

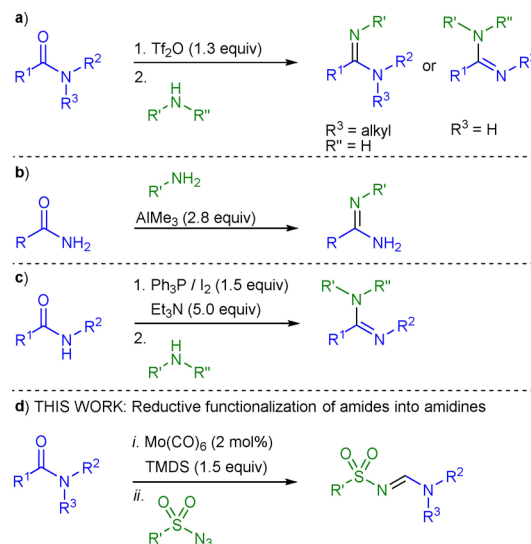
# Mild Reductive Functionalization of Amides into *N*-Sulfonylformamidines

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The development of a protocol for the reductive functionalization of amides into *N*-sulfonylformamidines is reported. The one-pot procedure is based on a mild catalytic reduction of tertiary amides into the corresponding enamines by the use of Mo(CO)<sub>6</sub> (molybdenum hexacarbonyl) and TMDS (1,1,3,3-tetra-methyldisiloxane). The formed enamines were allowed to react with sulfonyl azides to give the target compounds in moderate to good yields.

The amidine functional group is frequently found in biologically active compounds possessing anti-inflammatory, antibacterial, antiviral, antibiotic, and anesthetic properties.<sup>[1]</sup> They are also employed as intermediates and precursors in organic synthesis of important heterocyclic compounds such as imidazoles, quinazolines, isoquinolines, and pyrimidines.<sup>[2]</sup> Furthermore, amidines are employed as ligands in metal complexes and as protecting groups for primary amines.<sup>[3]</sup>

The stability of amides makes this functional group valuable to include in an array of different compounds such as pharmaceuticals, agrochemicals, and other organic materials.<sup>[4]</sup> On the other hand, the inherent stability is contributing to the reluctance of employing amides as synthetic intermediates. The concept of activation and functionalization of amides is well known and the discovery of triflic anhydride (Tf<sub>2</sub>O) as an amide activating agent constituted a major advance within this field.<sup>[5]</sup> In recent years, research based on Tf<sub>2</sub>O as an amide activator has progressed immensely and a broad variety of mild transformations have been reported.<sup>[6]</sup> Besides classical amide activation reagents such as POCl<sub>3</sub>,<sup>[7]</sup> SOCl<sub>2</sub>,<sup>[8]</sup> PCl<sub>3</sub>,<sup>[9]</sup> PCl<sub>5</sub>,<sup>[10]</sup> and (COCl)<sub>2</sub>,<sup>[11]</sup> triflic anhydride was also employed by Charette and Grenon for the transformation of amides into amidines (Scheme 1 a).<sup>[12]</sup> Later, protocols based on AlMe<sub>3</sub> and Ph<sub>3</sub>P/I<sub>2</sub> for



**Scheme 1.** Preparation of amidines through a–c) electrophilic amide activation and d) reductive functionalization of amides.

amide activation and subsequent amidine synthesis were also reported by Velavan et al. and Phakhodee et al. (Scheme 1 b and 1 c).<sup>[13, 14]</sup> The direct condensation of sulfonamides with *N,N*-dimethylformamide dimethyl acetal (DMF-DMA) was furthermore reported by Sharma and co-workers,<sup>[15]</sup> and *N*-sulfonylformamidines can also be prepared from cyanamides.<sup>[16]</sup>

The development of the chemoselective reduction of amides has been very successful and, today, functional groups such as ketones, aldehydes, and imines can be tolerated.<sup>[17]</sup> Consequently, the reductive functionalization of amides is now an emerging field within organic chemistry. This area of research can be divided in two divisions, reduction of amides for the formation of electrophilic species (iminium ion) or nucleophilic species (enamine) with the subsequent trapping/functionalization thereof.<sup>[18]</sup> Herein, we demonstrate a mild protocol for the reductive functionalization of amides (via enamines) for the formation of *N*-sulfonylformamidines (Scheme 1 d).

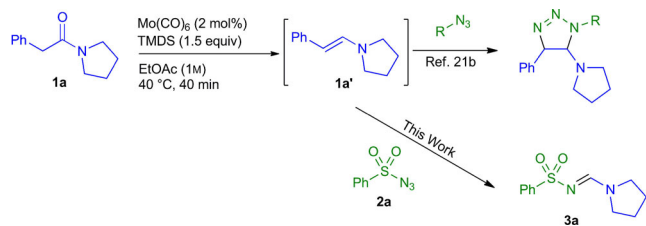
We have previously reported on a highly chemoselective protocol for amide reduction into either amines or aldehydes.<sup>[19]</sup> The Mo(CO)<sub>6</sub>-catalyzed system was further investigated and it was discovered that enamines could also be accessed.<sup>[20]</sup> Recently, we demonstrated the reductive functionalization of amides into 4,5-dihydroisoxazoles and triazoles.<sup>[21]</sup> In the case of the latter compounds, the generated enamines were trapped with organic azides and, during the evaluation of the substrate scope, it was observed that *N*-sulfonylformamidine was formed upon the use of sulfonyl azide (Scheme 2).

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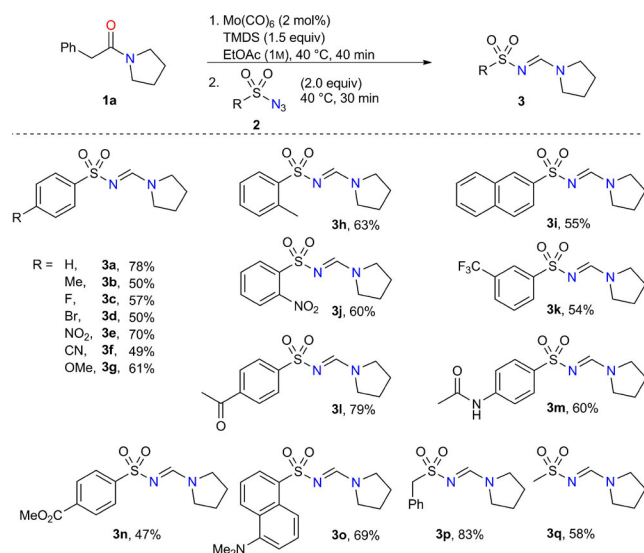
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**Scheme 2.** One-pot transformation of amides into *N*-sulfonylformamidines.

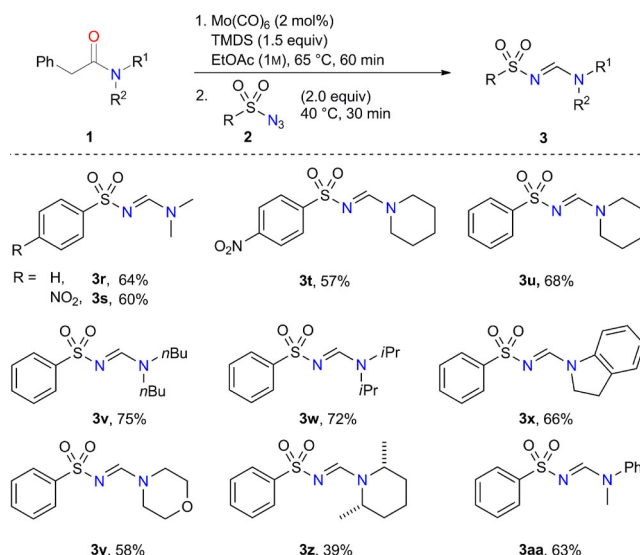
As the sulfonyl group is an important class of pharmacophore and *N*-sulfonylamidines, in particular, exhibit various important biological and pharmaceutical activities, we decided to optimize the conditions for the synthesis of this class of compounds.<sup>[22]</sup> The  $\text{Mo}(\text{CO})_6$ -catalyzed reduction of tertiary amide **1a** gives full conversion into the corresponding enamine **1a'**, as determined by  $^1\text{H}$  NMR spectroscopy using an internal standard.

The screening of the reaction conditions toward the formation of *N*-sulfonylformamidine showed that two equivalents of the sulfonyl azide were needed and the reaction then went to completion within 30 min. A wide variety of benzenesulfonyl azides were then evaluated, which gave the corresponding *N*-sulfonylformamidines in yields between 47 and 79% (Scheme 3, **3a–3o**). Several functional groups such as halide, ketone, secondary amide, ester, amine, cyano, and nitro groups were tolerated. Benzyl- and aliphatic-substituted sulfonyl azides could also be employed and compounds **3p** and **3q** were isolated in 83 and 58% yields, respectively.



**Scheme 3.** Evaluation of sulfonylazides in the transformation of amides into amidines.

Next, we performed an evaluation of different amides in the preparation of *N*-sulfonylformamidines (Scheme 4). During our previous investigation of amide transformation into triazolines, it was found that aliphatic amides constituted a challenging class of substrates for enamine formation.<sup>[21b]</sup> The product ratio



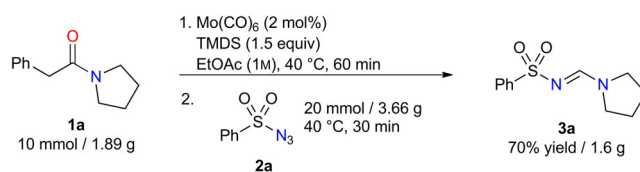
**Scheme 4.** Evaluation of the amide scope.

was in favor of enamine in the case of longer aliphatic chains; however, only amine was essentially formed when employing acetamides. Thus, it was necessary to use phenylacetamides throughout the scope. The reduction of the different amides was straightforward and produced the corresponding enamines in excellent yields (> 95%, according to  $^1\text{H}$  NMR spectroscopy). The subsequent in situ reaction with sulfonyl azide yielded a variety of formamidines substituted with *N,N*-dimethyl (**3r**, **3s**), piperidine (**3t**, **3u**), *N,N*-dibutyl (**3v**), *N,N*-diisopropyl (**3w**), indoline (**3x**), morpholine (**3y**), 2,6-dimethylpiperidine (**3z**), and *N*-methyl-*N*-phenyl (**3aa**).

The overall substrate evaluation shows that this protocol allows for *N*-sulfonylamidines to be synthesized with versatility in both the sulfonyl and the amine part. The products were obtained in moderate to good yields and most of the compounds are novel and have not been previously reported.

The developed protocol for the transformation of carboxamides into *N*-sulfonylformamidines was further evaluated on a preparative scale (Scheme 5). Although we never experienced any issues, one should always be aware of the explosion risks associated with organic azides.<sup>[23]</sup> The reaction with amide **1a** (10 mmol) was performed by using a two-necked round-bottomed flask under an inert atmosphere and amidine **3a** was isolated in 70% yield (1.6 g).

The decomposition of triazolines can lead to a variety of different compounds such as triazoles, aziridines, and amidines.<sup>[24]</sup> In a recent study, we demonstrated the preparation and isola-



**Scheme 5.** One-pot transformation of amide **1a** into sulfonylformamidine **3a** on a preparative scale.

tion of a wide variety of different triazolines.<sup>[21b]</sup> It was also shown that, in some cases, depending on the electronic nature of the amide or the azide, triazoles would form spontaneously by elimination of the amine moiety. The instability of sulfonyl-substituted triazolines is known, but their disintegration does not necessarily form amidines. For instance, Bakulev and co-workers reported on the synthesis of 1*H*-1,2,3-triazoles via sulfonyl-substituted triazolines derived from enamines and sulfonyl azides.<sup>[24c]</sup> Furthermore, the collapse of triazolines into amidines may also proceed via different pathways. Houk and co-workers recently investigated the reactivity of perfluorinated aryl azides in the (3 + 2) cycloaddition with enamines, which resulted in the formation of triazolines.<sup>[25]</sup> The spontaneous cleavage of these heterocyclic species with loss of N<sub>2</sub> was observed and the corresponding  $\alpha$ -substituted amidines were isolated (Scheme 6a).

Li and co-workers have developed a protocol for *N*-sulfonylformamidine synthesis based on tertiary amines and sulfonyl azides in combination with stoichiometric amounts of diethyl azodicarboxylate (DEAD).<sup>[26]</sup> In this case, the decomposition of the sulfonyl-substituted triazolines led to the formation of formamidines (Scheme 6b). The authors proposed diazomethane to be formed as a by-product, which was confirmed by a trapping experiment using carboxylic acid.<sup>[27]</sup> We speculated that, if the formation of *N*-sulfonylformamidine would proceed via the triazoline intermediate, then phenyldiazomethane would most likely be formed upon cleavage of the heterocycle in a similar fashion to that proposed by Li and co-workers (Scheme 6b).<sup>[26]</sup> Thus, we performed an experiment employing benzoic acid as

the trapping reagent for phenyldiazomethane. The *p*-methoxy-substituted amide **1g** was reduced to the corresponding enamine (**1g'**) and then treated with both sulfonyl azide **2a** and benzoic acid in situ. The side-product 1-(diazomethyl)-4-methoxybenzene (**5**) derived from triazoline **4g** was successfully intercepted (Scheme 6c). 4-Methoxybenzyl benzoate (**6**) could be confirmed by the crude <sup>1</sup>H NMR spectrum and also by subsequent isolation/characterization (see the Supporting Information), which supports the proposed mechanism in Scheme 6c.

In conclusion, we have developed a protocol for the reductive functionalization of carboxamides into *N*-sulfonylformamidines. The system is characterized by mild conditions and short reaction times and can be performed in the environmentally friendly solvent ethyl acetate.<sup>[28]</sup> A wide range of sulfonyl azides and amides were evaluated, and the majority of the *N*-sulfonylformamidines obtained have previously not been reported. It was further demonstrated that the protocol could be employed on a preparative scale. This mild and high-yielding strategy to obtain enamines from stable carboxamides and utilize them in situ for the formation of *N*-sulfonylformamidines should be of high value to organic and medicinal chemists.

## Experimental Section

Amide (1.0 mmol) and Mo(CO)<sub>6</sub> (0.0054 g, 0.02 mmol) were added to an oven-dried 10 mL vial equipped with a magnetic stirring bar. To the sealed tube, dry ethyl acetate (1 mL) was added and the atmosphere was exchanged to N<sub>2</sub> via the septum. The reaction mixture was heated at 80 °C for 10 min to activate the catalyst, which was followed by flushing the vial with N<sub>2</sub>. The reaction was allowed to reach the optimized reaction temperature, after which TMDS (1.5 mmol, 0.26 mL) was added and the reaction was stirred for the required amount of time to form the corresponding enamine. To the crude reaction, sulfonyl azide (2 mmol) was added at 40 °C. After 30 min, the crude reaction was transferred to a round-bottom flask and concentrated onto silica. *N*-Sulfonyl amidines were purified through column chromatography by using pentane/EtOAc as the eluent.

## Acknowledgements

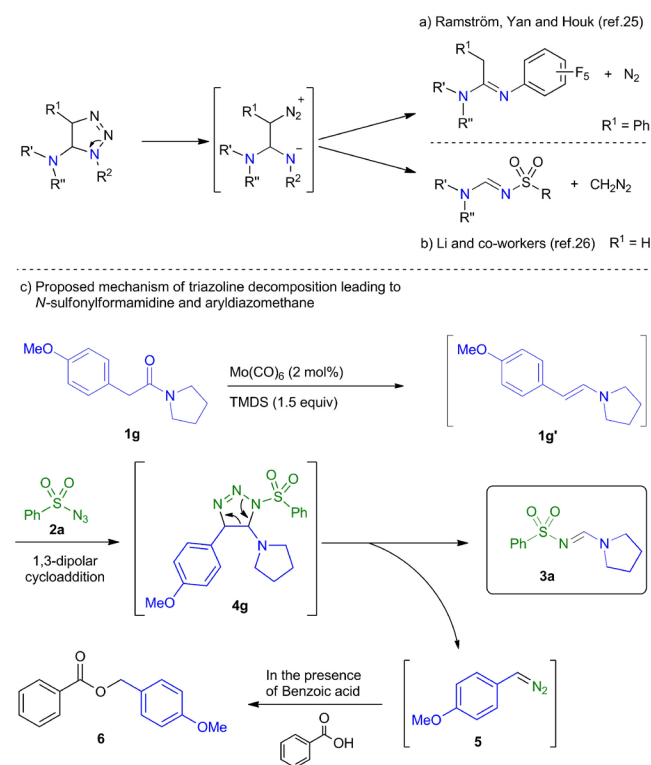
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## Conflict of Interest

The authors declare no conflict of interest.

**Keywords:** amides • amidines • enamines • reductive functionalization • sulfonyl azides

- [1] a) J. V. Greenhill, P. Lue, *Prog. Med. Chem.* **1993**, *30*, 203–326; b) S. Arya, N. Kumar, P. Roy, S. M. Sondhi, *Eur. J. Med. Chem.* **2013**, *59*, 7–14; c) S. D. Guile, L. Alcaraz, T. N. Birkinshaw, K. C. Bower, M. R. Ebden, M. Furber, M. J. Stocks, *J. Med. Chem.* **2009**, *52*, 3123–3141.  
[2] a) S. K. Alla, R. K. Kumar, P. Sadhu, T. Punniyamurthy, *Org. Lett.* **2013**, *15*, 1334–1337; b) Y. Zhu, C. Li, J. Zhang, M. She, W. Sun, K. Wan, Y. Wang, B. Yin, P. Liu, J. Li, *Org. Lett.* **2015**, *17*, 3872–3875; c) J.-P. Lin, F.-H.



**Scheme 6.** a,b) Decomposition pathways of triazolines into  $\alpha$ -substituted amidines or formamidines. c) Proposed mechanism.

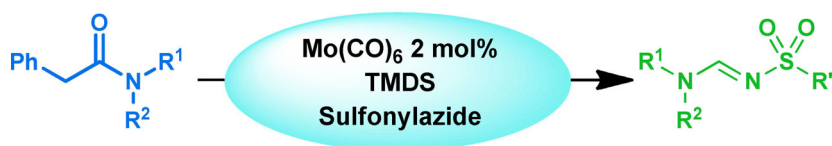
- Zhang, Y.-Q. Long, *Org. Lett.* **2014**, *16*, 2822–2825; d) J. Li, M. Tang, L. Zang, W. Zhang, Z. Zhang, L. Ackermann, *Org. Lett.* **2016**, *18*, 2742–2745; e) D. Tejedor, S. López-Tosco, F. J. García-Tellado, *J. Org. Chem.* **2013**, *78*, 3457–3463; f) M. Radi, S. Schenone, M. Botta, *Org. Biomol. Chem.* **2009**, *7*, 2841–2847; g) N. Deibl, K. Ament, R. Kempe, *J. Am. Chem. Soc.* **2015**, *137*, 12804–12807.
- [3] a) J. Barker, M. Kilner, *Coord. Chem. Rev.* **1994**, *133*, 219–300; b) D. Cornacchia, R. Z. Pellicani, F. P. Intini, C. Pacifico, G. Natile, *Inorg. Chem.* **2009**, *48*, 10800–10810; c) S. Enthaler, K. Schröder, S. Inoue, B. Eckhardt, K. Junge, M. Beller, M. Driß, *Eur. J. Org. Chem.* **2010**, 4893–4901; d) S. Tanaka, K. Mashima, *Dalton Trans.* **2013**, *42*, 2831–2840; e) E. C. Hansen, D. J. Pedro, A. C. Wotal, N. J. Gower, J. D. Nelson, S. Caron, D. J. Weix, *Nat. Chem.* **2016**, *8*, 1126–1130; f) S. J. Pastine, D. V. Gribkov, D. Sames, *J. Am. Chem. Soc.* **2006**, *128*, 14220–14221; g) S. Vincent, S. Mons, L. Lebeau, C. Mioskowski, *Tetrahedron Lett.* **1997**, *38*, 7527–7530.
- [4] J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, *4*, 2337–2347.
- [5] J.-B. Falmagne, J. Escudero, S. Taleb-Sahraoui, L. Ghosez, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 879–880; *Angew. Chem.* **1981**, *93*, 926–931.
- [6] a) S. A. Ruider, N. Maulide, *Angew. Chem. Int. Ed.* **2015**, *54*, 13856–13858; *Angew. Chem.* **2015**, *127*, 14062–14064; b) D. Kaiser, N. Maulide, *J. Org. Chem.* **2016**, *81*, 4421–4428; c) B. Peng, D. Geerdink, C. Fares, N. Maulide, *Angew. Chem. Int. Ed.* **2014**, *53*, 5462–5466; *Angew. Chem.* **2014**, *126*, 5566–5570; d) G. Pelletier, W. S. Bechara, A. B. Charette, *J. Am. Chem. Soc.* **2010**, *132*, 12817–12819; e) P.-Q. Huang, Q.-W. Lang, Y.-R. Wang, *J. Org. Chem.* **2016**, *81*, 4235–4243; f) V. Tona, A. de la Torre, M. Padmanaban, S. Ruider, L. González, N. Maulide, *J. Am. Chem. Soc.* **2016**, *138*, 8348–8351; g) W. S. Bechara, G. Pelletier, A. B. Charette, *Nat. Chem.* **2012**, *4*, 228–234; h) P.-Q. Huang, Y.-H. Huang, H. Geng, J.-L. Ye, *Sci. Rep.* **2016**, *6*, 28801; i) S. Régnier, W. S. Bechara, A. B. Charette, *J. Org. Chem.* **2016**, *81*, 10348–10356; j) J. W. Medley, M. Movassaghi, *Angew. Chem. Int. Ed.* **2012**, *51*, 4572–4576; *Angew. Chem.* **2012**, *124*, 4650–4654; k) G. Bélanger, M. Dupuis, R. Larouche-Gauthier, *J. Org. Chem.* **2012**, *77*, 3215–3221; l) J. Boudreault, F. Lévesque, G. Bélanger, *J. Org. Chem.* **2016**, *81*, 9247–9268.
- [7] H. Brederick, R. Gompfer, K. Klemm, H. Rempfer, *Chem. Ber.* **1959**, *92*, 837–849.
- [8] E. Kühle, *Angew. Chem. Int. Ed. Engl.* **1962**, *12*, 647–652; *Angew. Chem.* **1962**, *74*, 861–866.
- [9] A. J. Hill, I. Rabinowitz, *J. Am. Chem. Soc.* **1926**, *48*, 732–737.
- [10] A. J. Hill, J. V. Johnston, *J. Am. Chem. Soc.* **1954**, *76*, 920–922.
- [11] M. Gazvoda, M. Kočev, S. Polanc, *Eur. J. Org. Chem.* **2013**, 5381–5386.
- [12] A. B. Charette, M. Grenon, *Tetrahedron Lett.* **2000**, *41*, 1677–1680.
- [13] A. Velavan, S. Sumathi, K. K. Balasubramanian, *Eur. J. Org. Chem.* **2014**, 5806–5815.
- [14] W. Phakhodee, S. Wangngae, N. Wiriya, M. Pattarawarapan, *Tetrahedron Lett.* **2016**, *57*, 5351–5354.
- [15] N. Chandna, N. Chandak, P. Kumar, J. K. Kapoor, P. K. Sharma, *Green Chem.* **2013**, *15*, 2294–2301.
- [16] J. Hellmann, I. Rhotert, H. Westenberg, R. Fröhlich, B. Wibbeling, W. Uhl, E.-U. Würthwein, *Eur. J. Org. Chem.* **2013**, 3356–3368.
- [17] A. Volkov, F. Tinnis, T. Slagbrand, P. Trillo, H. Adolfsson, *Chem. Soc. Rev.* **2016**, *45*, 6685–6697 and references therein.
- [18] For reductive functionalization of amides via electrophilic species see a) S. Katohara, S. Kobayashi, K. Fujita, T. Matsumoto, T. Sato, N. Chida, *J. Am. Chem. Soc.* **2016**, *138*, 5246–5249; b) P.-Q. Huang, W. Ou, F. Han, *Chem. Commun.* **2016**, 52, 11967–11970; c) M. Nakajima, T. Sato, N. Chida, *Org. Lett.* **2015**, *17*, 1696–1699; d) K. Shirokane, T. Wada, M. Yoriata, R. Minamikawa, N. Takayama, T. Sato, N. Chida, *Angew. Chem. Int. Ed.* **2014**, *53*, 512–516; *Angew. Chem.* **2014**, *126*, 522–526; e) Á. L. Fuentes de Arriba, E. Lenci, M. Sonawane, O. Formery, D. J. Dixon, *Angew. Chem. Int. Ed.* **2017**, *56*, 3655–3659; *Angew. Chem.* **2017**, *129*, 3709–3713; For reductive functionalization of amides via nucleophilic species see f) P. W. Tan, J. Seayad, D. J. Dixon, *Angew. Chem. Int. Ed.* **2016**, *55*, 13436–13440; *Angew. Chem.* **2016**, *128*, 13634–13638; g) A. W. Gregory, A. Chambers, A. Hawkins, P. Jakubec, D. J. Dixon, *Chem. Eur. J.* **2015**, *21*, 111–114; h) Y. Nakayama, Y. Maeda, M. Kotatsu, R. Sekiya, M. Ichiki, T. Sato, N. Chida, *Chem. Eur. J.* **2016**, *22*, 3300–3303; i) H. Kobayashi, Y. Sasano, N. Kanoh, E. Kwon, Y. Iwabuchi, *Eur. J. Org. Chem.* **2016**, 270–273.
- [19] F. Tinnis, A. Volkov, T. Slagbrand, H. Adolfsson, *Angew. Chem. Int. Ed.* **2016**, *55*, 4562–4566; *Angew. Chem.* **2016**, *128*, 4638–4642.
- [20] Few protocols for amide reduction into enamines are known. a) Y. Motoyama, M. Aoki, N. Takaoka, R. Aoto, H. Nagashima, *Chem. Commun.* **2009**, 12, 1574–1576; b) S. Bower, K. A. Kreutzer, S. L. Buchwald, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1515–1516; *Angew. Chem.* **1996**, *108*, 1662–1664; c) A. Volkov, F. Tinnis, H. Adolfsson, *Org. Lett.* **2014**, *16*, 680–683; d) A. Tahara, Y. Miyamoto, R. Aoto, K. Shigeta, Y. Une, Y. Sunada, Y. Motoyama, H. Nagashima, *Organometallics* **2015**, *34*, 4895–4907.
- [21] a) T. Slagbrand, G. Kerverfors, F. Tinnis, H. Adolfsson, *Adv. Synth. Catal.* **2017**, <https://doi.org/10.1002/adsc.201700154>; b) T. Slagbrand, A. Volkov, P. Trillo, F. Tinnis, H. Adolfsson, *ACS Catal.* **2017**, *7*, 1771–1775.
- [22] a) H.-X. Dai, A. F. Stepan, M. S. Plummer, Y.-H. Zhang, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 7222–7228; b) M. Y. Lee, M. H. Kim, J. Kim, S. H. Kim, B. T. Kim, I. H. Jeong, S. Chang, S. H. Kim, S.-Y. Chang, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 541–545; c) N. K. Andersen, N. Chandak, L. Brulíková, P. Kumar, M. D. Jensen, F. Jensen, P. K. Sharma, P. Nielsen, *Bioorg. Med. Chem.* **2010**, *18*, 4702–4710; d) P. Kumar, N. Chandak, P. Nielsen, P. K. Sharma, *Bioorg. Med. Chem.* **2012**, *20*, 3843–3849; e) A. Goubet, A. Chardon, P. Kumar, P. K. Sharma, R. N. Veedu, *Bioorg. Med. Chem. Lett.* **2013**, *23*, 761–763; f) S.-Y. Chang, S. J. Bae, M. Y. Lee, S.-H. Baek, S. Chang, S. H. Kim, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 727–729; g) M.-J. Wang, Y.-Q. Liu, L.-C. Chang, C.-Y. Wang, Y.-L. Zhao, X.-B. Zhao, K. Qian, X. Nan, L. Yang, X.-M. Yang, H.-Y. Hung, J.-S. Yang, D.-H. Kuo, M. Goto, S. L. Morris-Natschke, S.-L. Pan, C.-M. Teng, S.-C. Kuo, T.-S. Wu, Y.-C. Wu, K.-H. Lee, *J. Med. Chem.* **2014**, *57*, 6008–6018.
- [23] S. Bräse, C. Gil, K. Knepper, V. Zimmerman, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–5240; *Angew. Chem.* **2005**, *117*, 5320–5374.
- [24] a) R. Fusco, G. Bianchetti, D. Pocar, R. Ugo, *Chem. Ber.* **1963**, *96*, 802–812; b) G. L'abbé, *Chem. Rev.* **1969**, *69*, 345–363; c) I. Efimov, V. Bakulev, N. Beliaev, T. Beryozkina, U. Knippschild, J. Leban, F. Zhi-Jin, O. Eltsov, P. Slepukhin, M. Ezhikova, W. Dehaen, *Eur. J. Org. Chem.* **2014**, 3684–3689.
- [25] S. Xie, S. A. Lopez, O. Ramström, M. Yan, K. N. Houk, *J. Am. Chem. Soc.* **2015**, *137*, 2958–2966.
- [26] X. Xu, X. Li, L. Ma, N. Ye, B. Weng, *J. Am. Chem. Soc.* **2008**, *130*, 14048–14049.
- [27] Carboxylic acids are known to react with diazo compounds to yield esters. a) M. E. Furrow, A. G. Myers, *J. Am. Chem. Soc.* **2004**, *126*, 12222–12223; b) R. A. Squitieri, G. P. Shearn-Nance, J. E. Hein, J. T. Shaw, *J. Org. Chem.* **2016**, *81*, 5278–5284.
- [28] D. Prat, A. Wells, J. Hayler, H. Sneddon, C. R. McElroy, S. Abou-Shehada, P. J. Dunn, *Green Chem.* **2016**, *18*, 288–296.

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## REDUCTIVE FUNCTIONALIZATION OF AMIDES



**Amidst the amidines:** A system for the reductive functionalization of amides into *N*-sulfonylformamidines is described. This one-pot protocol is based

on a  $\text{Mo}(\text{CO})_6$ -catalyzed reduction of amides into enamines and offers an access to a wide variety of amidines.

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