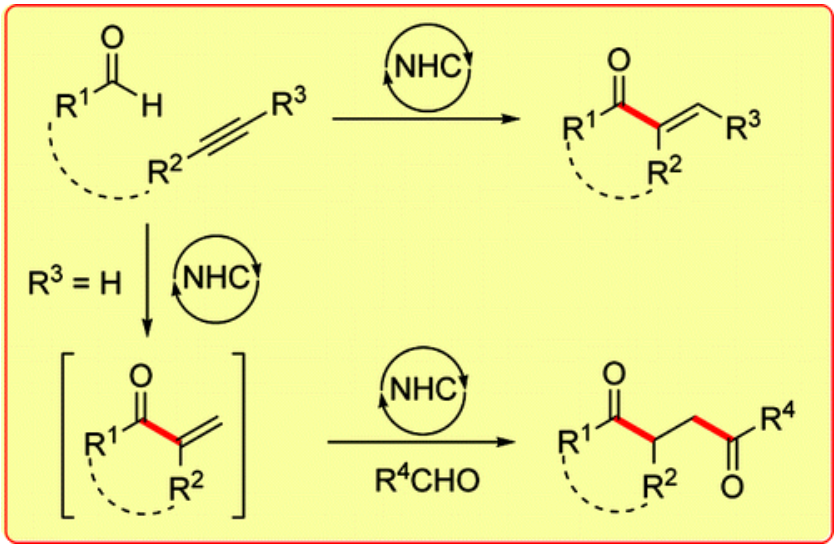
# N-Heterocyclic Carbene-Catalyzed Cascade Reaction Involving the Hydroacylation of Unactivated Alkynes

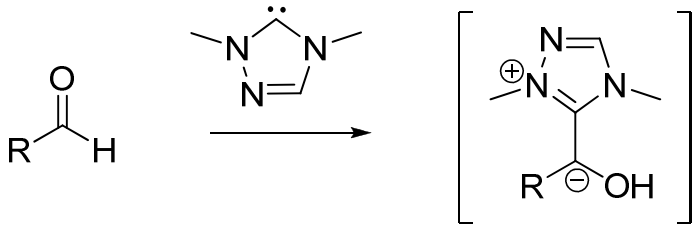



Akkattu T. Biju, Nathalie E. Wurz and Frank Glorius
J. Am. Chem. Soc. 2010, ASAP

**RCC 21/04/10 Maria del Mar Sanchez**

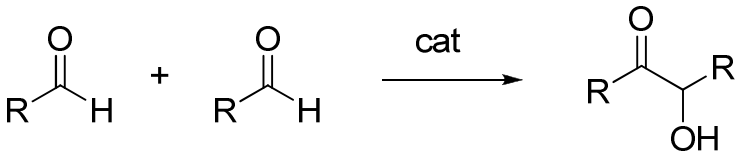
# Introduction

Reactivity of NHC with aldehydes:
Umpolung reactivity

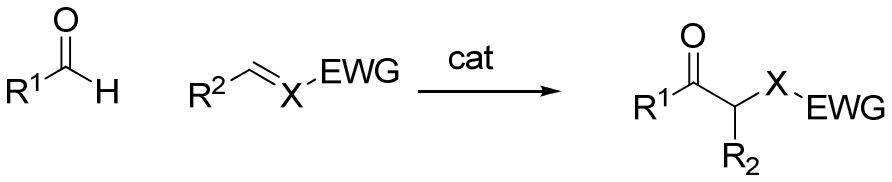


**Umpolung aldehyde or Acyl anion**

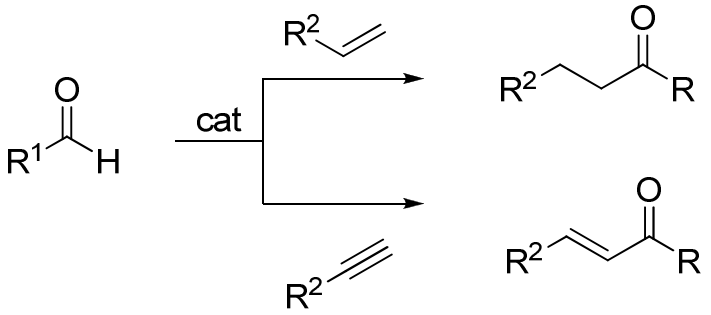
## Benzoin condensation



## Stetter reaction



## Hydroacylation

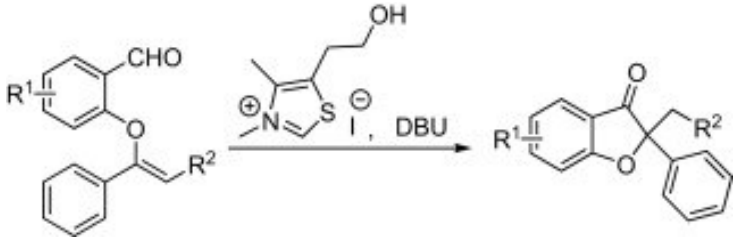


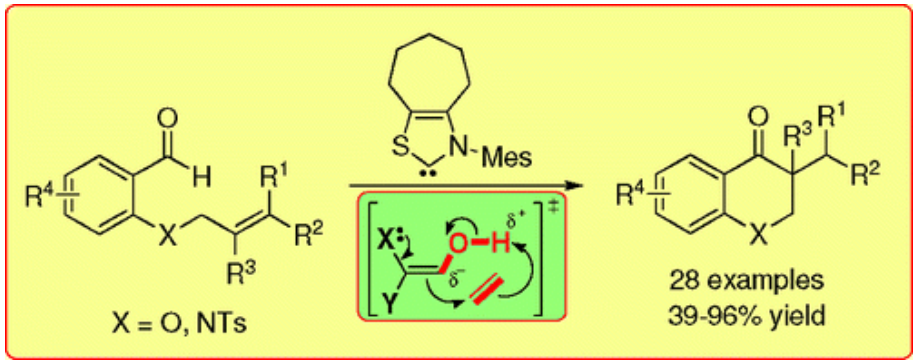
# From the litterature

## Addition of unreactive olefins, NHC-organocatalized :

**intramolecular nucleophilic addition of carbonyl anion equivalents to enol ethers**

Jinmei He, Shouchu Tang, Jian Liu, Yingpeng Su, Xinfu Pan, Xuegong She
*Tetrahedron*, **2008**, 64, 37, 8797-8800




**Hydroacylation of unactivated olefins**

Keiichi Hirano, Akkattu T. Biju, Isabel Piel and Frank Glorius
*J. Am. Chem. Soc.* **2009**, 131, 14190-14191

## $Rh^{I}$-catalyzed hydroacylation with alkynes

Chul-Ho Jun, Hyuk Lee, Jun-Bae Hong, Bong-Il Kwon
*Angew. Chem. Int. Ed.* **2002**, 41,2146-2147

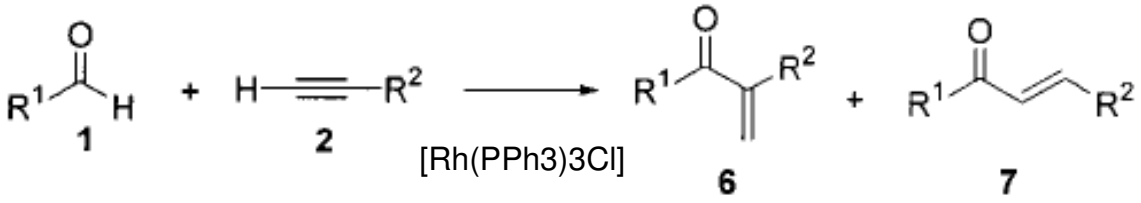
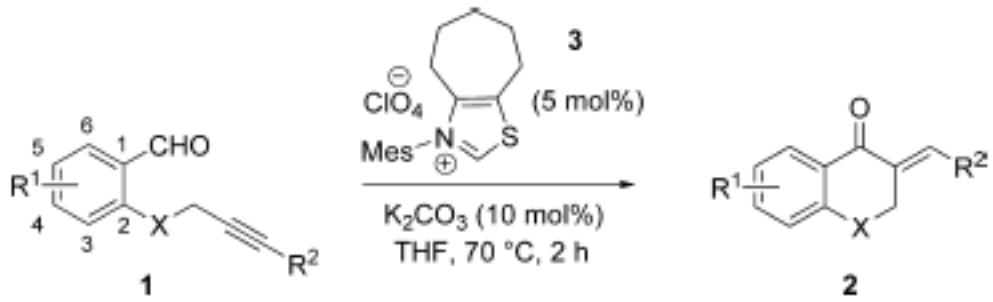


***Table 1.*** Hydroacylation of Unactivated Alkynes[a]

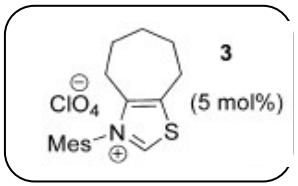


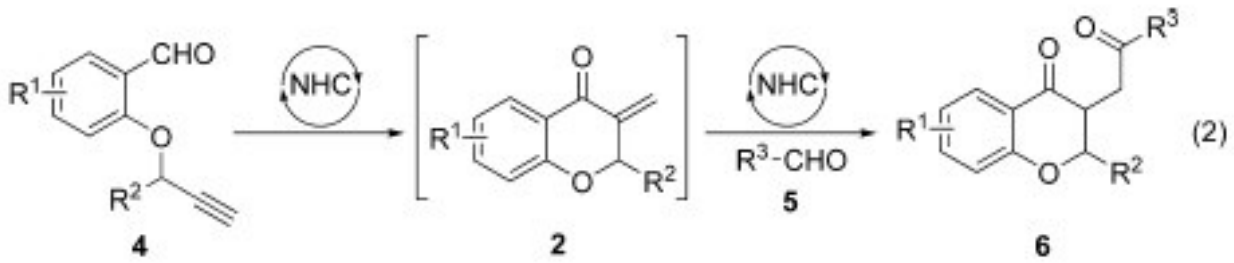

1 2

| entry | X | $R^1$ | $R^2$ | product | yield (%) |
|---|---|---|---|---|---|
| 1 | O | H | Ph | **2a** | 86 |
| 2 | O | 3-OMe | Ph | **2b** | 95 |
| 3 | O | 5-Cl | Ph | **2c** | 78 |
| 4 | O | 5-F | Ph | **2d** | 84 |
| 5 | O | H | 4-$MeOC_6H_4$ | **2e** | 72 |
| 6 | O | H | 4-$MeC_6H_4$ | **2f** | 74 |
| 7 | O | H | 4-$EtOC(O)C_6H_4$ | **2g** | 78 |
| 8 | O | H | 2-$FC_6H_4$ | **2h** | 80 |
| 9[b] | NTs | H | Ph | **2i** | 63 |

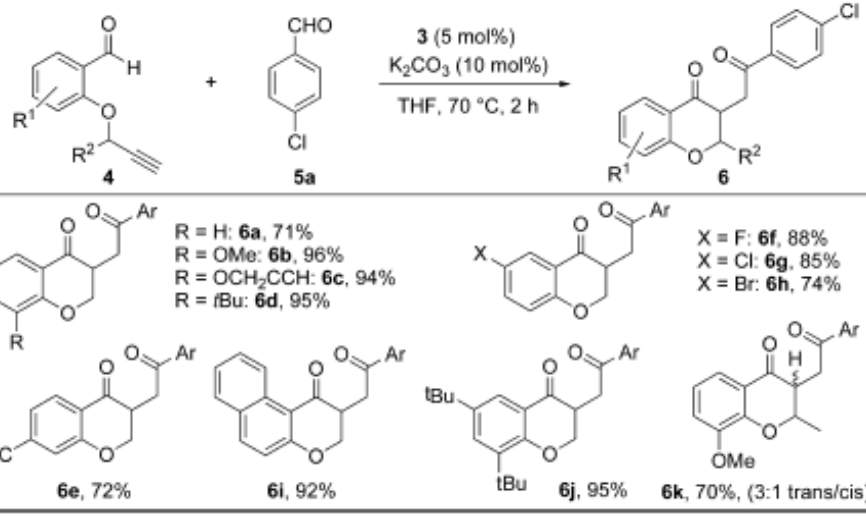
[a] General conditions: **1** (1.0 mmol), **3** (5 mol %), $K_2CO_3$ (10 mol %), THF (2.0 mL), 70 °C, 2 h; isolated yields are reported. [b] Run on a 0.35 mmol scale using 10 mol % **3** and 20 mol % $K_2CO_3$ for 4 h.

# NHC-Catalyzed Hydroacylation-Stetter Cascade:



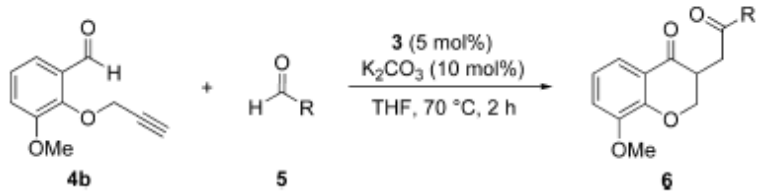




## Scope of Propargylic Aldehydes




[a] General conditions: **4** (1.0 mmol), **5a** (1.0 mmol), **3** (5 mol %), $K_2CO_3$ (10 mol %), THF (2.0 mL), 70 °C, 2 h; Ar = 4-$ClC_6H_4$. Isolated yields are given. [b] dr based on $^1H$ NMR analysis of the crude reaction mixture.

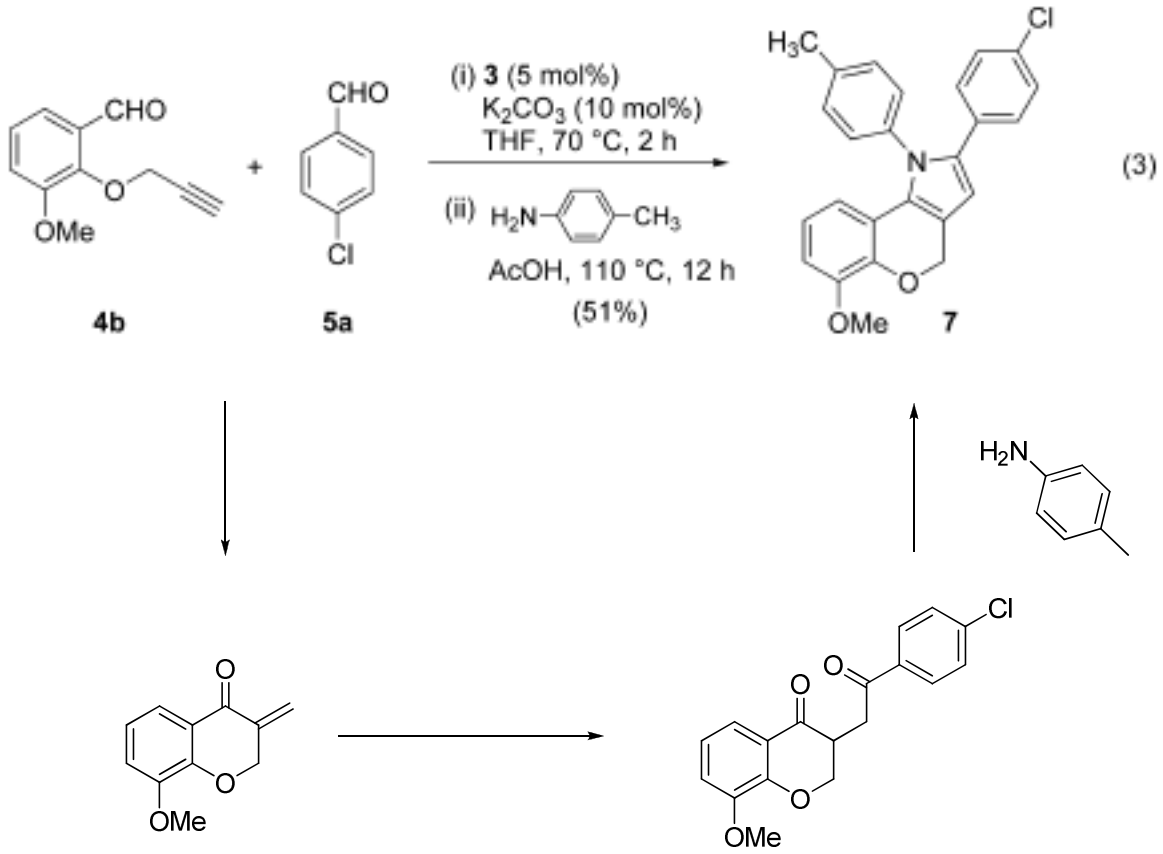
## Scope of the Coupling Aldehyde



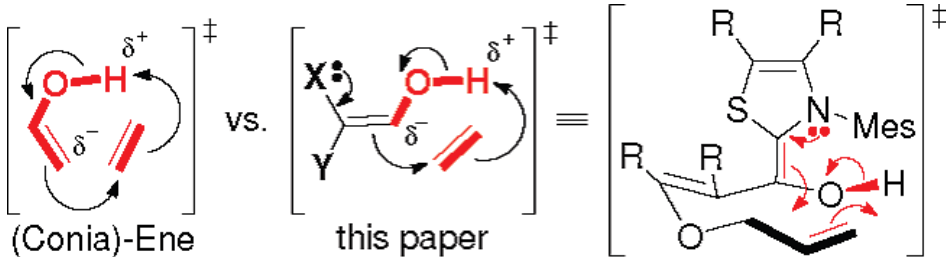

| entry | R | product | yield (%) |
|---|---|---|---|
| 1 | phenyl | **6l** | 90 |
| 2 | 2-chlorophenyl | **6m** | 66 |
| 3 | 2-methylphenyl | **6n** | 67 |
| 4 | 2-allyloxyphenyl | **6o** | 65 |
| 5 | 3-bromophenyl | **6p** | 82 |
| 6 | 3-methoxyphenyl | **6q** | 85 |
| 7 | 4-bromophenyl | **6r** | 93 |
| 8 | 4-methylphenyl | **6s** | 90 |
| 9 | 4-methoxyphenyl | **6t** | 88 |
| 10 | 4-carbomethoxyphenyl | **6u** | 77 |
| 11 | 1-naphthyl | **6v** | 86 |
| 12 | 2-furyl | **6w** | 85 |
| 13 | isopropyl | **6x** | 68 |

[a] General conditions: **4b** (1.0 mmol), **5** (1.0 mmol), **3** (5 mol %), $K_2CO_3$ (10 mol %), THF (2.0 mL), 70 °C, 2 h. Isolated yields are given.

# Application to the the one pot synthesis of of benzopyranopyrroles



# Mechanistic proposal

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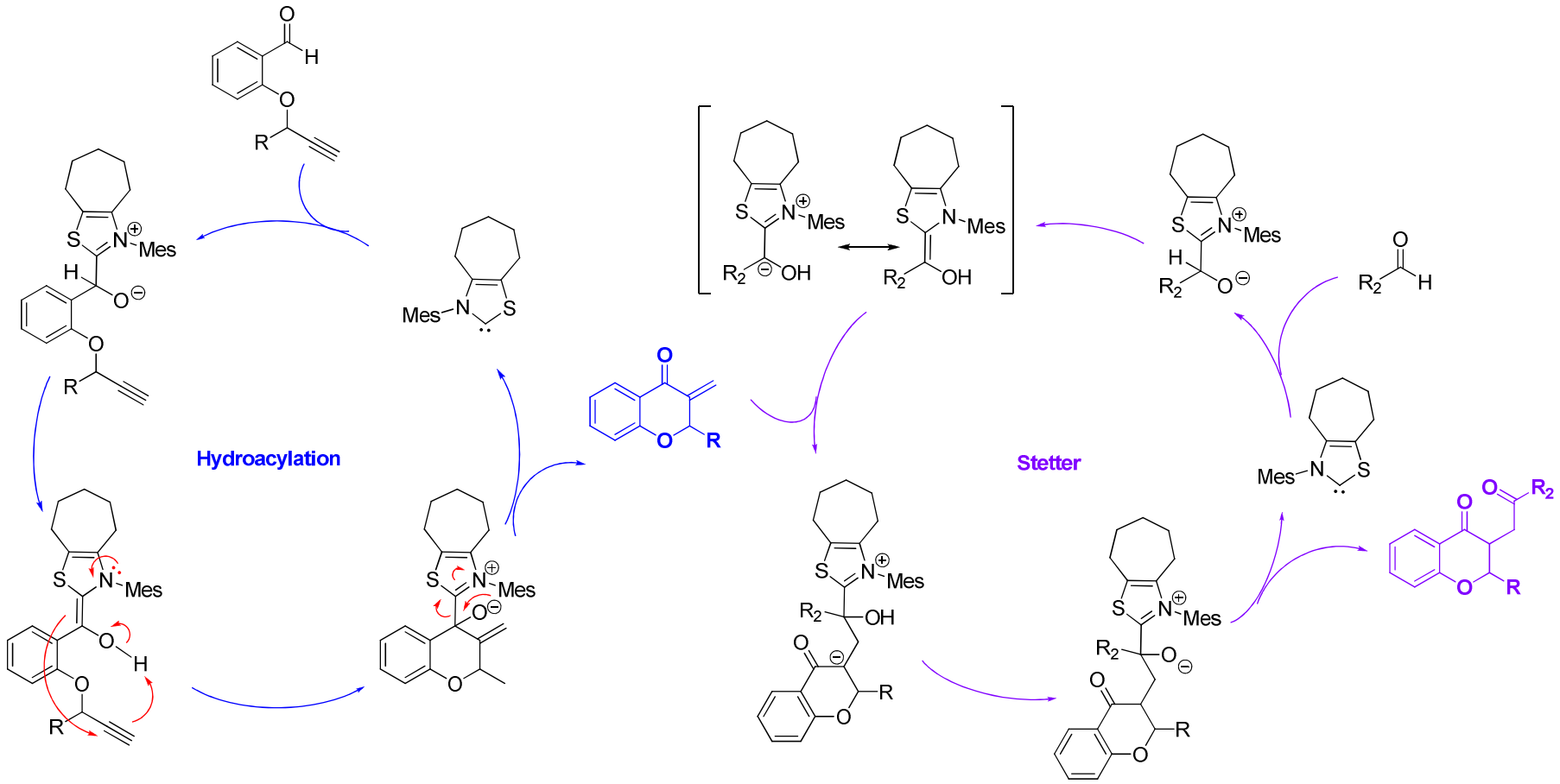
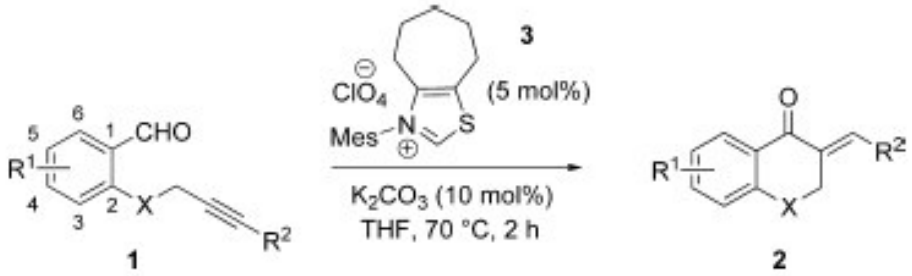
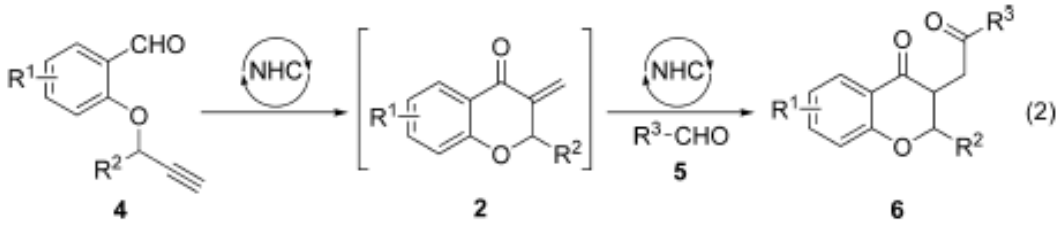


# Conclusion

First NHC-organocatalyzed hydroacylation of unactivated alkynes




An efficient an selective dually NHC-catalyzed cascade involving
The hydroacylation of alkynes and a subsequent intermolecular stetter reaction.




Thank you for your attention