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Chinese Chemical Letters 23 (2012) 293–296

CHINESE CHEMICAL LETTERS

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Amberlyst-15 as a recyclable heterogeneous catalyst for synthesis of *N-tert*-butylamides *via* Ritter-type reaction

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Received 6 October 2011
Available online 25 January 2012

Abstract

Highly efficient method for the preparation of *N-tert*-butylamides by reaction of nitriles with *tert*-butylacetate is described using Amberlyst-15 as a recyclable heterogeneous catalyst. Selective amidation of benzonitrile in the presence of acetonitrile was also achieved.

Keywords: Modified Ritter reaction; Amberlyst-15; Nitriles; *tert*-Butylacetate; *N-tert*-Butylamides

The application of polymer supports as reagent and catalyst has received special attention, due to easy work up of reaction products and some selectivity which is undoubtedly attractive features of this methodology [1]. Ion exchange resins are usually employed either as sulfonic acid cation exchangers in the hydrogen form or quaternary ammonium anion exchangers in the hydroxide form in both aqueous and non-aqueous media. It is noteworthy that these reagents are insoluble in reaction media and can be easily removed by simple filtration, therefore reducing the steps and equipments required for catalyst removal. Furthermore these reagents can be handled easily without any danger to personnel. The Ritter reaction makes possible the conversion of a group, capable of giving a relatively stable carbonium ion, to a substituted amide by reaction with a nitrile in the presence of a strong acid like concentrated sulfuric acid [2]. Several modifications have been attempted to improve Ritter reaction conditions. However, as an alternative to sulfuric acid, other acid catalysts such as $(CF_3SO_2)_2O$ [3], $BF_3{\cdot}Et_2O$ [4], Fe^{3+}-Montmorillonite [5], $Mg(HSO_4)_2$ [6], $Bi(OTf)_3$ [7], $CeCl_3{\cdot}7H_2O/AcCl$ [8], P_2O_5/SiO_2 [9] and Nafion [10] are employed in the Ritter reaction. Ritter reaction using *tert*-butylacetate instead of alcohol was also reported to be catalyzed by sulfuric acid [11,12], $FeCl_3{\cdot}6H_2O$ [13], $ZnCl_2/SiO_2$ [14], and I_2 [15].

However, most of these methods suffer from at least one of the following disadvantage: vigorous reaction conditions, strong protic and aqueous media, high cost and toxicity of the reagent, tedious work-up procedures, and instability and hygroscopic nature of the reagent. Substantial investigations have been done to introduce novel supported catalysts and chemical reagents. These include dispersing catalysts on inorganic supports such as metal oxide, alumina, silica, and zeolite. There are a number of advantages in using polymer supported catalysts over the conventional catalysis. The reactions can be performed under mild condition and purification of the product is simplified because of the use of an

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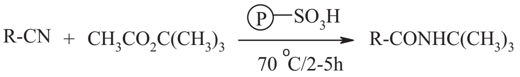
doi:10.1016/j.cclet.2011.11.026



$$\text{R-CN} + CH_3CO_2C(CH_3)_3 \xrightarrow[70\,^{\circ}C/2\text{-}5h]{Ⓟ-SO_3H} \text{R-CONHC}(CH_3)_3$$

Scheme 1.

insoluble solid support. Polymer supported catalysts can also be recycled after use [16]. Recently, Amberlyst-15 was efficiently used as catalyst in variety of chemical reactions like: synthesis of 1,5-benzodiazepines [17], bis and tris (1*H*-indol-3yl) methanes [18], β-acetamido ketones [19], regeneration of carbonyl compounds from oximes, hydrazones and semicarbazones [20], preparation of quinoline derivatives [21], oxidation of benzyl alcohols catalyzed by isoamyl nitrate [22] and synthesis of alkyl/aryl/heterocyclic phosphonates [23]. In connection with our research to develop application of Ritter reaction for synthesis of polyamides [24], polyether amides [25] and amidation of benzhydrol and tertiary alcohols with polyvinylpolypyrrolidone-boron trifluoride [26], herein, we found that Amberlyst-15 can be used for preparation of *N*-*tert*-butylamide derivatives from *tert*-butylacetate *via* Ritter type reaction in good to excellent yields. This method often leads to the development of eco-friendly protocols (Scheme 1).

Interestingly, this reagent not only gives good yields of the products but also Amberlyst-15 is easily regenerated and can be reused several times.

A variety of *N*-*tert*-butylamides were prepared from *tert*-butylacetate and the corresponding nitriles in the presence of Amberlyst-15 in good yields (Table 1, entries 1–8). *O*-Tolunitrile shows low yield of corresponding amides probably *via* steric hindrance of methyl group in *ortho* position of CN functional group (Table 1, entry 9). Aliphatic nitriles were converted to the corresponding amides in moderate yields (Table 1, entries 10 and 11). Also, using of *tert*-butanol and triphenyl methanol instead of *tert*-butylacetate lead to appropriate yield of corresponding amides (Table 1, entry 12 and 13). It is worth mentioning that the corresponding amide in each case was isolated by simple filtration of the catalyst followed by crystallization from the crude filtrate.

Additionally, competitive Amberlyst-15 catalyzed modified Ritter reaction of *tert*-butylacetate with equimolar amounts of benzonitrile and acetonitrile leads to the selective formation of *N*-*tert*-butylbenzamide in good yield, whereas acetonitrile remained unchanged (Scheme 2).

Mechanistically, we assume that the reaction likely proceeds *via* the protonation of *tert*-butylacetate by Amberlyst-15 and facilitation of C–O cleavage by attacking of nitrile group to give the nitrilium cation which subsequently reacts with water to furnish the desired amide (Scheme 3).

To check the reusability of the catalyst, it was employed the amidation of *tert*-butylacetate with benzonitrile five cycles under the optimum conditions. In the first run 90% of *N*-*tert*-butylbenzamide was obtained. The catalyst powder was recovered by filtration, washed with dichloromethane and immediately reused for amidation processes again, taking into account the partial loss of catalyst during the recovery. After recycling five times, the catalytic activity of Amberlyst-15 still remained at a high level (Table 2).

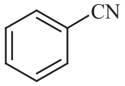
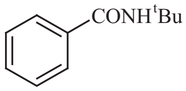
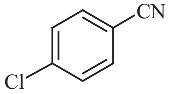
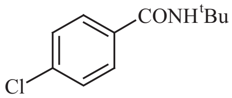
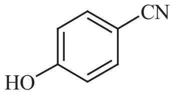
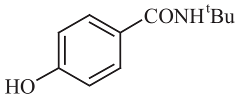
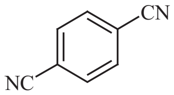
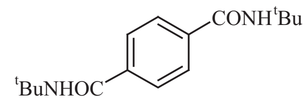
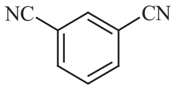
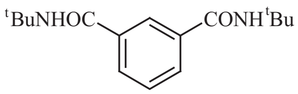
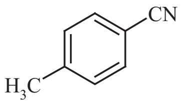
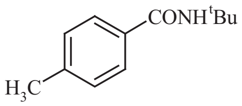
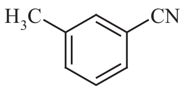
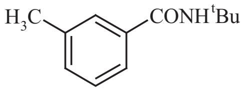
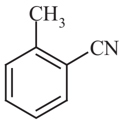
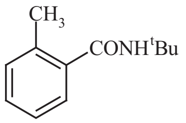
Cross-linked polystyrene tolerates well a broad range of reaction conditions, including treatment with weak oxidants (ozone, DDQ), strong bases (LDA), and acids (HBr, TfOH). Strong oxidants at high temperatures and other reagents which lead to a chemical modification of alkyl benzenes, however, not surprisingly, also attack polystyrene [27]. In general, the maximum working temperature for acid resins is approximately 125 °C, so, Amberlyst-15 is stable and decomposition not occurred in this reaction conditions.

In conclusion, we have developed a simple methodology for modified Ritter reaction using Amberlyst-15 as a recyclable heterogonous catalyst, and represent effective catalytic activity for the amidation of *tert*-butylacetate with nitriles. This catalyst can be recovered from reaction system and reused many times without significant loss of catalytic ability.

1. Experimental

All chemicals were purchased from Merck chemical company. Melting points were recorded on an electro thermal melting point apparatus. The NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard on a Bruker advance DRX 400 MHz spectrometer. IR spectra were determined on a SP-1100, P-UV-Com instrument. Purity determination of the products was accomplished by TLC on silica gel poly gram SIL G/UV 254 plates. Products were separated by simple filtration, and identified by comparison IR, and ^1H NMR spectra, with those reported for authentic samples.

Table 1
Amidation of *tert*-butylacetate and *tert*-alcohol with nitriles using Amberlyst-15.

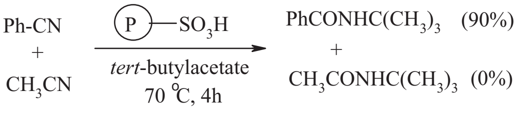
Entry	Substrate	Nitriles	Product[a]	Time/h	Yield %[b]
1	$CH_3CO_2C(CH_3)_3$			2	90
2	$CH_3CO_2C(CH_3)_3$			2	92
3	$CH_3CO_2C(CH_3)_3$			4	76
4	$CH_3CO_2C(CH_3)_3$			5	87
5	$CH_3CO_2C(CH_3)_3$			5	85
6	$CH_3CO_2C(CH_3)_3$			2	84
7	$CH_3CO_2C(CH_3)_3$			2	92
8	$CH_3CO_2C(CH_3)_3$			3	25
9	$CH_3CO_2C(CH_3)_3$			3	74
10	$CH_3CO_2C(CH_3)_3$	$ClCH_2CN$	$ClCH_2CONH^tBu$	3	48
11	$CH_3CO_2C(CH_3)_3$	$NCCH_2COOEt$	$^tBuNHCOCH_2COOEt$	3	56
12	$(CH_3)_3COH$	CH_3CN	CH_3CONH^tBu	3	76
13	$(Ph_3)_3COH$	CH_3CN	$CH_3CONHC(Ph)_3$	3	85

[a] All the products were characterized by IR, ^1H NMR spectra and comparison with authentic samples.
[b] All yields refer to isolated products.

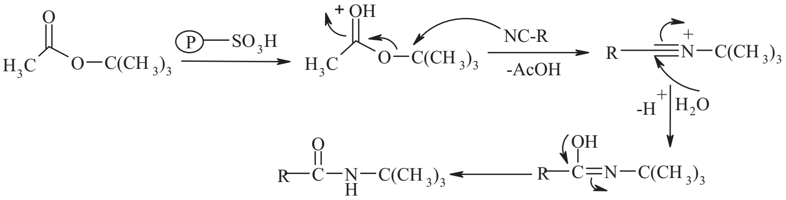
1.1. General procedure:

A solution of 3 mmol nitrile in 3 mmol *tert*-butylacetate or *tert*-butylalcohol was prepared. Amberlyst-15 (1 g) was added to the solution and the reaction mixture was stirred for 2–5 h under 70 °C until TLC analysis showed that no nitrile remained. The reaction mixture was filtered, and the solvent was evaporated on a rotatory evaporator under diminished pressure. The solid residue was recrystallized from water to afford pure crystals of the proper amides in 48–92% yields.

N,N′-Di-tert-butylisophtalamide (entry 5): Yield 85%; mp: 204–207 °C. IR (KBr): 3272, 3068, 2969, 1639, 1548, 1307, 680 cm^{-1}. ^1H NMR (400 MHz $CDCl_3$): δ 1.49 (s, 18H), 6 (br, s, 2H), 7.28–8.11 (m, 4H).



Scheme 2.



Scheme 3.

Table 2
The recycling of Amberlyst-15 in the amidation of *tert*-butyl acetate to *N*-*tert*-butylbenzamide.

Cycle	1	2	3	4	5
Yield (%)[a]	90	88	86	85	84

[a] Isolated yields.

N-tert-Butyl-3-methylbenzamide (entry 7): Yield 92%; mp: 96–97 °C. IR (KBr): 3382, 2962, 1643, 1529, 1447, 748 cm^{-1}. ^1H NMR (400 MHz $CDCl_3$): δ 1.49 (s, 9H), 2.4 (s, 3H), 5.95 (br, s, 1H), 7.28–7.56 (m, 4H).

N-tert-Butylchloromethylacetamide (entry 10): Yield 48%; mp: 79–81 °C. IR (KBr): 3311, 2977, 1683, 1554, 1222, 673 cm^{-1}. ^1H NMR (400 MHz $CDCl_3$): δ 1.40 (s, 9H), 3–96 (s, 2H), 6.38 (br, s, 1H).

N-tert-Butylmethylacetatoamide (entry 11): Yield 56%; mp: 90–93 °C; IR (KBr): 2991, 2979, 1720, 1629, 1498, 1043, 736 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.45 (s, 9H), 1.47 (t, 3H), 2.43(s, 2H), 4.54 (q, 2 H, $J = 6.8$) 11.25 (br, s, 1H).

Acknowledgment

We are grateful to Islamic Azad University of Rasht Branch for financial assistance of this work.

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