Unprecedented Catalytic Aurone Synthesis from Simple Chalcones Enabled by Design of a Pd-on-Au Bimetallic Nanoparticle Catalyst Supported on CeO_2

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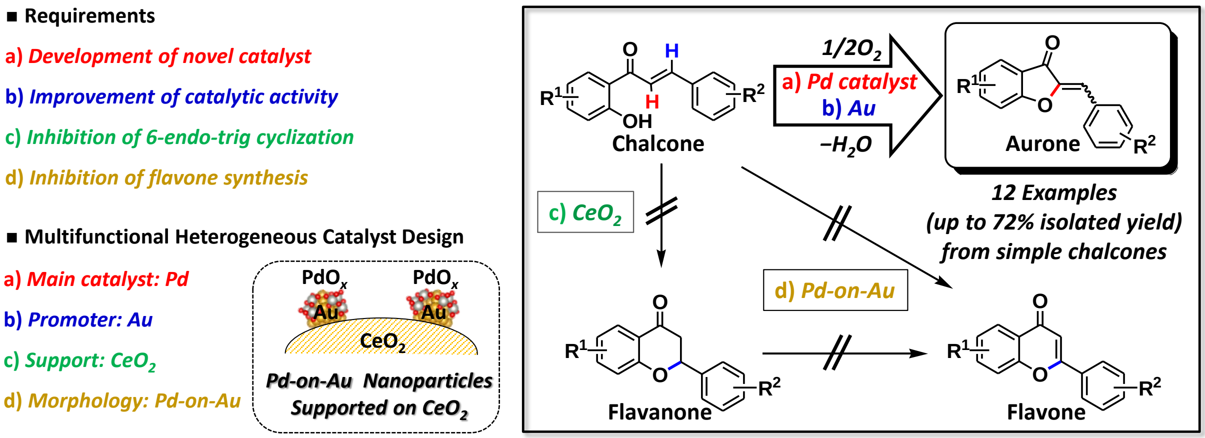
Abstract: Aurones, which are a class of flavonoids, plant secondary metabolites derived from chalcones, show various biological activities. From the viewpoint of their pharmaceutical application, the chemical synthesis of aurones from chalcones is attractive because chalcones are easily obtained. Their catalytic synthesis, however, has not yet been reported because of preferential 6-membered ring formation and the need for rare intramolecular α-olefinic C–H functionalization. Herein, we developed the first catalytic synthesis of various aurones from simple chalcones *via* selectivity reversal enabled by design of a Pd-on-Au bimetallic nanoparticle catalyst supported on CeO_2 using O_2 in air as the sole oxidant.

Keywords: Pd-on-Au bimetallic nanoparticle, Heterogeneous catalyst design, Aurone synthesis.

1. Introduction

From the view of aurones' pharmaceutical application, the direct synthesis of aurones from chalcones as with the biosynthesis is attractive because chalcones are easily available by extracting from plants or synthesizing from simple aldehydes and ketones through the Claisen–Schmidt condensation. (Super)stoichiometric amounts of $Hg(OAc)_2$, however, are typically used for the synthesis to inhibit the preferential 6-*endo*-*trig* cyclization toward flavanone and the successive oxidation of flavanone. In addition, the catalytic aurone synthesis from chalcones is regarded as a catalytic "intramolecular α-olefinic C–H functionalization", which is rarely reported[1]. So far, there is no reliable report regarding catalytic synthesis of aurones from chalcones. To achieve catalytic aurone synthesis, the following four points should be considered; a) the development of catalyst for aurone synthesis, b) an improvement of the catalytic activity, c) the inhibition of the 6-*endo*-*trig* cyclization, and d) the inhibition of flavone synthesis. In this study, the aforementioned four requirements have been controlled by a) a supported Pd species, b) an Au promoter, c) a CeO_2 support, and d) a Pd-on-Au structure (Figure 1). That is, we have developed the first catalytic aurone synthesis over a Pd-on-Au bimetallic nanoparticle catalyst supported on CeO_2 ($Pd/Au/CeO_2$).

Figure 1. Strategy used in this work: Design of multifunctional heterogeneous catalysts controlling each reaction.



2. Experimental

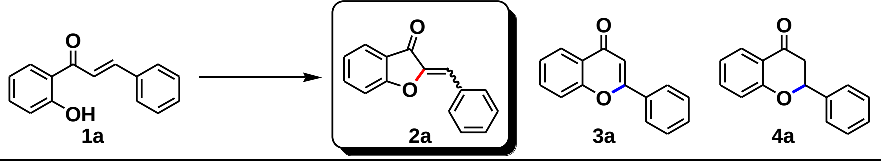
Referring to the previous report[2], we prepared $Pd/Au/CeO_2$ through calcination at 300 °C for 2 h after Au and Pd species were supported on CeO_2 separately in this order *via* a deposition–precipitation method. The catalytic reaction was typically carried out as follows. Into a Pyrex glass reactor (volume: *ca.* 20 mL) were successively added Pd/Au/CeO_2 (100 mg, Au: 4.6 mol%, Pd: 4.7 mol%), biphenyl (0.1 mmol, internal standard), 2′-hydroxychalcone (**1a**, 0.3 mmol), BuOAc (2 mL), and a Teflon-coated magnetic stir bar; the mixture was then stirred at 100 °C under an open air atmosphere for 24 h.

3. Results and discussion

The synthesis of aurone (**2a**) from 2'-hydroxychalcone (**1a**) was carried out using various catalysts (Table 1). Using a homogeneous Pd catalyst, the reaction stopped in the middle with the formation of Pd black (entry 1). Pd/Al_2O_3 or Pd/TiO_2 were effective to increase **2a** yield, though flavanone (**4a**) was formed to some extent (entries 3 and 4). Pd/CeO_2 was effective to inhibit **4a** production, though **2a** was obtained in a low yield (entries 2 and 10). Au–Pd bimetallic nanoparticles supported on CeO_2 boosted the production of **2a**, concomitantly with the considerable flavone (**3a**) production by Au catalysis[3] (entries 5 and 6). Pd/Au/CeO_2 retained the Au promotion effect and inhibited the Au catalysis, which resulted in the high yield of and selectivity to **2a**; the optimized **2a** yield reached 79% (entries 7 and 8). Under an Ar atmosphere, **2a** was hardly obtained, which reveals that O_2 in air worked as the sole oxidant in this system (entry 9).

The observed catalysis for this aurone synthesis is truly heterogeneous and the catalyst can be reused. This system is applicable to the synthesis of various aurones from chalcones including natural compounds (12 examples, up to 72% isolated yield). In the presentation, the detailed mechanism will be also discussed.

Table 1. Effect of catalysts on the synthesis of aurone (**2a**).



Entry	Catalyst	Conv. [%]	Yield [%]		
		1a	**2a**	**3a**	**4a**
1	Pd(TFA)$_2$	38	12	2	16
2[a]	Pd/CeO_2	7	3	<1	4
3[a]	Pd/TiO_2	37	19	1	13
4[a]	Pd/Al_2O_3	47	16	3	25
5	Au/CeO_2	>99	6	80	8
6	Au–Pd/CeO_2	90	52	22	8
7	Pd/Au/CeO_2	60	46	6	9
8[b]	Pd/Au/CeO_2	94	79	11	5
9[b,c]	Pd/Au/CeO_2	21	1	<1	13
10	none	16	<1	<1	16

Reaction conditions: **1a** (0.3 mmol), catalyst (Au and/or Pd: 2 mol%), BuOAc (2 mL), open air (1 atm), 100 °C, 24 h. Yields and conversions were determined by GC. [a] Supported Pd catalyst (50 mg, Pd: 1 mol%). [b] Catalyst (100 mg). [c] Under Ar (1 atm). TFA = trifluoroacetate.

4. Conclusions

We have achieved the first catalytic aurone synthesis from simple chalcones over Pd-on-Au bimetallic nanoparticles supported on CeO_2. This study demonstrates the potential of heterogeneous catalyst design for novel difficult organic syntheses not yet achieved using homogeneous catalysts.

References

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