Aerobic Oxidative Cross-Coupling Reaction of Catehols and Active Methylene Compounds Using Supported Metal Catalysts

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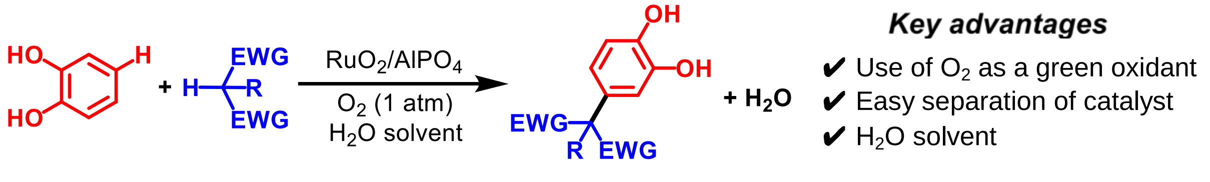
Abstract: The oxidative cross-coupling reaction of catechols and active methylene compounds with O_2 as a green oxidant was achieved using the $AlPO_4$-supported RuO_2 nanoparticle catalyst. The present catalyst system is simple and clean because H_2O is theoretically formed as the sole byproduct and the catalyst can be easily separated from the reaction mixture by filtration.

Keywords: Oxidative cross coupling, Catechol, Active methylene compound, Ruthenium.

1. Introduction

Carbon quaternary centers covalently bonded to 1,2-dihydroxylated aromatic rings are important structures in natural and pharmaceutical compounds. These structures were constructed through coupling reactions of halogen- or boronic acid-substituted catechols. Despite their high synthetic efficiencies, these methods required the prefunctionalization of catechols and suffered from the concomitant formation of salt wastes derived from the above substitution groups. From the standpoint of Green Sustainable Chemistry, a simple and atom-economical method to introduce C−C bonds to catechol aromatic rings is highly demanded.

Aerobic oxidative coupling reaction is an environmentally-benign molecular transformation because it can directly build a new C−C bond with formation of H_2O as the sole byproduct. Our research group has developed several supported metal catalysts promoting the regioselective homo-coupling reactions of phenols.[1] Herein, we developed the $AlPO_4$-supported RuO_2 nanoparticle catalyst ($RuO_2/AlPO_4$) for cross-coupling reaction of catechols and active methylene compounds using O_2 as a green oxidant (Scheme). To date, the coupling reaction of catechols and active methylene compounds has been conducted through stoichiometric reaction using periodate salts or enzymatic reaction using oxidase. However, these methods suffer from occurrence of over-oxidation of the product or difficulty in separation of enzyme from the reaction mixture, respectively. The present catalytic system could avoid the over-oxidation of the product and was recyclable by simple filtration after the reaction.



Scheme. Oxidative cross-coupling reaction of catechols and active methylene compounds with O_2 using $RuO_2/AlPO_4$ catalyst.

2. Experimental

2-1. Preparation and characterization of $RuO_2/AlPO_4$

$RuO_2/AlPO_4$ was prepared by impregnation of $Ru(acac)_3$ to $AlPO_4$ followed by calcination. The characterization was conducted by XRD and TEM measurements.

2-2. Typical procedure of oxidative coupling of catechols and active methylene compounds

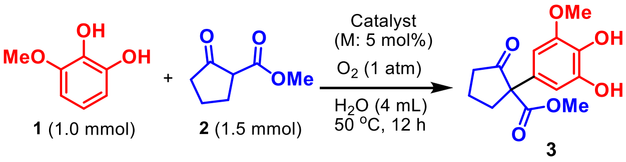
$RuO_2/AlPO_4$ was added to aqueous solution containing catechol and active methylene compound, and then the mixture was stirred under O_2 (1 atm) at 50 °C. Following completion of the reaction, hexadecane was added as an internal standard and the organic phase was extracted for ^1H NMR analysis.

3. Results and discussion

The XRD spectrum of $RuO_2/AlPO_4$ was similar to that of $AlPO_4$, showing that $AlPO_4$ structure was maintained. The peak attributed to RuO_2 (110) around $2\theta = 28^{\circ}$ was observed, indicating that the Ru species existed as RuO_2. The TEM images represented the presence of RuO_2 nanoparticles on $AlPO_4$.

Initially, the oxidative cross-coupling reaction of 3-methoxycatechol (**1**) and methyl 2-oxocyclopentanecarboxylate (**2**) was investigated using several $AlPO_4$-supported metal catalysts (Table 1). $RuO_2/AlPO_4$ selectively promoted the reaction under O_2 (1 atm) in H_2O solvent, affording a 90% yield of the desired cross-coupling product (**3**) (entry 1). Although $PdO/AlPO_4$ and $Rh_2O_3/AlPO_4$ catalyzed the reaction, the yields of **3** were lower than that obtained by $RuO_2/AlPO_4$ (entries 2 and 3). The use of $PtO_2/AlPO_4$ decreased the yield of **3** to 13% due to the occurrence of over-oxidation and/or decomposition of **3** (entry 4). We also prepared the RuO_2 nanoparticles immobilized to other supports and examined their catalytic activities. $Mg_3(PO_4)_2$, AlOOH, and SiO_2-supported RuO_2 exhibited low activity and the yield of **3** were 27, 30 and 8%, respectively (entries 5-7). The above results show that the combination of RuO_2 and $AlPO_4$ is essential to obtain a high yield of the cross-coupling product.

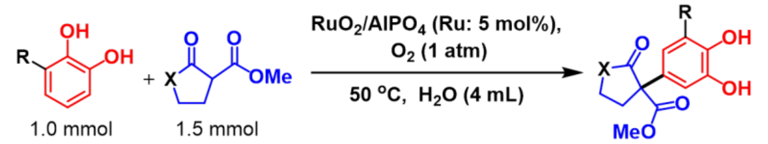
Table 1. Cross-coupling reaction of 3-methoxycatechol (**1**) and methyl 2-oxocyclopentanecarboxylate (**2**) with O_2 using various supported metal catalysts.

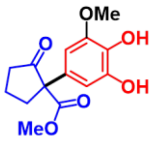
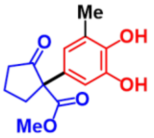
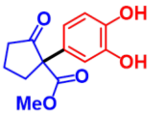
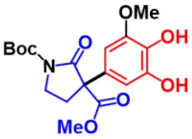


Entry	Catalyst	Yield [%]
1	$RuO_2/AlPO_4$	90
2	$PdO/AlPO_4$	69
3	$Rh_2O_3/AlPO_4$	67
4	$PtO_2/AlPO_4$	13
5	$RuO_2/Mg_3(PO_4)_2$	27
6	$RuO_2/AlOOH$	30
7	RuO_2/SiO_2	8

$RuO_2/AlPO_4$ selectively promoted the cross-coupling reaction of various catechols and active methylene compounds in H_2O solvent (Table 2). For example, the coupling reaction of 3-methoxycatechol and 3-methyl 2-oxopyrrolidine-1,3-dicarboxylate proceeded to afford the corresponding product, which is useful for total synthesis of amaryllidaceae alkaloids, such as Powelline and Buphanidrine, in 90% yield. The $RuO_2/AlPO_4$ catalyst is easily separated from the reaction mixture after the reaction. $AlPO_4$ efficiently promotes the nucleophilic addition of active methylene compounds to *o*-quinone intermediates generated by aerobic oxidation of catechols by RuO_2, enabling the selective cross-coupling reaction.

Table 2. Cross-coupling reaction of catechols and active methylene compounds with O_2 using $RuO_2/AlPO_4$ catalyst.



Product				
Yield, Time	90%, 12 h	83%, 24 h	76%, 24 h	90%, 12 h

4. Conclusions

We achieved in the development of $RuO_2/AlPO_4$ promoting aerobic oxidative cross-coupling reaction of catechols and active methylene compounds. This is the first example of heterogeneous catalyst system for the cross-coupling reaction. The present system has many advantages, including the use of O_2 and H_2O as green oxidant and solvent, respectively, the production of only H_2O as the byproduct, and easy separation of the catalyst from the reaction mixture.

References

1. Z. Maeno, T. Mitsudome, T. Mizugaki, K. Jitsukawa, K. Kaneda, Molecules 20 (2015) 3089; Z. Maeno, T. Mitsudome, T. Mizugaki, K. Jitsukawa, Catal. Sci. Tech. 7 (2017) 3205.