Synthesis of Cyclopropyl-Substituted Furans by Brønsted Acid Promoted Cascade Reactions

J. S. Clark, F. Romiti, K. F. Hogg, M. H. S. A. Hamid, S. C. Richter, A. Boyer, J. C. Redman and L. Farrugia, *Angew. Chem. Int. Ed .* **2015**, asap

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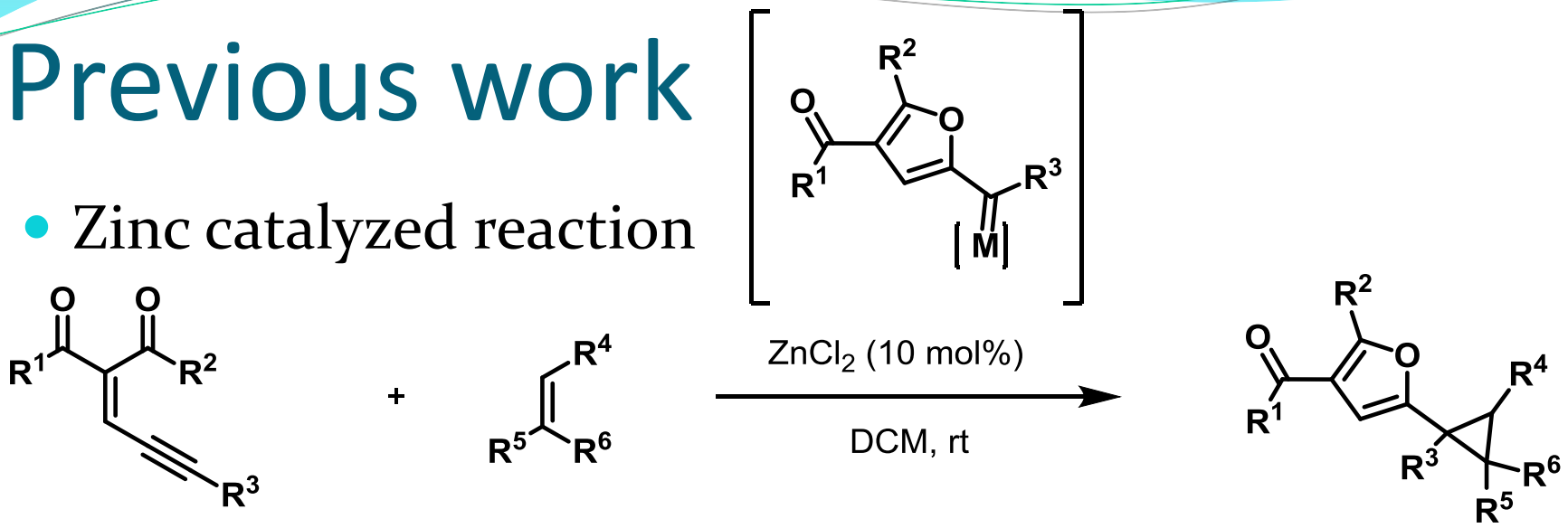
Why this paper ?

- Bioactive compounds and natural products precursors
- Valuables building blocks
- Few organocatalyzed processes

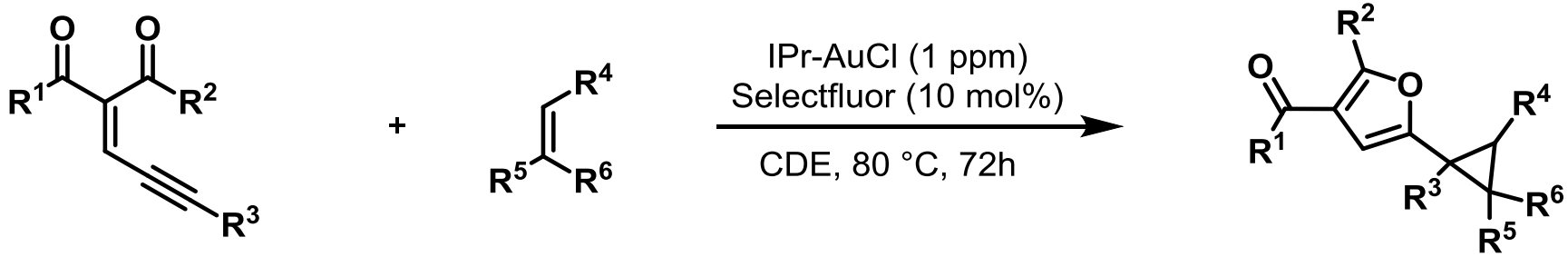
Previous work

- Zinc catalyzed reaction



R. Vicente, J. Gonzalez, L. Riesgo, J. Gonzalez, , and L. A. Lopez, *Angew. Chem. Int. Ed.* **2012**, *51*, 8063

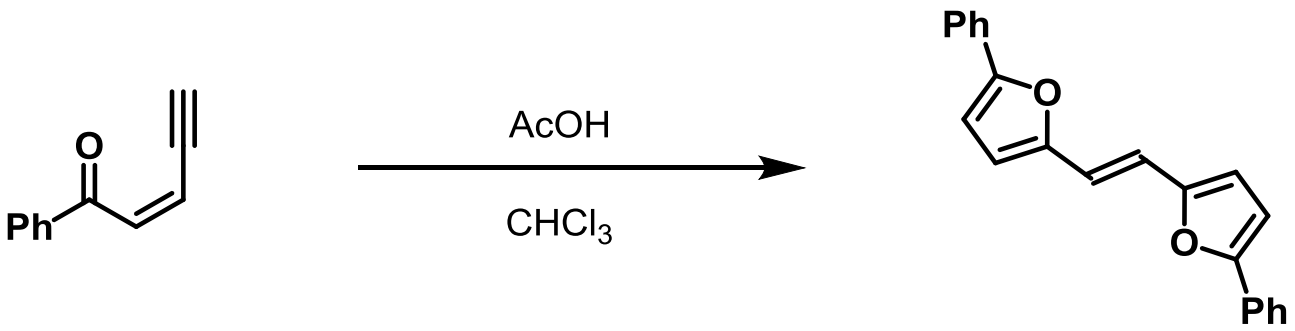
- Gold catalyzed reaction



J. Ma, H. Jiang, and S. Zhu, *Org. Lett.* **2014**, *16*, 4472

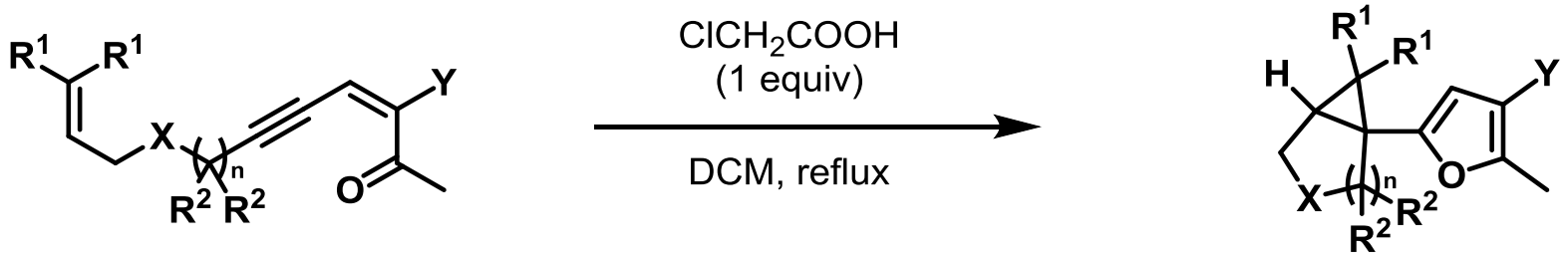
Previous work

- Brønsted acid catalyzed furan forming reaction

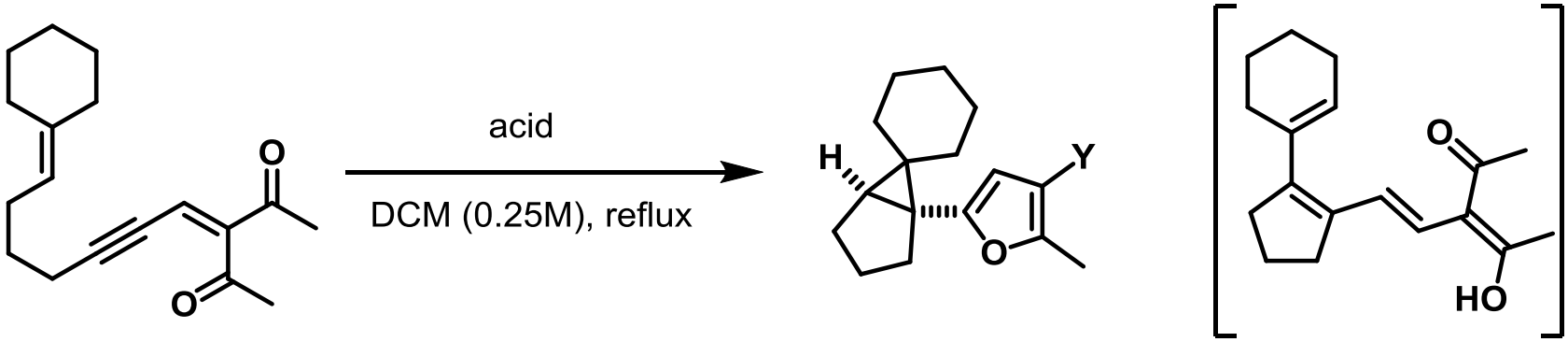


C. P. Casey and N. A. Strotman, *J. Org. Chem.* **2005**, *70*, 2576

This work

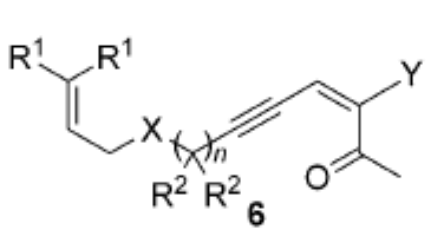


Role of acid



Entry	Acid (pK_a)	Loading (equiv)	Time (h)
1	$(CF_3)_2CHOH$ (11)	1.0	120
2	$MeCO_2H$ (4.8)	1.0	72
3	$PhCO_2H$ (4.2)	1.0	72
4	$ClCH_2CO_2H$ (2.9)	1.0	20
5	CF_3CO_2H (0.2)	1.0	/
6	$ClCH_2CO_2H$ (2.9)	0,25	24
7	$ClCH_2CO_2H$ (2.9)	0,1	/

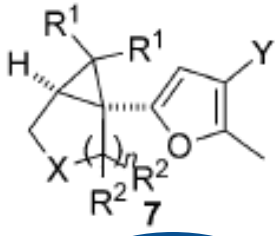
Scope



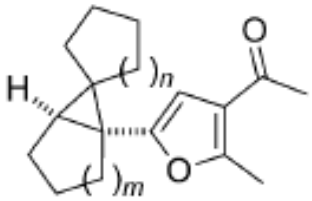
6

$ClCH_2CO_2H$ (1 equiv)

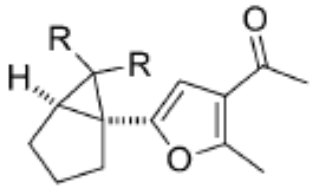
CH_2Cl_2 (0.25 M)
reflux, 18–72 h
d.r. ≥ 98:2



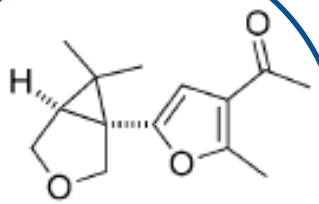
7



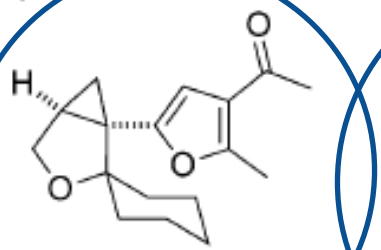
7a *m* = 1 *n* = 2 86%
7b *m* = 1 *n* = 1 66%[a]
7c *m* = 2 *n* = 2 85%



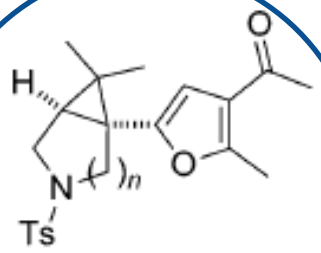
7d R = H 94%
7e R = Me 71%



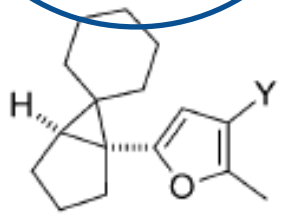
7f R = H 61%[b]



7g 88%

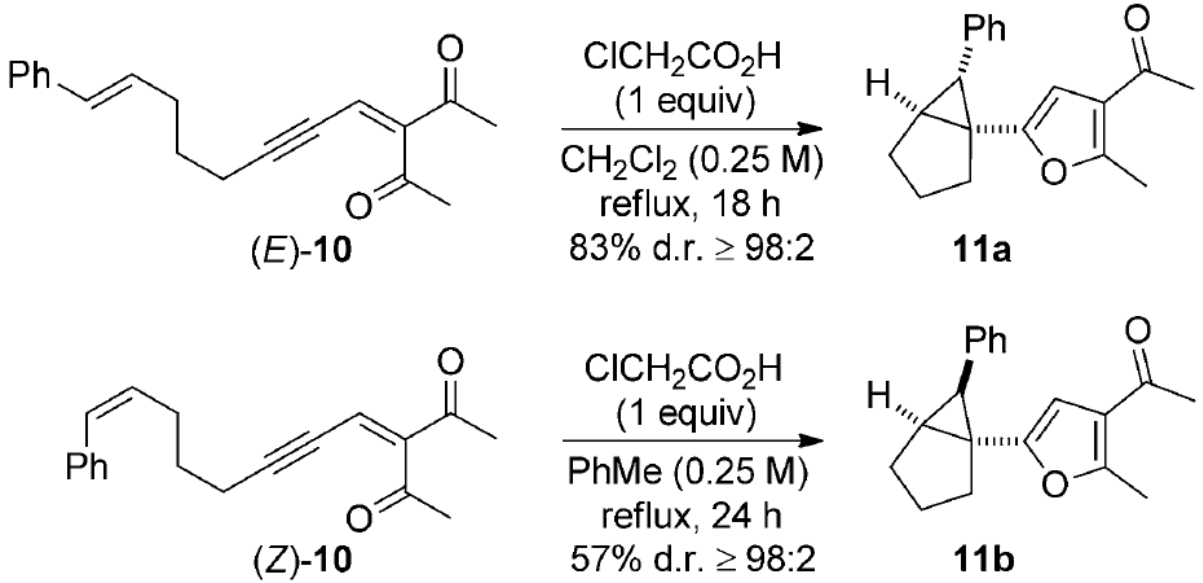


7h *n* = 1 58%[b]
7i *n* = 2 82%

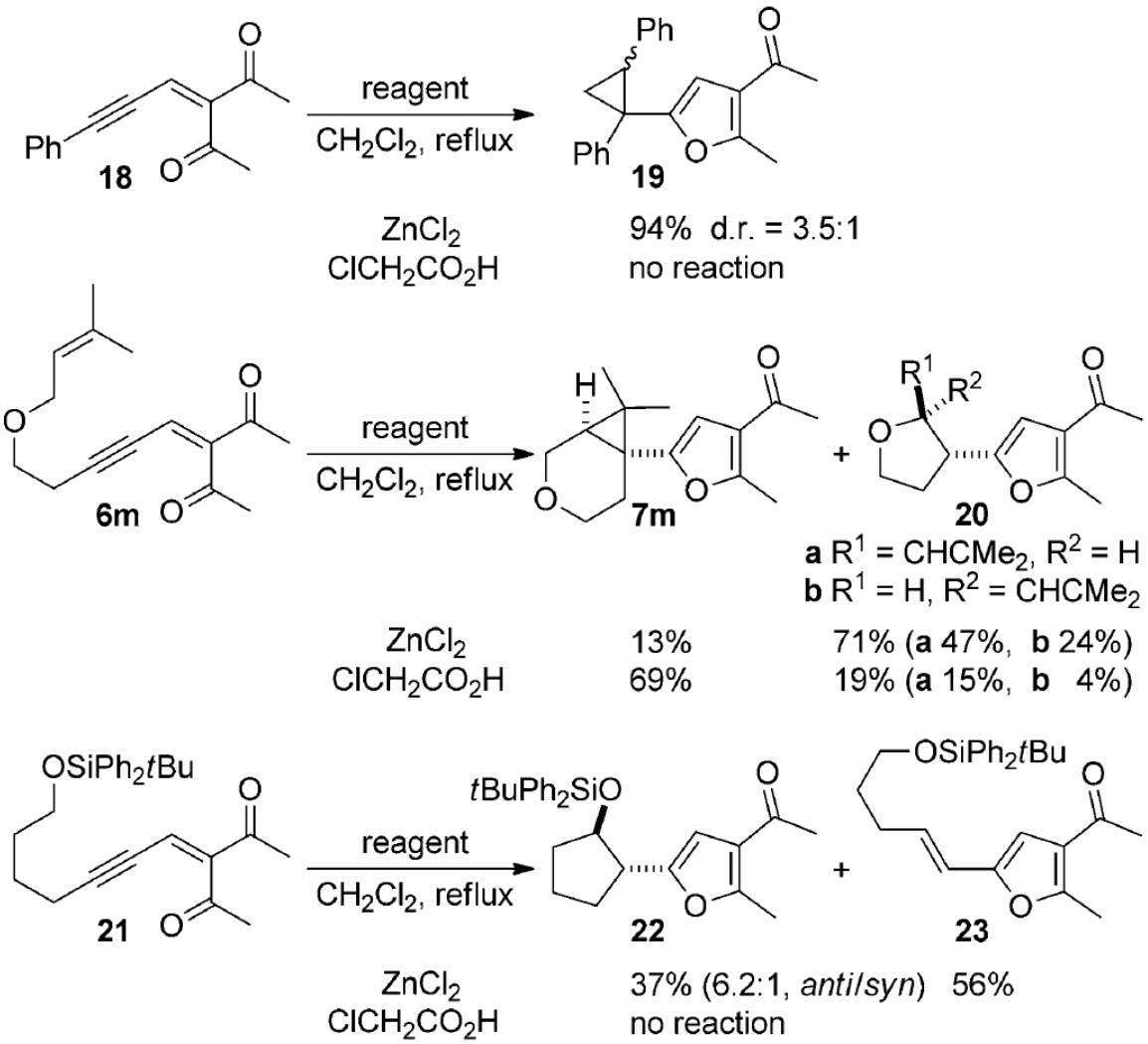


7j Y = CO_2Et 60%
7k Y = $P(O)(OMe)_2$ 88%
7l Y = SO_2Ph 87%

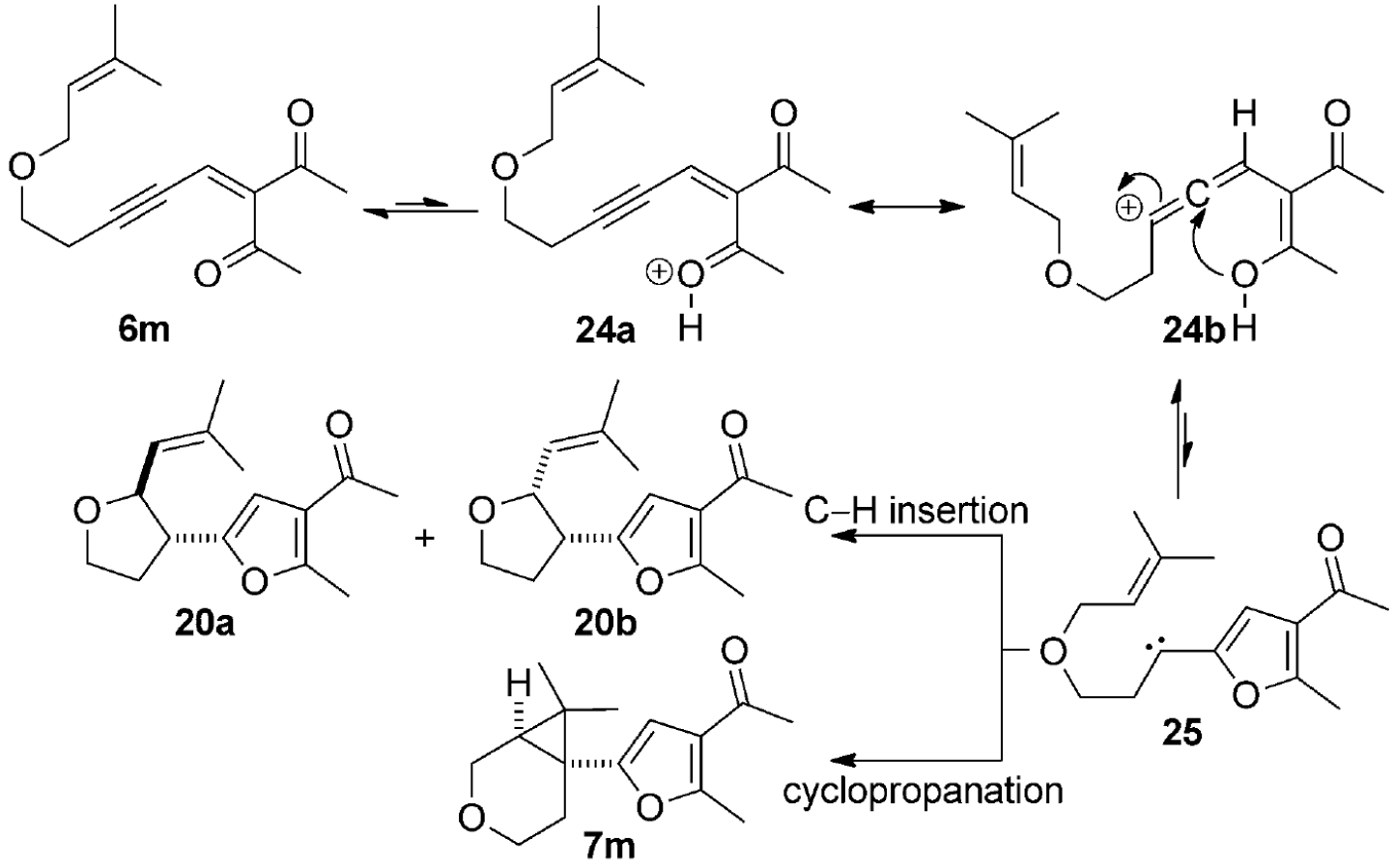
Scope


Ph
O
O
(E)-10
ClCH2CO2H
(1 equiv)
CH2Cl2 (0.25 M)
reflux, 18 h
83% d.r. ≥ 98:2
Ph
H
O
O
11a
Ph
O
O
(Z)-10
ClCH2CO2H
(1 equiv)
PhMe (0.25 M)
reflux, 24 h
57% d.r. ≥ 98:2
Ph
H
O
O
11b

Comparison study



Reaction mecanism



Conclusion

- High yield and diastereoselectivity
- Useful building blocks
- Mecanism needs to be further investigated

Thank you
for
your attention