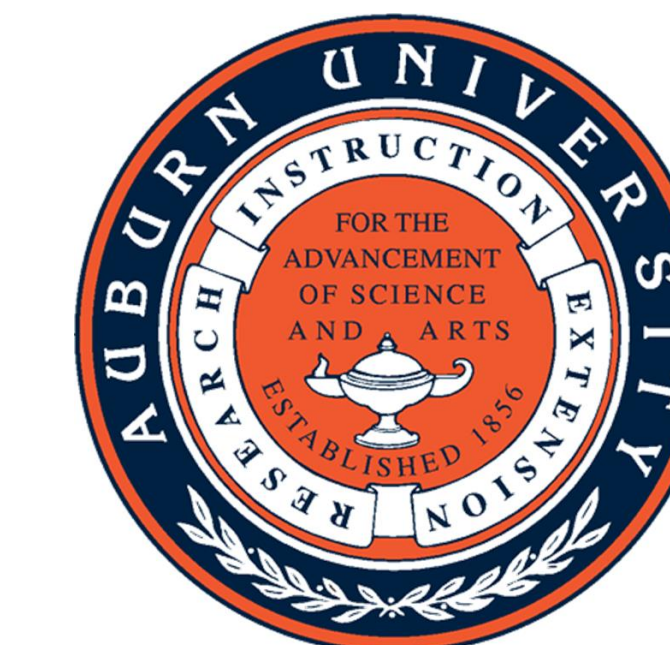




# Oxidative Mannich reactions using Cu(II) 2-quinoxalino salen catalyst and tert-butyl hydroperoxide

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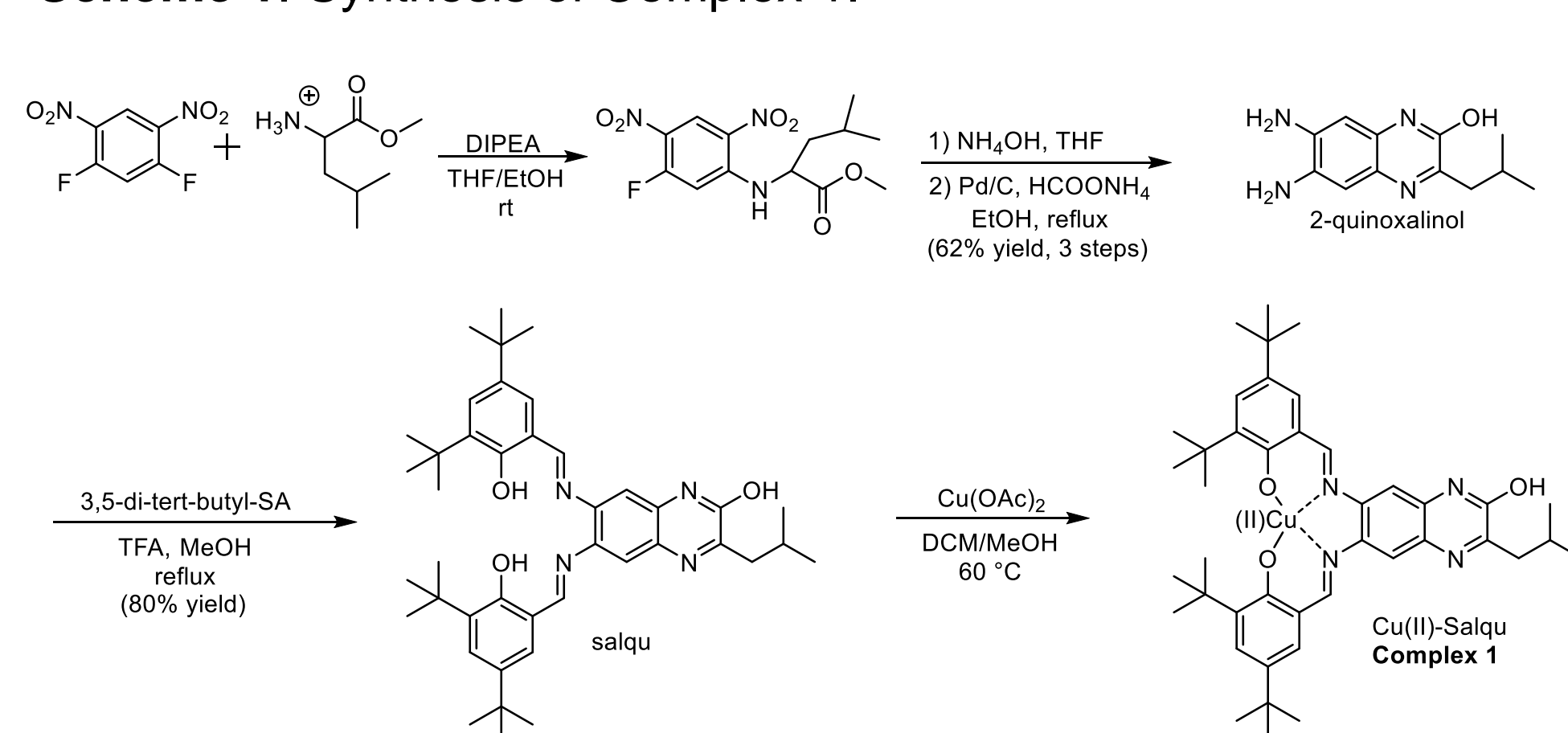


## INTRODUCTION

- The Mannich reaction is a useful tool to form carbon-carbon bonds.
- Many historical syntheses require key Mannich couplings.
- Several challenges arise when forming the iminium ion intermediate.
  - harsh conditions, long reaction times, expensive transition metals, or high catalyst loading.
- C-H oxidation could provide a direct route to forming the iminium ion.
  - Previous examples require expensive catalyst such as  $Rh_2(cap)_4$  or low yielding Cu(I).<sup>1,2</sup>
- Herein, we report the use of Cu(II) 2-quinoxalino salen (Salqu) catalyst for oxidative Mannich reactions.<sup>3</sup>

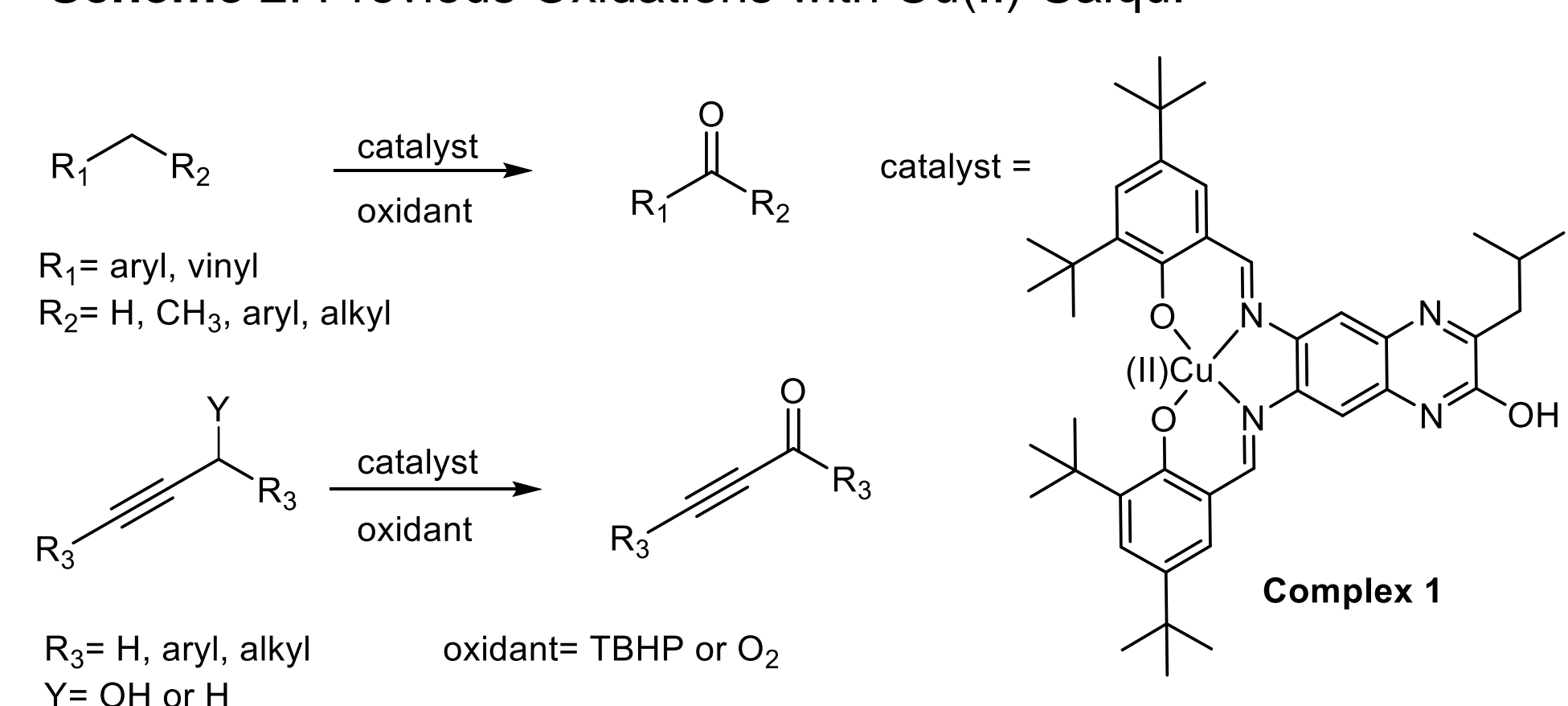
## CATALYST PREPARATION

Scheme 1. Synthesis of Complex 1.



## PREVIOUS OXIDATIONS

Scheme 2. Previous Oxidations with Cu(II)-Salqu.



## RESULTS AND DISCUSSION

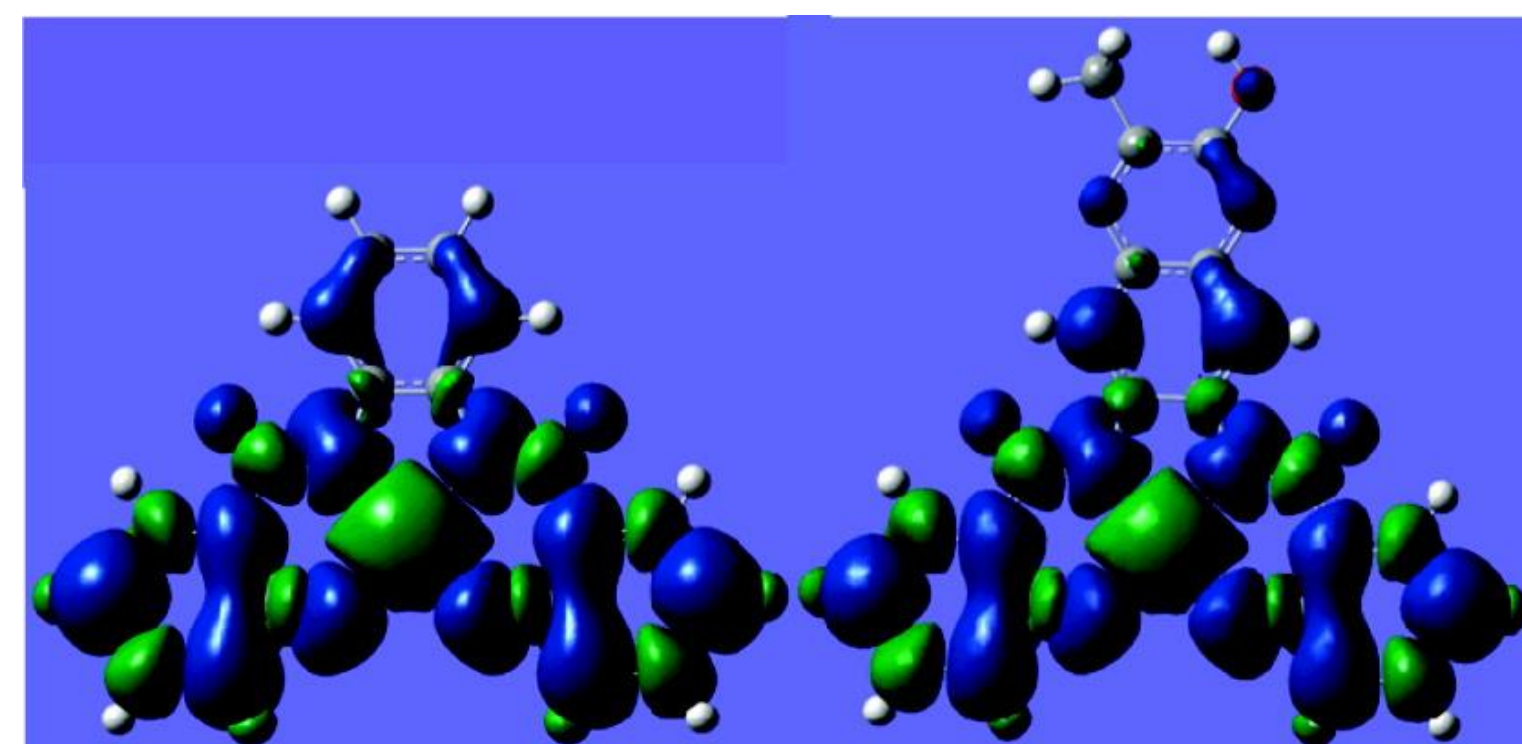
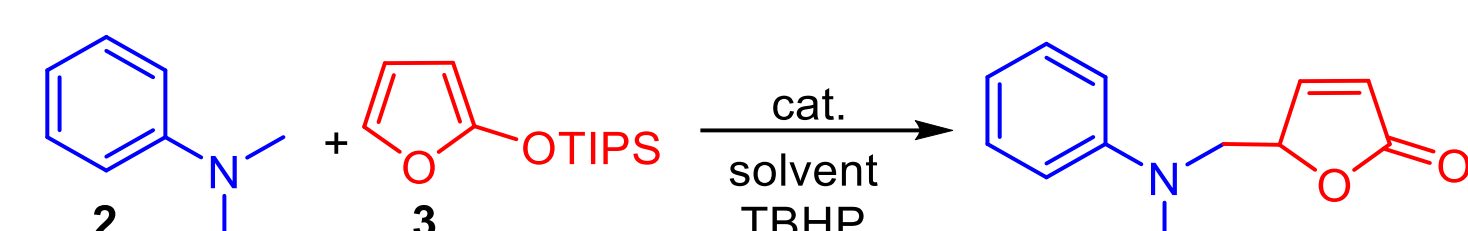


Figure 1. DFT comparison of salophen and Salqu, the Spin density of  $[LCu(III)]^+$  with 0.0004 a.u. isosurface density (L = salophen and salqu).

Table 1. Optimization of Reaction Conditions.



entry	conditions <sup>a</sup>	time	yield <sup>b</sup> (%)
1	1 (1 mol%), MeOH, 60 °C	1	64
2	1 (1 mol%), MeOH, 60 °C	2	81
3	1 (1 mol%), MeOH, 60 °C	3	92
4	1 (1 mol%), MeOH, 60 °C	4	98
5	1 (1 mol%), 3 (1 equiv), MeOH, 60 °C	4	82
6	1 (1 mol%), $K_2CO_3$ MeOH, 60 °C	4	trace
7	1 (1 mol%), MeCN, 60 °C	4	52
8	$Cu(OAc)_2$ (5 mol%), MeOH, 60 °C	4	62
9 <sup>c</sup>	1 (1 mol%), MeOH, 60 °C	4	51

<sup>a</sup>Reactions were done using 2 (1 mmol), 3 (0.5 mmol), T-HYDRO (1.2 equiv), solvent (1 mL). <sup>b</sup>Yield determined by GC using internal standard or isolated yields after column chromatography. <sup>c</sup> $H_2O_2$  instead of T-HYDRO.

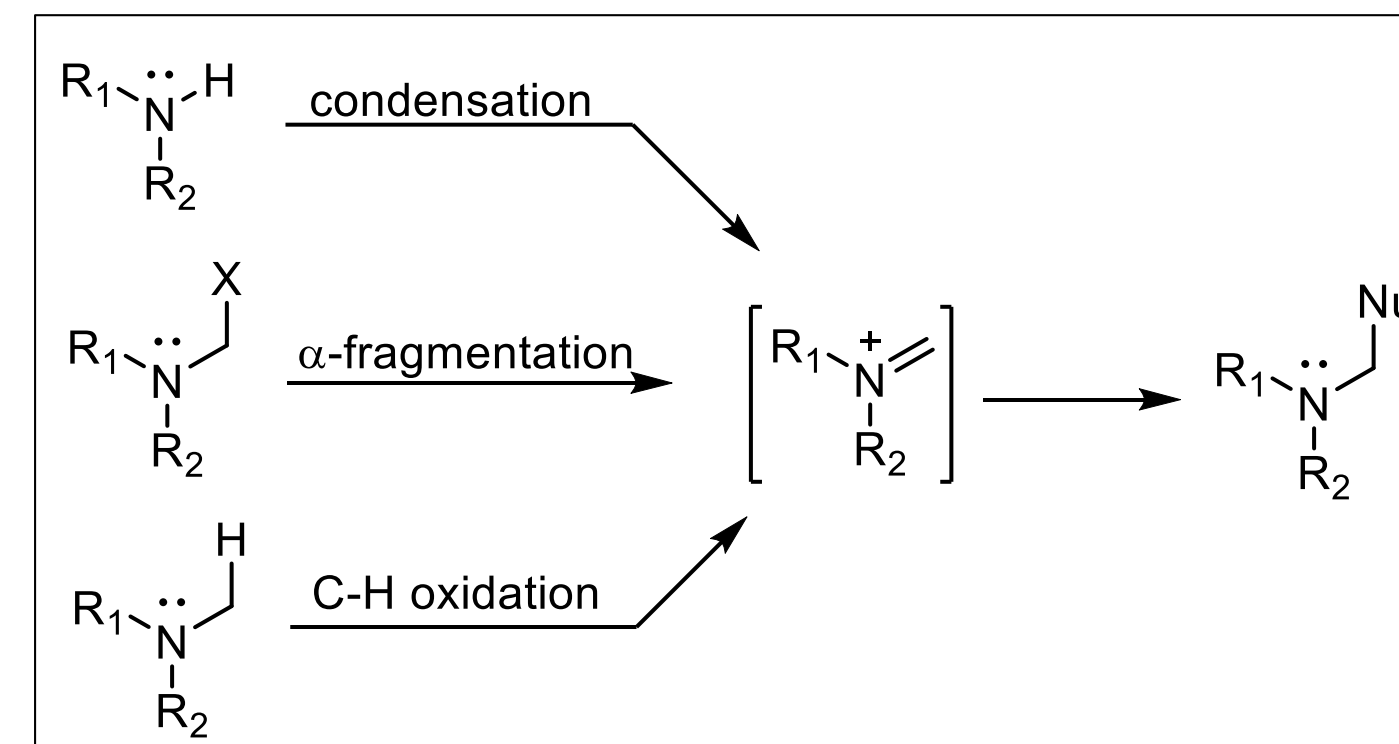
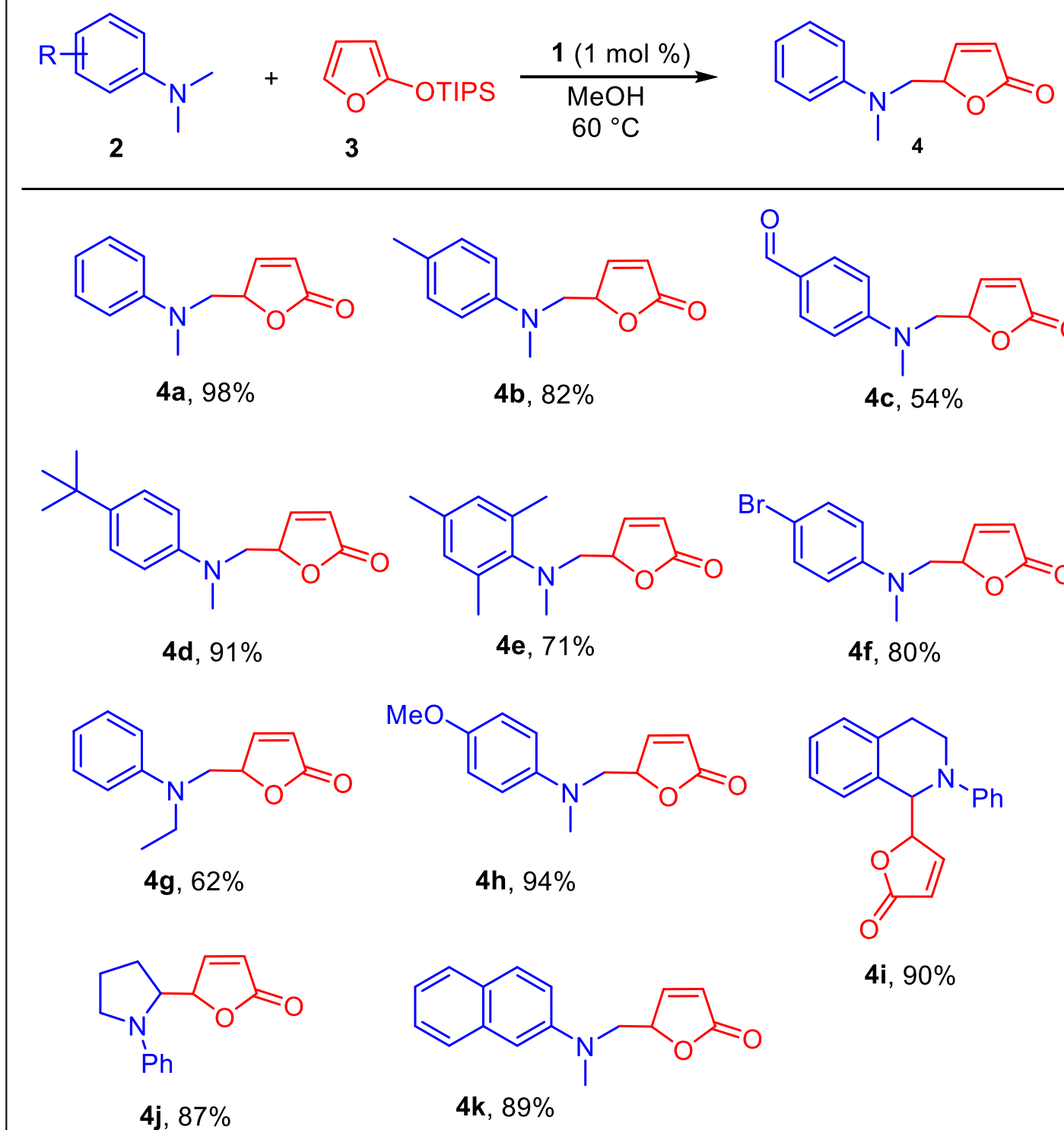


Figure 2. Formation of iminium ion using different methods

Table 2. Substrate Scope of Various Amines.



<sup>a</sup>Reaction conditions: N,N dimethylaniline 2a (1.0 mmol), 2-triisopropoxysilylfuran (0.5 mmol), MeOH (1 mL), Cu(II)-Salqu (1 mol%), T-HYDRO (1.2 equiv), 60 °C, 3-4 h. <sup>b</sup>Yields of isolated products.

## CONCLUSIONS

- We report the use of an earth abundant transition metal copper for oxidative Mannich reactions.
- A range of different 3° amine substrates were tested producing yields up to 98% in 3-4 h.
- A simple catalytic cycle has been proposed which we believe is generating Cu(III); however, more studies will be done to better understand this reaction.

## REFERENCES

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