Repurposing *n*-butyl stannoic acid as highly efficient catalyst for direct amidation of carboxylic acids with amines

Santoshkumar M. Potadar, Anil S. Mali, Krishnakant T. Waghmode, Ganesh U. Chaturbhuj

PII: S0040-4039(18)31364-9
DOI: https://doi.org/10.1016/j.tetlet.2018.11.036
Reference: TETL 50421

To appear in: *Tetrahedron Letters*

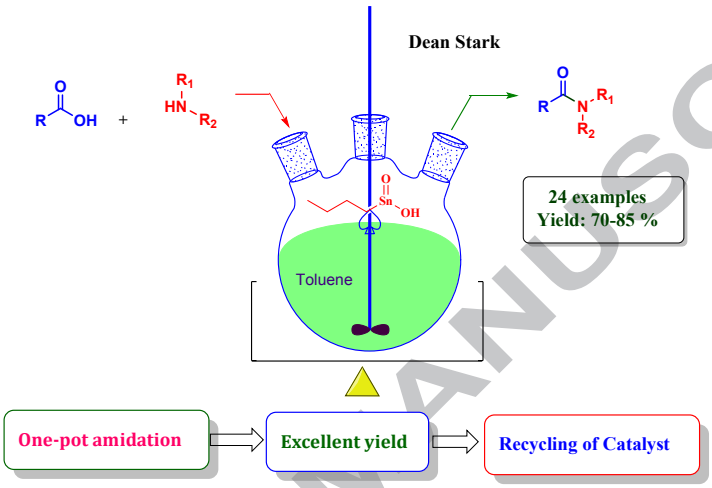
Received Date: 4 July 2018
Revised Date: 7 November 2018
Accepted Date: 11 November 2018

Please cite this article as: Potadar, S.M., Mali, A.S., Waghmode, K.T., Chaturbhuj, G.U., Repurposing *n*-butyl stannoic acid as highly efficient catalyst for direct amidation of carboxylic acids with amines, *Tetrahedron Letters* (2018), doi: https://doi.org/10.1016/j.tetlet.2018.11.036

Abstract

Repurposing *n*-butyl stannoic acid as highly efficient catalyst for direct amidation of carboxylic acids with amines

Santoshkumar M. Potadar,[a] Anil S. Mali[b], Krishnakant T. Waghmode[a] and Ganesh U. Chaturbhuj[b]*



ELSEVIER

Tetrahedron Letters

journal homepage: www.elsevier.com

Repurposing *n*-butyl stannoic acid as highly efficient catalyst for direct amidation of carboxylic acids with amines

Santoshkumar M. Potadar,[a] Anil S. Mali,[b] Krishnakant T. Waghmode,[a] and Ganesh U. Chaturbhuj[b]*

[a]Organic Chemistry Research Laboratory, Department of Chemistry, D. G. Ruparel College, Mumbai- 400016, India

[b]Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Mumbai- 400019, India

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
n-Butyl stannoic acid
Direct amidation
Carboxylic acids
Amines

ABSTRACT

This is the first-time report on the repurposing n-butyl stannoic acid as a catalyst for direct amidation of carboxylic acids with amines. Notably, efficient amidation observed in comparison with all other catalytic methods reported up until now. The protocol has successfully applied to the synthesis of a variety of amides. Moderate reaction parameters, clean amidation with excellent yields of desired amides, ability to tolerate a variety of functional groups, easy product isolation; commercial availability and recyclability of the catalyst are key advantages of the current protocol.

Carboxamide is a valuable functional group in organic chemistry found in a number of biologically active compounds.[1] Amides employed as important building blocks in the preparation of pharmaceuticals, agrochemicals, dyes, pigments, polymers, and photographic products.[2-5] Today, amide synthesis is one of the most important processes in the chemical and pharmaceutical industries.[6] In fact currently, about 30 % of active pharmaceutical ingredients (APIs) *viz.* paracetamol, valsartan, moclobemide, nikethamide, atorvastatin, captopril, diltiazem, lidocaine, and acetazolamide, benzipram (Fig. 1), contains one more amide linkage indicating its significance in process chemistry.

The amide synthesis is a significant transformation for both industrial and academic research. In 2007, The American Chemical Society Green Chemistry Institute of Pharmaceutical Roundtable (ACS GCIPR) has estimated amidation as the challenging goal in organic chemistry for which green, efficient, improved and sustainable alternative methods are required.[7] Amide synthesis was first described in 1833 by German chemists Carl Schotten and Eugen Baumann from acid chloride and amine in known as Schotten-Baumann reaction.[8, 9] Currently, there are various methods for amide synthesis, classical commercially used process involves the use of carboxylic acid chloride as electrophile which reacts with amine[10-13] (Scheme 1). This method suffers from various limitation, significantly additional step required for the preparation of acid chloride and there is a stability issue with several of them.

Moreover, preparation of acid chloride involves uses of hazardous reagents like thionyl chloride, oxalyl chloride, which liberates

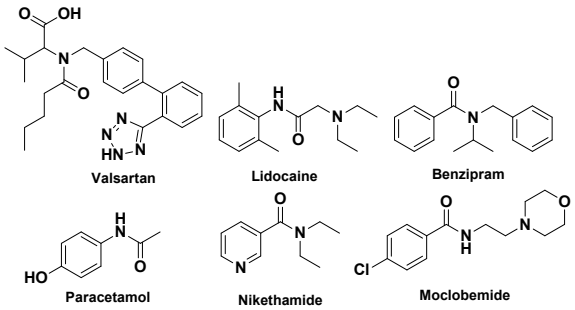
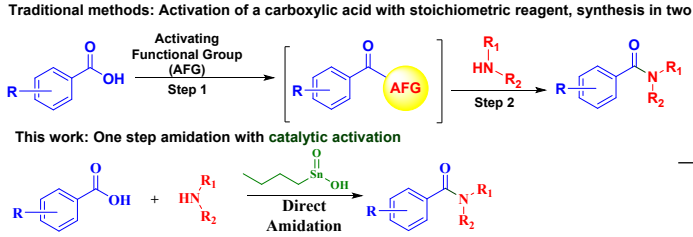


Fig. 1. Amide linkages containing APIs and agrochemicals.

corrosive by-products. Aminolysis of ester requires a strong basic condition., all these conventional methods[14] for the preparation of amides are unsuitable for multitone scale as now-a-days environmental protection is one of major concern in the industry. Hence the development of alternatives for amides preparation direct amidation carboxylic acid is always the desirable method

In 1979 Grieco et al. first reported the direct conversion of a carboxylic acid into amides.[15] Rachel M. Lanigan and Tom D. Sheppard published a review on direct amidation with reaction mechanism.[16] Alternative approaches to activate carboxylic acids towards nucleophilic attack by using various coupling reagents methods have been developed including $B(OCH_2CF_3)_3$[16-18], $B(OMe)_3$,[19, 20] $AlMe_3$,[21] XtalFluor-E,[22] Ph_3PCl_2,[23] nano sulfated TiO_2,[24] DMT-MM, [25] oxalates,[26] but all these reagents are required in stoichiometric or in excess quantity, some of them are air

* Corresponding author. Tel.: +91-22-33612212; fax:+91-22 24145614; e-mail: gu.chaturbhuj@gmail.com



Scheme 1. Comparing present amidation with classical ones.

sensitive difficult to handle. Excess use of coupling reagents on multitone scale generates of waste, compromises on efficiency and economy of the processes.

Up to now, for direct amidation of carboxylic acid and amine, only a few catalytic methods have been developed, using heterogeneous catalysts such as $B(OH)_3$,[27-29] $ZrCp_2Cl_2$,[30] BH_3,[31] and aryl boronic acids as homogeneous catalysts.[34, 35] Use of HATU, HBTU, TBTU, EDCI, and PyBOP are reviewed recently.[32, 33] Some of these catalytic protocols do have synthetic efficiency but still associated with one or more drawbacks, *viz.* commercial unavailability or cost, difficult recovery, and recyclability, long reaction time, unsatisfactory yields. In the case of homogeneous catalysts, a trace amount of the catalyst recovered leading the product contamination.

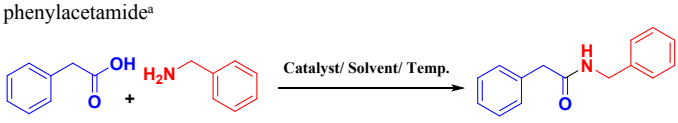
In light of addressing the issue of atom economy and eco-friendliness, our research group has developed few eco-friendly catalysts *viz.* sulfated polyborate,[36] aluminized polyborate,[37] activated Fuller's earth,[38] and applied them for various organic transformations efficiently.[36-55]

There are reports on the use of compounds of group IV metals as a catalyst for direct amidation *viz.* $ZrCl_4$ [65, 66] $Hf(Cp)_2Cl_2$,[67] $Ti(OiPr)_4$,[60, 68] Though, further improvement in catalytic activity and development of efficient, high yielding, rapid, and safe reaction system with the commercially available catalyst in a short reaction period for direct amidation is expected. To achieve these objectives, herein we report the study for direct conversion of a carboxylic acid into amide using group IV organo-metallic catalysts such as *n*-butyl stannoic acid, dibutyltin oxide [56,57] as well as sulfated polyborate under moderate reaction condition.

The condensation reaction of carboxylic acids and amines are highly desirable because they are readily available, and the only side product is water hence the process is clean. Typically, the equilibrium is shifted towards amide formation by removal of water from the reaction mixture azeotropically. The development of a novel protocol with maximum efficiency and minimum waste is currently in demand. This is the first report on the repurposing *n*-butyl stannoic acid for direct amidation of carboxylic acids with amines, which was otherwise used for polymeric ester and transesterification.[61,62] Several industries manufacture this catalyst hence commercially available with CAS No. 2273-43-0.[58] The present protocol shall be extended for the manufacturing of pharmaceutical important molecules or their intermediates containing amide linkages (Scheme 1).

Initially, the study was designed to investigate the suitable catalyst and solvent for one-pot amidation of carboxylic acid and amine. For a selection of suitable catalyst, the effect of *n*-butyl stannoic acid, dibutyltin oxide as well as sulfated polyborate was assessed. Initial studies were performed using an equimolar mixture phenylacetic acid and benzylamine with these catalysts in toluene under Dean-Stark trap (Scheme 1). The effect of these catalysts on the yield of the reaction was ascertained. Among these catalysts *n*-butyl stannoic acid was found to be the best yielding *N*-benzyl-2-phenylacetamide in 82 % yield within 3 hours (Table 1,

Table 1: Selective Catalyst and solvent study for synthesis of *N*-benzyl-2-phenylacetamide[a]



Entry	Solvent	Catalyst	Loading (mol %)	Temp (°C)	Yield [b] (%)
1	Toluene	Bu Sn(=O) OH	5	110	50
2	Toluene	Bu Sn(=O) OH	10	110	82
3	Toluene	Bu Sn(=O)H	10	110	75
4	Toluene	Bu_2 Sn(=O)	10	110	30
5	Toluene	Sulfated Polyborate	10	110	78
6	Xylene	Bu Sn(=O) OH	10	110	84
7	MeCN	Bu Sn(=O) OH	10	80	40
8	Dioxane	Bu Sn(=O) OH	10	100	30
9	DMF	Bu Sn(=O) OH	10	140	NR[c]
10	DMSO	Bu Sn(=O) OH	10	150	NR[c]

[a]Reaction condition: Phenylacetic acid (2.5 gm, 19.68 mmol), benzylamine (2.10 gm 19.68 mmol) and catalyst, 3 h, [b]Isolated yield. [c]No reaction

entry 2). Further, to establish the role of solvents, the reaction also performed in different solvents like xylene, acetonitrile, 1,4-dioxane, DMSO, and DMF. Maximum yield was obtained in toluene comprised of other solvents; it was adopted for further study (Table 1, entries 7-10).

Prior to substrate study, types of amides **2a-c** with varying substrates on both side were selected (Table 2) and experiments were conducted to optimize the catalyst loading and reaction time for maximum conversion with higher isolated yields for desired amides. The study was conducted in toluene and xylene. The experiments were conducted with varying catalyst loading. the progress of reaction monitored and continued until the maximum conversion of starting materials.

To establish the catalyst role, control experiments were performed in absence of a catalyst, resulted in the yield in the range of 8-20 % after 3-15 hours of reflux in toluene. Phenylacetic acid and benzylamine react smoothly within 3 hours with 97 % yield of desired amide **2a** were achieved using 18 mol% of *n*-butyl stannoic acid (Table 2, entry 1). Amidation reaction between a benzoic acid and benzylamine provide 80 % yield of desired amide **2b** with 15 mol% of catalyst loading in 11 hours (Table 2, entry 2). Amidation of aniline with phenylacetic acid afford 75 % desired amide **2c** with 15 mol% of catalyst in 15 hours, as aniline being week base and less reactive (Table 2, entry 3). Therefore, aniline and benzoic acid reaction required more reaction time as compare to benzylamine and phenylacetic acid (Table 2, entries 1-3). The use of slightly higher mol% *n*-butyl stannoic acid could effectively catalyze the amidation of non-activated carboxylic acid with an amine at the reflux temperature of toluene. Xylene showed no major advantage in yield compared to toluene. Depending on the nature of substrates 10 to 18 mol% of catalyst loading and toluene as a solvent were optimized for further study.

Furthermore, it was clearly observed that almost all useful active pharmaceutical ingredients of amide class contain aromatic substituent on one side whereas the aliphatic on another (Fig.1). Hence, the present study was focused on the synthesis of amides with one aliphatic and other aliphatic reactants. With the optimized condition in hand, a number of structurally diverse acids and amines were screened to demonstrate and expand the scope of the present protocol (Table 3, 4 and scheme 2)[70]**.** A variety of

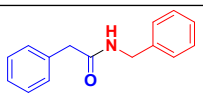
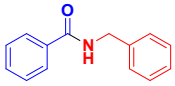
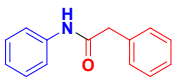
aliphatic, α,β-unsaturated and aromatic carboxylic acids with either electron withdrawing or electron-donating functionalities reacted efficiently with benzylamine and afforded the desired amides in moderate to excellent yields (Table 3, **3a-d)**. Similarly, upon treating heterocyclic and α,β-unsaturated acids with benzylamine, desired amides **3g** and **3h** were isolated in 76 % and 70 % respectively. 2- and 4-methoxyphenylacetic acid reacted smoothly with benzylamine giving **3k and 3l**, 75 and 70 % yield within 3 and 10 hours respectively. An aromatic carboxylic acid having electron-withdrawing substituent provided higher yield as compared to electron donating substituent. However, optimized protocol when applied to 4-chloro-3,5-dinitrobenzoic acid and 2,5-dihydroxybenzoic acid was unable to give products, presumably due to extreme electronic effects. (Table 3, entries 3e and 3j).

The scope of this optimized protocol was further investigated for amine variants. Aromatic amines bearing electron withdrawing as well as electron donating functional groups reacted smoothly with phenylacetic acid, gave amides **4a-i** in 75-85 % isolated yield (Table 4). Interestingly, the chemoselectivity of present protocol for amidation over esterification was observed in the case of 4-aminophenol bearing two functionalities (NH_2 and OH), amidation observed instead of esterification to yield **4c**. Importantly, heterocyclic amines like 2-aminopyridine and 2-aminothiazole also reacted with a phenylacetic acid to obtain amides **4d** and **4e** in 75 % and 76 % yield, respectively. Furthermore, alicyclic 2° amines like morpholine, piperidine, pyrrolidine, and aliphatic *n*-butylamine are also reacted efficiently giving corresponding amides in excellent yields 80, 82, 84, 85 % respectively (Table 4, entries **4f-i**). All reactions proceeded cleanly and no undesired side reactions were observed. The present optimized protocol is also extendable to aliphatic acid and aliphatic amines. Caproic acid reacted equally well with *n*-butylamine (**5a**) and 3-methoxy propylamine (**5b**) to yield corresponding amides in excellent yield (Scheme 2). The reactions were monitored by gas chromatography.

A plausible mechanism for amide synthesis is depicted in Figure 3. As proposed by Chandrasekhar, V. et al.[69] the carboxylic acid might have reacted with *n*-butyl stannoic acid to form anhydride intermediate II *via* an intermediate I. Intermediate II might have attacked by strongly nucleophilic amines to form amides and *n*-butyl stannoic acid recycles.

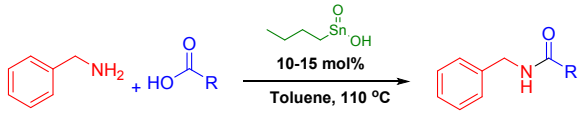
The reusability of the catalyst under an optimized condition in the model reaction was assessed. After completion of each cycle, the catalyst was separated by extraction of the solid with acetone,

Table 2: Optimization of reaction time, catalyst loading for different types of amides with varying reactants.

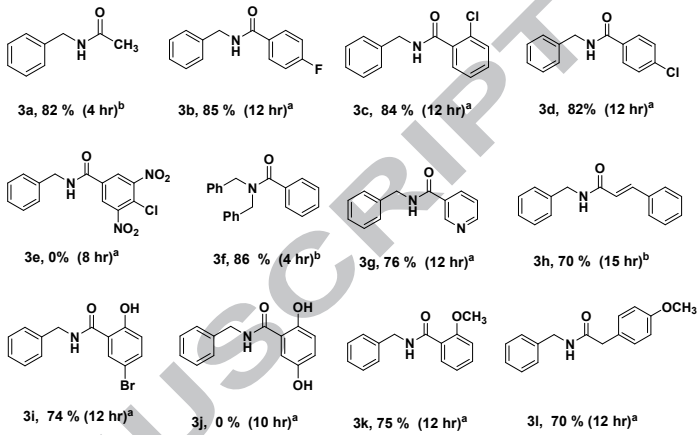
Entry	Solvent	Catalyst (mol %)	Time (h)	Amides	Yield[b] (%)
1	Toluene	0	3		20
		12	3		85
		15	3		90
		18	3		97
				2a	
2	Toluene	0	11		10
		10	11		64
		15	11		80
	Xylene	15	11		84
				2b	
3	Toluene	0	15		8
		10	15		60
		15	15		75
	Xylene	15	15		78
				2c	

[a]Reaction condition: amine (1 equiv.), carboxylic acid (1 equiv.), reflux (110 °C) in toluene with azeotropic removal of water. [b]Isolated average yield (3 batches) .

Table 3: Substrate scope for carboxylic acids for direct amidation with benzylamine [a,70]

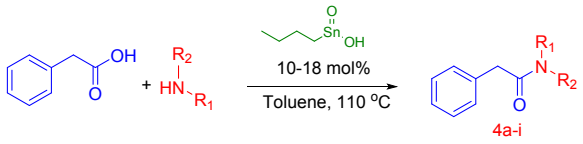


3a-l

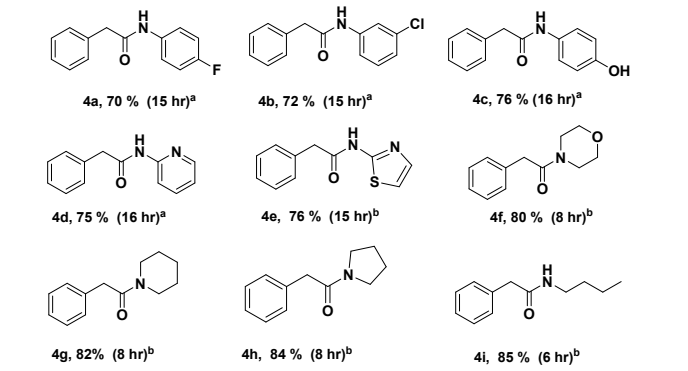


[a]Reaction condition: benzylamine (1 equiv.), carboxylic acid (1 equiv.), Bu Sn(=O)OH [a](15 mol%), [b](10 mol%), reflux in toluene with azeotropic removal of water, Average yields (3 batches) of the isolated products are given.

Table 4: Substrate scope for amines for direct amidation with phenylacetic acid [a, 70]

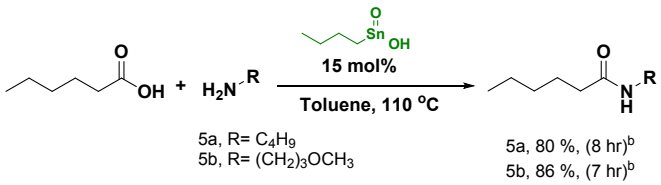


4a-i



[a]Reaction condition: phenylacetic acid (1 equiv.) amine (1 equiv.), Bu Sn(=O)OH (18 mol%)[a], (10 mol%), [b]Reflux in toluene with azeotropic removal of water. Average yields (3 batches) of the isolated products are given

Scheme 2: Substrate scope for aliphatic acid and aliphatic carboxylic direct amidation[a, 70]

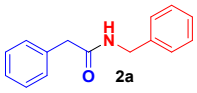


5a, R= C_4H_9
5b, R= $(CH_2)_3OCH_3$

5a, 80 %, (8 hr)b
5b, 86 %, (7 hr)b

[a] Reaction yield and purity by gas chromatography [b]Isolated yield

Table 5: Efficiency of *n*-butyl stannoic acid catalyst in comparison with reported catalysts for synthesis of *N*-benzyl-2-phenylacetamide, **2a**



Sr. No.	Catalyst	Solvent	Time	Yield (%)	Ref.
1.	15 mol %, *n*-Butyl stannoic acid	Toluene	3	90	This work
2.	18 mol %, *n*-Butyl stannoic acid	Toluene	3	97	This work
3.	20 mol % Titanium(IV)isopropoxide, 90 °C	Neat	4	92	60
4.	10 mol%, Zirconium(IV) chloride, 70 °C	THF	6	95	65
5.	100 mg, Fe^{3+}-K 10 Montmorillonite, 70 °C	$CHCl_3$	7	96	59
6.	0.796 mmol, bis(bis(trimethylsilyl)amido) tin(II), reflux	THF	14	82	64
7.	1 equiv., Trimethyl borate, 80 °C	MeCN	15	92	63
8.	2 mol %, $ZrCl_4$, 4Å MS, 100 °C	THF	24	99	66
9.	10 mol %, Ti(O*i*-Pr)$_4$, 4 Å MS, 70 °C	Dry THF	24	91	60

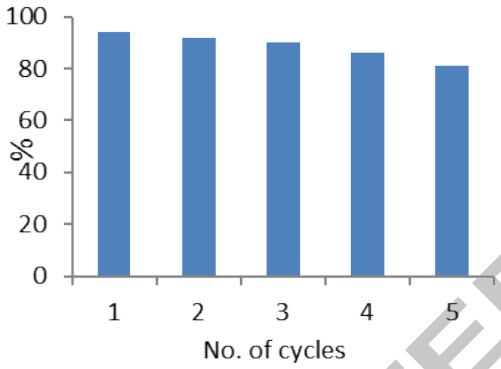


Fig. 2. Reusability of the catalyst.

catalyst remains insoluble in acetone, hence recovered by filtration. Recovered catalyst dried for 1 hour at 55 °C and was reused four times with n significant loss in a catalytic (Fig.2).

The efficiency of *n*-butyl stannoic acid catalyst for synthesis of *N*-benzyl-2-phenylacetamide, **2a** is compared with the catalyst reported in the literature. *n*-butyl stannoic acid at 18% loading was found to be much efficient (Table 5).

In conclusion, a new highly efficient and practical one-step catalytic method for direct amidation of the variety of carboxylic acids and amines is developed. A number of carboxylic acids and amines bearing different substituents were converted into corresponding amides conveniently in excellent to high yields. An important advantage of this protocol is that there is an activation of the carboxylic acid not by stoichiometric reagent but by *n*-butyl stannoic acid. Heterogeneous catalyst, moderate reaction condition, shorter reaction time, higher yields, easy work-up procedure are key features of a present protocol. This protocol can be adapted for the manufacturing of active pharmaceutical ingredients on a preparative scale of course with suitable optimization.

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.dol,org/10.

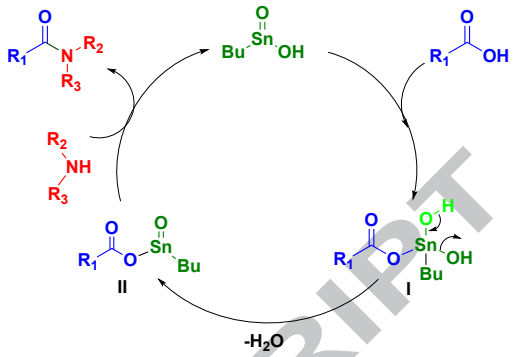


Fig. 3. A plausible mechanism for *n*-Butyl stannoic acid catalyzed amidation

Acknowledgments: Authors are thankful to University of Mumbai, India for their financial support.

References:

1. Kung, P.P.; Huang, B.; Zhang, G.; Zhou, J.Z.; Wang, J.; Digits, J.A.; Skaptason, J.; Yamazaki, S.; Neul, D.; Zientek, M.; Elleraas, J. *J. Med. Chem.*, **2010**, 53, 499-503.
2. Wang, G.W.; Yuan, T.T.; Li, D.D. *Angew. Chem.*, **2011**, 123, 1416-1419.
3. Zhang, X.; Teo, W.T.; Chan, P.W.H., *J. Organomet. Chem.*, **2011**, 69, 331-337.
4. Glomb, M.A.; Pfahler, C. *J Biol. Chem.*, **2001**, 276, 41638-41647.
5. Armelin, E.; Franco, L.; Rodriguez-Galan, A.; Puiggalí, J., *Macromol. Chem. Phys.*, **2002**, 203, 48-58
6. Carey, J.S.; Laffan, D.; Thomason, C.; Williams, M. T. *Org Biomol. Chem*. **2006**, 4, 2337-2347.
7. Montallbetti, C.A.G.N.; Falque, V. *Tetrahedron*, **2005**, 61, 10827-10852.
8. Constable, D.J.; Dunn, P.J.; Hayler, J.D.; Humphrey, G.R.; Leazer, Jr J.L.; Linderman, R.J.; Lorenz, K.; Manley, J.; Pearlman, B.A.; Wells, A.; Zaks A. *Green Chem.* **2007**, 9, 411-420.
9. Schotten, C. *Ber. Dtsch. Chem. Ges.* **1884**,17, 2544-2547.
10. Baumann, E. *Ber. Dtsch. Chem. Ges.***1886**; 19, 3218-3222.
11. Bailey P. D.; Collier I. D. and Morgan K. M., In: Comprehensive Organic Functional Group Transformations, ed. Katritzky A. R.; Meth-Cohn O. and Rees C. W., Pergamon, Cambridge, 1995, vol. 5, ch. 6.
12. Larock, R.C.; *Comprehensive Organic Transformation,* Wiley-VCH, Weinheim, **1999**.
13. Iqbala, N.; Cho, E. *J. Org, Chem*, **2016**, 81, 1905-1911.
14. Liana, C.; Allen, A. A.; Lapkin, J. M.; Williams, J. *Tetrahedron Lett*., **2009**, 50, 4262- 4264.
15. Paul, A.; Grieco, D. S.; Clark, G. P. W. *J. Org. Chem*, **1979**, 44, 2945 – 2947.
16. Lanigan, R.M.; Pavel, S.; Sheppard. T.D. *Eur. J. Org, Chem*, **2013**, 7453 – 7465.
17. Lanigan, R. M.; Karaluka, V.; Sabatini, M. T.; Starkov, P.; Badland, M.; Boulton, L.; and Sheppard, T. D. *Chem. Commun.*, **2016**, 52, 8846-8849.
18. Sabatini, M. T.; Boulton, L. T.; and Sheppard, T. D. *Sci. Adv.*, 2017, 3, e1701028.
19. Lanigan, R.M.; Pavel, S.; Sheppard. T.D. *J. Org, Chem*, **2013**, 78, 4512- 4523.
20. Pelter, A.; Levitt, T.E.; Melson, P. *Tetrahedron*, **1970**, 26, 1536-1544.
21. Chung, S.; Uccello, D. P.; Choi, H.; Montgomery, J. I.; Chen, J. *Synlett*, **2011**, 14, 2072-2074.
22. Orliac, A.; Pardo, D. B.; Bombrim, A.; Cossy, J. *Org. Lett.*, **2013**, 15, 902-905.
23. Azumaya, T. O.; Imabeppu, F.; Takayanagi, H. *Tetrahedron*, **2003**, 59, 2325-2331.

24. Hosseini, S. M.; Sodagar, E.; Doroodmand, M. M. *J. Org. Chem.*, **2011**, 76, 2853-2859.
25. Munetaka, K.; Chiho, K.; Kazuhito, H.; Keiji, T.; Shohei T. *Tetrahedron*, **2001**, 57, 1551-1558.
26. Takeda, K.; Sawada I.; Suzuki, A.; Ogura, H. *Tetrahedron Lett.,* **1983,** 24, 4451-4454.
27. Tang P. *Org. Synth.*, **2005**, 81, 262-272.
28. Mylavarapu, R. K.; Kondaiah G.C.M.; Kolla, N.; Bhattacharyan A.; Bandichhor R. *Org. Process Res. Dev.*, **2007**, 11, 1065-1068.
29. Yun, F.; Chunhui, C. *Synthesis,* **2017**, 49, 1583-1596.
30. Allen, C. L.; Chhatwal A. R.; Williams J. M. J. *Chem. Commun.* **2012**, 48, 666-668.
31. Huang, Z.; Reilly, J. R.; Buckle, R. N., *Synlett*, **2007**, 1026-1030.
32. Han, S. Y.; Kim, Y. A. *Tetrahedron*, **2004**, 60; 2447-2467.
33. Valeur, E.; and Bradley, M. *Chem. Soc. Rev.*, **2009**, 38, 606-631.
34. Gernigon N.; Al-zoubi R. M.; Hall D. G., *J. Org. Chem.*, **2012,** 77. 8386-8400.
35. El Dine, T. M.; W. Erb, Berhault Y.; Rouden J.; Blanchet J. *J. Org. Chem.*, **2015**, 80, 4532-4544.
36. Khatri, C.K.; Rekunge, D.S.; Chaturbhuj, G.U. *New J. Chem*. **2016,** 40, 10412-10417.
37. Mali, A. S.; Potnis, C. S.; Chaturbhuj, G. U. *J. Iran. Chem. Soc*., **2018**, 15, 1399-1409.
38. Rekunge, D.S.; Indalkar, K.S.; Chaturbhuj, G.U. *Tetrahedron Lett*., **2016**, 57, 5815-5819.
39. Indalkar, K.S.; Khatri, C.K.; Chaturbhuj, G.U. *J. Chem. Sci*., **2017**, 129, 141-148.
40. Indalkar, K.S.; Khatri, C.K.; Chaturbhuj, G.U. *J. Chem. Sci*., **2017**, 129, 415-420.
41. Indalkar, K.S.; Khatri, C.K.; Chaturbhuj, G.U. *Tetrahedron Lett*. **2017**, 58, 2144-2148.
42. Khatri, C.K.; Mali, A.S.; Chaturbhuj, G.U. *Monatsh. Chem*., **2017**, 148, 1463-1468.
43. Khatri, C.K.; Patil, M.S.; Chaturbhuj, G.U. *J. Iran. Chem. Soc*., **2017**, 8, 1683-1689.
44. Khatri, C.K.; Potadar, S.M.; Chaturbhuj, G.U. *Tetrahedron Lett*., **2017**, 58, 1778-1780.
45. Khatri C.K.; Satalkar, V.B.; Chaturbhuj, G.U. *Tetrahedron Lett*., **2017**, 58, 694-698.
46. Patil, M.S.; Palav, A.V.; Khatri, C.K.; Chaturbhuj, G. U. *Tetrahedron Lett*., **2017**, 58, 2859-2864.
47. Rekunge, D. S.; Khatri, C.K.; Chaturbhuj, G.U. *Tetrahedron Lett*., **2017**, 58, 1240-1244.
48. Khatri, C.K.; Chaturbhuj, G.U. *J. Iran. Chem. Soc*., **2017**, 14, 2513-2519.
49. Rekunge, D.S.; Khatri, C.K.; Chaturbhuj, G.U. *Monatsh. Chem*., **2017**, 148, 2091-2295.
50. Rekunge, D.S.; Khatri, C.K.; Chaturbhuj, G.U. *Tetrahedron Lett*., **2017**, 58, 4304-4307.
51. Patil, M.S.; Mudaliar, C., Chaturbhuj, G.U., *Tetrahedron Lett*., **2017**, 58, 3256–3261.
52. Indalkar, K.S., Patil, M.S., Chaturbhuj, G.U. *Tetrahedron Lett*., **2017**, 58, 4496-4502.
53. Jejurkar, V.P.; Khatri, C.K.; Chaturbhuj, G.U. Saha S., *ChemistrySelect***, 2017,** 35, 11693–11696.
54. Patil, M.S.; Khatri, C.K.; Chaturbhuj, G.U. *Monatsh. Chem*. **2018**, 149, 1463-1457.
55. Rekunge, D.S., Kale, I.A., Chaturbhuj, G.U. 2018. *J. Iran. Chem. Soc.*, **2018**, 15, 2455-2462.
56. Meneghetti, M. R.; Meneghetti, S.M.P. *Catal. Sci. Tech.*, **2015,** 5, 765-771.
57. Brito, Y. C.; Ferreira D. A.; Danielle M. D. A.; Mendes P. R.; Oliveira C. M.; De, Meneghetti M. R.; Meneghetti S. M. *Appl. Catal. A: Gen.*, **2012**, 443, 202-206.
58. Sigma Aldrich catalog no. 8.40126 EMD MILLIPORE
59. Srinivas, K.V.N.S.; Das, B. *J. Org. Chem.,* **2003**, 68, 1165-1167.
60. Maria, A.; Svetlana, E.; Gerhard, M. *RSC Adv*., **2014**, 4, 56506-56517.
61. Technical information: bulletin 345 revision 3/91, bulletin 346, revision 7/92 and bulletin 362 revision 10/93, Elf Atochem North America, Inc.
62. Technical information: bulletin LIOCAT 118 revision 08/99, Miracema-Nuodex Ind. Qu´ımica Ltda.
63. Starkov, P.; Sheppard, T. D. *Org. Biomol. Chem*. **2011**, 9, 1320-1323.
64. Burnell-Curty, C.; Roskamp, E. J.; *Tetrahedron Lett.* **1993**, 34, 5193-5196.
65. Lundberg, H.; Tinnis, F.; Zhang, J.; Algarra, A. G.; Himo, F.; Adolfsson, H. *J. Amer. Chem. Soc*. **2017**, 139, 2286-2295.
66. Lundberg, H., Tinnis, F., and Adolfsson, H. *Chem, Eur. J.*, **2012,** *18*, 3822-3826.
67. Lundberg, H., and Adolfsson, H. *ACS Catal.*, **2015**., 5, 3271-3277.
68. Lundberg, H., Tinnis, F., and Adolfsson, H. *Synlett,* **2012**, 23, 2201-2204.
69. Chandrasekhar, V.; Nagendran, S.; Bansal, S.; Cordes, A. W.; and Vij, A. *Organometallics*, **2002**, 21, 3297-3300.
70. ***General procedure for the synthesis of Amides:*** To a 250 mL three-necked reaction flask equipped with an agitator, Dean-Stark trap with a reflux condenser, temperature sensor, added 50 mL toluene, phenylacetic acid (2.5 g, 19.68 mmol), benzylamine (1.96 g, 19.68 mmol) and catalyst (0.82 g, 18 mol%). The mixture was stirred under gentle reflux at 110 °C in an oil bath. Water collected in the Dean-Stark trap, and the progress of the reaction was monitored by TLC. After consumption of starting materials, the reaction mixture was concentrated under reduced pressure to recovered 40 mL of toluene. The mixture was cooled to 20-25 ˚C to this added 100 mL hexane and stirred for 2 h. The precipitated solid was filtered. Solid containing product and the catalyst washed with 25 mL $NaHCO_3$ (5%) solution, 25 mL of water and dried in an oven at 60 ˚C for 3 h. Dried solid extracted with acetone or methanol and filtered to separate the catalyst and filtrate containing amide was concentrated under reduced pressure to afford target amide, **2a** as white solid, 4.01 gm, yield 97 %.

    Similarly, the scalability of the reaction was assessed, phenylacetic acid 25 gm (183 mmol) with benzylamine 19.68 gm (183 mmol) and 18 mol % of *n*-butyl stannoic acid (6.9g, 33 mmol) in 500 mL toluene after 3 h, maximum conversion of amide was observed, and the product was isolated by the procedure mentioned above to give 40.5 gm, yield 98 %.

Highlights

- *N*-Butyl stannoic acid is economic and commercially available.
- This is the first report on repurposing *n*-Butyl stannoic acid for direct amidation.
- Heterogeneous, recyclable and reusable catalyst.
- Activation of the carboxylic acids via anhydride of *n*-Butyl stannoic acid.
- Good to excellent yields of the amides.