Alkylation of Nitriles with Alcohols Catalyzed by a Well-Defined Cobalt Complex Supported by a Tripodal N, P Mixed-Donor Ligand

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Abstract

The construction of a C-C bond is one of the central goals in both academia as well as industry. Among them, the alkylation of nitriles with alcohols is highly significant because nitriles products are the versatile structural motif for the construction of value-added products such as amides, carboxylic acids, ketones, and oxazolines. In addition, many drugs and natural products also contain nitriles group. There are many approaches for the alkylation of nitriles with alcohols; among them, transition metal catalyzed alkylation reaction is environmentally benign because it releases water as the sole byproduct. However, most of the catalysts for nitrile alkylation are based on noble metals such as Os, Rh, Ir, and Pd. These noble metals are not only expensive and rare but also toxic. So, it is desirable to develop a catalyst based on cheap, earth-abundant and less toxic transition metals. Recently, our group developed an air-stable catalyst based on cobalt metal which offers additional economic and ecological benefits than precious metals. This well-defined cobalt catalyst showed remarkable catalytic activities in ketone, ester, imine, and amine synthesis. Herein, we further explored its catalytic activities for the synthesis of nitrile products. We successfully synthesized nitriles products in good to excellent yields. The reaction releases water as the only byproduct and tolerates a wide variety of functional groups and heterocyclic moieties.

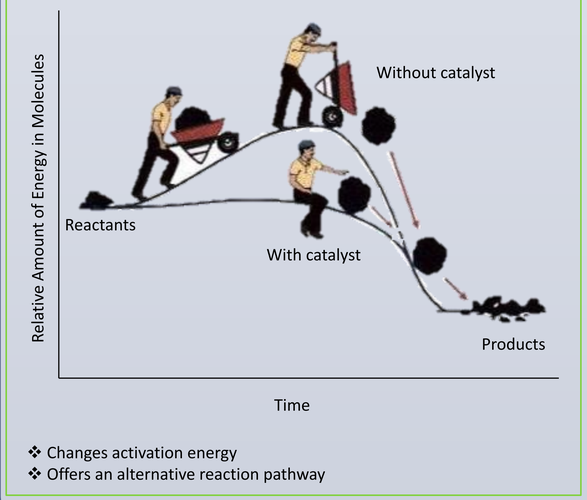
Objectives

- To design a catalyst based on earth-abundant metals.
- To use the above-designed catalyst for the synthesis of various value-added products through alkylation of nitriles with alcohols.

Contribution From Catalysis

- Economic → Contributes 40% of Global GDP[1]
- Manufacturing Process → over 80% of all Manufactured Products are made from catalysis[2]

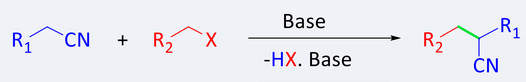
How does Catalyst Work ?



- Changes activation energy
- Offers an alternative reaction pathway

Methods of Synthesis for Nitriles Product

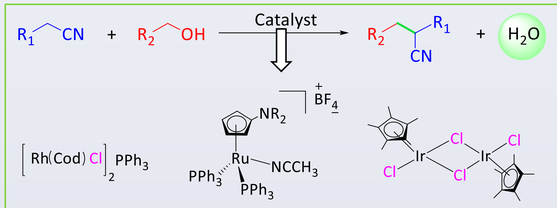
1. Traditional Method



Drawbacks

- Mutagenic and toxic reagents
- Stoichiometric amount of base
- Stoichiometric salt waste
- Potential for dialkylated byproducts

2. Catalytic Method Developed by Other Groups

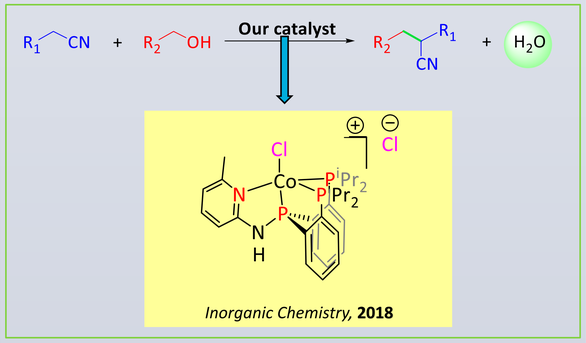


Adv. Synth. Catal. **2015** | *Dalton Trans.* **2010** | *J. Org. Chem.* **2006**

Drawbacks

- Limited
- Expensive
- Toxic

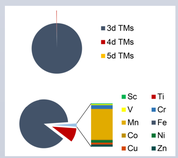
3. Catalytic Method Developed by Our Group



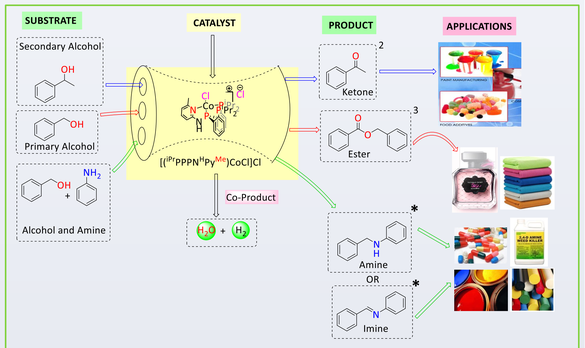
Inorganic Chemistry, **2018**

Advantages of our catalyst

- Used earth abundant cobalt metal[3] for catalysis
- Cheap
  - 31 Eur/Kg[3]
  - 240 times cheaper than Ru
  - 1300 times cheaper than Ir
  - 2700 times cheaper than Rh
- Release only water as a byproduct

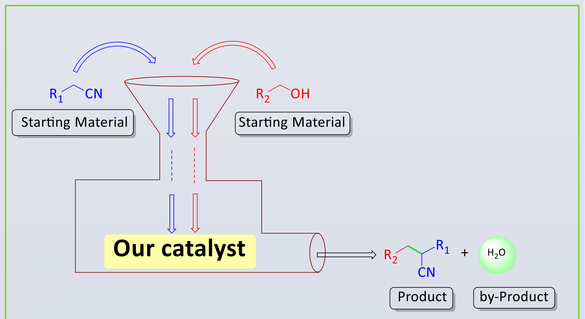


Remarkable Catalytic Activities Showed by Our Catalyst for the Construction of Various Value-Added Products



Inorganic Chemistry, **2018** , *Organic Letters,* **2018** , ∗ = *Manuscript ready for submission*

Further Catalytic Activities Showed by Our Catalyst for the Construction of α-Alkylated Nitriles Product



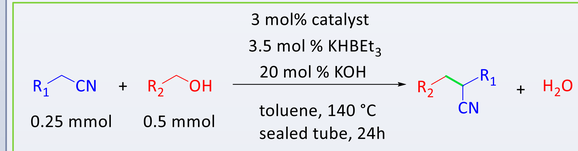
Advantages of Alcohol as a Starting Material

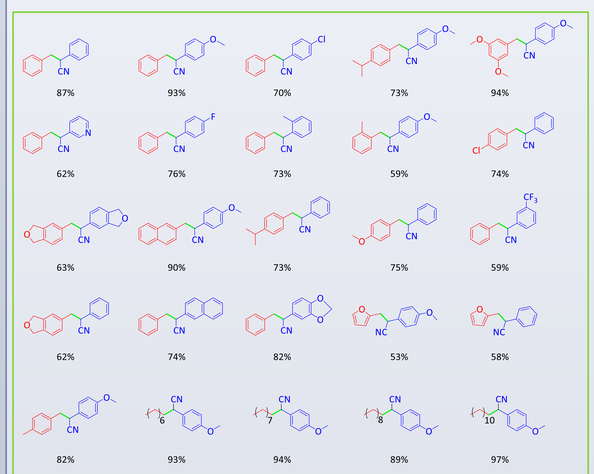
- Can be obtained from the fermentation of inedible lignocellulose
- Cheap
- Non-toxic

Applications of α-Alkylated Nitriles Product

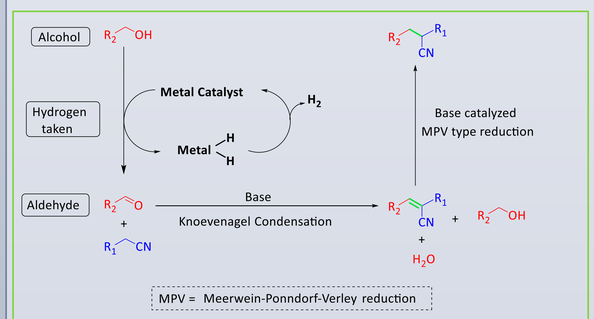
- Building blocks in organic synthesis
- Drugs such as **Ruxolitinib, Vildagliptin** and **Anastrazole** contains nitrile groups

Selective Synthesis of Nitriles Product With Our Cobalt Catalyst (Results)





Proposed Mechanism



Conclusion

In summary, the cobalt catalyst designed in our lab is a promising example of a homogeneous earth-abundant metal catalyst. This catalyst showed excellent catalytic activity for the synthesis of value-added products such as ketone and esters. Herein, we further used our catalyst for the selective synthesis of α-alkylated nitriles product with water as the sole by-product.

References

1. Davidson, M. *Modern Developments in Catalysis,* ISBN: 978-1-78634-122-8
2. Chris, A. *North American Catalysis Society , accessed on* **3/22/2020**
3. Halka, M.; Nordstrom, B. *Transition metals*; Facts On File:London, **2011**.

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