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Polyvinylpolypyrrolidone-Supported Boron Trifluoride; Highly Efficient Catalyst for the Synthesis of *N-tert*-Butyl Amides

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Abstract: Highly efficient method for the preparation of *N*-tert-butyl amides by reaction of nitriles with tert-butyl acetate is described using polyvinylpolypyrrolidone-supported boron trifluoride (PVPP-BF₃) at 70 °C in good to excellent yields. Selective amidation of benzonitrile in the presence of acetonitrile was also achieved. polyvinylpolypyrrolidone-boron trifluoride complex shows non-corrosive and stable solid catalyst elevated Lewis acid property.

Keywords: Polyvinylpolypyrrolidone, Boron trifluoride, Nitriles, Tert-butyl acetate, Tert-butyl amide.

Introduction

Among the reported routes, use of the Ritter reaction is an attractive method for the synthesis of amide. The Ritter reaction makes possible the conversion of a group, easily converted to relatively stable carbonium ion to a substituted amide by reaction with a nitrile in the presence of strong acid¹. The conversion of a nitrile to the corresponding *N-tert* butyl amide is a very important transformation in organic synthesis. The product *N-tert*-butyl amides are pharmaceutically applicable² and also serve as precursors to the corresponding amines. The classical Ritter reaction involves the reaction of alkenes and of tertiary and benzylic alcohols with nitriles in the presence of conc. sulfuric acid³⁻⁵. As an alternative to sulfuric acid, other acid catalysts such as (CF₃SO₂)₂O⁶, BF₃.Et₂O⁷, Fe (III) - montmorillonite⁸, Mg(HSO₄)₂⁹, Bi(OTf)₃¹⁰, CeCl₃.7H₂O/AcCl¹¹, P₂O₅/SiO₂⁻¹² and nafion¹³ have been employed to improve the classical Ritter reaction. The Ritter reaction using *tert*-butyl acetate instead of *tert*-butyl alcohol was also reported by sulfuric acid^{14,15}, FeCl₃.6H₂O¹⁶, I₂⁻¹⁷ and ZnCl₂/SiO₂⁻¹⁸.

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, unsatisfactory yields, 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 of 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 insoluble solid support. Polymer supported catalysts can also be recycled after use. Poly (vinyl pyrrolidone) displays a strong binding affinity toward small molecules, its iodine complex, povidon-iodine, is widely used as an anti-infective agent in clinical treatments¹⁹. In spite of boron trifluoride etharate, PVPP-BF₃ is non-corrosive and stable solid catalyst elevated Lewis acid property. Following our interest on the use of the Ritter reaction for the synthesis of polyamides²⁰, polyether amides²¹ and amidation of benzhydrol with nitriles via polyvinylpolypyrrolidone-boron trifluoride (PVPP-BF₃)²², we found that PVPP-BF₃ can be used for the preparation of N-tert-butyl amides by tert-butyl acetate in good to excellent vields (Scheme 1). This method leads to the development of eco-friendly protocols. Interestingly, this reagent not only gives good yields of the products but also PVPP-BF₃ is easily regenerated and can be reused several times and retains its activity after several months of storage.

$$\begin{array}{c} \text{R-CN} + \text{CH}_{3}\text{CO}_{2}\text{C}(\text{CH}_{3})_{3} \xrightarrow{\text{PVPP-BF}_{3}} \text{R-CONHC}(\text{CH}_{3})_{3} \\ \hline \text{ClCH}_{2}\text{CH}_{2}\text{Cl}_{2}\text{Cl} \\ 70 \text{ °C}/2-5 \text{ h} \\ \hline \text{Scheme 1} \end{array}$$

Experimental

Polyvinylpolypyrrolidone (PVPP) was purchased from Fluka chemical company. Other chemicals were purchased from Merck chemical company. Melting points were recorded on an electro thermal melting point apparatus. The NMR spectra were recorded in CDCl₃ 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. Products were separated by simple filtration, and identified by comparison IR, and 1H NMR spectra, with those reported for authentic samples.

Catalyst preparation

In this method boron trifluoride etherate was immobilized on polyvinylpolypyrrolidone to give a stable polymeric Lewis acid reagent according to our previous article²². To a suspension of 3 g PVPP in 25 ml CH₂Cl₂, a solution of 5 ml BF₃.Et₂O in 15 ml CH₂Cl₂ was added dropwise and the mixture stirred for 1 h at room temperature. The resulting resin was filtered and washed with 2×10 ml CH₂Cl₂ and dried in a vacuum desiccator to give a stable and non hygroscopic powder.

Synthesis of tert-butyl amides: General procedure

To a solution of 3 mmol nitrile and 3 mmol *tert*-butyl acetate in 5 mL 1,2-dichloroethane was added 3 mmol (0.3 g) PVPP-BF₃ and the reaction mixture was stirred for 2-5 h at 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 recrystalized from water to afford pure crystals of the corresponding amides in 72-96% yields. *N-tert-butyl-benzamide* (1)

FT- IR (KBr): $\upsilon = 3322$, 3064, 2962, 1638, 1537, 1482, 858 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.47$ (s, 9H), 6.04 (br s, 1H), 7.52 (d, 2H), 7.58 (d, 2H) ppm.

N-tert-butyl-4-chlorobenzamide (2)

FT- IR (KBr): v = 3322, 3067, 2927, 1639, 1529, 1540, 1483, 1315, 1220 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.49$ (s, 9H), 5.94 (br s, 1H), 7.29 (d, 2H) 7.66 (d, 2H) ppm.

N-tert-butyl-4-methylbenzamide (3)

FT- IR (KBr): v = 3351, 3029, 2971, 1639, 1542, 1447, 1311 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.49$ (s, 9H), 2.37 (s, 3H), 5.96 (br s, 1H), 7.18 (d, 2H), 7.61 (d, 2H) ppm.

N-tert-butyl-3-methylbenzamide (4)

FT- IR (KBr): v = 3382, 2962, 1643, 1529, 1447, 748 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.49$ (s, 9H), 2.4 (s, 3H), 5.95 (br s, 1H), 7.28-7.56 (m, 4H) ppm.

N-tert-butyl-4-hydroxybenzamide (5)

FT- IR (KBr): $\upsilon = 3274$, 3068, 2969, 1639, 1548, 1307, 935 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.49$ (s, 9H), 5.97 (br s, 1H), 6.84 (d, 2H), 7.59 (d, 2H) ppm.

N,*N*'-di-tert-butylterphtalamide (6)

FT-IR (KBr): v = 3301, 2969, 1639, 1546, 1324, 864 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.50$ (s, 18H), 5.97 (br s, 2H), 7.77 (s, 4H) ppm.

N,*N*'-*di*-*tert*-*butylisophtalamide* (7)

FT-IR (KBr): v = 3272, 3068, 2969, 1639, 1548, 1307, 680 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.49$ (s, 18H), 6 (br s, 2H), 7.28-8.11 (m, 4H) ppm.

N-tert-butylacrylamide (8)

FT-IR (KBr): v = 3263, 3072, 2964, 1656, 1567, 1403, 1226 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.39$ (s, 9H), 5.55 (dd, 1H), 5.82 (br s, 1H), 6.02-6.16 (m, 1H), 6.16-6.29 (m, 1H) ppm.

N-tert-butylchloromethylacetamide (9)

FT-IR (KBr): v = 3311, 2977, 1683, 1554, 1222, 673 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.40$ (s, 9H), 3-96 (s, 2H), 6.38 (br s, 1H) ppm.

Ethyl 3-(tert-butylamino)3-oxopropanoate (10)

FT-IR (KBr): v = 2991, 2979, 1720, 1629, 1498, 1043, 736 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) $\delta = 1.45$ (s, 9H), 1.47 (t, 3H), 2.43(s, 2H), 4.54 (q, J=6.8, 2 H) 11.25 (br, s, 1H) ppm.

Results and Discussion

Characterization of the Lewis-acid sites present on the polymer was performed by recording the FT-IR spectrum of PVPP-BF₃, which shows a strong broad absorption at 1000-1060 cm⁻¹ for the BF bonds and a moderate absorption at 1646 cm⁻¹ corresponds to the imine group on the backbone (Figure 1). The capacity of the reagent was determined by titration and found to be 10 mmol/g, whereas its silica supported analogue has a loading capacity of less than 4 mmol/g^{23,24}.



Figure 1. The Fourier transform infrared spectroscopy (FT-IR) spectrum of polyvinylpolypyrrolidone (PVPP) and (PVPP-BF₃) complex.

A variety of *N*-tert-butylamides were prepared from tert-butyl acetate and the corresponding nitriles in the presence of PVPP-BF₃ in good to excellent yields (Table 1, entries 1-10). 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, a competitive reaction of tert-butyl acetate with equimolar amounts of benzonitrile and acetonitrile lead to the selective formation of *N*-tert-butylbenzamide in good yield, whereas acetonitrile remained unchanged (Scheme 2).

It is reasonable to assume that the present reaction is initiated by Lewis acidity and oxophilicity of PVPP-BF₃ which promote the Ritter reaction via coordination to oxygen atoms of ester and facilitation of C-O cleavage by attack of nitrile group (Scheme 3). An interesting feature of this method is that the spent resin can be regenerated at the end of the reaction after washing with organic solvent and back to the starting polyvinylpolypyrrolidone-boron triflouride complex and can be used several times without losing its activity.

Ph-CN PVPP-BF₃ PhCONHC(CH₃)₃ (90%)
+
$$tert$$
-butyl acetate $ClCH_2CH_2Cl/70^{\circ}C, 2h$ $CH_3CONHC(CH_3)_3$ (0%)

Scheme 2

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Entry	Nitriles	Product	Time/h	Yield	m.p., °C
1	CN	CONH'Bu	2	90	135-136
2	CI	Cl CONH ¹ Bu	2	92	129-132
3	H ₃ C CN	H ₃ C CONH'Bu	2	87	99-102
4	H ₃ C CN	H ₃ C CONH ^t Bu	2	96	96-97
5	HO	HO CONH ^t Bu	4	72	189-192
6	NC	^t BuNHOC	5	92°	272-276
7	NC CN	^t BuNHOC CONH ^t Bu	5	82 ^c	204-207
8		CONH Bu	3	74	128-131
9	CICH ₂ CN	ClCH2CONH ^t Bu	3	95	79-81
10	NCCH ₂ COOEt	^t BuNHCOCH ₂ COOEt	3	84	89-93

^{*a*}All entries were carried on nitrile (3 mmol), t-BuOAc (3 mmol) and PVPP-BF₃ (3 mmol) in 1,2-dichloromethane (5 ml) at 70 °C. ^{*b*}All yields refer to isolated products. ^{*C*}Nitrile (1.5 mmol) is used.

Conclusion

We have developed a simple and efficient method for the modified Ritter reaction using polyvinylpolypyrrolidone-boron trifluoride as a high loading of Lewis acid, which is stable, easy to prepared and handle, and represent effective activity for the amidation of *tert*-butyl acetate with nitriles. This method provides an easy access to a variety of *tert*-butyl amides.



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References

- 1. Ritter J J and Paul P P, J Am Chem Soc., 1948, 70, 4045-4048.
- 2. Ikeda K, Tatsuno T, Nishihara N, Nagata T and Nishi H, *J Patent.*, 2000-90274 20000329.
- 3. Benson F R and Ritter J J, J Am Chem Soc., 1949, 70, 4128-4129.
- 4. Parris C L and Christenson R M, J Org Chem., 1960, 25, 1888-1889.
- 5. Hathaway B A, J Chem Ed., 1989, 66, 776.
- 6. Garcia Martinez A, Martinez alvarez R, Teso Vilar E, Garcia Fraile A, Hanach M and Subramanian L R, *Tetrahedron Lett.*, 1989, **30**, 581-582.
- 7. Firouzabadi H, Sardarian A. R, Badparva H, Synth Commun., 1994, 24, 601-607.
- 8. Lakouraj M M, Movassagh B and Fasihi J, Synth Commun., 2000, 30, 821-827.
- 9. Salehi P, Khodaei M M, Zolfigol M A and Keyvan A, Synth Commun., 2001, 31, 1947-1957.
- 10. Callens E, Burton A J and Barrett A G M, Tetrahedron Lett., 2006, 47, 8699-8701.
- 11. Yadav J S, Subba Reddy B V, Narayana Kumar G G K S and Madhusudhan Reddy G, *Tetrahedron Lett.*, 2007, **48**, 4903-4906.
- 12. Tamaddon F, Khoobi M and Keshavarz E, Tetrahedron Lett., 2007, 48, 3643-3646.
- 13. Polshettiwar V and Varma R S, Tetrahedron Lett., 2008, 49, 2661-2664.
- 14. Reddy L K, Tetrahedron Lett., 2003, 44, 1453-1455.
- 15. Baum J C, Milne J E, Murry J A and Thiel O R, J Org Chem., 2009, 74, 2207-2209.
- 16. Anxionnat B, Guérinot A, Reymond S and Cossy J, *Tetrahedron Lett.*, 2009, **50**, 3470-3473.

- 17. Theerthagiri P, Lalitha A and Arunachalam P N, *Tetrahedron Lett.*, 2010, **51**, 2813-2819.
- 18. Tamaddon F and Tavakoli F, J Mol Catal A: Chem., 2011, 337, 52-55.
- 19. Liu C, Cui S, Wang Z and Zhang X, J Phys Chem. B., 2005, 109, 14807-14812.
- 20. Lakouraj M M. and Mokhtary M, Polym Int., 2009, 58, 1167-1172.
- 21. Lakouraj M M and Mokhtary M, J Polym Res., 2009, 16, 681-686.
- 22. Lakouraj M M and Mokhtary M, Monash Chem., 2009, 140, 53-56.
- 23. Wilson K and Clark J H, Chem Commun., 1998, 2135-2136.
- 24. Wilson K, Adams D J, Rothenberg G and Clark J H, *J Mol Catal A: Chem.*, 2000, **156**, 309-314.



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