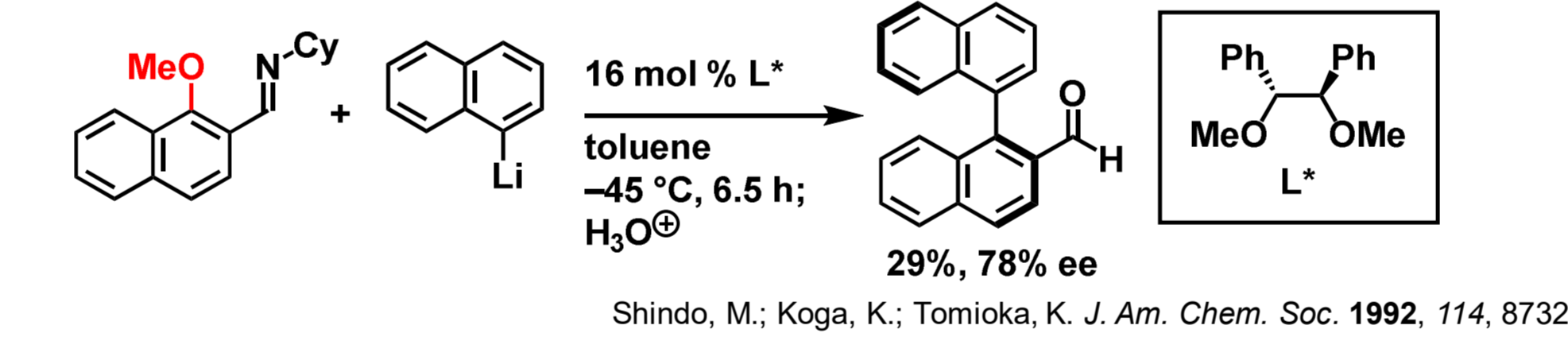
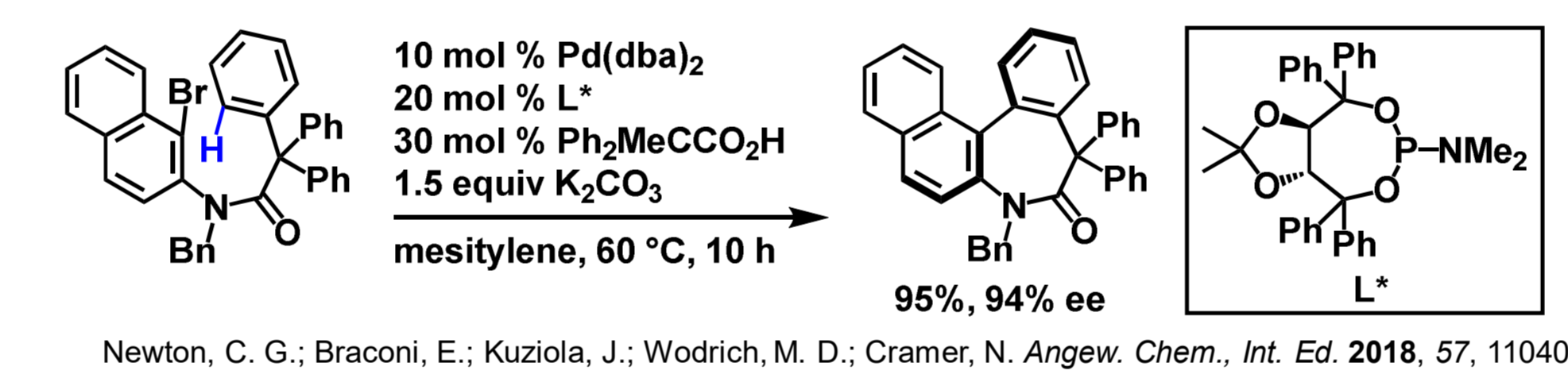
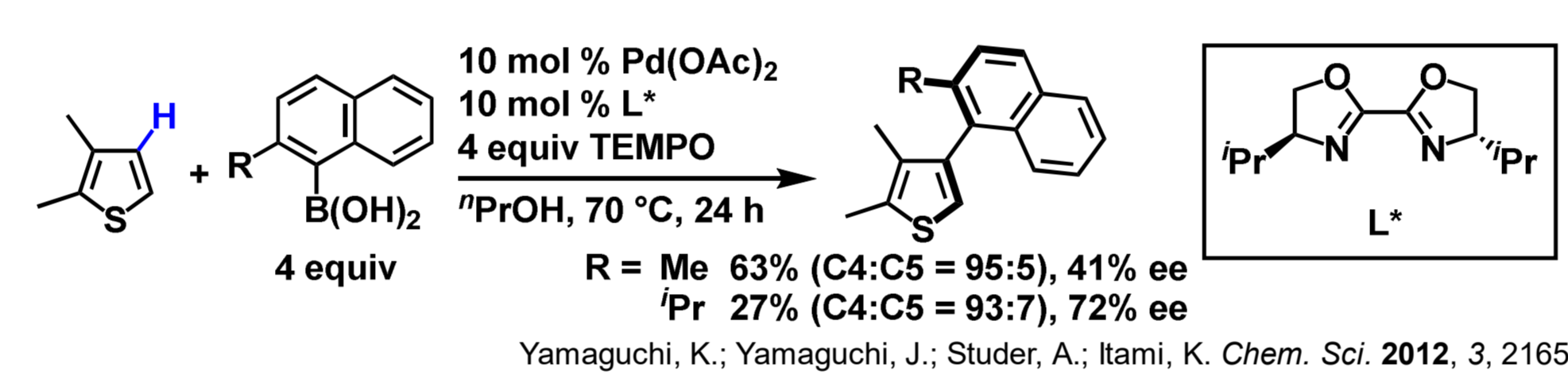
Ni-catalyzed atropselective biaryl synthesis using Grignard reagent



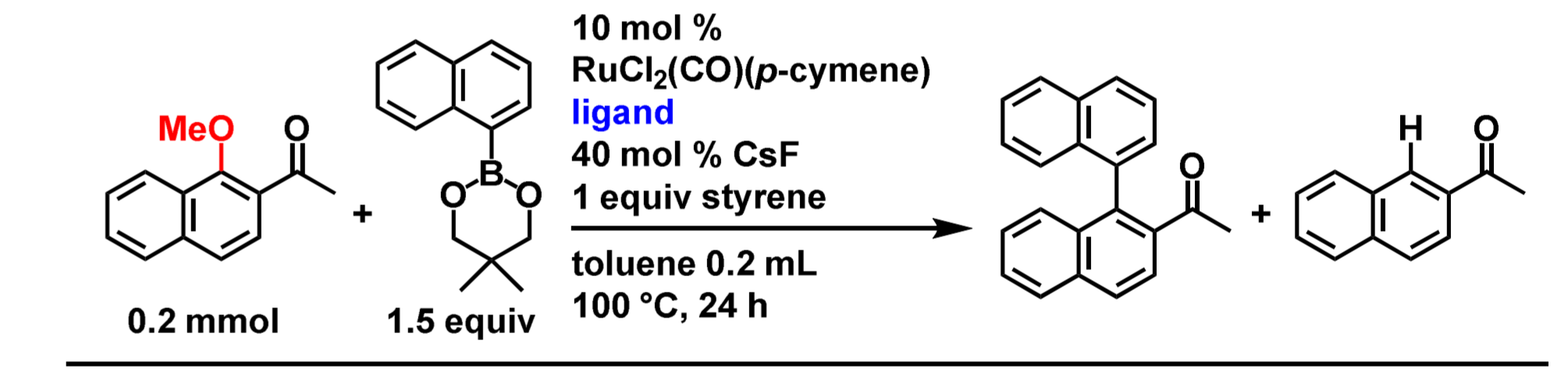
Pd-catalyzed atropselective biaryl synthesis using organoboron reagent



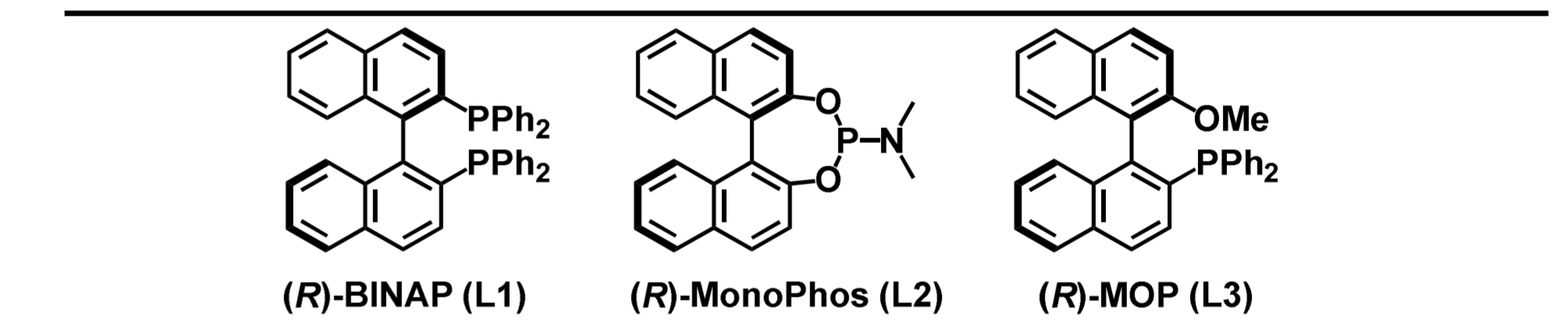
Syntheses of Axially Chiral Biaryls through Inert C-H and C-O Bond Arylation



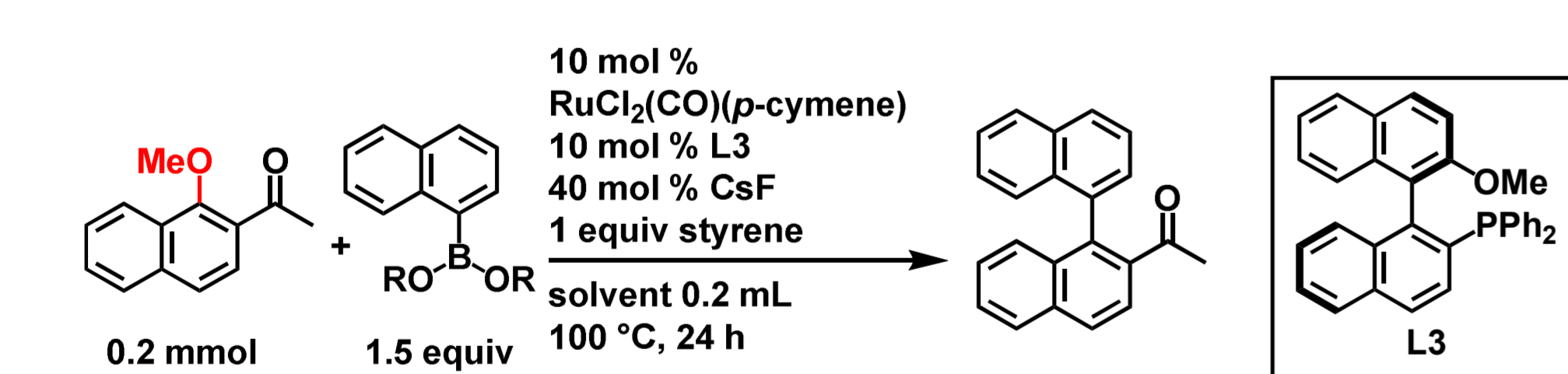
Initial Screening of Phosphine Ligands



| entry | ligand | conv. | arylation product | | hydrogenolysis product |
|-------|-------------|-------|-------------------|---|------------------------|
| | | | NMR yield / ee | | |
| 1 | 10 mol % L1 | 16% | trace / - | - | 3% |
| 2 | 20 mol % L2 | 40% | 29% / 29% ee | - | 1% |
| 3 | 20 mol % L3 | 77% | 50% / 36% ee | - | 4% |
| 4 | 10 mol % L3 | 64% | 49% / 46% ee | - | 3% |

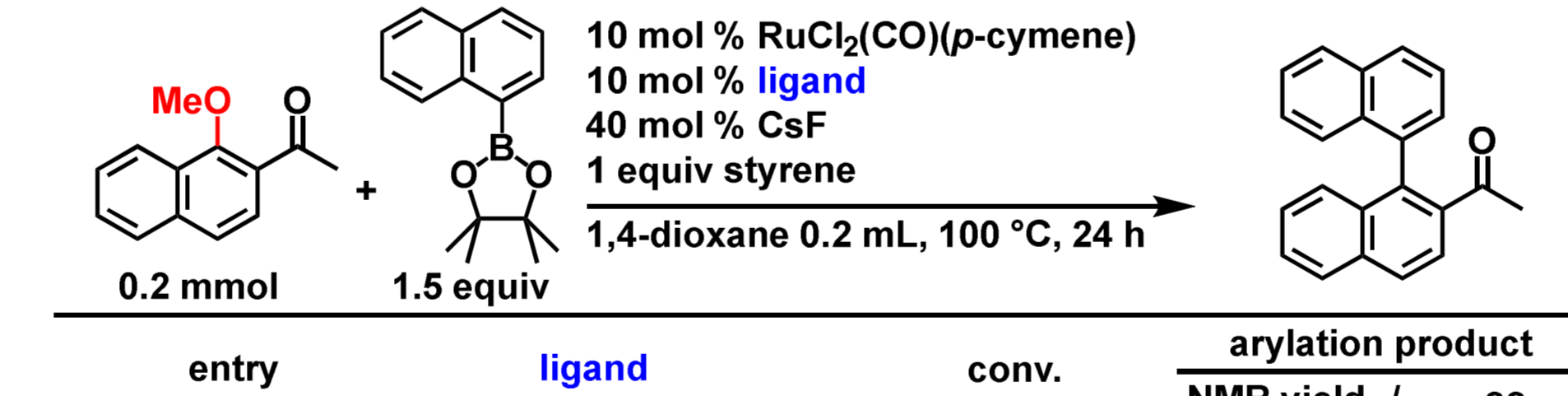


Screening of Solvents and Arylboronates

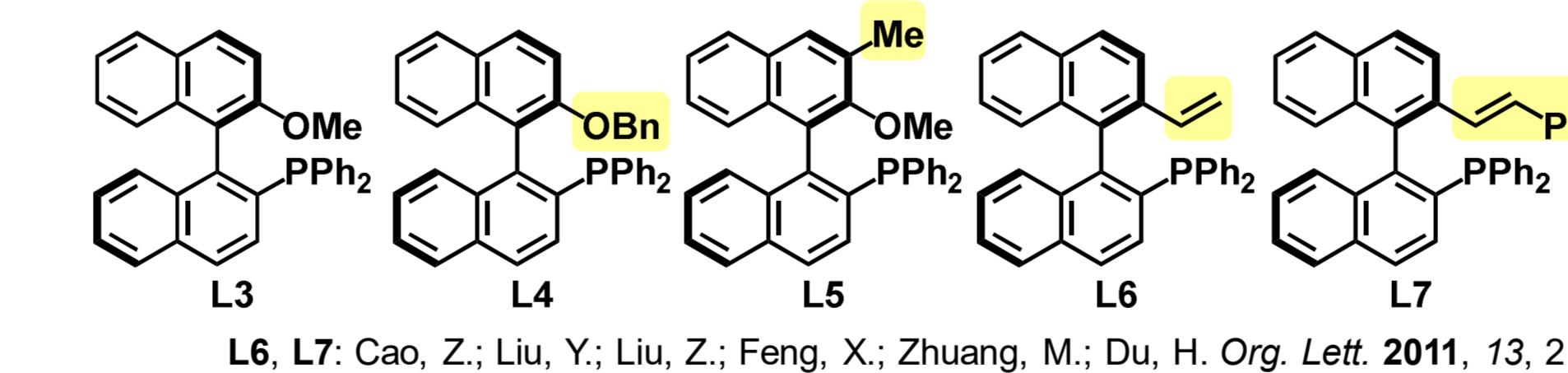


| entry | boronate | solvent | conv. | arylation product | |
|-------|-----------------------|-------------|-------|-------------------|--------|
| | | | | NMR yield / ee | |
| 1 | Ar-B(OH) ₂ | toluene | 64% | 49% | 46% ee |
| 2 | Ar-B(OH) ₂ | 1,4-dioxane | 83% | 59% | 53% ee |
| 3 | Ar-B(OH) ₂ | 1,4-dioxane | 71% | 56% | 53% ee |

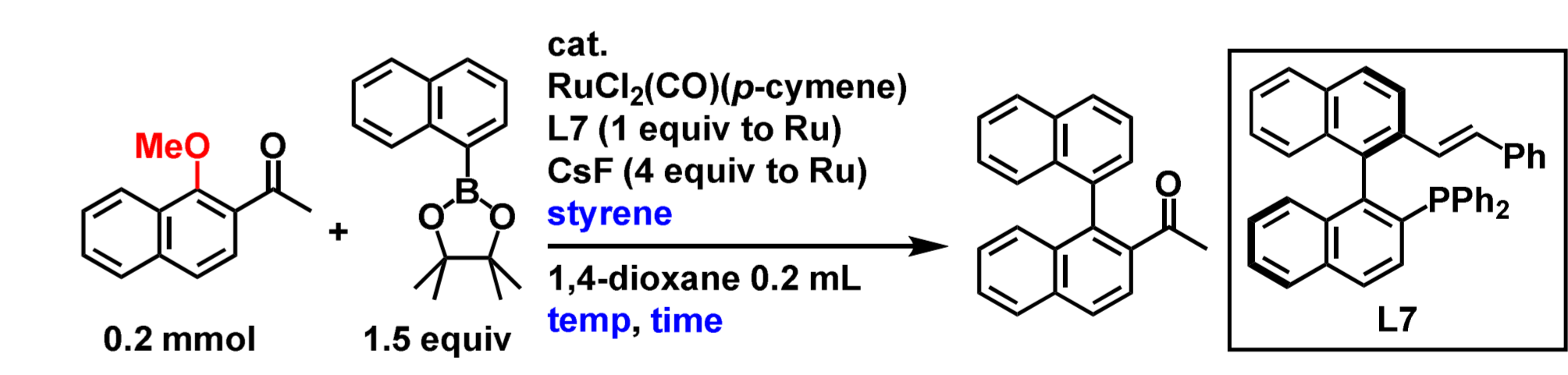
Screening of MOP Ligands



| entry | ligand | conv. | arylation product | |
|-------|--------|-------|-------------------|---------|
| | | | NMR yield / ee | |
| 1 | L3 | 71% | 56% | 53% ee |
| 2 | L4 | 56% | 47% | 57% ee |
| 3 | L5 | 40% | 32% | 42% ee |
| 4 | L6 | 25% | 18% | -30% ee |
| 5 | L7 | 77% | 63% | -61% ee |

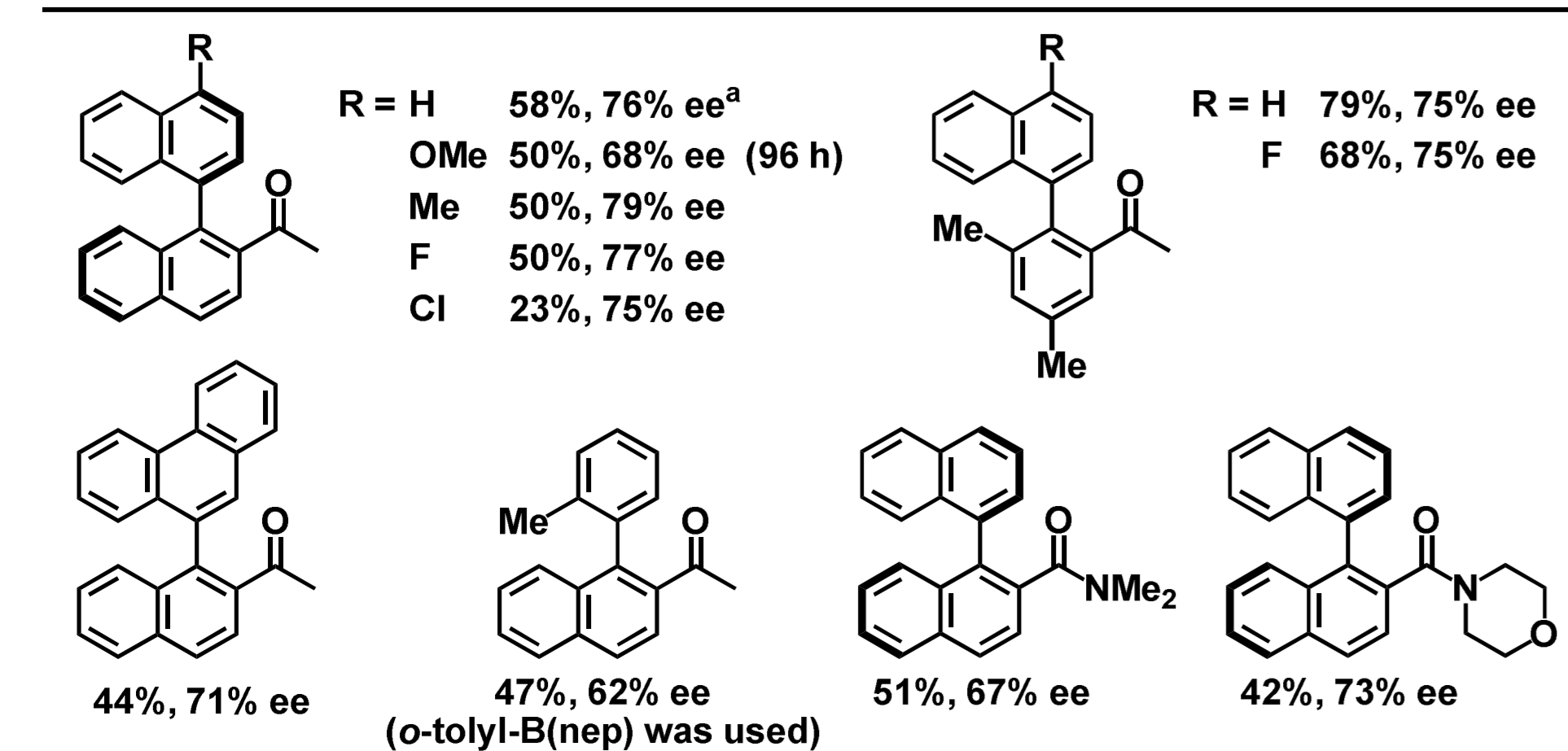
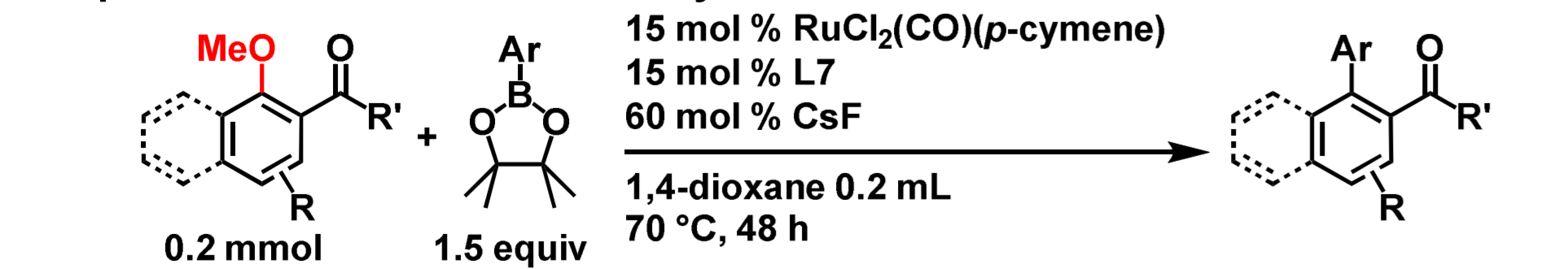


Optimization of Reaction Conditions



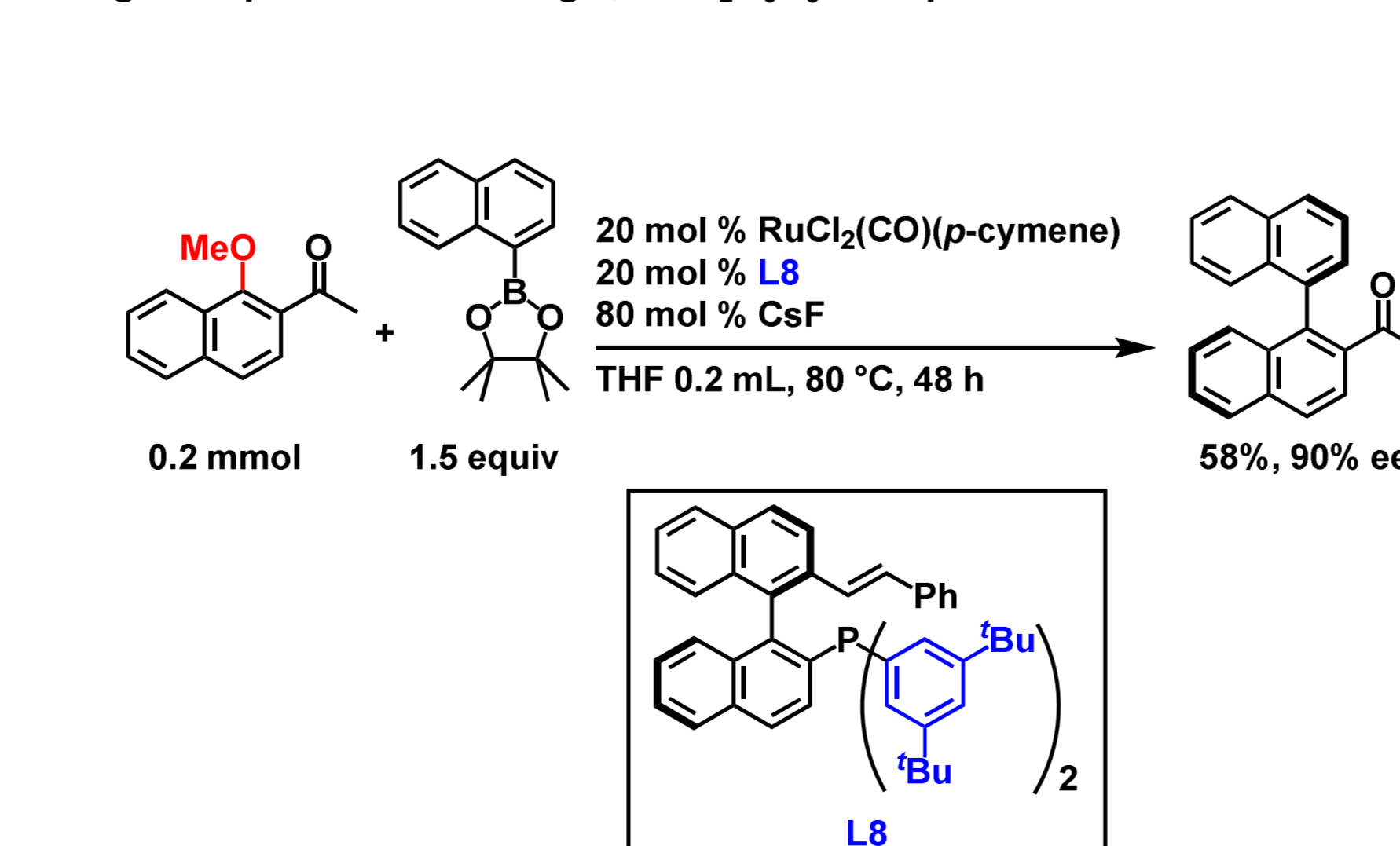
| entry | Ru cat. | styrene | temp | time | conv. | arylation product | |
|-------|----------|---------|--------|------|-------|-------------------|---------|
| | | | | | | NMR yield / ee | |
| 1 | 10 mol % | 1 equiv | 100 °C | 24 h | 77% | 63% | -61% ee |
| 2 | 10 mol % | none | 100 °C | 24 h | 80% | 71% | -62% ee |
| 3 | 10 mol % | none | 70 °C | 24 h | 35% | 31% | -78% ee |
| 4 | 15 mol % | none | 70 °C | 24 h | 41% | 37% | -79% ee |
| 5 | 15 mol % | none | 70 °C | 48 h | 67% | 61% | -76% ee |

Scope of Aromatic Ketones and Arylboronates



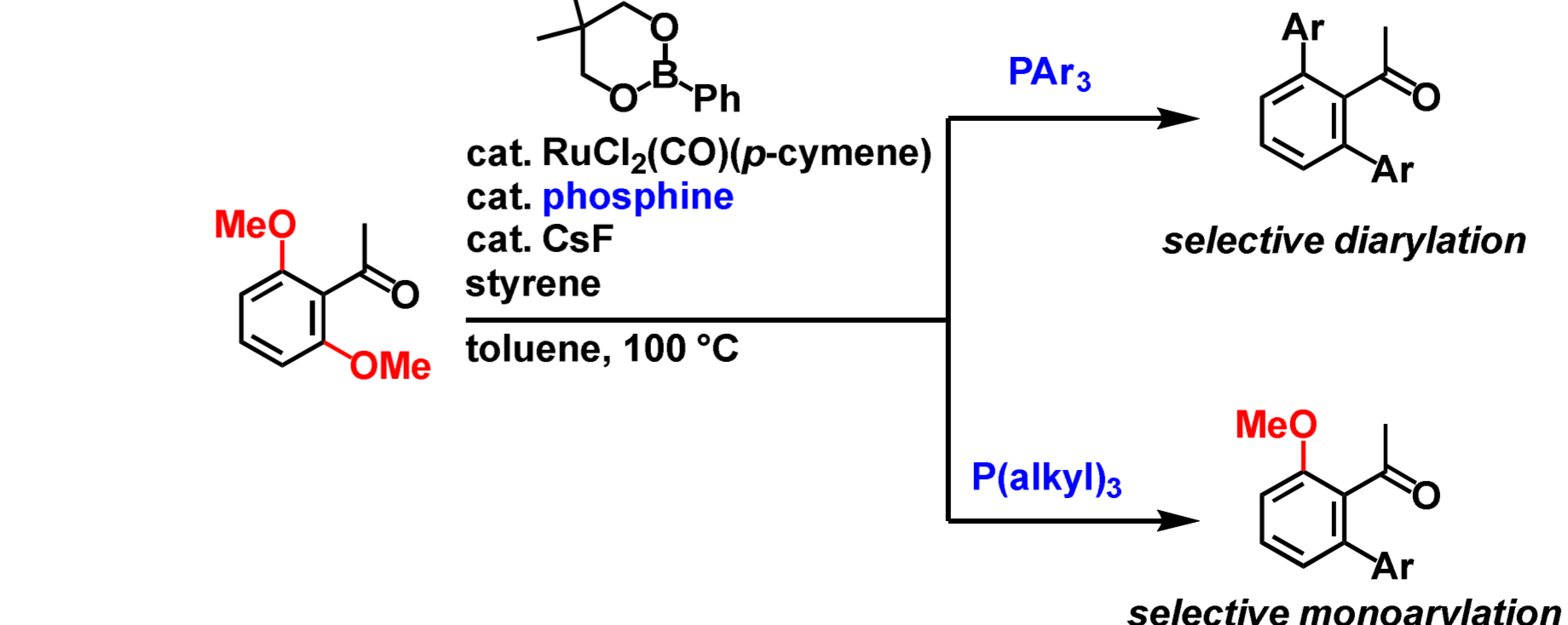
a) Absolute configuration assignment: Liu, J.; Hu, K.-F.; Qu, J.-P.; Kang, Y.-B. *Org. Lett.* 2017, 19, 5593

Using Phosphine Possessing 3,5-^tBu₂C₆H₃ Groups

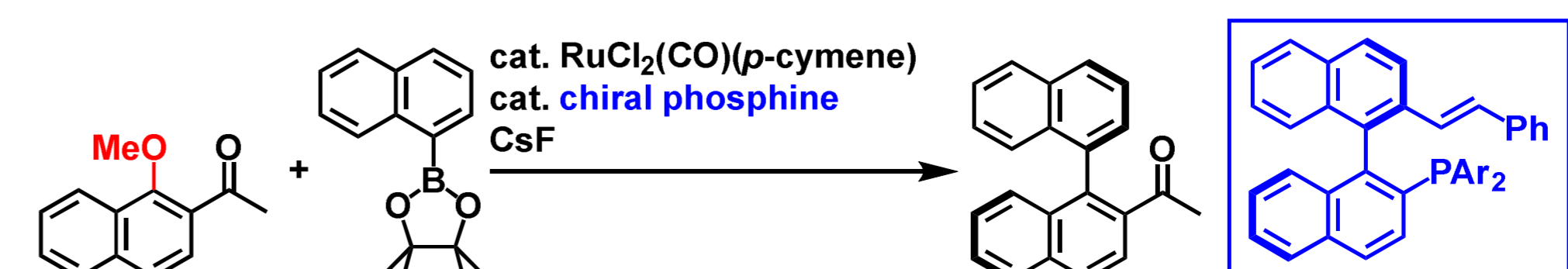


Summary

> in situ generation of ruthenium phosphine catalyst for C-O mono/diarylation



> atropo-enantioselective synthesis of axially chiral biaryls



Kondo, H.; Kochi, T.; Kakiuchi, F. *Chem. Eur. J.* 2020, 16, 1737-1741.



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