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# Mechanochemical Iron-Catalyzed Nitrene Transfer Reactions: Direct Synthesis of *N*-Acyl Sulfonimidamides from Sulfinamides and Dioxazolones

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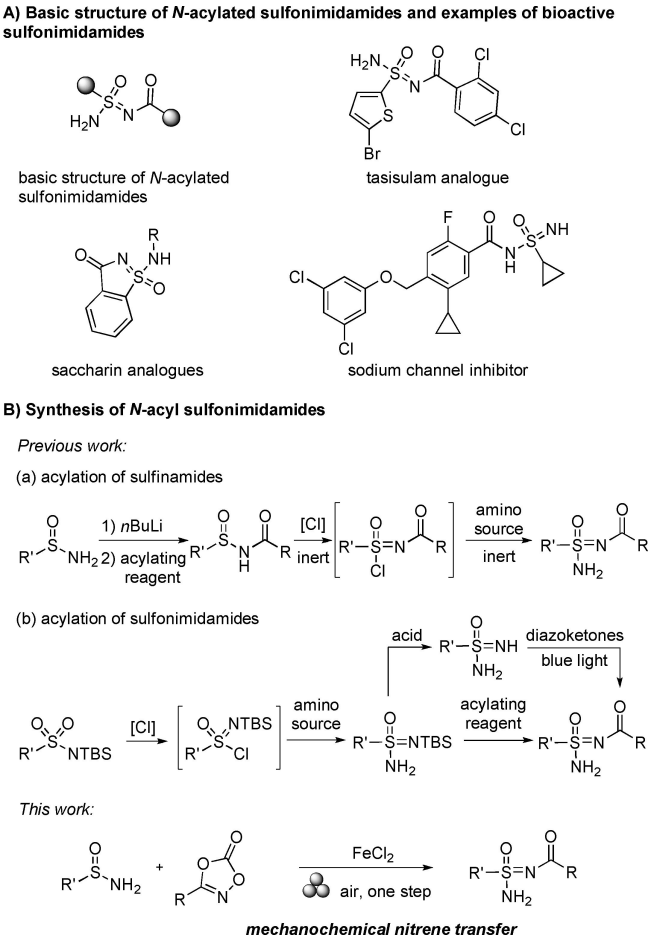
**Abstract:** A mechanochemical synthesis of sulfonimidamides by iron(II)-catalyzed exogenous ligand-free *N*-acyl nitrene transfer to sulfinamides is reported. The one-step method tolerates a wide range of sulfinamides with various substituents under solvent-free ambient conditions. Compared to its solution-phase counterpart, this mechanochemical approach shows better conversion and chemoselectivity. Mechanistic investigations by ESI-MS revealed the generation of crucial nitrene iron intermediates.

**S**ulfonimidamides are monoaza analogs of sulfonamides, which have garnered significant attention in medicinal chemistry due to their unique pharmacophore.[1,2] *N*-acylated derivatives exhibit biological activities across diverse medical domains. Examples include an analog to the anticancer agent tasisulam,[3] an innovative saccharin aza-bioisostere,[4] and a sodium channel inhibitor[5] (Scheme 1A). Arvidsson and Pemberton independently demonstrated that *N*-acylated sulfonimidamides can be regarded as carboxylic acid bioisosteres with tunable biological and physiochemical properties.[1d,6] If the imino moiety of the sulfonimidamide is shielded by a protecting group, the remaining amino substituent can selectively be functionalized through arylation,[7] acylation,[1d,8] and nitrene transfer reaction.[9] These structural alternations significantly broaden the accessible chemical space in sulfur(VI) chemistry and permit novel applications of such compounds in medicinal chemistry.

Most acylated sulfonimidamides are prepared by a traditional, well-established protocol [Scheme 1B, previous work, (a)].[10] It starts from a sulfinamide, which is acylated by deprotonation with *n*BuLi and subsequent treatment of the resulting anion with a carboxylic chloride or an anhydride. Oxidation of the acylated intermediate with a potent electrophilic chlorinating agent such as *t*BuOCl or NCS provides an *N*-acyl sulfonimidoyl chloride, which upon substitution of the halo group with an ammonia source yields the desired acylated sulfonimidamide. This approach requires stringent and inert reaction conditions due to the high reactivity of *n*BuLi and the susceptibility of the sulfonimidoyl halo intermediate to hydrolysis and decom-




***Scheme 1.*** A) Basic structure of *N*-acylated sulfonimidamides and examples of bioactive sulfonimidamides, B) synthesis of sulfonimidamides in a traditional and the newly discovered mechanochemical way.

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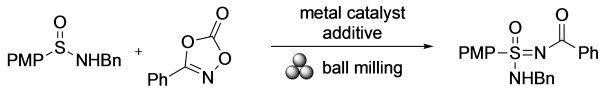
position. An alternative method for the preparation of *N*-acylated sulfonimidamides makes use of *N*-TBS (*N*-*tert*-butyldimethylsilyl) or *N*-unsubstituted precursors which are reacted with acyl donors [Scheme 1B, previous work, (b)].[11] These approaches are straightforward but require multistep preparations of the starting materials, rendering these methods less efficient and limiting their applicability.

Nitrene transfer has emerged as a highly effective approach for synthesizing sulfilimines and sulfoximines through sulfur imidation from their respective low-valence sulfide and sulfoxide precursors.[12] Surprisingly, this strategy has only scarcely been applied for the conversion of sulfinamides to sulfonimidamides.[13] If so, stoichiometric amounts of hypervalent iodine reagents were mostly used as oxidants. An alternative was reported in 2021 by Dinér and co-workers, who developed a light-promoted nitrene-involving strategy for such transformations.[14] Although synthetically appealing, the applicability of this method remained limited due to the use of toxic and explosive azides as nitrene precursors and the requirement of a fluorinated organic solvent and inert reaction conditions. Realizing these severe restrictions in current protocols, we initiated a search for practical and safe sulfinamides imidations to give sulfonimidamides. Dioxazolones, which are well-established, stable acyl nitrene precursors with numerous applications in related sulfur imidations[15] and C–H-bond amidations,[16] were identified as attractive reagents. In addition, we set the goal to search for a simple and non-precious metal catalyst to be applied under mechanochemical conditions, which we envisaged to have two additional advantages over existing technologies: First, being able to avoid a solvent and, second, reaching a higher efficiency with improved sustainability.[17–19] As a results of this endeavor, we now report an iron-catalyzed mechanochemical approach to sulfonimidamides from sulfinamides and dioxazolones under ambient conditions in air (Scheme 1B, bottom).

The investigation was initiated with *N*-benzyl-4-methoxybenzenesulfinamide (**1a**) and 3-phenyl-1,4,2-dioxazol-5-one (**2a**) as representative starting materials. Table 1 summarizes the results of the optimization study. The first experiments were conducted with a range of iron catalysts in the presence of silica as grinding auxiliary in a 10 mL stainless steel jar with a 10 mm stainless steel ball in a mixer mill at 25 Hz for 60 min (Table 1, entries 1–6). $FeCl_2$, as an inexpensive iron(II) catalyst, was the best among all the catalysts that were tested, giving product **3aa** in 42 % yield (as determined from the crude product by $^1$H NMR spectroscopy using an internal standard). Extending the milling time from 60 min to 90 min or 120 min slightly increased the yields (Table 1, entries 7 and 8). Applying $Al_2O_3$ instead of silica in this reaction and milling for 90 min affording **3aa** in a significantly increased yield (74 %, Table 1, entry 9). When 1.2 or 1.5 equivalents of **2a** were used, product **3aa** was obtained in 76 % yield. Decreasing or increasing the amount of $Al_2O_3$ resulted in a decrease in yield for **3aa** to 67 % and 36 %, respectively (Table 1, entries 12 and 13). Subsequently, the amount of $FeCl_2$ was screened, and the yield of **3aa** slightly increased to 78 % with 20 mol % of $FeCl_2$ (Table 1, entry 15). Inspired by recent observations,[20] $Al_2O_3$ was substituted by talcum in the next set of experiments, and to our delight, a positive effect was observed here too. Now, after milling at 25 Hz for 120 min **3aa** was obtained in 88 % yield (Table 1, entry 17). Performing the reaction under argon atmosphere did not improve the yield, showing the insensitivity of the reaction to air (Table 1, entry 18). A control experiment without the iron catalyst confirmed its central role, giving no tractable yield (Table 1, entry 19). Without the addition of an additive, the yield of **3aa** dropped sharply to 17 % (Table 1, entry 20).

To compare the conversion and the chemoselectivity of the reaction in the ball mill and in solution, a series of control experiments was carried out (for details, see the Supporting Information). As mentioned before, **3aa** was obtained as single product in 88 % yield under the optimized mechanochemical conditions (Table 1, entry 17). In contrast, performing the same reaction in toluene or DCM led to low yields of **3aa** (8 % and 6 %, respectively), and as byproduct, thiosulfonate PMP-$SO_2$-S-PMP (**4**)[21] was formed in 4 % and 6 %, respectively (Table S1, entries 1 and 2). No product formation occurred in MeCN (Table S1, entry 3). Extending the reaction time from 2 h to 24 h and raising the ambient reaction temperature to 60 °C increased the yield of **3aa** to

***Table 1:*** Optimization of the reaction conditions.[a]




**1a** **2a** PMP = *p*-methoxyphenyl **3aa**

| Entry | Catalyst | Milling conditions | Additive | Yield of **3aa** [%][b] |
|---|---|---|---|---|
| 1 | $FeCl_2$ | 25 Hz, 60 min | silica | 42 |
| 2 | $Fe(OTf)_2$ | 25 Hz, 60 min | silica | 13 |
| 3[c] | $Fe^{II}Pc$ | 25 Hz, 60 min | silica | trace |
| 4 | $Fe(acac)_2$ | 25 Hz, 60 min | silica | – |
| 5 | $FeBr_2$ | 25 Hz, 60 min | silica | 36 |
| 6 | $FeCl_3$ | 25 Hz, 60 min | silica | 14 |
| 7 | $FeCl_2$ | 25 Hz, 90 min | silica | 45 |
| 8 | $FeCl_2$ | 25 Hz, 120 min | silica | 46 |
| 9 | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 74 |
| 10[d] | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 76 |
| 11[e] | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 76 |
| 12[d,f] | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 67 |
| 13[d,g] | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 36 |
| 14[d,h] | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 58 |
| 15[d,i] | $FeCl_2$ | 25 Hz, 90 min | $Al_2O_3$ | 78 |
| 16[d,i] | $FeCl_2$ | 25 Hz, 90 min | talcum | 83 |
| **17**[d,i] | **$FeCl_2$** | **25 Hz, 120 min** | **talcum** | **88(75)**[j] |
| 18[d,i,k] | $FeCl_2$ | 25 Hz, 120 min | talcum | 86 |
| 19[d,i] | - | 25 Hz, 90 min | talcum | – |
| 20[d,i] | $FeCl_2$ | 25 Hz, 90 min | – | 17 |

[a] Reaction conditions: Into a stainless steel jar (10 mL) with one stainless steel ball (Ø: 10 mm), **1a** (0.2 mmol), **2a** (0.2 mmol), the metal catalyst (10 mol %), and the additive (60 mg) were added under air and milled at 25 Hz for 60–120 min. [b] Determined by $^1$H NMR analysis using $CH_2Br_2$ as internal standard. [c] $Fe^{II}Pc$ = Iron(II) phthalocyanine. [d] Use of 1.2 equiv. of **2a**. [e] Use of 1.5 equiv. of **2a**. [f] Use of 30 mg of additive. [g] Use of 90 mg of additive. [h] Use of 5 mol % of $FeCl_2$. [i] Use of 20 mol % of $FeCl_2$ [j] After isolation by column chromatography. [k] Under argon atmosphere.

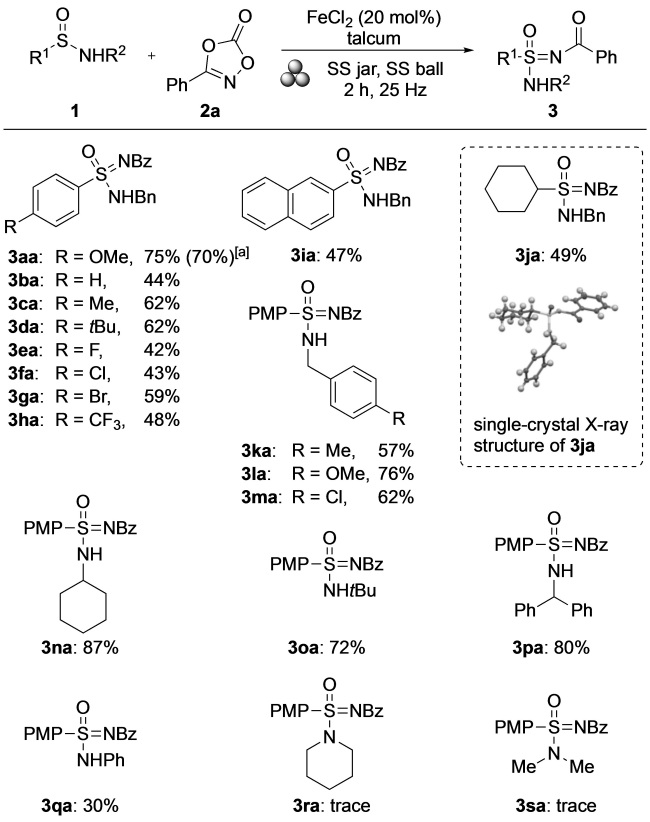
27 % at best. At the same time, more of byproduct **4** was formed (Table S1, entries 4–6). In toluene, talcum did not promote the reaction (Table S1, entry 7). From these results it is evident that the mechanochemical conditions employed here are beneficial for both conversion and chemoselectivity when compared to its solution-based counterpart.

Next, the scope of the reaction was investigated under the optimized mechanochemical conditions. The results are shown in Scheme 2. First, various *N*-substituted sulfinamides **1** were reacted with dioxazolone **2a**. *S*-Aryl *N*-benzyl sulfinamides with a range of *para*-substituents on the arene tolerated well, providing the corresponding products **3aa**–**ha** in yields ranging from 42 % to 75 %. Generally, sulfinamides with electron-donating groups (**1a**–**d**) gave slightly higher yields than those bearing electron-withdrawing substituents (**1e**–**h**). *S*-2-Naphthyl- and *S*-cyclohexyl sulfinamides reacted smoothly with **2a**, affording **3ia** and **3ja** in 47 % and 49 % yield, respectively. The molecular structure of **3ja** in the solid state was confirmed by single-crystal X-ray diffraction and is depicted in Scheme 2. When the *N*-benzyl group of sulfinamide was substituted with methyl, methoxy, and chloro in *para*-position of the arene, the corresponding products **3ka**–**ma** were isolated in yields of 57–76 %. *N*-Cyclohexyl, *tert*-butyl, and benzhydryl sulfinamides were all suitable substrates, leading to **3na**, **3oa**, and **3pa** in yields of 87 %, 72 %, and 80 %, respectively.

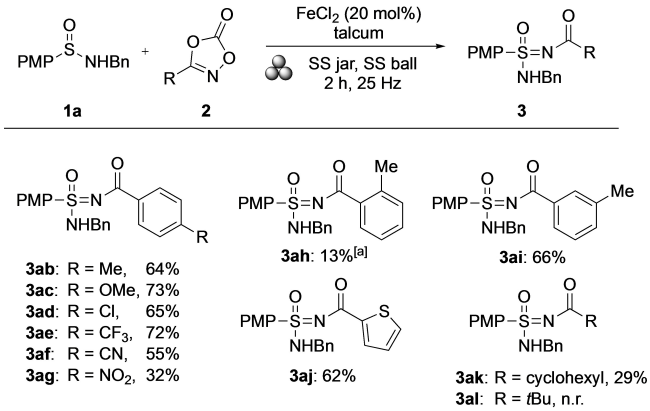
Compared with *N*-alkyl sulfinamides, *N*-phenyl sulfinamide **1q** was less reactive, providing the corresponding product **3qa** in only 30 % yield. Noteworthy, *N,N*-disubstituted sulfinamides (**1r** and **1s**) gave the expected products (**3ra** and **3sa**) in only trace amounts, revealing the necessity of the proton on the nitrogen of the sulfinamide. An upscaling was demonstrated by performing the imidation of **1a** on a 1 mmol scale, leading to **3aa** in 70 % yield.

Next, various dioxazolones **2** were examined in reactions with sulfinamide **1a** (Scheme 3). In general, the imidations proceeded well with aryl-substituted dioxazolones **2** bearing both electron-donating and electron-withdrawing groups at the *para*-position on the arene, providing the corresponding products **3ab**–**ag** in yields of 32–73 %. Among them, substrate **2c** having a *para*-methoxy group gave the best result (**3ac**, 73 % yield), while **2g** with a *para*-nitro substituent afforded product **3ag** in only 32 % yield. Comparing the yields of the products with methyl groups at different positions of aryl ring revealed a significant impact of steric effects. Dioxazolones with a methyl group at the *para* and *meta*-position reacted smoothly, giving products **3ab** and **3ai** in 64 % and 66 % yield, respectively, while **2h** being substituted at the *ortho*-position gave **3ah** in only 13 % yield even after an extended reaction time (4 h). Applying thiofuranyl-substituted dioxazolone **2j** in the imidation of **1a** provided **3aj** in 62 % yield. Contrasting those positive results, alkyl-substituted dioxazolones proved less suitable. Thus, cyclohexyl-substituted dioxazolone **2k** gave **3ak** in only 29 % yield, and **2l** with a *tert*-butyl substituent did not react with sulfinamide **1a**, probably due to steric hindrance.

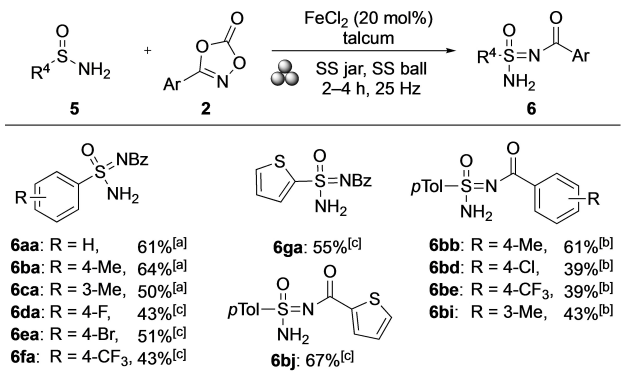
The applicability of *N*-unsubstituted (primary) sulfinamides **5** was explored on a 0.5 mmol scale (Scheme 4). The results revealed that electron-rich aromatic sulfinamides (**5b** and **5c**) gave somewhat higher yields than their electron-deficient counterparts (**5d**, **5e**, and **5f**), which paralleled the




***Scheme 2.*** Substrate scope of substituted sulfinamides **1a–s**. Reaction conditions: Into a stainless steel jar (10 mL) with one stainless steel ball (Ø:10 mm, weight: ca. 3.5 g), **1** (0.2 mmol), **2a** (0.24 mmol), $FeCl_2$ (20 mol %), and talcum (60 mg) were added, and the mixture was milled at 25 Hz for 2 h. [a] The reaction was conducted on a 1.0 mmol scale.



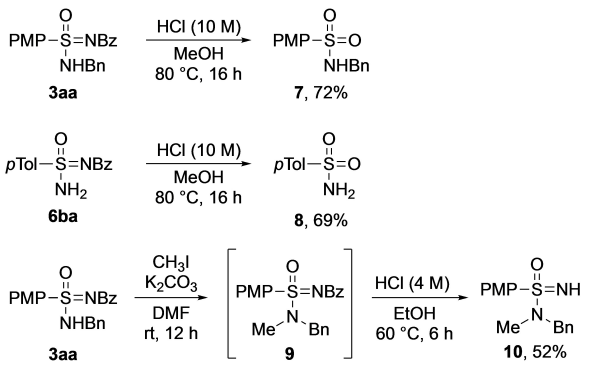

***Scheme 3.*** Substrate scope of dioxazolones **2b–l**. Reaction conditions: Into a stainless steel jar (10 mL) with one stainless steel ball (Ø:10 mm, weight: ca. 3.5 g), **1a** (0.2 mmol), **2** (0.24 mmol), $FeCl_2$ (20 mol %), and talcum (60 mg) were added, and the mixture was milled at 25 Hz for 2 h. [a] Milled for 4 h.




***Scheme 4.*** Substrate scope of *primary* sulfinamides **5** with a range of dioxazolones **2**. Reaction conditions: Into a stainless steel jar (10 mL) with one stainless steel ball (Ø:10 mm, weight: ca. 3.5 g), **5** (0.5 mmol), **2** (0.6 mmol), $FeCl_2$ (20 mol%), and talcum (150 mg) were added, and the mixture was milled at 25 Hz for the given time. [a] Milled for 2 h. [b] Milled for 3 h. [c] Milled for 4 h.

trend observed for the *N*-substituted analogs. Taking that into account, the reaction time was extended (from 2 h to 4 h), when electron-poor substrates were applied. *S*-Thiofuranyl sulfinamide was a suitable substrate too, providing **6ga** in 55% yield. Finally, imidations of **5b** with other dioxazolones were investigated. In general, all reactions worked well, with dioxazolones substituted with a *para*- or a *meta*-methyl on the phenyl ring (**2b** and **2i**) leading to slightly higher yields than the *para*-chloro- and their *para*-trifluoromethyl-substituted counterparts **2d** and **2e**, respectively. Thiofuranyl-based dioxazolone **2j** reacted smoothly also, affording **6bj** in 67% yield after milling for 4 h.

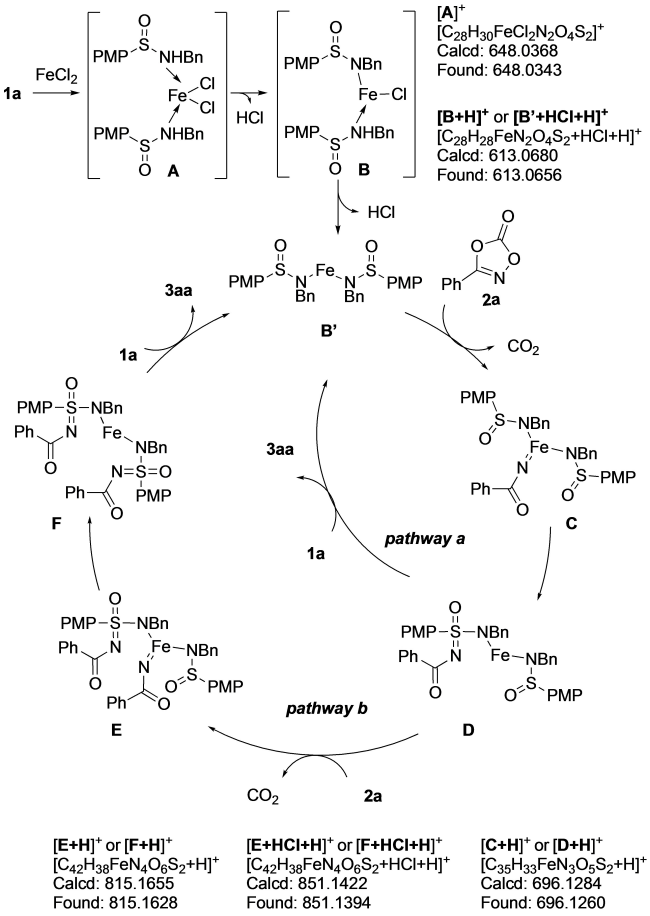
The synthetic utility of the synthesized sulfonimidamides was demonstrated through subsequent transformations, as depicted in Scheme 5. Upon treatment with 10 M aq. HCl in MeOH at 80 °C, both *N*-Bn-protected sulfonimidamide **3aa** and $NH_2$-sulfonimidamide **6ba** converted to sulfonamides in yields of 72% for **7** and 69% for **8** (Scheme 5, top and middle). Apparently, these conditions led to hydrolysis, and the *N*-benzoyl imino groups of the sulfonimidamides were substituted by oxygen. Methylation of **3aa** with methyl iodide afforded intermediate **9**, which could be deprotected with an HCl solution (4 M in dioxane), to give the desired




***Scheme 5.*** Product transformations.

*sp*$^2$-*N*H sulfonimidamide **10** in 52% yield (Scheme 5, bottom). This transformation offers an approach to expanding the structural diversity of sulfonimidamides in organic synthesis.

To gain mechanistic insight in this mechanochemical imidation reaction, radical scavenging experiments and ESI-MS analyses with substrates **1a** and **2a** were carried out (for further details, see the Supporting Information). Only minor yield reductions for **3aa** were observed upon addition of either 1 or 2 equiv. of radical scavenger 2,6-di-*tert*-butyl-4-methyl phenol (BHT), which suggested the absence of relevant radicals in this transformation. Important intermediates were detected by ESI-MS in reactions that were interrupted after 1 min. Particularly noteworthy is the detection of intermediates **C**/**D** and **E**/**F**. On the basis of previous work[15,16] and the aforementioned observation, two possible pathways can be proposed (Scheme 6). In pathway **a**, two molecules of sulfinamide **1a** coordinate to iron(II) chloride to produce intermediate **A**, followed by the formation of **B** and **B**′ upon loss of HCl. Intermediate **B**′ then reacts with dioxazolone **2a** to give acyl nitrene iron complex **C** by extrusion of $CO_2$. Subsequently, **D** is formed by intramolecular nitrene transfer of **C** (from iron to sulfur), which finally releases product **3aa** and closes the catalytic cycle in the presence of **1a**. Ligand scrambling explains the




***Scheme 6.*** Proposed mechanistic pathways.

formation of intermediates **E**/**F**. In pathway **b**, intermediate **D** undergoes a second imidization process involving another molecule of dioxazolone **2a** to afford **E**, which gives the intermediate **F** by a subsequent intramolecular nitrene transfer. Finally, **3aa** is produced in the presence of **1a**. In both pathways, the initial formation of intermediate **B** explains the requirement of a proton on the sulfinamide nitrogen, which is consistent with the experimental result that *N*,*N*-disubstituted sulfinamides (**1r** and **1s**) did not react smoothly. Besides, the loss of HCl in this process provides an explanation of the lower conversion and chemoselectivity of the solution-based reactions: trapping HCl in the solvent cage may hamper the formation of intermediate **C** and favor the formation of the observed byproduct **4**.[21]

In summary, we present a mechanochemical synthesis of acylated sulfonimidamides by iron(II)-catalyzed nitrene transfer to sulfinamides. The method accommodates a wide range of sulfinamides bearing diverse substituents. Notably, this one-step, solvent-free procedure can be performed under ambient air conditions. Compared to its more conventional solvent-based counterpart, this mechanochemical approach exhibits impoved reactivity and chemoselectivity, revealing the potential of mechanochemistry as a promising technique for efficient and sustainable synthesis. Hydrolysis of sulfonimidamides under acidic conditions affords sulfonamides. Methylation and subsequent deprotection can lead to structurally diverse and synthetically valuable *N*-unsubstituted sulfonimidamides. Mechanistic investigations suggest the formation of iron nitrene intermediates.

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## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available in the Supporting Information of this article. Deposition Number CCDC-2302866 (for **3ja**), contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service

**Keywords:** Ball Mill · Iron Catalysis · Mechanochemistry · Nitrene Transfer · Sulfonimidamides

[1] For selected reviews and examples of applications of sulfonimidamides in medicinal chemistry, see: a) B. E. Cathers, J. V. Schloss, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1527–1532; b) P. K. Chinthakindi, T. Naicker, N. Thota, T. Govender, H. G. Kruger, P. I. Arvidsson, *Angew. Chem. Int. Ed.* **2017**, *56*, 4100–4109; c) G. C. Nandi, P. I. Arvidsson, *Adv. Synth. Catal.* **2018**, *360*, 2976–3001; d) S. R. Borhade, R. Svensson, P. Brandt, P. Artursson, P. I. Arvidsson, A. Sandström, *ChemMedChem* **2015**, *10*, 455–460; e) A. Benediktsdottir, L. Lu, S. Cao, E. Zamaratski, A. Karlen, S. L. Mowbray, D. Hughes, A. Sandström, *Eur. J. Med. Chem.* **2021**, *224*, 113699–113710; f) D.-D. Liang, N. Lional, B. Scheepmaker, M. Subramaniam, G. Li, F. M. Miloserdoc, H. Zuilhof, *Org. Lett.* **2023**, *25*, 5666–5670; g) F. Romanoc-Michailidis, C.-C. Hsiao, L. M. Urner, S. Jerhaoui, M. Surkyn, B. Miller, A. Vos, M. D. Blanco, R. Bueters, P. Vinken, M. Bekkers, D. Walker, B. Pietrak, W. Eyckmans, J. L. Dores-Sousa, S. J. Koo, W. Lento, M. Bauser, U. Philippar, F. J. R. Rombouts, *J. Med. Chem.* **2023**, *66*, 6122–6148 and references therein.

[2] For applications of sulfonimidamides in crop protection, see: C. Gnamm, A. Jeanguenat, A. C. Dutton, C. Grimm, D. P. Kloer, A. J. Crossthwaite, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3800–3806.

[3] A. D. Steinkamp, L. Schmitt, X. Chen, K. Fietkau, R. Heise, J. M. Baron, C. Bolm, *Skin Pharmacol. Physiol.* **2016**, *29*, 281–290.

[4] Y. Chen, C. J. Aurell, A. Pettersen, R. J. Lewis, M. A. Hayes, M. Lepisto, A. C. Jonson, H. Leek, L. Thunberg, *ACS Med. Chem. Lett.* **2017**, *8*, 672–677.

[5] S. Chowdhury, C. M. Dehnhardt, T. Focken, M. E. Grimwood, I. W. Hemeon, S. McKerrall, D. Sutherlin, (Genentech, Inc.). WO 2017172802, **2017**.

[6] N. Pemberton, H. Graden, E. Evertsson, E. Bratt, M. Lepisto, P. Johannesson, P. H. Svensson, *ACS Med. Chem. Lett.* **2012**, *3*, 574–578.

[7] a) C. Worch, C. Bolm, *Synthesis* **2008**, 739–742; b) S. Azzaro, M. Desage-El Murr, L. Fensterbank, E. Lacôte, M. Malacria, *Synlett* **2011**, 849–851; c) M. F. Maldonado, F. Sggelmeble, F. Bjarnemark, M. Svensson, J. Åhman, P. I. Arvidsson, *Tetrahedron* **2012**, *68*, 7456–7462; d) I. Sen, S. Sasmal, R. G. Hall, S. Pal, *Synthesis* **2016**, *48*, 3743–3752.

[8] a) C. Worch, C. Bolm, *Synlett* **2009**, 2425–2428; b) S. R. Borhade, A. Sandström, P. I. Arvidsson, *Org. Lett.* **2013**, *15*, 1056–1059; c) P. B. Wakchaure, S. R. Borhade, A. Sandström, P. I. Arvidsson, *Eur. J. Org. Chem.* **2015**, 213–219.

[9] a) P. H. Di Chenna, F. Robert-Peillard, P. Dauban, R. H. Dodd, *Org. Lett.* **2004**, *6*, 4503–4505; b) D. Leca, A. Toussaint, C. Mareau, L. Fensterbank, E. Lacôte, M. Malacria, *Org. Lett.* **2004**, *6*, 3573–3575; c) C. Fruit, F. Robert-Peillard, G. Bernardinelli, P. Müller, R. H. Dodd, P. Dauban, *Tetrahedron: Asymmetry* **2005**, *16*, 3484–3487; d) C. Liang, F. Robert-Peillard, C. Fruit, P. Müller, R. H. Dodd, P. Dauban, *Angew. Chem. Int. Ed.* **2006**, *45*, 4641–4644; e) F. Collet, R. H. Dodd, P. Dauban, *Org. Lett.* **2008**, *10*, 5473–5476; f) C. Liang, F. Collet, F. Robert-Peillard, P. Müller, R. H. Dodd, P. Dauban, *J. Am. Chem. Soc.* **2008**, *130*, 343–350; g) A. Lei, W. Liu, C. Liu, M. Chen, *Dalton Trans.* **2010**, *39*, 10352–10361; h) F. Robert-Peillard, P. H. Di Chenna, C. Liang, C. Lescot, F. Collet, R. H. Dodd, P. Dauban, *Tetrahedron: Asymmetry* **2010**, *21*, 1447–1457; i) Á. Beltrán, C. Lescot, M. Mar Díaz-Requejo, P. J. Pérez, P. Dauban, *Tetrahedron* **2013**, *69*, 4488–4492.

[10] a) O. García Mancheño, C. Bolm, *Beilstein J. Org. Chem.* **2007**, *3*, 25; b) C. Worch, I. Atodiresei, G. Raabe, C. Bolm, *Chem. Eur. J.* **2010**, *16*, 677–683.
[11] a) Y. Chen, *Synthesis* **2016**, *48*, 1019–1028; b) J. Feng, H. Liu, Y. Yao, C.-D. Lu, *J. Org. Chem.* **2022**, *87*, 5005–5016; c) S. Pan, M. T. Passia, X. Wang, P. Wu, D. Ma, C. Bolm, *Adv. Synth. Catal.* **2023**, *365*, 31–36.
[12] For selected reviews of sulfur imidation from sulfides and sulfoxides, see: a) V. Bizet, C. M. Hendriks, C. Bolm, *Chem. Soc. Rev.* **2015**, *44*, 3378–3390; b) J. A. Bull, L. Degennaro, R. Luisi, *Synlett* **2017**, *28*, 2525–2538; c) M. Andresini, A. Tota, L. Degennaro, J. A. Bull, R. Luisi, *Chem. Eur. J.* **2021**, *27*, 17293–17321; d) R. Luisi, J. A. Bull, *Molecules* **2023**, *28*, 1120–1135.
[13] For selected examples of sulfur imidations starting from sulfinamides, see: a) F. Izzo, M. Schäfer, R. Stockman, U. A. Lücking, *Chem. Eur. J.* **2017**, *23*, 15189–15193; b) E. L. Briggs, A. Tota, M. Colella, L. Degennaro, R. Luisi, J. A. Bull, *Angew. Chem. Int. Ed.* **2019**, *58*, 14303–14310; c) M. Ding, Z. X. Zhang, T. Q. Davies, M. C. Willis, *Org. Lett.* **2022**, *24*, 1711–1715.
[14] G. Proietti, J. Kuzmin, A. Z. Temerdashev, P. Dinér, *J. Org. Chem.* **2021**, *86*, 17119–17128.
[15] For selected examples and reviews on the use of dioxazolones as nitrene precursors in sulfur imidations, see: a) J. Sauer, K. K. Mayer, *Tetrahedron Lett.* **1968**, *9*, 319–324; b) V. Bizet, L. Buglioni, C. Bolm, *Angew. Chem. Int. Ed.* **2014**, *53*, 5639–5642; c) V. Bizet, C. Bolm, *Eur. J. Org. Chem.* **2015**, 2854–2860; d) L. Buglioni, V. Bizet, C. Bolm, *Adv. Synth. Catal.* **2014**, *356*, 2209–2213; e) C. M. M. Hendriks, P. Nürnberg, C. Bolm, *Synthesis* **2015**, *47*, 1190–1194; f) J.-J. Tang, X. Yu, Y. Wang, Y. Yamamoto, M. Bao, *Angew. Chem. Int. Ed.* **2021**, *60*, 16426–16435; g) K. M. van Vliet, B. de Bruin, *ACS Catal.* **2020**, *10*, 4751–4769; h) T. Shimbayashi, K. Sasakura, A. Eguchi, K. Okamoto, K. Ohe, *Chem. Eur. J.* **2019**, *25*, 3156–3180; i) Z. Bai, S. Zhu, Y. Hu, P. Yang, X. Chu, G. He, H. Wang, G. Chen, *Nat. Commun.* **2022**, *13*, 6445.
[16] For guiding references, see: a) S. Y. Hong, Y. Hwang, M. Lee, S. Chang, *Acc. Chem. Res.* **2021**, *54*, 2683–2700; b) Y. Park, S. Jee, J. G. Kim, S. Chang, *Org. Process Res. Dev.* **2015**, *19*, 1024–1029; c) J. Kweon, S. Chang, *Angew. Chem. Int. Ed.* **2021**, *60*, 2909–2914; d) H. Jung, J. Kweon, J.-M. Suh, M. H. Lim, D. Kim, S. Chang, *Science* **2023**, *381*, 525–532.
[17] For relevant overviews on mechanochemistry, see: a) M. T. J. Williams, L. C. Morrill, D. L. Browne, *ChemSusChem* **2022**, *15*, e202102157; b) D. Virieux, F. Delogu, A. Procheddu, F. Garcìa, E. Colacino, *J. Org. Chem.* **2021**, *86*, 13885–13894; c) K. J. Ardila-Fierro, J. G. Hernández, *ChemSusChem* **2021**, *14*, 2145–2162; d) S. Mateti, M. Mathesh, Z. Liu, T. Tao, T. Ramireddy, A. M. Glushenkov, W. Yang, Y. I. Chen, *Chem. Commun.* **2021**, *57*, 1080–1092; e) T. Friščić, C. Mottillo, H. M. Titi, *Angew. Chem. Int. Ed.* **2020**, *59*, 1018–1029; f) A. Porcheddu, E. Colacino, L. de Luca, F. Delogu, *ACS Catal.* **2020**, *10*, 8344–8394; g) M. Pérez-Venegas, E. Juaristi, *ACS Sustainable Chem. Eng.* **2020**, *8*, 8881–8893; h) W. Pickhardt, S. Grätz, L. Borchardt, *Chem. Eur. J.* **2020**, *26*, 12903–12911; i) K. Kubota, H. Ito, *Trends Chem.* **2020**, *2*, 1066–1081; j) I. N. Egorov, S. Santra, D. S. Kopchuk, I. S. Kovalev, G. V. Zyryanov, A. Majee, B. C. Ranu, V. L. Rusinov, O. N. Chupakhin, *Green Chem.* **2020**, *22*, 302–315; k) C. Bolm, J. G. Hernández, *Angew. Chem. Int. Ed.* **2019**, *58*, 3285–3299; l) E. Colacino, A. Porcheddu, C. Charnay, F. Delogu, *React. Chem. Eng.* **2019**, *4*, 1179–1188; m) J. L. Howard, Q. Cao, D. L. Browne, *Chem. Sci.* **2018**, *9*, 3080–3094; n) J. G. Hernández, C. Bolm, *ChemSusChem* **2018**, *11*, 1410–1420; o) D. Tan, T. Friščić, *Eur. J. Org. Chem.* **2018**, 18–33; p) J. G. Hernández, C. Bolm, *J. Org. Chem.* **2017**, *82*, 4007–4019; q) J. L. Do, T. Friscic, *ACS Cent. Sci.* **2017**, *3*, 13–19; r) D. Tan, L. Loots, T. Friščić, *Chem. Commun.* **2016**, *52*, 7760–7781; s) S. L. James, C. J. Adams, C. Bolm, D. Braga, P. Collier, T. Friščić, F. Grepioni, K. D. M. Harris, G. Hyett, W. Jones, A. Krebs, J. Mack, L. Maini, A. G. Orpen, I. P. Parkin, W. C. Shearouse, J. W. Steed, D. C. Waddell, *Chem. Soc. Rev.* **2012**, *41*, 413–447; t) E. Juaristi, C. G. Avila-Ortiz, *Synthesis* **2023**, *55*, 2439–2459; u) C. Patel, E. André-Joyaux, J. A. Leitch, X. M. de Irujo-Labalde, F. Ibba, J. Struijs, M. A. Ellwanger, R. Paton, D. L. Browne, G. Pupo, S. Aldridge, M. A. Hayward, V. Gouverneur, *Science* **2023**, *381*, 302–306; v) Y. S. Zholdassov, L. Yuan, S. Romero Garcia, R. W. Kwok, A. Boscoboinik, D. J. Valles, M. Marianski, A. Martini, R. W. Carpick, A. B. Braunschweig, *Science* **2023**, *380*, 1053–1058; w) I. d′Anciães, A. Silva, E. Bartalucci, C. Bolm, T. Wiegand, *Adv. Mater.* **2023**, https://doi.org/10.1022/adma.202304092.
[18] For a mechanochemical sulfonimidamide synthesis by a two-step protocol involving oxidative chlorination and amine substitution, see: S. Terhorst, T. Jansen, T. Langletz, C. Bolm, *Org. Lett.* **2022**, *24*, 4109–4113.
[19] For a mechanochemical intramolecular amidation involving an iron-catalyzed dioxazolone activation, see: P. Shi, Y. Tu, D. Kong, P. Wu, D. Ma, C. Bolm, *Angew. Chem. Int. Ed.* **2022**, *61*, e202204874.
[20] T. Jansen, L. Adarve Cardona, C. Bolm, to be published.
[21] Y.-Z. Ji, C. Zhang, J.-H. Wang, H.-J. Li, Y.-C. Wu, *Org. Biomol. Chem.* **2021**, *19*, 9291–9298.

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