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The Effect of Variation of N-Substituents on Oxidopyridinium Ions in (4+3) Cycloadditions

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Introduction/Background

A (4 + 3) cycloaddition reaction is an attractive method for the generation of seven-membered rings in organic chemistry. The reaction between a four-atom π -system and a three-atom π -system is required for such a reaction to proceed. Traditionally, a diene is used for the four-atom system while either an allylic or oxyallylic cation is used as the three-atom system (Figure 1).¹ In the example shown, the product will evolve to a specific product based on the identity of the "Z" group.

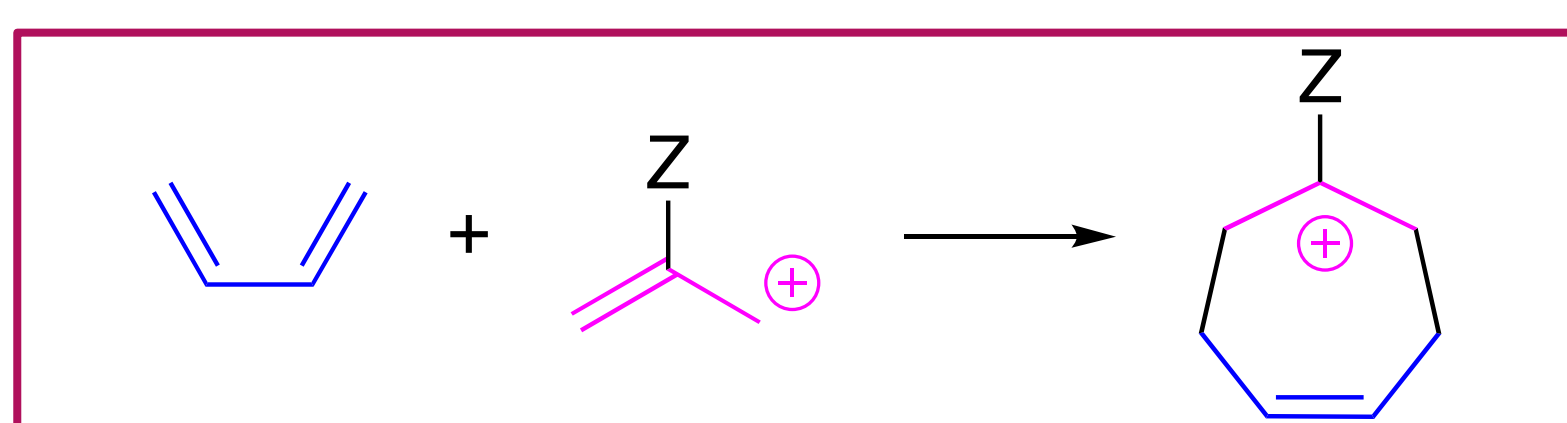
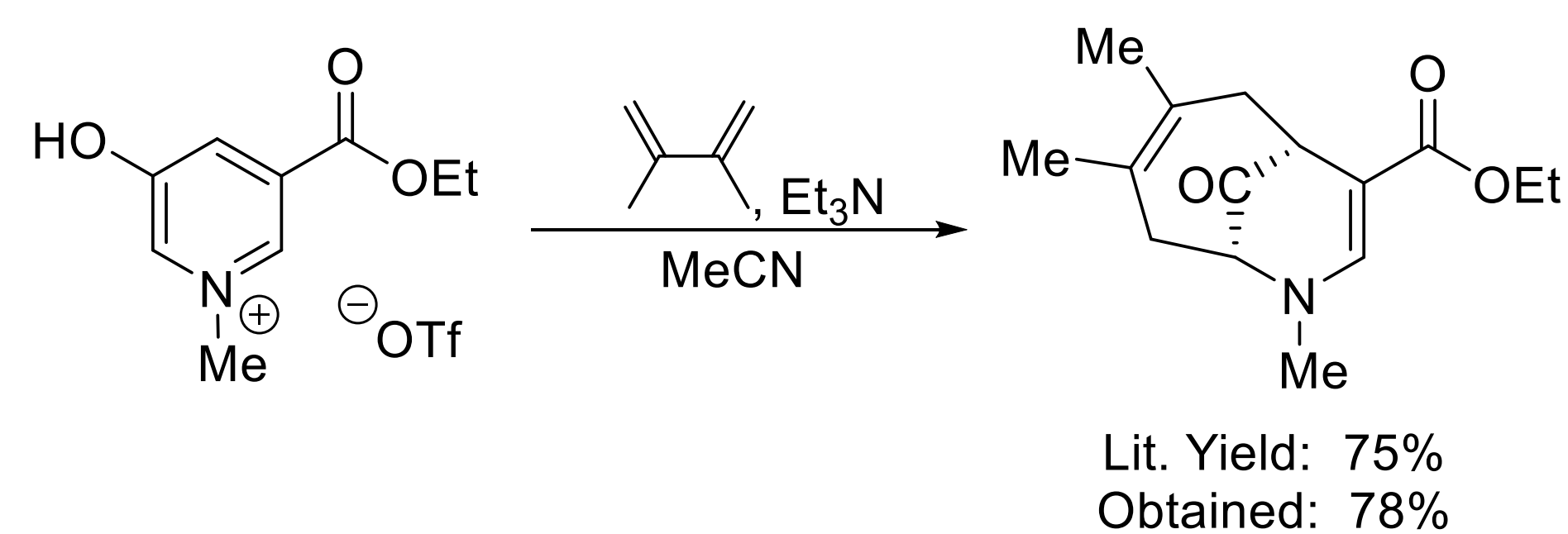
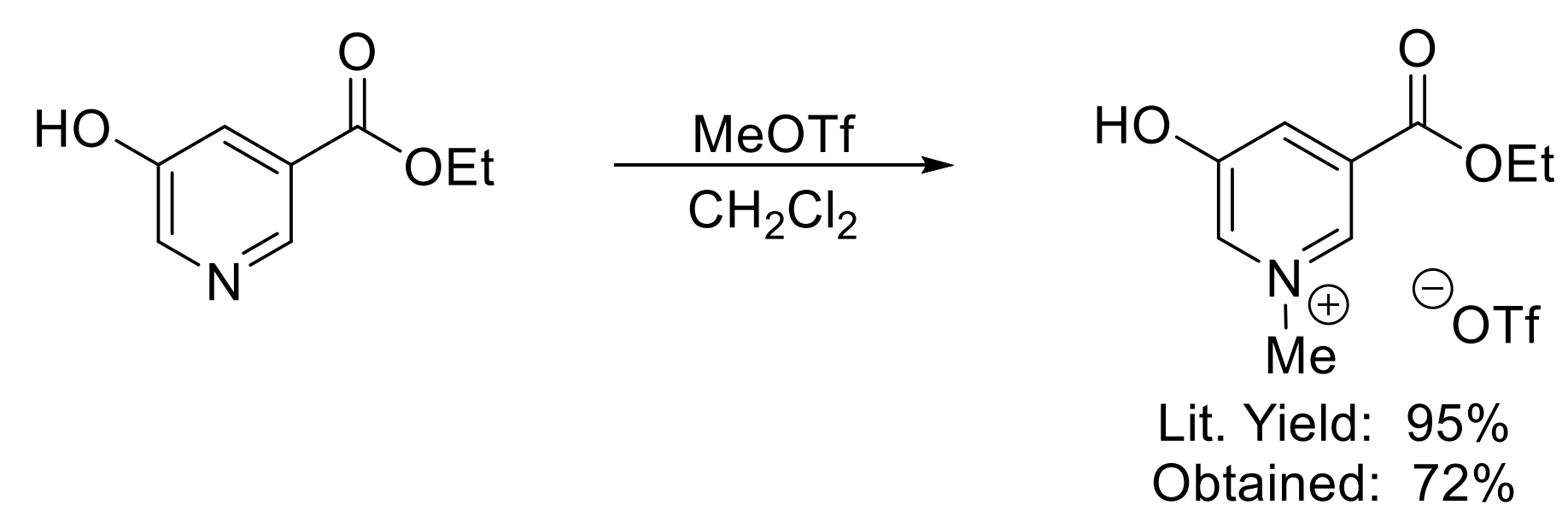
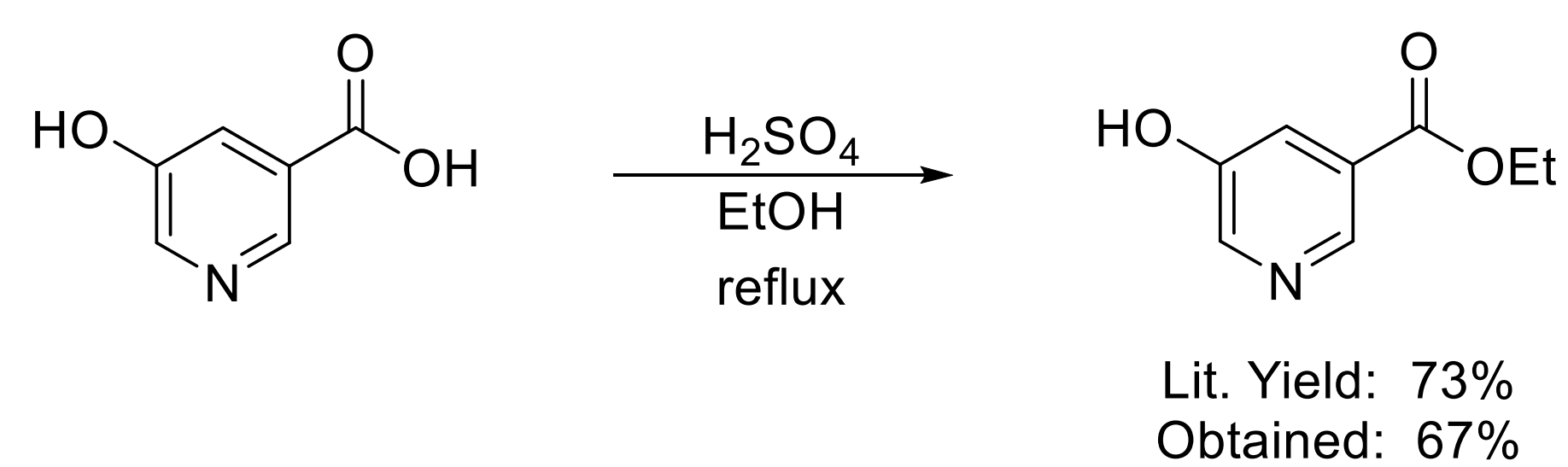


Figure 1. Generic (4+3) cycloaddition reaction.

Our group has currently been studying the production of (4+3) cycloadducts using oxidopyridinium ions. We have published several papers on *N*-methylated oxidopyridinium ions that undergo (4+3) cycloadditions in high yields.¹

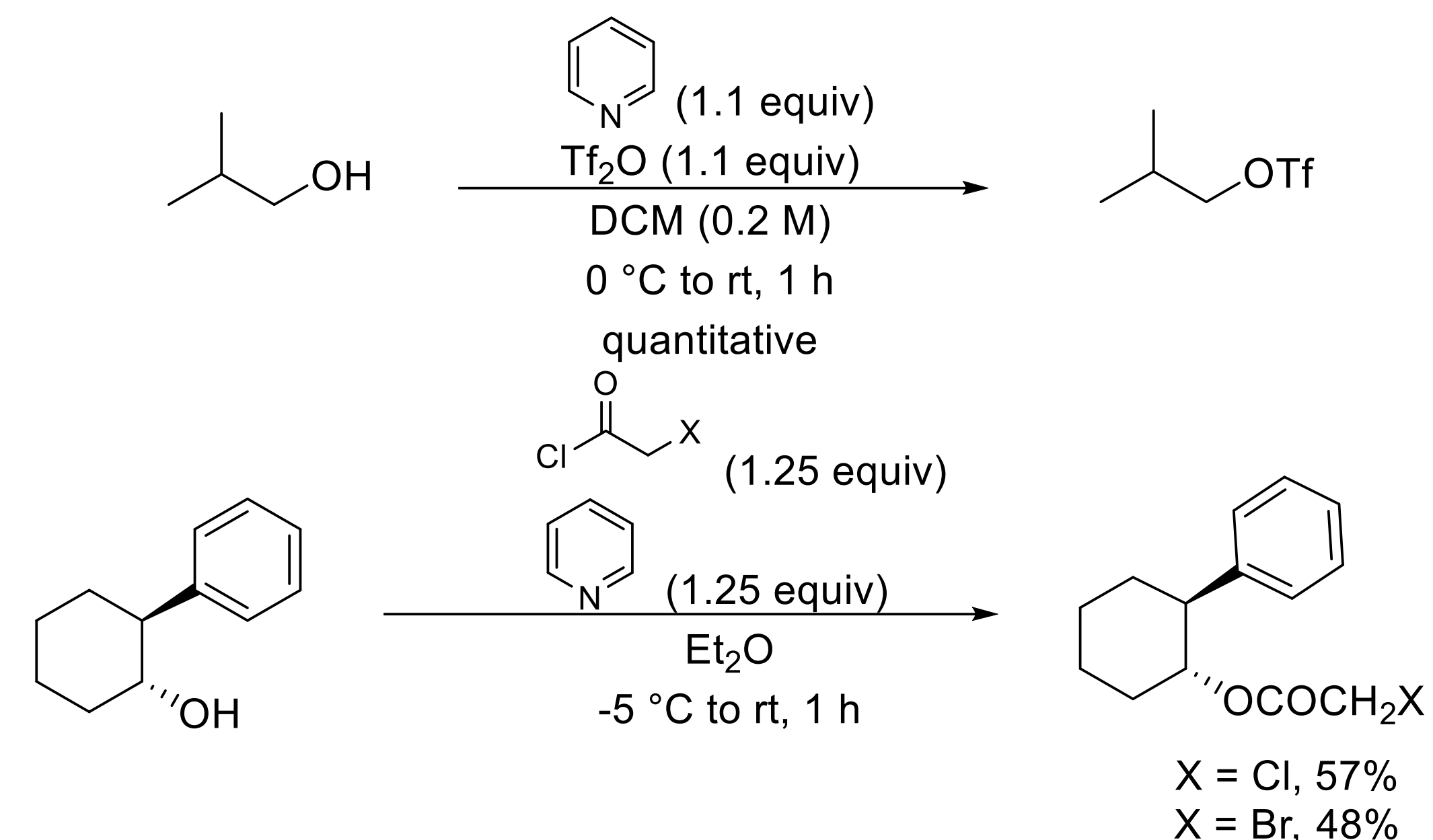
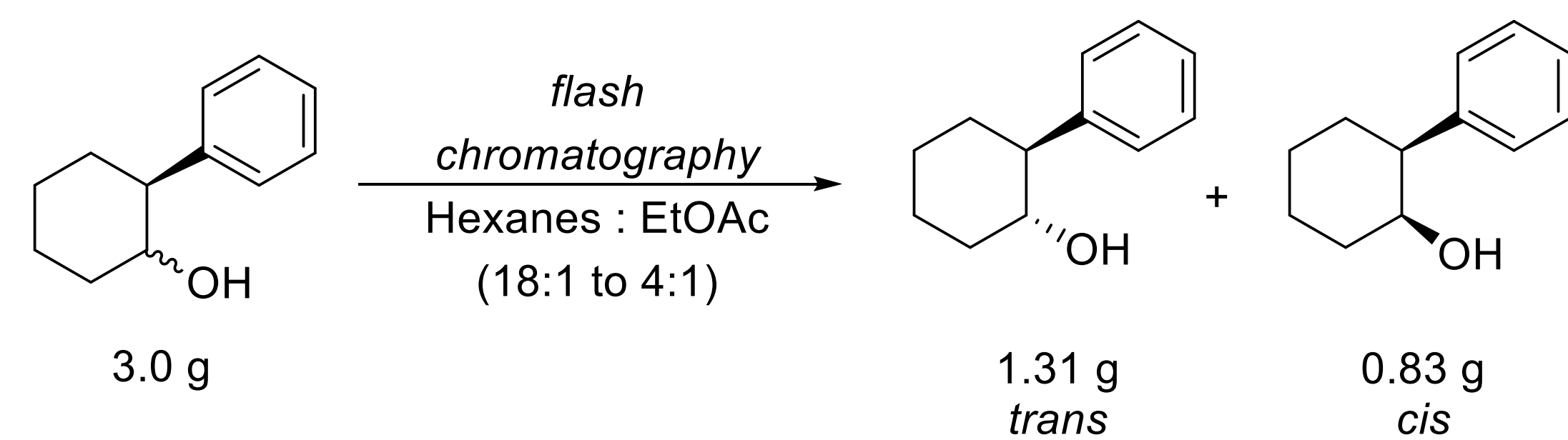
We wanted to determine if there were bulkier *N*-alkyl and *N*-acyl derivatives that could participate in these (4+3) cycloaddition reactions and, if so, to what extent? We began with checking our own ability to carry out the reaction that had been published.

Reproducing Literature Results²

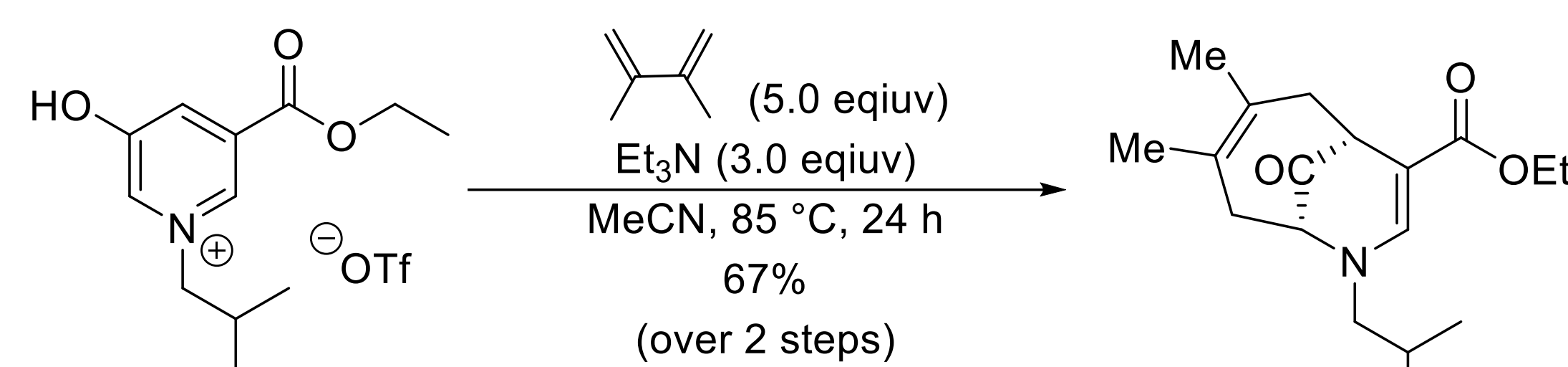
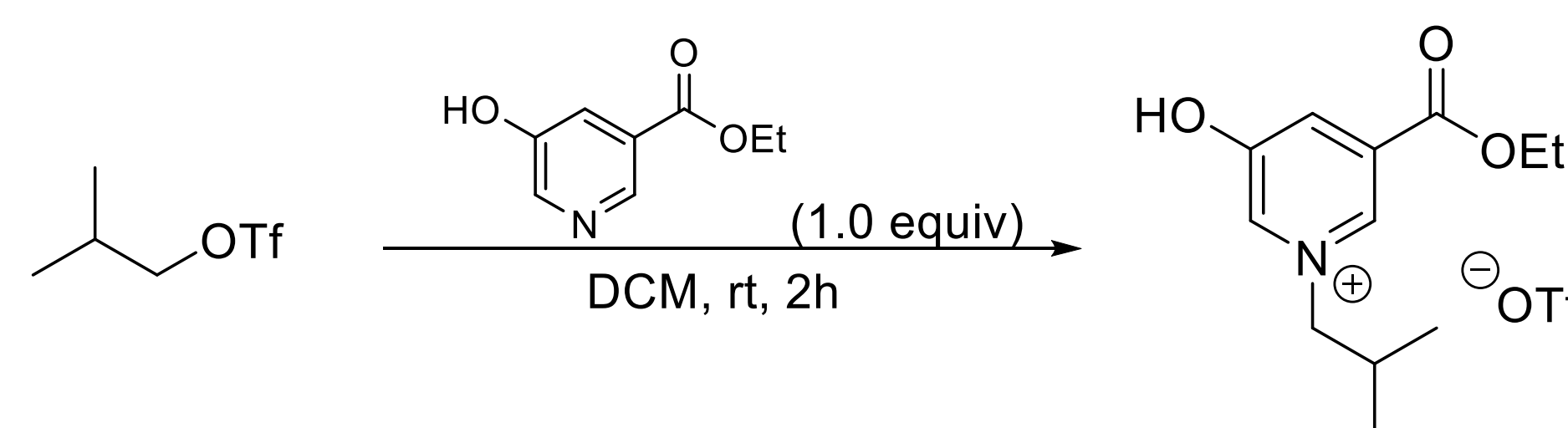


Chemistry (Results)

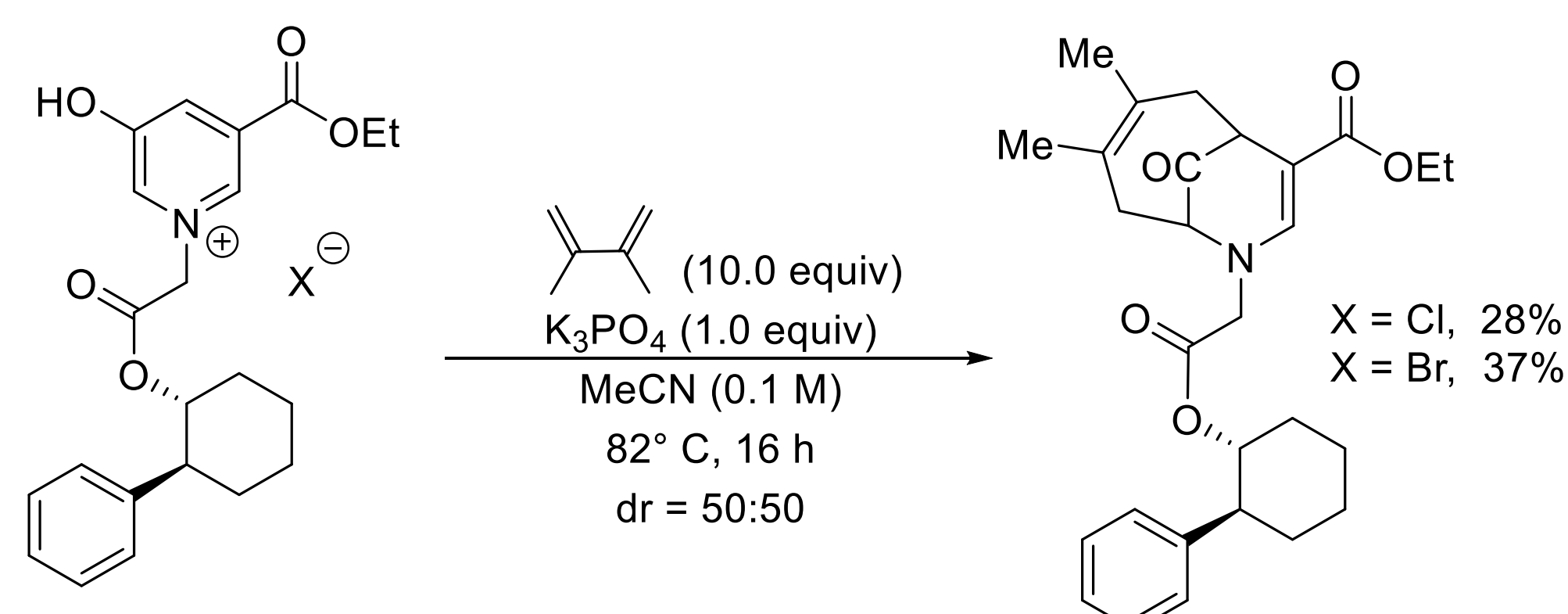
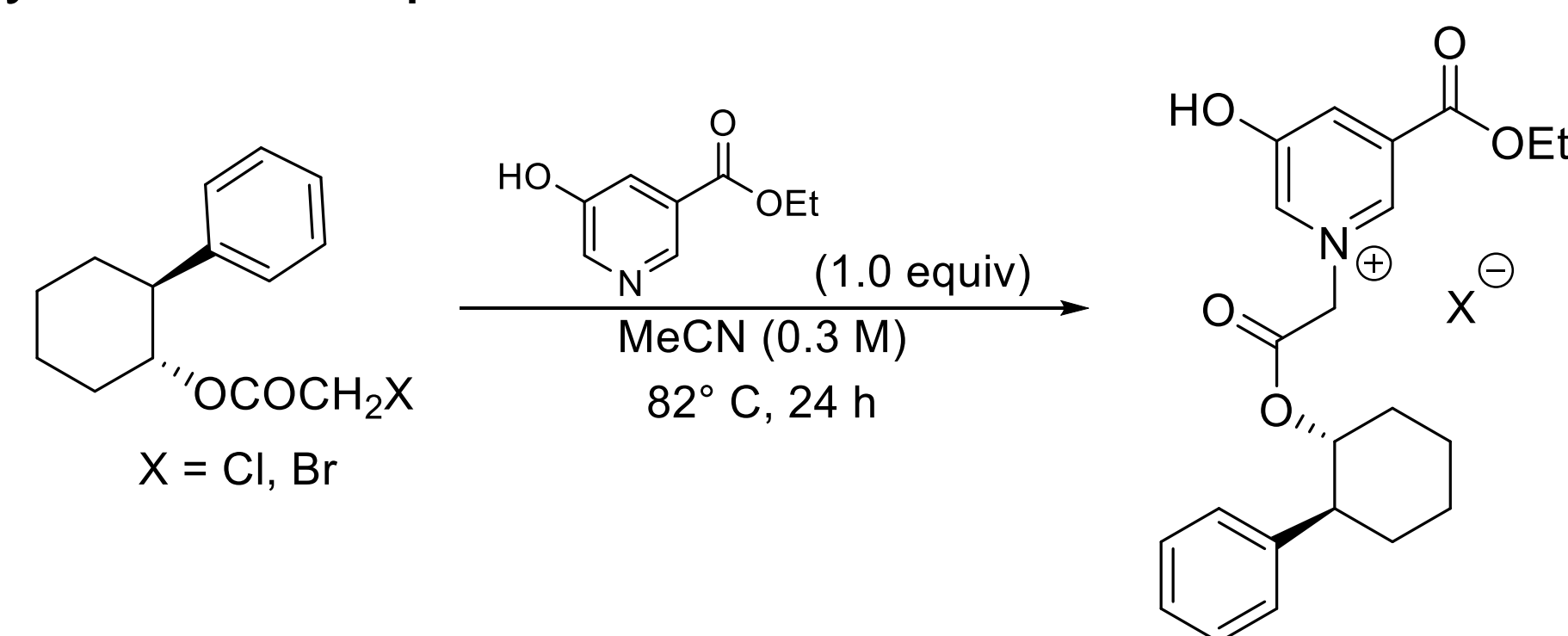
❖ Synthesis and purification of starting materials



❖ *N*-alkylation of ethyl 5-hydroxynicotinate and (4+3) cycloaddition product



❖ *N*-acylation of ethyl 5-hydroxynicotinate and (4+3) cycloaddition product



Discussion/Conclusion

- ❖ Increasing the steric bulk of functional groups bound to oxidopyridinium ions did not hinder our ability to produce cycloadduct products.
- ❖ While testing the purity of our acetyl chloride (4+3) product, we noticed that it started to degrade when left out signaling that it is air sensitive which could have had an effect on our final yield.

In conclusion, attaching bulkier functional groups onto oxidopyridinium ions and using them in (4+3) cycloaddition reactions proved to be possible. While the derivatives included here were not as high yielding as such oxidopyridinium derivatives containing an *N*-methyl group, further optimization of reaction conditions would be required for each unique functional group introduced.

References

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