A sustainable approach to amide bond formation via C-O bond cleavage of simple esters in water

Nanthini Rajendran[‡,a] Kiruthigadevi Kamaraj[‡,a] Saranya Janakiraman,[a] Mary Saral,[a] Pierre H. Dixneuf, [b] and Charles Beromeo Bheeter[*a]

a. Department of chemistry, School of advanced science, Vellore institute of technology, vellore-632014, Tamilnadu, India.
E-mail: charlesbheeter@vit.ac.in

b. Pierre Dixneuf, (Institut sciences chimiques de Rennes)
University or Rennes: Rennes, Bretagne, France.
E-mail: pierre.dixneuf@univ-rennes1.fr

A simple and efficient method has been developed for the formation of amides by coupling of simple esters and amine in the presence of greener solvent. Amidation is a prevalent reaction from carboxylic acids, by the use of activating reagents, can be transformed into reactive acylating intermediates such as acyl chlorides, anhydrides, activated esters which directly react in situ with the suitable amines without their initial isolation and purification. Since, Amides are biologically pivotal and among the more important transformations in the design of the synthetic plan. In this context, herein, we developed a simple and efficient synthetic approach for the direct amidation through esters, simply in water, affording the desired products in moderate to excellent yields. Interestingly, this method features metal-free, additive-free and base-free characteristics, and it also used water as a green solvent. Therefore, it is a new and eco-friendly way to realize the direct amide bond formation. Applying this methodology, a development of catalyst free reaction that couples (hetero) aromatic/aliphatic esters with a broad scope to form (hetero) aromatic/aliphatic amide products, which including the drug molecule Diethyltoluamide in good yield. Finally, this approach was successfully applied to the gram-scale synthesis of a representative amide product.

The amide bond formation is an important step in pharmaceutical industries, synthetic polymers, and material products as amide bonds are the most essential constituent in peptide derivatives, natural products and drug designing.[1] The exploitation of carboxylic acid esters as electrophiles in cross-coupling reactions is increasingly popular, as environmentally friendly and readily available ester derivatives can

be powerful alternatives to the commonly used organo halides, acid chlorides, alkenes etc. Cracking of petroleum products oils, fatty acids, triesters of glycerol, fruits are the sources of esters and thus the methods of conversion of esters into amides becomes significant.[2]

Traditionally, most of the pharmaceutical industries follow acid-amine coupling method with over stoichiometric amount of coupling reagents and bases for amide bond formation.[3]

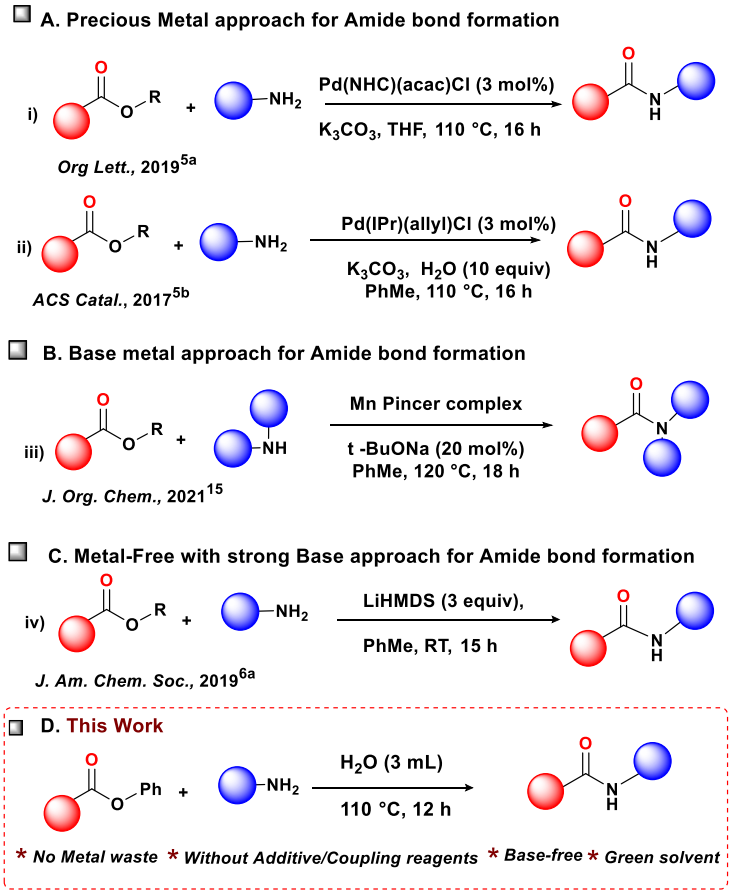
Also, in the earlier methods of catalytic synthesis of amides the use of CO gas by amino carbonylation methodology was successfully carried out by Wu and Beller et. al.[4] Another well-known approach in amide bond formation is the C(acyl)-O bond cleavage of esters through catalytic pathway, but using metal catalysts,[5] (Figure1, Part A) strong base[6] (Figure 1, Part C), with various additives,[5g, 7] and often non-greener solvents.[8] Sometimes also suitable substituents are required[5g, 7e, 9]for effective conversion.

When the cleavage of esters yields carbonylative and decarbonylative[10] products, intermittently, the selectivity was controlled by the nature of the ligands.[5b, 11] For instance catalyst Ni(IPr)-NHC with N-heterocyclic carbene ligand made carbonylative product[12] while $[Ni(dcype)]^-$ with bis-phosphine ligand composed decarbonylative product.[10e, 13] Other non-noble metals also cleaved the esters of C(acyl)-O bond with hybrid ligands such as NHC and nitrogen donors in Mn(pincer)[14] (Figure 1, Part B) and with La(OTf)3 lewis acid catalyst.[15] Moreover the C(acyl)-N bond cleavage of tertiary amides[5a, 8b, 16] is comparatively easier than with secondary amides.[8a, 17] Direct amide formation from aromatic amine and Unactivated esters are seldom utilized due to the need to deprotonate the amine with an aggressive Organometallic reagents such as BuLi, AlMe3, Al(O-tBu) along with Ni(cod)[5g] were found to require for amidation. Likely Aromatic amines such as Aniline are deprotonated readily by strong base like LiHMDS,[6a] NaH[18]. Besides, amidation through highly activated esters and aromatic amine where successfully achieved through K_2CO_3[19] has been established. Also deprotonating the non-nucleophilic amines with transition metals and complexes such as Pd-NHC[5a, 5b, 20], Ni-NHC,[5h, 12] Pd-Phosphine ligands, Mn pincer complex[14] and heterobimetallic lanthanide sodium alkaloids[21] were utilized.

As far as reported the way to deprotonate the aromatic amines no simple way has been found. Various amines were deprotonated and activated the non-nucleophilic amines part through transition metals, ligands, Strong bases, flammable organometallic reagents are desired. Hence there is a necessity for an environmentally friendly methodology for the industrial synthesis of amides in large quantities. Herein, To the best of our knowledge, we are reporting a coupling of unactived ester with non-nucleophilic amines which undergoes, only with green solvent such as water at 110 °C in oil bath. Overall the conversion of simple esters into amides under metal and base-free conditions using the green solvent water only and

avoiding the use/emission of CO, which is an atom economic method leading to environmentally friendly preparation of amides with reduced cost is the advantageous progress of our work.

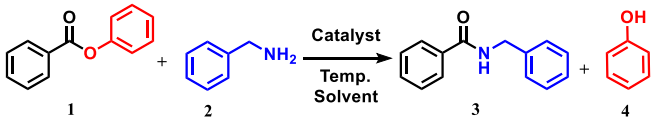
Fig. 1 Different approaches towards C(acyl)-O bond cleavage of esters to amides



Results and Discussion:

At the outset, we have outlined the model scheme for amidation of esters using phenyl benzoate (1) and benzylamine (2) as the ester and amine source respectively (Scheme 1). Initially, we anticipated that the use of heterogeneous catalyst[22] would bring more advantageous compared to homogenous catalysts. In this regard, the catalyst can be recycled and reused several times. In this context, the reaction was performed in the presence of recyclable silica materials with and without metal catalyst, namely, Fe-KIT-6, KIT-6 (mesoporous silica nanoparticles10 – 100 µm), SBA-15, (mesoporous silica nanoparticles<150 µm), and mesoporous silica 200-400mesh (25 mg) with water 3 ml at 110 °C furnished amidation product (3) in 82%, 78%, 60%, 80% respectively (Table 1, Entry 1-4).

Table 1 Reaction Optimization



Entry.	Catalyst	Solvent	Yield (%)
1 [a]	Fe KIT-6	Water	82
2 [a]	KIT-6	Water	78
3 [a]	SBA-15	Water	60
4 [a]	Silica	Water	80
5[b]	Catalyst-free	THF	80
6[b]	Catalyst-free	CH_3CN	78
7[b]	**Catalyst-free**	**Water**	**95**
8[b]	Catalyst-free	Ethanol	45
9[b]	Catalyst-free	Methanol	32

[a)]conditions: Phenyl benzoate 0.2525 mmol, benzylamine 0.5050 mmol, catalyst 25 mg, solvent 3 mL, 110 °C in oil bath, 12 h, Isolated yields. [b)]No catalyst, solvent 3 mL, 110 °C, 12 h, isolated yields.

To examine the importance of solvents we have randomly chosen four solvents among which the polar aprotic solvents like tetrahydrofuran and acetonitrile ended-up with good yield 80% and 78% (Table 1, entry 5 and 6). The polar protic ethanol and methanol showed low yields of 45% and 32% respectively (Table 1, entry 8 and 9). But to our delight the reaction produced good yield with the only use of water. Surprisingly, water afforded the amidation product with high yield of 95% after 12 h (Table 1, entry 7). Exploration of different solvents revealed that the universal solvent-water was optimal. During this investigation, we screened optimal time with a set of reactions on simple ester and benzylamine as a model substrate under different durations (Figure 2). In the row of 3 h, product (3) yield raised, then after 12 h remains constant. Hence, we fixed 12 h as a constant time for every reaction. The effect of temperature was also examined, in the oil bath at 110 °C led the reaction to be completed within 12 h with 95% yield (Table 1). Hence, the optimal condition to achieve maximum yield in the reaction between phenyl benzoate (1) at 110 °C and benzylamine (2) with 3 mL water in an oil bath for a duration of 12 h.

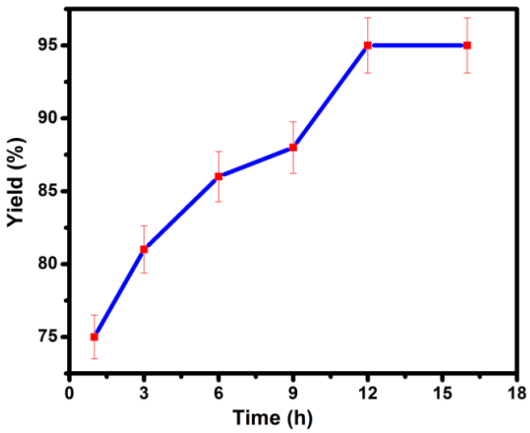
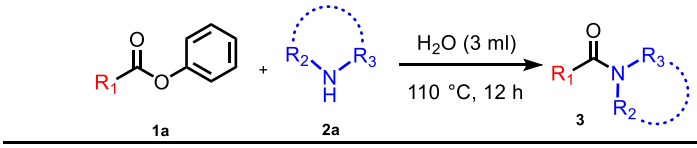
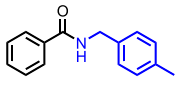


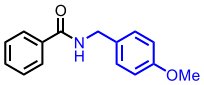
Fig. 2 Time Optimization

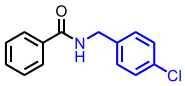
Under these optimal conditions, we turned our attention to the scope of esters and amines that can participate in this reaction (Scheme 1). Benzyl amine bearing electron donating groups gives 76% yield (Scheme 1, 3a) on the other hand, electron withdrawing groups in their para position gives 89%,84% yields (Scheme 1, 3b & 3c). On varying the aryl esters with electron withdrawing and donating groups, the corresponding amide yield was not affected (Scheme 1, 3d to 3g). Mostly, in benzyl amine derivative substitutents in para position resulted in high yield when compared to ortho or meta position (Scheme 1, 3b to 3g). Later we introduced halogenated derivatives in amines in ortho and para positions which were converted effectively into amides with 39% to 96% yield (Scheme 1, 3h to 3l). Surprisingly we obtained moderate yields when methoxy groups were introduced in amines with 49% to 57% of yield (Scheme 1, 3m to 3p). In the case of electron withdrawing substituents in both aryl groups we obtained very good yield of 73% of product (Scheme 1, 3q). On adding *p*-bromo phenyl benzoate with benzyl amine gives 94% (Scheme 1, 3r) and with morpholine gives 89% (3s) of yield. Since aliphatic esters coupled well, we introduced bulky aliphatic ester phenyl 2,2 diphenyl acetate with benzylamine gives 48% (3t) No reaction was observed between aryl ester (1) with n-Boc piperazine (Scheme 1 3w). Surprisingly, Water plays a similar role in amidation of various esters with cyclic secondary amines which resulted in excellent yield of corresponding amides. Several substituted esters underwent the aminolysis with Pyrrolidine, Piperidine, Morpholine, to the corresponding amides with good to excellent yields (Scheme 1, 3y in 78%, 3z in 91%, 3aa in 94%, 3ab in 48%, 3ac in 59%, and 3ad in 98% isolated yield).

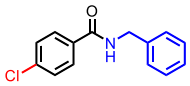
Scheme 1 Substrate scope for amidation of ester

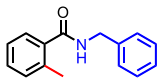


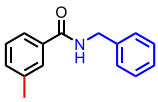

3a 76%

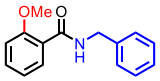

3b 89%

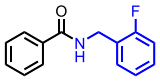

3c 84%

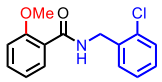

3d 94%

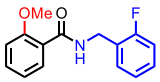

3e 94%

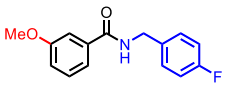

3f 96%

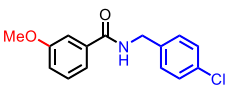

3g 73%

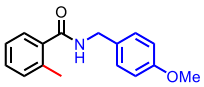

3h 39%

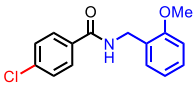

3i 79%

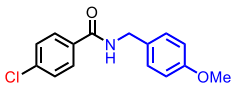

3j 96%

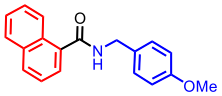

3k 77%

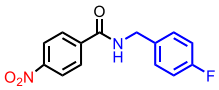

3l 72%

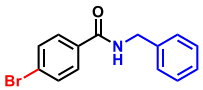

3m 55%

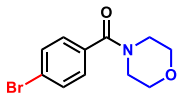

3n 49%

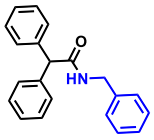

3o 55%


3p 57%

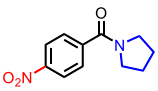

3q 73%

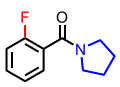

[b] 3r 94%

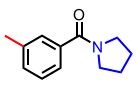

[b] **3s 89%**

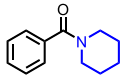

[b] 3t 48%

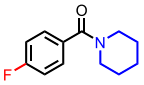

3w No reaction

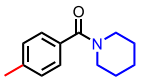

3y 78%

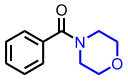

3z 91%

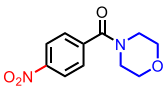

3aa 94%

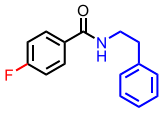

3ab 48%

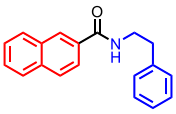

3ac 59%

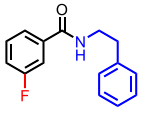

3ad 98%

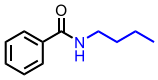

3ae 48%

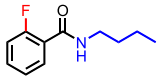

3af 27%

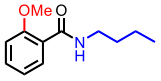

3ag 63%

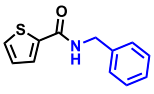

3ah 63%

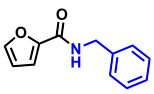

3ai 80%

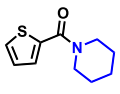

3aj 38%

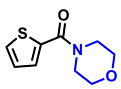

3ak 85%


3al 95%


[a] 3am 87%


[a] 3an 88%


[b] 3ao 44%


[b] 3ap 56%

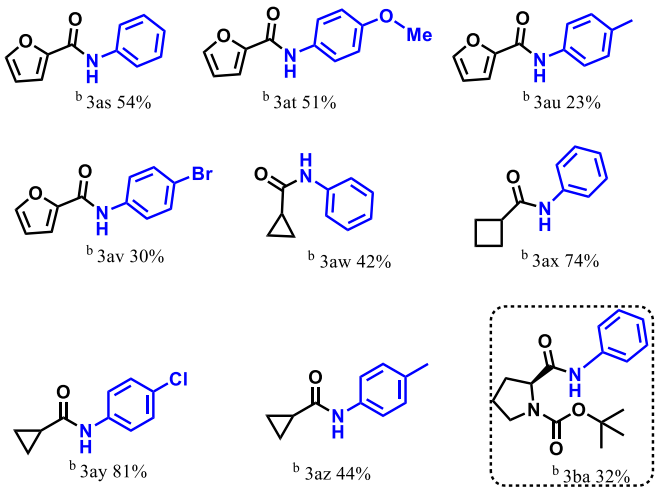
[b] 3aq 96%

[b] 3ar TRACE

Conditions: Ester (1 eqv.), amine (2 eqv.), solvent 3 mL, 110 °C, 12 h.

Notably, the morpholine and phenethylamine showed moderate reactivity with various esters (Scheme 1, 3ae) in 48%, (3af) in 27%. Particularly, when the alkyl chain of the amine was lengthened, the activated ester was converted smoothly into the corresponding amides with good yield (3ag, 3ah) of 63% & (3ai) of 80% yield. Interestingly, we achieved positive result with primary amine namely n-butylamine (3aj) in 38%, (3ak) in 85% & (3al) in 95%. Given the plausible implications of this discovered reaction process to this project, a small range of heterocyclic ring system were smoothly introduced in the reaction system with moderate to excellent yields obtained when benzylamine introduced with phenyl thiophene-2-carboxylate (3am, 87%), phenyl furan-2-carboxylate (3an,88%). To evaluate the scope of aromatic amines with a diverse range of ester were explored, Scheme (1). Meanwhile phenyl thiophene-2-carboxylate coupled with Piperidine gives (3ao) 44% and with morpholine gives (3ap) 56%. And introducing phenyl cyclopropane carboxylate with benzylamine which yields 96% (3aq) and phenyl cyclobutane carboxylate with morpholine gives only a trace (3ar).

Scheme 2 Substrate scope for amidation via aromatic amines

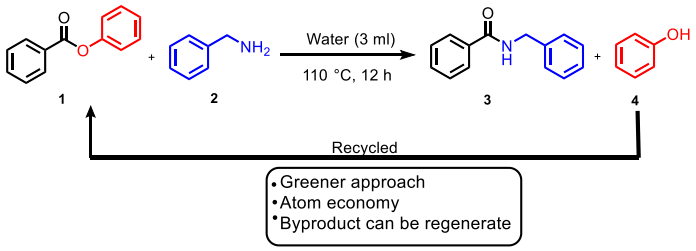


Conditions: [a] Ester (1 eqv.), amine (1.2 eqv.) , solvent 3 mL, 110 °C, 12 h.[b] amine (2 eqv.).

To imply the simplicity of the work we have improved the amine substrates to aromatic system with heteroaromatic esters and aliphatic esters. Surprisingly heteroaromatic esters Phenyl furan-2-carboxylate coupled successfully with aniline and gives (3as)54% yield, followed by substituted p-anisidine gives (3at)51% yield, p-toluidine gives (3au)23%, modestly with p-bromo aniline (3av)30% yield. As well, a selection of aliphatic esters phenyl cyclopropane carboxylate with aniline gives (3aw) 42%, and with p-

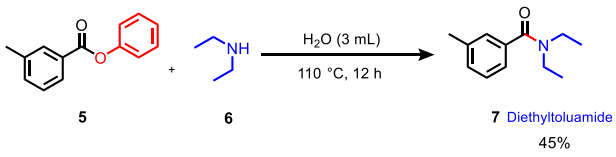
chloroaniline gives 3ay (81%),also with p-methyl aniline gives 3az (not yet calculated), and in-between phenyl cyclobutane carboxylate reacts with aniline were coupled with moderate yield of 74% (3qx).Also this reaction was also effective in the context of the direct synthesis of biologically relevant compounds like tert-butyl (S)-2-(phenyl carbamoyl)pyrrolidine-1-carboxylate (3ba) 32% which is prepared from n-boc L-proline an amino acid that is used as a drug in the treatment of hepatitis C virus (HCV).

Scheme 3 Identification of side product reaction



In order to prove the environment friendly of the proposed methodology the corresponding side product phenol (4) was recovered pure to give 60-70% yield which could be used further in the preparation of ester derivatives (Scheme 3). The amount of phenol presence in the bulk reaction has been detected by HPTLC instrumentation. (SI) Significantly we prepared the drug, Diethyltoluamide which is an insect repellent[23] by following the proposed optimized protocol (Scheme 4). Aminolysis of meta-methyl phenyl benzoate (5) with diethylamine (6) was carried out to give amide (7) with moderate yield of 45%.

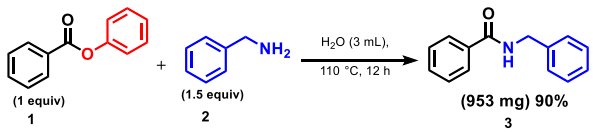
Scheme 4 Synthesis of Diethyltoluamide



Gram Scale:

Finally, we assessed the gram scale procedure (scheme 5) with a mixture of Phenyl benzoate (1), 1 g (1 equiv.), Benzylamine (2), 810 mg (1.5 equiv.) which was stirred in the presence of H2O at 110 °C for 12 h to afford the formation of 953 mg of benzyl benzamide (3) with 90% yield.

Scheme 5 Gram scale synthesis



Conclusion

In past few years a breakthrough study of amide formation through aromatic amines were envisioned. But we have succeeded in finding a metal-free, base /additive- free amidation protocol under aqueous conditions. This report explores the importance of water as an Eco-friendly benign solvent. Based on the substrate scope and gram scale experiment, combination of aromatic esters derivatives of phenol and aliphatic amines showed good activity under the standard protocol. To the best of knowledge this is the first report on ester Acyl(C-O) bond cleavage to amide with catalyst-free, base-free and additive- free and green solvent such as water. Those substantial progress has been made via costly metal catalysts, bases, additives.

Acknowledgement

We acknowledge Dr. Ganesh Babu for fruitful discussions. NR and KK acknowledge VIT for providing a fellowship. Authors acknowledge seed grant for financial support and VIT for infrastructure and instrumentation facilities.

Author Contributions

NR: methodology, writing, editing. KK: methodology, writing. SJ: methodology. MS: editing. PHD: co-supervision, editing, review & supervision. CBB: conceptualization, editing, supervision, project administration.

References

[1] a)M. T. Sabatini, L. T. Boulton, H. F. Sneddon, T. D. Sheppard, *Nat. Catal.* **2019**, *2*, 10-17; b)C. L. Allen, J. M. J. Williams, *Chem. Soc. Rev.* **2011**, *40*, 3405-3415; c)E. Valeur, M. Bradley, *Chem. Soc. Rev.* **2009**, *38*, 606-631; d)G. A. Filonenko, R. van Putten, E. J. M. Hensen, E. A. Pidko, *Chem. Soc. Rev.* **2018**, *47*, 1459-1483; e)D. G. Brown, J. Boström, *J. Med. Chem.* **2016**, *59*, 4443-4458.

[2] a)R. Takise, K. Muto, J. Yamaguchi, *Chem. Soc. Rev.* **2017**, *46*, 5864-5888; b)M. Ishikawa, Y. Warita, E. Takahisa, Y. Ohkubo, in *Comprehensive Natural Products II* (Eds.: H.-W. Liu, L. Mander), Elsevier, Oxford, **2010**, pp. 595-629; c)A. J. Meléndez-Martínez, P. Mapelli-Brahm, D. Hornero-Méndez, I. M. Vicario, in *Carotenoid Esters in*

Foods: Physical, Chemical and Biological Properties, The Royal Society of Chemistry, **2019**, pp. 1-50.

[3] a)N. G. Anderson, in *Practical Process Research and Development (Second Edition)* (Ed.: N. G. Anderson), Academic Press, Oxford, **2012**, pp. 89-120; b)R. M. de Figueiredo, J.-S. Suppo, J.-M. Campagne, *Chem. Rev.* **2016**, *116*, 12029-12122; c)F. Albericio, A. El-Faham, *Org. Process Res. Dev.* **2018**, *22*, 760-772.

[4] L. Wu, X. Fang, Q. Liu, R. Jackstell, M. Beller, X.-F. Wu, *ACS Catal.* **2014**, *4*, 2977-2989.

[5] a)T. Zhou, G. Li, S. P. Nolan, M. Szostak, *Org. Lett.* **2019**, *21*, 3304-3309; b)T. Ben Halima, J. K. Vandavasi, M. Shkoor, S. G. Newman, *ACS Catal.* **2017**, *7*, 2176-2180; c)A. Mondal, M. Subaramanian, A. Nandakumar, E. Balaraman, *Org.Lett.* **2018**, *20*, 3381-3384; d)M. B. Kurosawa, R. Isshiki, K. Muto, J. Yamaguchi, *J. Am. Chem. Soc.* **2020**, *142*, 7386-7392; e)A. H. Dardir, P. R. Melvin, R. M. Davis, N. Hazari, M. Mohadjer Beromi, *J. Org. Chem.* **2018**, *83*, 469-477; f)K. Kim, S. H. Hong, *J. Org. Chem.* **2015**, *80*, 4152-4156; g)L. Hie, N. F. Fine Nathel, X. Hong, Y.-F. Yang, K. N. Houk, N. K. Garg, *Angew. Chem., Int. Ed.* **2016**, *55*, 2810-2814; h)Y.-L. Zheng, S. Newman, *ACS Catal.* **2019**, *9*, 4426-4433; i)W. B. Wang, E. J. Roskamp, *J. Org. Chem.* **1992**, *57*, 6101-6103.

[6] a)G. Li, C.-L. Ji, X. Hong, M. Szostak, *J. Am. Chem. Soc.* **2019**, *141*, 11161-11172; b)L. H.-G. Kim BoRam, Kang Seung-Beom, Sung GiHyeon, Kim Jeum-Jong, Park JongKeun, Lee Sang-Gyeong, Yoon Yong-Jin, *Synthesis* **2012**, *44*, 42-50; c)R. Zhang, W.-Z. Yao, L. Qian, W. Sang, Y. Yuan, M.-C. Du, H. Cheng, C. Chen, X. Qin, *Green Chem.* **2021**, *23*, 3972-3982; d)W. I. Nicholson, F. Barreteau, J. A. Leitch, R. Payne, I. Priestley, E. Godineau, C. Battilocchio, D. L. Browne, *Angew. Chem. Int. Ed.* **2021**, *60*, 21868-21874; e)T. Ohshima, Y. Hayashi, K. Agura, Y. Fujii, A. Yoshiyama, K. Mashima, *Chem. Commun.* **2012**, *48*, 5434-5436.

[7] a)G. Li, M. Szostak, *Synthesis* **2020**, *52*, 2579-2599; b)N. Caldwell, C. Jamieson, I. Simpson, A. J. B. Watson, *Chem. Commun.* **2015**, *51*, 9495-9498; c)A. Ramirez, B. Mudryk, L. Rossano, S. Tummala, *J. Org. Chem.* **2012**, *77*, 775-779; d)C. G. McPherson, N. Caldwell, C. Jamieson, I. Simpson, A. J. B. Watson, *Org. Biomol. Chem* **2017**, *15*, 3507-3518; e)G. Li, M. Szostak, *Nat. Commun.* **2018**, *9*, 4165; f)D. A. Rankic, C. M. Stiff, C. W. am Ende, J. M. Humphrey, *J. Org. Chem.* **2017**, *82*, 12791-12797; g)K. E. Price, C. Larrivée-Aboussafy, B. M. Lillie, R. W. McLaughlin, J. Mustakis, K. W. Hettenbach, J. M. Hawkins, R. Vaidyanathan, *Org. Lett.* **2009**, *11*, 2003-2006.

[8] a)Y. Liu, S. Shi, M. Achtenhagen, R. Liu, M. Szostak, *Org Lett.* **2017**, *19*, 1614-1617; b)M. M. Rahman, G. Li, M. Szostak, *J. Org. Chem.* **2019**, *84*, 12091-12100; c)P. V. Ramachandran, H. J. Hamann, S. Choudhary, *Org. Lett.* **2020**, *22*, 8593-8597.

[9] a)L. Ling, C. Chen, M. Luo, X. Zeng, *Org. Lett.* **2019**, *21*, 1912-1916; b)C. W. Cheung, N. Shen, S.-P. Wang, A. Ullah, X. Hu, J.-A. Ma, *Org. Chem. Front.* **2019**, *6*, 756-761; c)L.-Y. Chen, M.-F. Wu, *Synthesis* **2019**, *51*, 1595-1602; d)T. Ooi, E. Tayama, M. Yamada, K. J. S. Maruoka, *Synlett* **1999**, *6*, 729-730; e)J. L. Vrijdag, F. Delgado, N. Alonso, W. M. De Borggraeve, N. Pérez-Macias, J. Alcázar, *Chem. Commun.* **2014**, *50*, 15094-15097; f)X. Yang, V. B. Birman, *Org. Lett.* **2009**, *11*, 1499-1502; g)Y. Dongqiang, X. Jiaxi, *Curr. Microw. Chem.* **2020**, *7*, 74-82.

[10] a)K. Amaike, K. Muto, J. Yamaguchi, K. Itami, *J. Am. Chem. Soc.*, **2012**, *134*, 13573-13576; b)K. Muto, J. Yamaguchi, D. G. Musaev, K. Itami, *Nat. Commun.* **2015**, *6*, 7508;

c)A. Chatupheeraphat, H.-H. Liao, W. Srimontree, L. Guo, Y. Minenkov, A. Poater, L. Cavallo, M. Rueping, *J. Am. Chem. Soc.* **2018**, *140*, 3724-3735; d)T. B. Boit, A. S. Bulger, J. E. Dander, N. K. Garg, *ACS Catal.* **2020**, *10*, 12109-12126; e)L. Guo, M. Rueping, *Acc. Chem. Res.* **2018**, *51*, 1185-1195.

[11] B. D. Mkhonazi, M. Shandu, R. Tshinavhe, S. B. Simelane, P. T. Moshapo, *Molecules* **2020**, *25*, 1040.

[12] T. Ben Halima, J. Masson-Makdissi, S. G. Newman, *Angew. Chem., Int. Ed.* **2018**, *57*, 12925-12929.

[13] C. A. Malapit, M. Borrell, M. W. Milbauer, C. E. Brigham, M. S. Sanford, *J. Am. Chem. Soc.* **2020**, *142*, 5918-5923.

[14] Z. Fu, X. Wang, S. Tao, Q. Bu, D. Wei, N. Liu, *J. Org. Chem.* **2021**, *86*, 2339-2358.

[15] H. Morimoto, R. Fujiwara, Y. Shimizu, K. Morisaki, T. Ohshima, *Org.Lett.* **2014**, *16*, 2018-2021.

[16] S. Shi, R. Lalancette, R. Szostak, M. Szostak, *Org. Lett.* **2019**, *21*, 1253-1257.

[17] a)G. Meng, P. Lei, M. Szostak, *Org Lett.* **2017**, *19*, 2158-2161; b)S. Yu, T. Shin, M. Zhang, Y. Xia, H. Kim, S. Lee, *Org Lett.* **2018**, *20*, 7563-7566; c)D. Joseph, M. S. Park, S. Lee, *Org. Biomol. Chem.* **2021**, *19*, 6227-6232.

[18] S. A. Rzhevskiy, A. A. Ageshina, G. A. Chesnokov, P. S. Gribanov, M. A. Topchiy, M. S. Nechaev, A. F. Asachenko, *RSC Adv.* **2019**, *9*, 1536-1540.

[19] S. Karthik, R. Sreedharan, T. Gandhi, *ChemistrySelect* **2019**, *4*, 175-180.

[20] S. Shi, M. Szostak, *ChemComm* **2017**, *53*, 10584-10587.

[21] Z. Li, C. Wang, Y. Wang, D. Yuan, Y. Yao, *Asian J. Org. Chem.* **2018**, *7*, 810-814.

[22] a)A. Kaithal, D. Kalsi, V. Krishnakumar, S. Pattanaik, A. Bordet, W. Leitner, C. Gunanathan, *ACS Catal.* **2020**, *10*, 14390-14397; b)R. V. Jagadeesh, K. Murugesan, A. S. Alshammari, H. Neumann, M. M. Pohl, J. Radnik, M. Beller, *Science (New York, N.Y.)* **2017**, *358*, 326-332.

[23] D. L. Sudakin, T. Osimitz, in *Hayes' Handbook of Pesticide Toxicology (Third Edition)* (Ed.: R. Krieger), Academic Press, New York, **2010**, pp. 2111-2125.