Organic and Materials Chemistry

29th Symposium on Chemistry Postgraduate Research in Hong Kong

Thiamine Carbene Ligated Gold (I) Chloride Catalyzes an Efficient Aldehyde-Alkyne-Amine (A3) Coupling Reaction in Water

Rajashekar Reddy Narra,† Vignesh Gopalakrishnan Unnithan,† and Zhihong Guo*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China.

INTRODUCTION

Propargylamines are versatile synthetic precursors that are widely used in the synthesis of pharmaceuticals and other bioactive molecules. Noticeably, the A3 coupling reaction is high-yielding and simple to operate under relatively mild conditions – providing an efficient route toward propargylamines. As a result, it has been widely used in the synthesis of significant scaffolds.

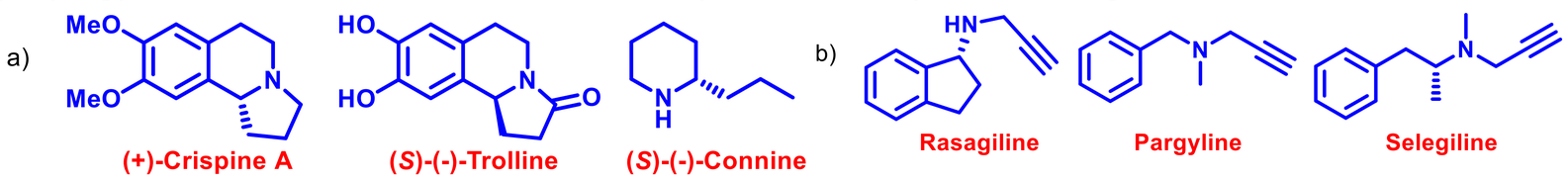


Figure 1. a) Representative natural products synthesized from propargylamine; b) Propargylamine core containing drug molecules

SYNTHESIS OF THIAMINE-GOLD(I) CATALYST

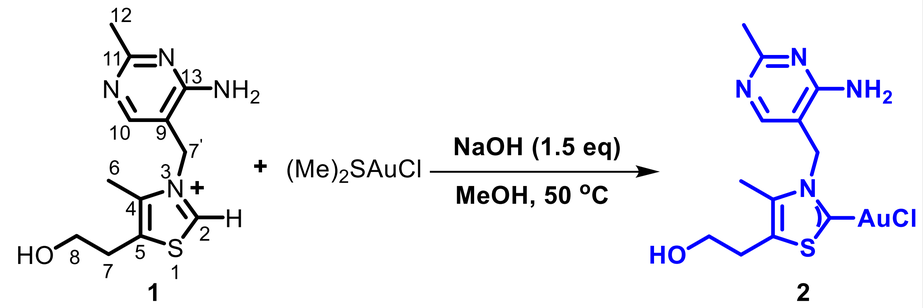
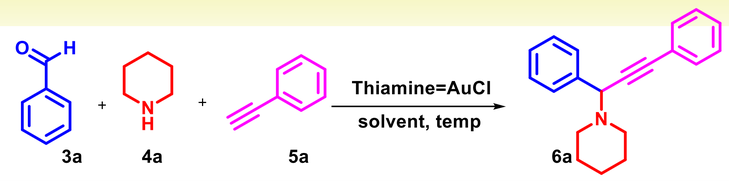


Figure 2. Synthesis of the thiamine-gold (I) catalyst

OPTIMIZATION OF THE REACTION CONDITIONS

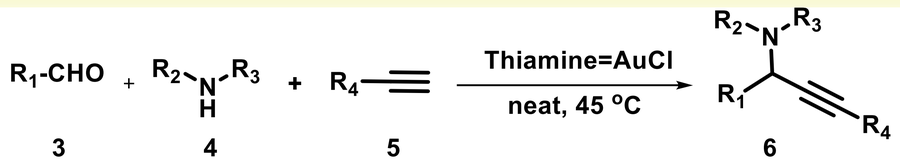


entry	catalyst **2** (%)	solvent	temp (°C)	time (h)	conv (%)
1	1	H_2O	45	24	60
2	2	H_2O:ACN(9:1)	RT	24	98[b]
3	2	H_2O:ACN(9:1)	45	5.5	98
4	2	H_2O:ACN(9:1)	80	24	95
5	2	MeOH	RT	24	55
6	2	MeOH	45	8	85
7	2	MeOH:H_2O	RT	24	50
8	2	iPrOH	RT	24	50
9	2	DCM	RT	24	65
10	2	THF	RT	24	20
11	2	CH_3CN	RT	24	20
12	2	1-BuOH	RT	24	50

[a] Isolated yields.

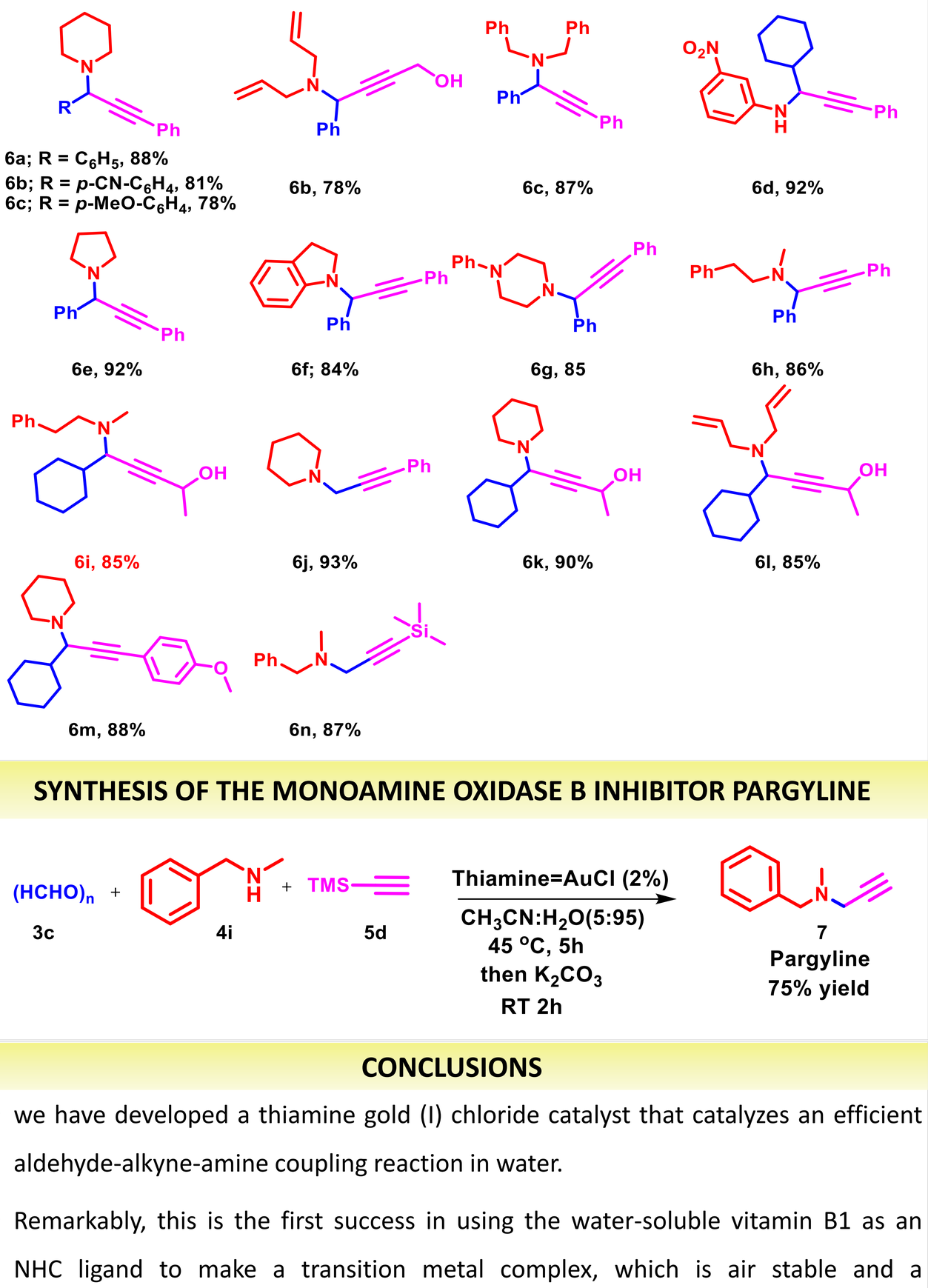
[b] after formation of propargylamine added K_2CO_3 to the reaction mixture.

SYNTHESIS OF PROPARGYLAMINES UNDER SOLVENT-FREE CONDITIONS



Entry	aldehyde	amine	alkyne	Time [h]	Product	Yield [%][a]
1	Ph—CHO (3a)	4a	5a		6a	85
2	$(HCHO)_n$ (3c)	4b	5b		6j	81
3	3b	4a	5a		6b	86
4	3c	4a	5a		6c	83

SUBSTRATE SCOPE



SYNTHESIS OF THE MONOAMINE OXIDASE B INHIBITOR PARGYLINE

CONCLUSIONS

- we have developed a thiamine gold (I) chloride catalyst that catalyzes an efficient aldehyde-alkyne-amine coupling reaction in water.
- Remarkably, this is the first success in using the water-soluble vitamin B1 as an NHC ligand to make a transition metal complex, which is air stable and a homogenous catalyst in both aqueous and organic environment.

Acknowledgements

This work was supported by the GRF16301922 from the Research Grants Council of the government of Hong Kong SAR.

Contact information

Prof. Dr. Zhihang Guo (chguo@ust.hk)