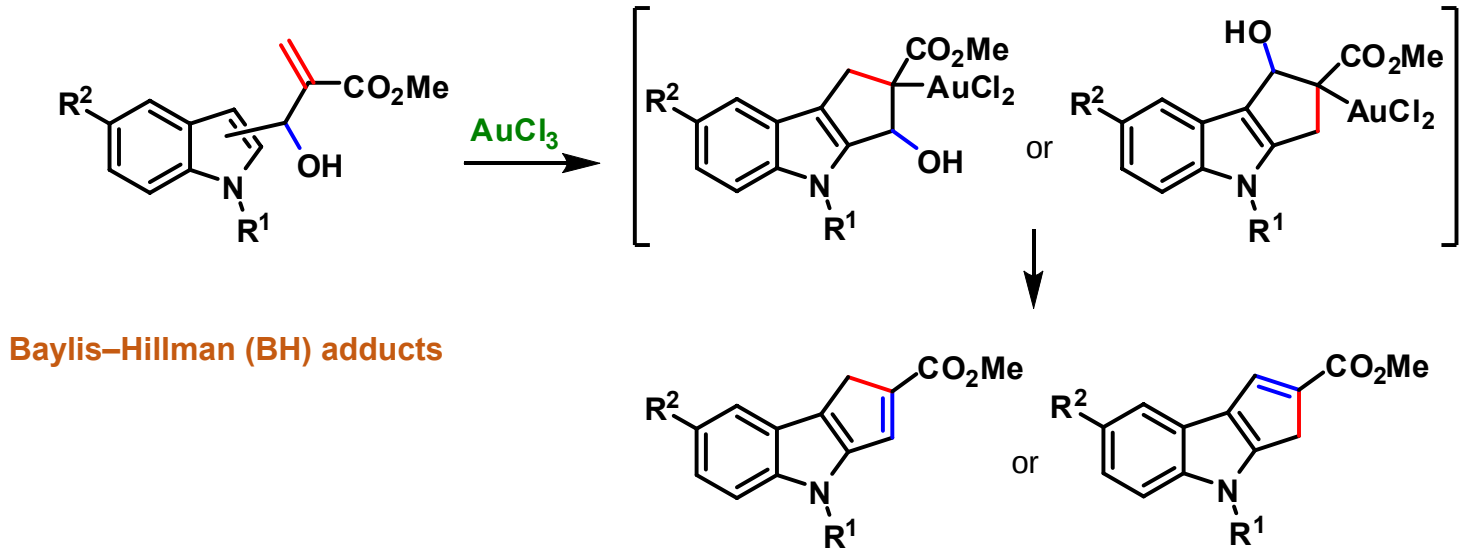
UNIVERSIDAD COMPLUTENSE DE MADRID
FACULTAD DE CIENCIAS QUÍMICAS
Grupo de Lactamas y Heterociclos Bioactivos,
Departamento de Química Orgánica I, Unidad Asociada al CSIC

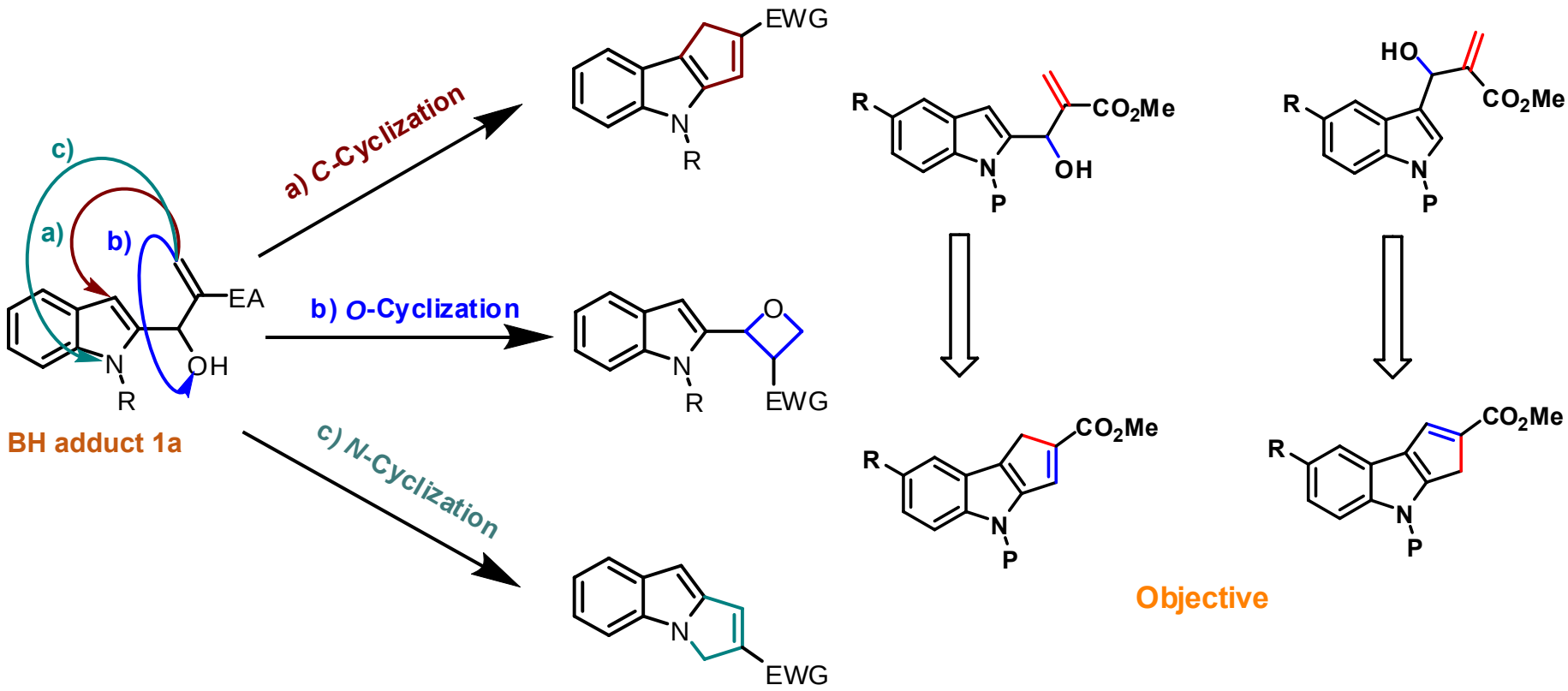
Gold-catalyzed cyclization of Baylis–Hillman adducts Derived from formyl-indoles

Benito Alcaide,[a,*] Pedro Almendros,[b,*] Alejandro Escobar,[a] Fernando Herrera,[a] and Amparo Luna[a]

The use of **gold salts** has gained a lot of attention in the recent times because of their powerful soft Lewis acidic nature. Such a property allows gold catalysts to activate unsaturated functionalities such as alkynes, alkenes, and allenes, to create **C–C** bonds under extremely mild conditions.
On the other hand, **Baylis–Hillman (BH) adducts** are usually flexible and multifunctional products which can be easily transformed in a huge number of derivatives.

A methodology for the direct preparation of **dihydrocyclopenta[*b*]indoles** from **indole-tethered α-hydroxacrylates** under **gold catalysis** has been developed

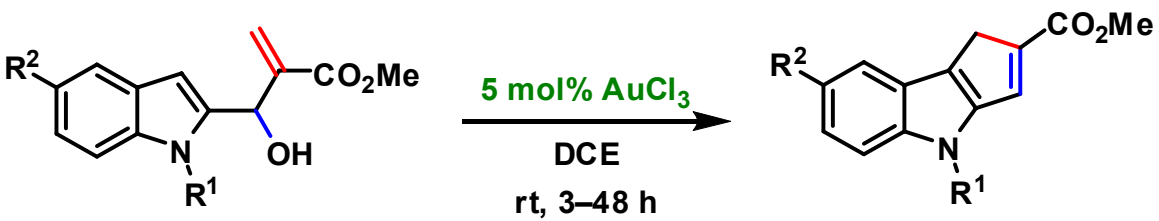




Initially, we started to evaluate the cyclization reaction by employing **BH adduct 1a** as model substrate. **NH-Indole-tethered α-hydroxacrylate 1a** has diverse reactive sites, at which at least three different transformations (***C*-cyclization** *versus* ***O*-cyclization** *versus* ***N*-cyclization**)

Our catalyst screening led to the identification of **$AuCl_3$** as **the most suitable promoter**.

AuCl and Gagosz' catalyst [(Ph3P)AuNTf$_2$] were less effective for the tricycle formation. Our solvent screening led to the identification of 1,2-dichloroethane (DCE) as the most suitable solvent. It was found that **$AuCl_3$** is an effective reagent for the room temperature **carbocyclization** of indole-linked acrylate **1a** to afford the cyclopentene-fused indole **3a**

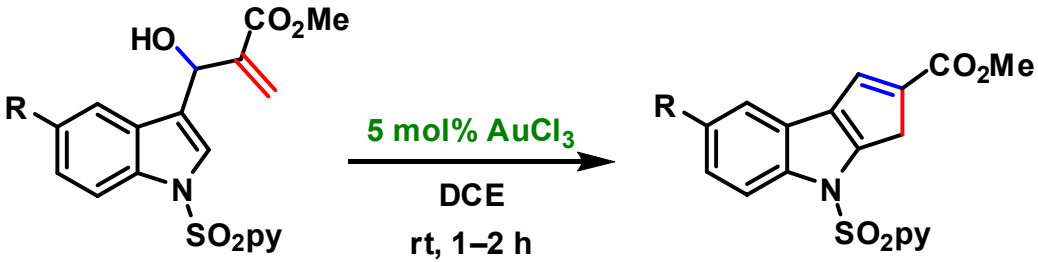


1a R^1 = H, R^2 = H
1b R^1 = SO_2py, R^2 = H
1c R^1 = SO_2py, R^2 = MeO
1d R^1 = SO_2py, R^2 = Cl

3a (50%)
3b (64%)
3c (57%)
3d (52%)

Due to the fact that the C3-position of an indole is the most reactive site for electrophilic functionalization, carbocyclization of indole-tethered alkenes to the C2 indole position is considerably less studied and is mainly restricted to 1,2-dienes.

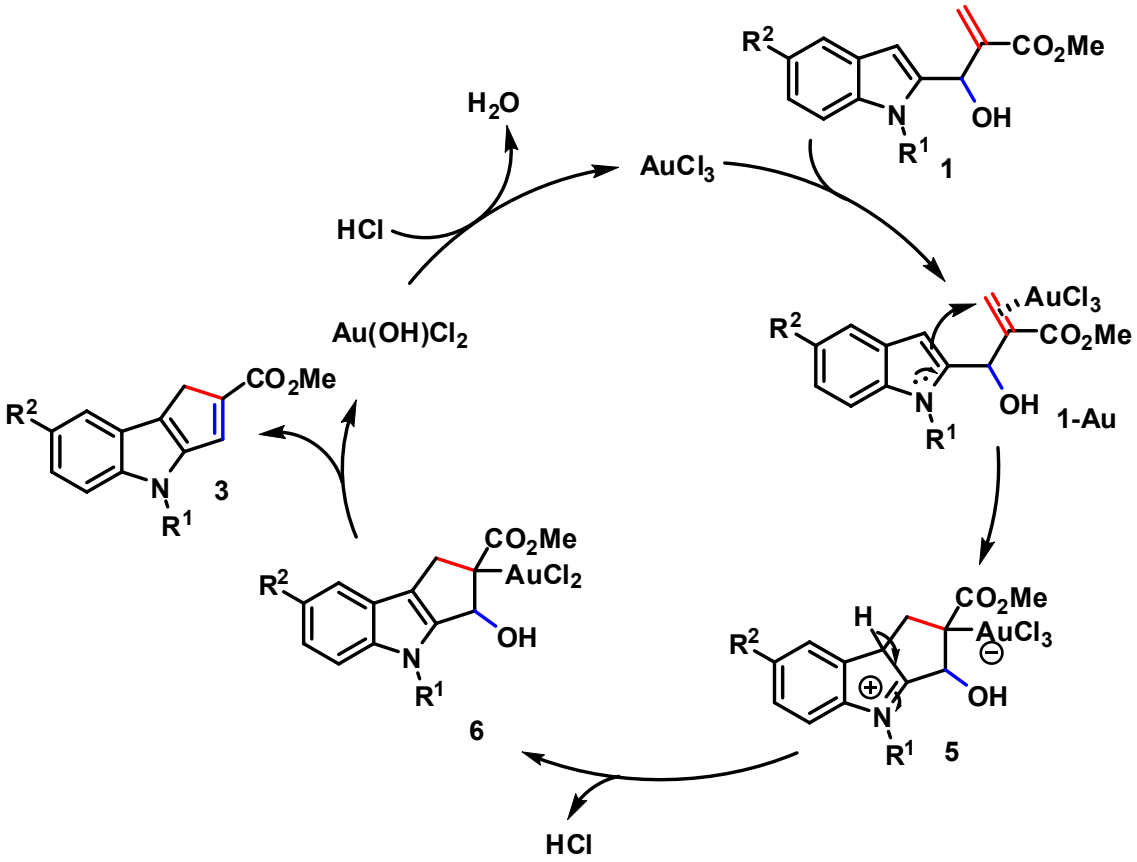
Fortunately, the **gold-catalyzed reaction** of **indole-tethered α-hydroxacrylates 2** was also successful. As shown in Scheme 2, under gold(III) catalysis, the C3–C2 annulation products **4** were obtained, but in in modest yields.



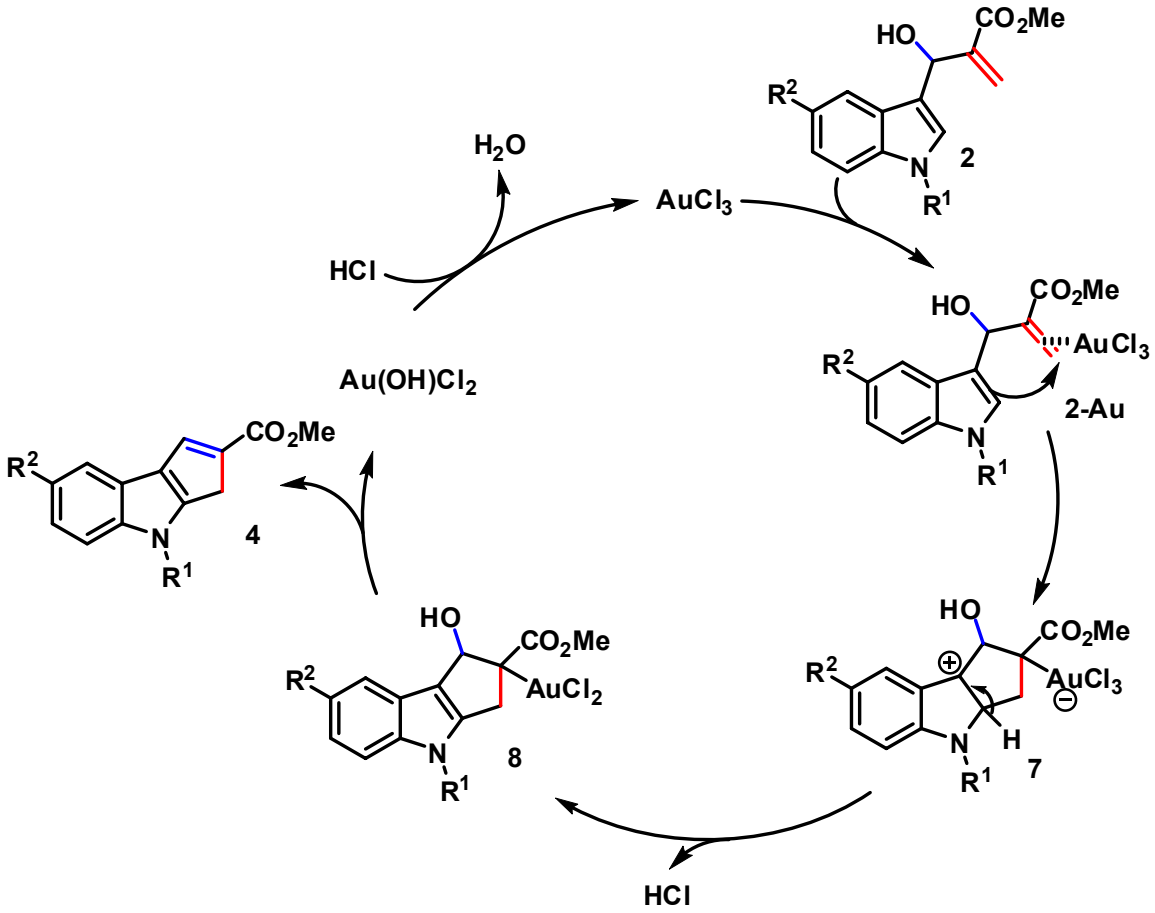
2a R = H
2b R = Me

4a (38%)
4b (31%)

The next scheme describes a putative mechanism for generating **1,4-dihydrocyclopenta[*b*]indoles 3** from the **carbocyclization** of indole-C2-tethered **α-hydroxacrylates 1.**

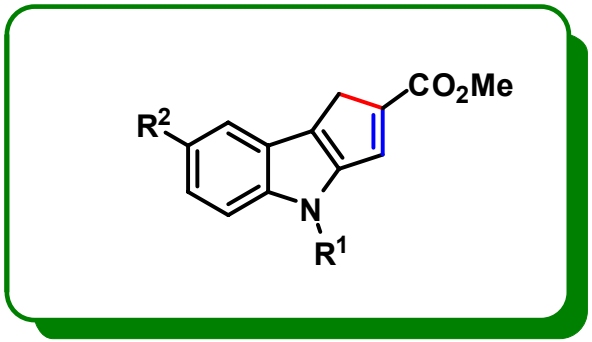


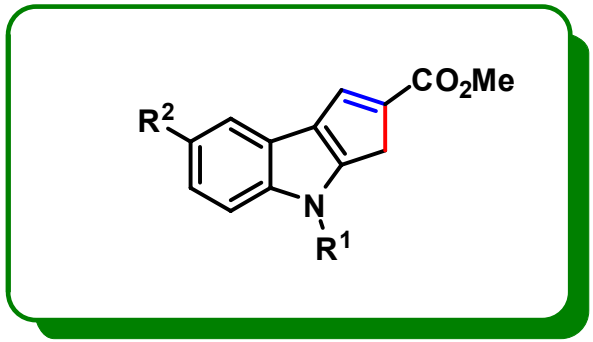
Our proposed mechanism for the gold-catalyzed generation of **3,4-dihydrocyclopenta[*b*]indole-2-carboxylates 4** is shown in the next scheme.



Conclusions

In conclusion, we have developed a convenient methodology for the **gold-catalyzed direct synthesis** of **dihydrocyclopenta[*b*]indoles** **from Baylis–Hillman adducts** derived from formyl-indoles. A conceivable mechanism for the achievement of **cyclopentene-fused indoles** may imply a selective indole hydroarylation followed by dehydration.





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