A C–N bond breaking reaction: Esterification of tertiary amides over a reusable CeO_2 catalyst

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Abstract: CeO_2 has been found to promote ester forming alcoholysis reactions of tertiary amides with alcohols. The present catalytic system is convenient, recyclable, and it does not require additives. In addition, the process has a wide substrates scope (43 examples; up to 92% isolated yield). A plausible mechanism, involving rate limiting nucleophilic addition of a CeO_2 lattice oxygen to the amide carbonyl, have been proposed for the process based on combined results from density functional theory (DFT) and *in situ* FT-IR studies. The theoretical results show the cooperative roles that acid and base sites of CeO_2 play in the reaction.

Keywords: CeO_2, Acid-base cooperation, Alcoholysis, Tertiary amides.

1. Introduction

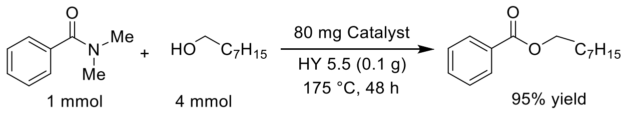
Amide groups are present in a broad range of natural and synthetic compounds. Despite its importance as key building blocks for such compounds, synthetic application of amide is limited owing to poor electrophilic nature and resonance stability of amide bond. As a consequence of the difficulties, cleaving C–N bond of amide still remains challenging and attracts much interests. In particular, so much effort has been devoted to alcoholysis reactions of amides. Although various non-catalytic methods of amide alcoholysis have been reported, they suffer from use of excess amount of promoters such as HCl and $NaNO_2$ as well as generation of resultant wastes. There has been substantial progress by utilizing homogeneous catalytic systems in recent years that enables conversion of amides to esters via alcoholysis reactions.[1] In these cases, however, the processes require additives and/or the use of elaborate catalytic ligand such as NHC, and difficulties are encountered with catalyst recycling.[2] In order to realize environmentally benign processes and large-scale applications, catalyst employed for these transformation reactions should be readily prepared, heterogeneous, and recyclable.[3] We herein report a general catalytic system for direct C–N bond cleavage to one-pot esterification of several tertiary amides with alcohols under additive-free condition using CeO_2 as reusable heterogeneous catalyst.

2. Experimental

CeO_2 (JRC-CEO2) supplied from the Catalysis Society of Japan was calcined at 600 °C for 3 h and used as a catalyst. Typical catalytic reactions condition is as follows: amide (1.0 mmol), alcohol (4.0 mmol), CeO_2 (80.0 mg) and dodecane (0.3 mmol) as an internal standard were added to a Pyrex reaction tube (18.0 ml). HY zeolite (0.1 g) wrapped by a filter paper was also placed at the upper portion of the reaction tube for removal of formed amine as a by-product. The reaction mixture was heated at 175 °C and stirred for 48 h under N_2 atmosphere. After completion of the reaction, the products were analyzed by GC, GC-MS, NMR.

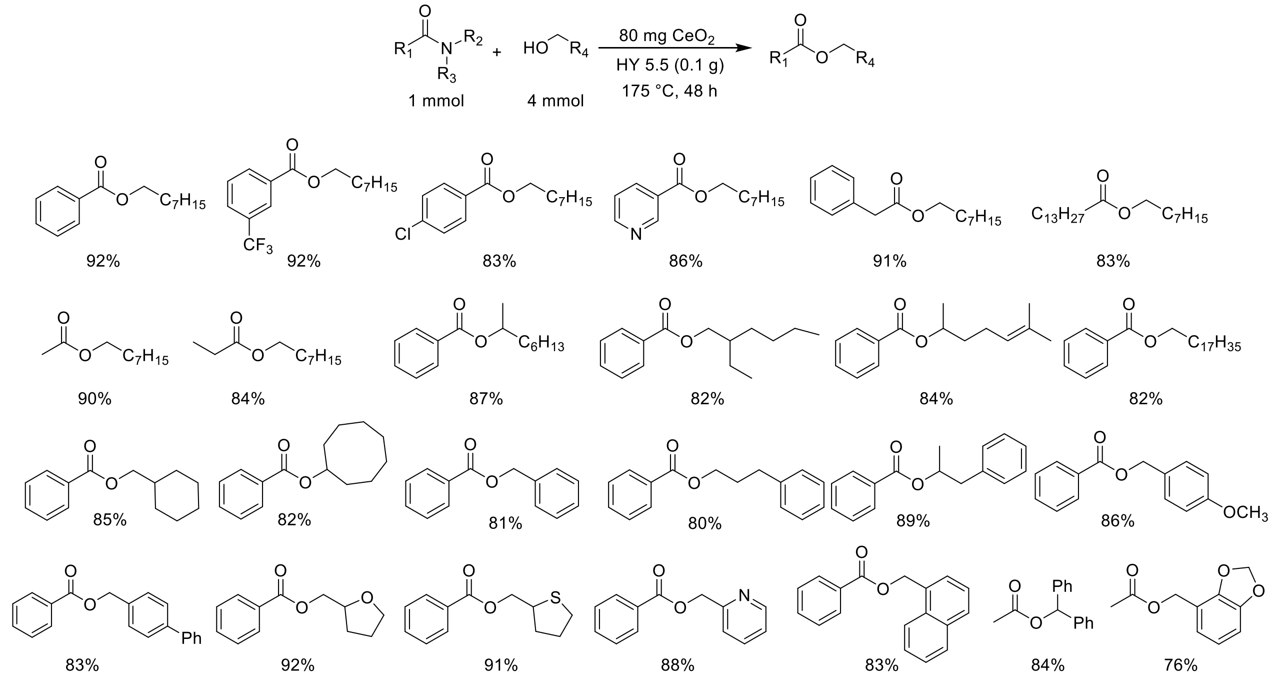
3. Results and discussion

The catalyst was screened with the following model reaction (1). Among various metal oxides and solid acid catalysts tested (metal oxides: CeO_2, CaO, MgO, ZnO, TiO_2, ZrO_2, Nb_2O_5, Al_2O_3, SiO_2, Fe-mont, solid acids: Amberlyst-15, HBEA-150, Niobic acid, Nafion-SiO_2), CeO_2 gave the highest yield of ester (95%) within 48 h.



(1)

Subsequently, substrate scope was investigated to show potential applicability of the CeO_2-catalyzed system. Various alcohols containing cyclic, linear, aliphatic and aromatic moieties were efficiently converted to give the corresponding esters. In addition to the scope of alcohols, amide substrate scope was also investigated by employing 1-octanol (Figure 1). The obtained results indicate that the proposed catalytic system is applicable to various amides alcoholysis. Furthermore, on the basis of *in situ* FT-IR findings, periodic DFT calculations were performed to explore the mechanistic pathway proposed for the reaction of *N,N*-dimethylacetamide and benzylalcohol on the CeO_2 (111) surface.[4] The computational results showed that the rate determining step for the alcoholysis reaction involves addition of a lattice oxygen of CeO_2 to the carbonyl carbon atom of the amide. In addition, catalyst reusability was also investigated. There was no significant loss in activity even after five times of recycling, indicating that CeO_2 possesses high stability for the reaction. Moreover, the catalytic system was also applicable for gram scale synthesis of esters up to 91% isolated yield.



Scheme 1. Substrate scope for CeO_2-catalyzed ester formation reaction from various amides and alcohols.

4. Conclusion

We have developed an efficient way to convert tertiary amides to esters using CeO_2 as a heterogenous catalyst. Unlike typical reactions utilizing homogeneous catalytic systems, the new process is operationally simple and does not require additives. The esterification process displays a wide substrates scope (43 examples; up to 92% isolated yield). Moreover, combined results of DFT and *in situ* FT-IR studies suggested the reaction proceeds through nucleophilic attack of lattice oxygen of CeO_2. It is our hope and expectation that the area of amide C–N bond breaking using CeO_2 catalyst will continue to flourish the growing use of tertiary amides as synthons in organic synthesis.

References

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