

Exploring the Utility of Ionic Liquids as Solvents for the Selectivity of Copper-catalysed Phosphoramidate Synthesis

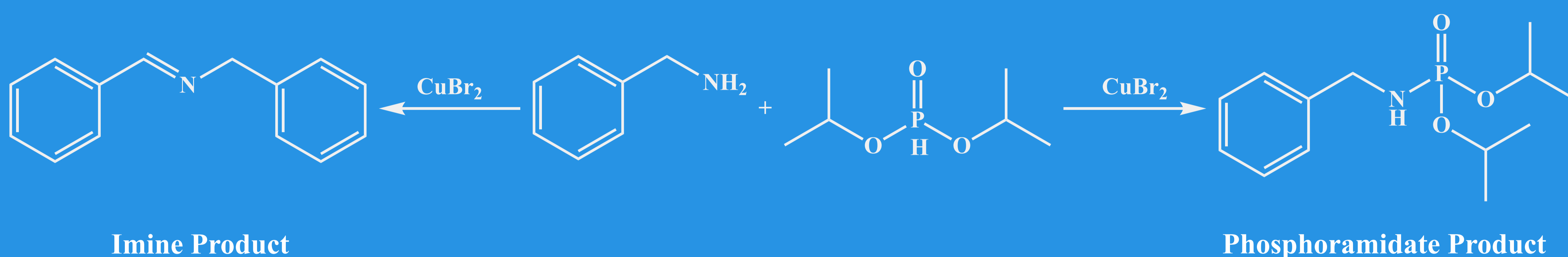
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Introduction

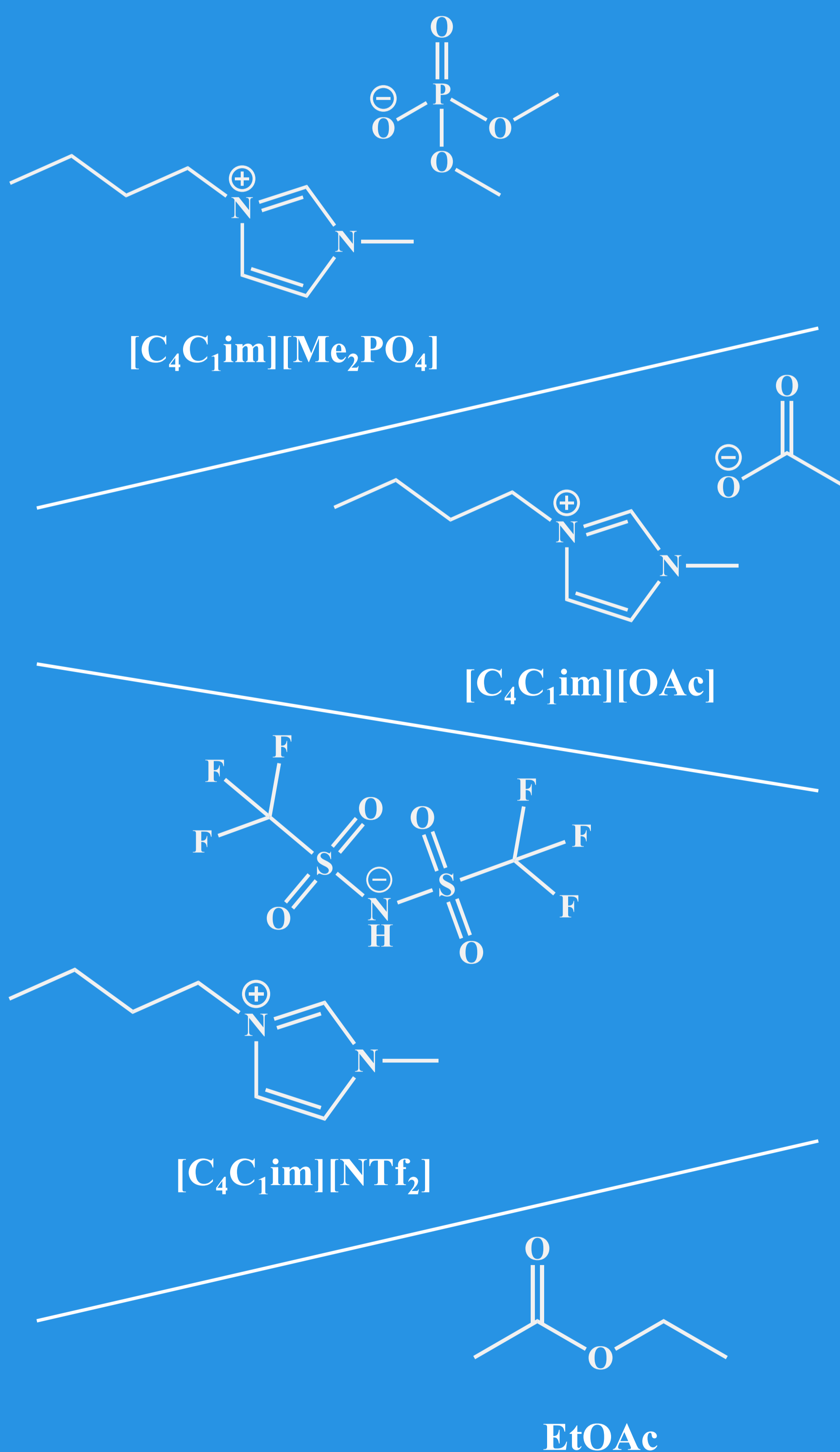
- Phosphoramidates previously have been synthesized by the nucleophilic substitution of chlorophosphonates with amides in the presence of a strong base such as *n*-butyllithium.¹
- Recent methods involve aerobic oxidative dehydrocoupling: phosphite interacting with a copper(II) bromide catalyst to produce halogenated phosphite and copper(I) bromide.² The reduced copper is re-oxidized by air to complete the catalytic cycle.
- Aerobic oxidative dehydrocoupling was performed using ionic liquids, exploring kinetic and thermodynamic effects. Solvents [C₄C₁im][Me₂PO₄], [C₄C₁im][OAc], and [C₄C₁im][NTf₂] were used to be compared against ethyl acetate (EtOAc).
- Literature indicates an anion effect on the aerobic oxidation of amines, controlling selectivity between imine and nitrile products.³



Imine Product

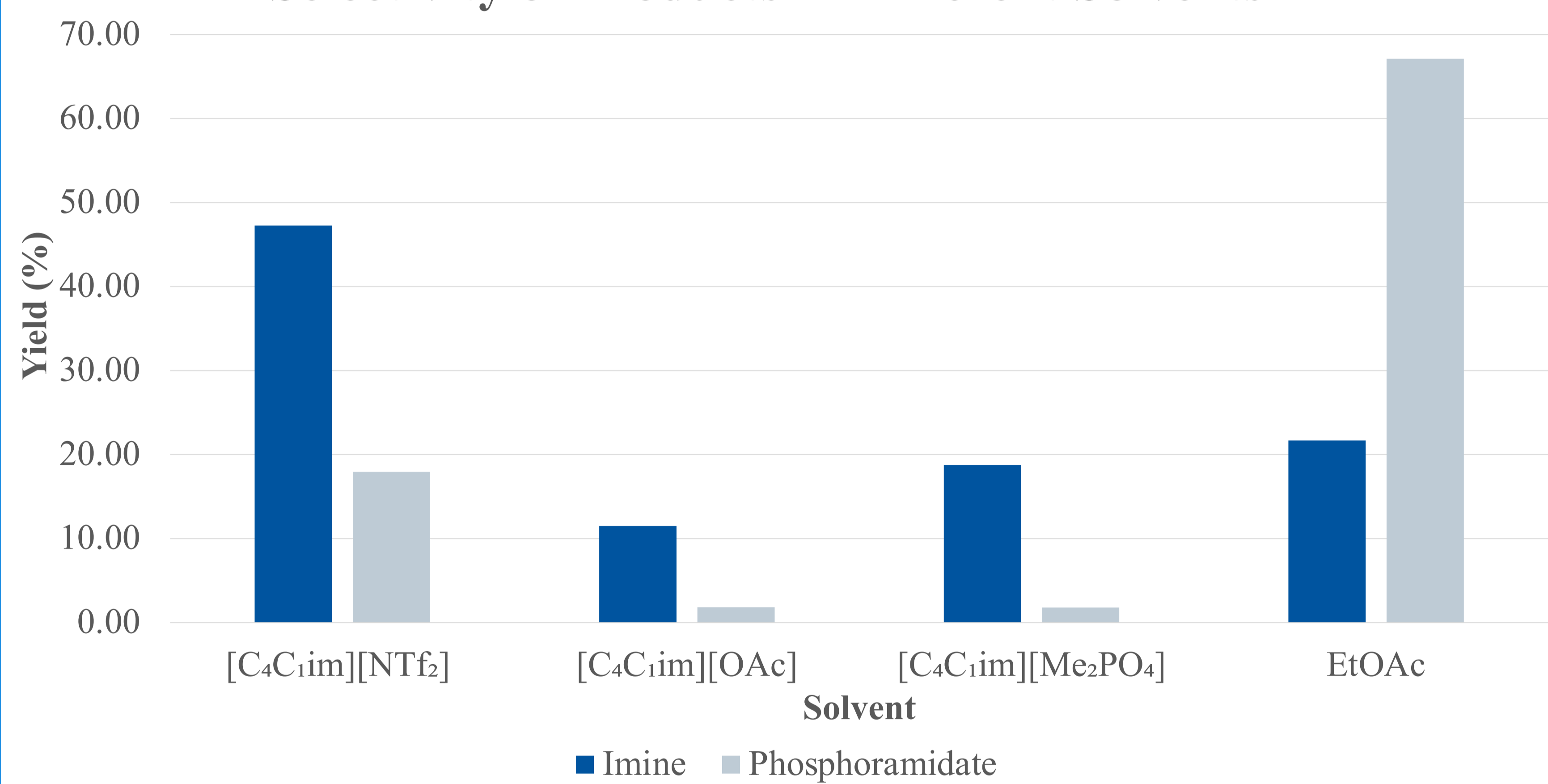
Phosphoramidate Product

Solvents



Results and Discussion

Selectivity of Products in Different Solvents



Effect of using different solvents with 6 hours of reaction time under air at room temperature

- Postulated that the difference in yields is caused by ionic liquid ion exchange. Literature states that ion exchange can occur if stronger interactions can be formed upon the exchange of ions.⁴
- Phosphoramidate likely forms due to a halogenated active catalyst derived from copper(II) bromide. When an ionic liquid (i.e. [C₄C₁im][NTf₂]) is used as a solvent, the effects of the halogenated active catalyst are deterred, resulting in imine product.

Conclusion

- Ionic liquids facilitate the formation of imines over phosphoramidates when used in tandem with a copper bromide catalyst.
- Ultimately, the observed effects could likely be produced with an appropriate anion on the copper catalyst, even without ionic liquids.

References

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