One-pot Green Synthesis of Flavones Using Gold Nanoparticles Supported on Layered Double Hydroxides

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Flavones, which are ubiquitous in fruits and vegetables, show various biological activities such as antioxidant, antitumor, and antiallergy. Therefore, many synthetic procedures for flavones have been developed, but in terms of environmental burden they are still problematic. In this study, a novel heterogeneous one-pot synthesis of flavones was developed starting from simple substrates, benzaldehydes and 2'-hydroxyacetiophenones, using gold nanoparticles supported on Mg–Al layered double hydroxides (Au/LDH). Au/LDH efficiently catalyzed the Claisen–Schmidt condensation, oxa-Michael addition, and oxidative dehydrogenation through multiple catalysis and concerted catalysis (Figure 1)[1]. This system has many environmentally-friendly characteristics, such as the employment of molecular oxidant as the terminal oxidant, no need for isolation of intermediates, and the use of the reusable heterogeneous catalyst.

Various metal supported catalysts were tested for the synthesis of flavone (**3aa**) starting from 2'-hydroxyacetophenone (**1a**) and benzaldehyde (**2a**) (Table 1). When using Ru, Rh, Pd, or Pt catalysts supported on LDH, **3aa** was hardly synthesized although 2'-hydroxychalcone (**4aa**) and flavanone (**5aa**) were obtained through Claisen–Schmidt condensation and oxa-Michael addition catalyzed by LDH support (entries 2–5). On the other hand, Au/LDH efficiently catalyzed the oxidative dehydrogenation of **5aa** to produce **3aa** in 76% yield (entry 1). In the presence of Au/Al_2O_3, Au/TiO_2, or Au/CeO_2, the yield of **3aa** did not match that of Au/LDH (entries 1 and 6–8). Under argon atmosphere the catalytic activity steeply decreased, indicating molecular oxygen is the terminal oxidant in air (entry 9). Therefore, Au/LDH is the best catalyst for the synthesis of **3aa** from **1a** and **2a** using O_2 as the terminal oxidant.

The substrate scope of this system is significantly broad as shown in Figure 2. This system was confirmed to be truly heterogeneous, and Au/LDH could be reused.

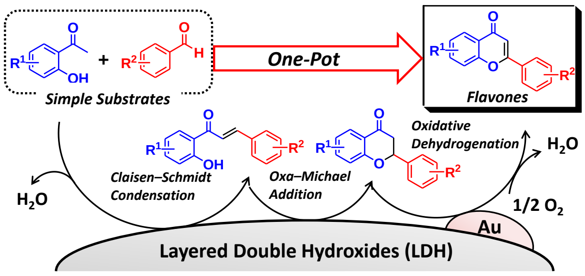
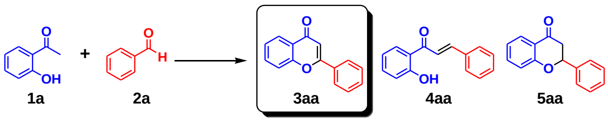


Fig. 1 Strategy of this study.

Table 1 Effect of catalysts.



Entry	Catalysts	Conv. [%] 1a	Conv. [%] 2a	Yield [%] 3aa	Yield [%] 4aa	Yield [%] 5aa
1	Au/LDH	>99	97	76	<1	<1
2	Ru/LDH	70	78	<1	5	16
3	Rh/LDH	79	74	<1	20	39
4	Pd/LDH	84	>99	2	2	22
5	Pt/LDH	91	96	<1	20	44
6	Au/Al_2O_3	79	83	58	2	3
7	Au/TiO_2	46	56	34	<1	<1
8	Au/CeO_2	40	78	3	<1	<1
9[a]	Au/LDH	>99	>99	24	15	34

Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), catalyst (130 mg), mesitylene (2 mL), open air (1 atm), 130 °C, 24 h. [a] Under Ar atmosphere (1 atm).

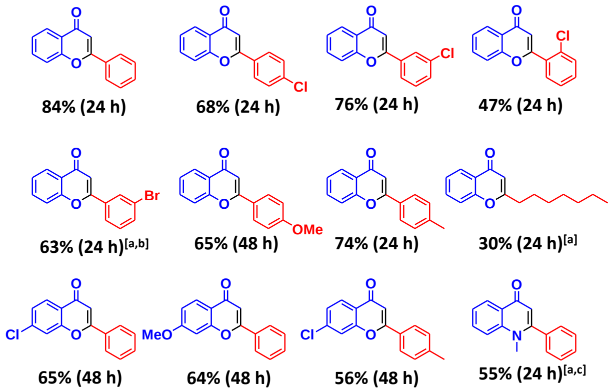


Fig. 2 Substrate scope.

Reaction conditions: ketone (0.3 mmol), aldehyde (0.6 mmol), Au/LDH (100 mg, Au: 4 mol%), mesitylene (2 mL), open air (1 atm), 130 °C. Isolated yields (based on ketone) were shown. [a] Au/LDH (200 mg). [b] **3aa** was also formed (8%). [c] The product was isolated as a monohydrate.

REFERENCES

[1] T. Yatabe, X. Jin, K. Yamagichi, N. Mizuno, Angew. Chem. Int. Ed., 54 (2015) 13302.