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Nafion®-catalyzed microwave-assisted Ritter reaction: an atom-economic solvent-free synthesis of amides

Vivek Polshettiwar, Rajender S. Varma *

Sustainable Technology Division, National Risk Management Research Laboratory, US Environmental Protection Agency, 26 W. Martin Luther King Dr., MS 443, Cincinnati, OH 45268, USA

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Abstract

An atom-economic solvent-free synthesis of amides by the Ritter reaction of alcohols and nitriles under microwave irradiation is reported. This green protocol is catalyzed by solid-supported Nafion®NR50 with improved efficiency and reduced waste production.

Keywords: Ritter reaction; Amides; Nafion®NR50; Solvent-free reaction; Microwave irradiation

Amides are common moieties in naturally occurring substances like peptides and proteins and are also found in various synthetic materials.[1,2] This makes the amide functionality an important building block in synthetic chemistry and many methods for its synthesis were reported in the literature.[1] In general, amides are formed by the condensation of carboxylic acid and amines, using various coupling agents.[3] Although good results were obtained using this protocol, the reaction conditions were very harsh. In 1948, Ritter reported the efficient synthesis of amide by the reaction of alkenes with nitriles,[4] in which alcohols can also be used instead of alkenes.[5,6] In recent years, several alternative methodologies have been developed for Ritter reaction using sulfuric and other acid catalysts,[7–10] metal complexes,[11] trifluoromethanesulfonic anhydride,[12] and boron trifluoride etherate.[13] The main disadvantages of these methods are the use of toxic catalysts or corrosive acids.

Use of solid-supported acids, such as silica-sulfuric acid, P_2O_5/SiO_2,[10] and $Cs_{2.5}H_{0.5}PW_{12}O_{40}$, was also made for this reaction;[14] however, reuse of these catalysts is not possible. Olah et al. in 1987 reported the use of Nafion-H as an efficient catalyst for the Ritter reaction.[15] This is an excellent protocol in terms of catalyst reusability and product yield; however, harsh reaction conditions, longer reaction time, and the use of excessive nitrile make this method non-sustainable. In view of the emerging interest in microwave chemistry,[16,17] and in keeping with our emphasis on the development of green synthetic methods,[17,18] we revisited this protocol. The primary objective of this project was to find an economical and greener method for the conversion of nitrile into the corresponding N-monosubstituted amide, and herein we report Nafion®NR50[18a,19]-catalyzed atom-economic solvent-free Ritter reaction under microwave (MW) irradiation (Scheme 1).

After screening a range of MW power, reaction temperature, and time, and exploring the scope of various solvents, we found that the solid-supported Nafion®NR50 was the most efficient catalyst for Ritter protocol at 130 °C under MW irradiation (200 W), in the absence of any solvent. The efficiency of this protocol was then studied for the synthesis of various amides, and the results are summarized in Table 1.

Various alcohols reacted efficiently with nitriles to afford the corresponding amides in good yields (entries 1–15). The generality and scope of this protocol was evaluated for a wide range of alcohols, bearing both electron withdrawing

* Corresponding author. Tel.: +1 513 487 2701; fax: +1 513 569 7677.
E-mail address: varma.rajender@epa.gov (R. S. Varma).

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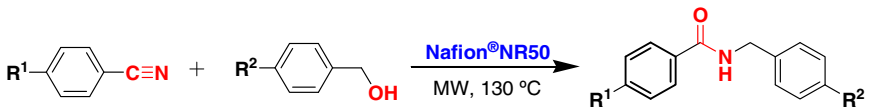
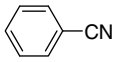
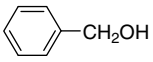
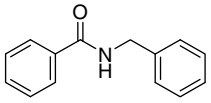
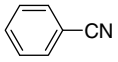
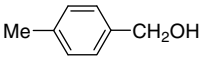
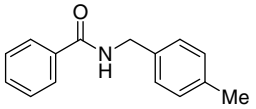
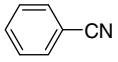
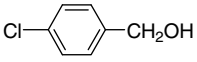
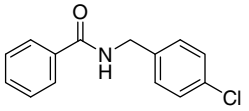
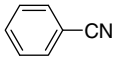
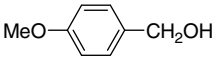
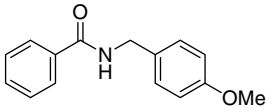
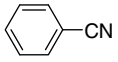
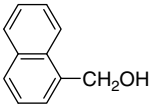
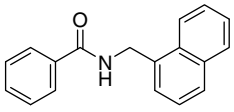
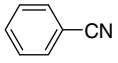
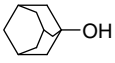
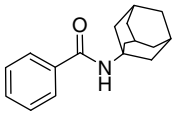
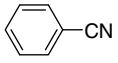
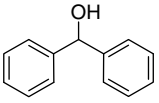
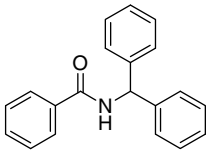
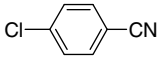
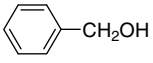
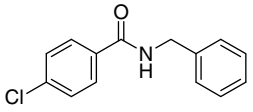
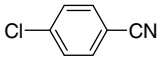
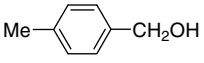
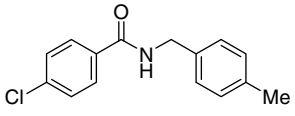
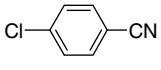
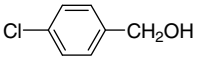
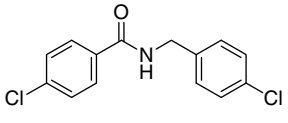


R^1 = H, OMe, Cl
R^2 = H, Me, OMe, Cl, naphthyl, adamantyl etc

Scheme 1. Nafion®NR50-catalyzed solvent-free Ritter reaction under MW irradiation.

Table 1
Nafion®NR50-catalyzed Ritter synthesis of amides under MW irradiation[a]

Entry	Nitrile	Alcohol	Product	Yield[b] (%)
1				92
2				88
3				86
4				86
5				82
6				90
7				72
8				88
9				86
10				85