

Letter

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# Iron-Catalyzed Amination of Sulfides and Sulfoxides with Azides in Photochemical Continuous Flow Synthesis.

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KEYWORDS. sulfilimines, sulfoximines, iron(III) acetylacetonate, stereospecific amination, nitrene

**ABSTRACT:** A photochemical (UVA) continuous flow process for the amination of thioethers and sulfoxides was performed with trichloroethoxysulfonyl azide in presence of catalytic iron(III) acetylacetonate. Aromatic and aliphatic sulfilimines and sulfoximines were produced in high yields and short reaction times. The reaction with chiral sulfoxides was stereospecific, producing enantioenriched sulfoximines in excellent yields.

Sulfilimines and sulfoximines are highly valuable building blocks due to their importance in biologically active agents (Figure 1).<sup>1</sup> While azides are the most commonly used reagents to aminate sulfides and sulfoxides to yield sulfilimines and sulfoximines,<sup>2,3,4</sup> their application often raises safety concerns, as many azide reagents are highly energetic and may be explosive.<sup>5</sup> Strong acids and high temperature are typically required to undergo metal-free amination reactions.<sup>6,7</sup> Metal-catalyzed processes employing iron<sup>3a,b,f</sup> and ruthenium<sup>2a,3c,d,e</sup> complexes were reported to proceed under milder reaction conditions, albeit for longer reaction times (12–24 h). In addition, an excess of substrate was required for iron-catalyzed or mediated reaction.<sup>3a,b,f</sup>



Figure 1. Selected Examples of Biologically Relevant Sulfilimines and Sulfoximines

To the best of our knowledge, there are no accounts that combine the application of a commercially available catalyst with a stable azide reagent to enable a broad substrate scope and a short reaction time (<2 h). Although the photochemical decomposition of azides to produce nitrenes is known,<sup>8</sup> their subsequent exploitation in synthetic methods to produce nitrogen-containing molecules has not yet been reported. We reasoned that the photochemical decomposition of azide reagents could be assisted by the use of a metal catalyst. Furthermore, continuous flow synthesis could be advantageous to decrease the reaction time by maximizing the light exposure. Herein, we disclose the photochemical continuous flow synthesis of sulfilimines and sulfoximines with trichloroethoxysulfonyl azide using catalytic iron(III) acetylacetonate that proceeds in under 90 min.

Continuous flow synthesis is an emerging technology that has numerous advantages over conventional batch transformations.9 Benefits include enhanced heat and mass transfer, reduced reaction volumes, as well as improved reagent mixing. The combination of these, in addition to the fact the build up of hazardous intermediates is mitigated, lead to enhanced reaction safety parameters.<sup>10</sup> Continuous flow synthesis has also been demonstrated to be efficient in photochemical processes due to improved light penetration.<sup>11</sup> We hypothesized that a continuous flow process could be used to decompose azide reagents to produce reactive metal nitrene species that would undergo amination of sulfides and sulfoxides. A variety of inexpensive, readily available metal complexes and azide reagents were tested for the amination of thioanisole using a Luzchem LZC-5 photoreactor<sup>11h</sup> equipped with 8 x 8W black light blue UVA (365 nm) tubes.<sup>12,13</sup> Whereas no reaction was observed with copper(II) and cobalt(II) acetylacetonate, the desired product was obtained with corresponding iron catalysts. Iron(III) proved superior to iron(II) acetylacetonate.<sup>14</sup> Analysis by UV spectroscopy revealed that among the tested metal complexes, only Fe(acac)<sub>3</sub> wascapable of absorbing UVA light. Using trichloroethoxy-

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sulfonyl azide (TcesN<sub>3</sub>)<sup>15,16</sup> sulfilimine **1** derived from thioanisole was produced in 90% yield with a residence time ( $t_R$ ) of 150 min. In sharp contrast, no photodecomposition of aryl and alkyl azides (*p*-tolN<sub>3</sub> and BnN<sub>3</sub>) was observed under the same catalytic conditions and starting material was recovered. Conversely, acyl azides (CBzN<sub>3</sub> or TrocN<sub>3</sub>) were decomposed, but only the Troc-protected sulfilimine was produced albeit in low yield. Only trace amounts of the desired product were obtained using TsN<sub>3</sub>. In the absence of catalyst, only traces of sulfilimine **1** were produced and TcesN<sub>3</sub> was not decomposed in the absence of UV light.

To accelerate the rate of the reaction (thus decrease the residence time), a novel photoreactor was designed to maximize the exposure of the tubing to the light (Figure 2). The PFA tubing was wrapped around four small metal tubes to create a big cylinder around the light bulb. Three cylinders were connected in a row to a Syrris pump, and the system could be safely operated in laboratory fume hood using an aluminum foil-lined photobox.<sup>17</sup>



#### Figure 2. Capillary Cylinder Photoreactor

The residence time and the catalyst loading were optimized using the described photoreactor for the amination of thioanisole with TcesN<sub>3</sub>. The use of 5 mol % of Fe(acac)<sub>3</sub> in a 90 min residence time afforded the desired product in 94% yield. The optimal result was obtained using 10 mol % of the iron catalyst and 50 min residence time (Table 1, entry 1). Given the concentration and the flow rate, the productivity of the process was calculated to produce 1.34 g/h of sulfilimine **1**. The reaction time could be even shorter if 20 mol% of Fe(acac)<sub>3</sub> was used, affording 89% of sulfilimine **1** with a residence time of 15 min.

The substrate scope was then investigated (Table 1). Phenyl thioethers containing larger alkyl groups were reacted in good yields (entries 2, 3). Electron withdrawing and donating aryl substituents were compatible with the reaction conditions (entries 4, 5). Sulfilimine **6** was produced in 86% yield, with no side-reaction on the boronate substituent (entry 6). Ortho-substituted thioethers are also compatible (entry 7) Sulfides containing pyridine and thiophene moiety produced desired sulfilimines **8** and **9**, in 75% and 71% yield respectively (entries 8, 9). With less reactive thioethers, it is possible to perform two cycles. This strategy was used to synthesize pyrimidinesubstituted sulfilimine **10** (entry 10).



Entry <sup>a</sup>	Product	t <sub>R</sub> (min)	Yield (%) <sup>b</sup>
1	<sup>©</sup> NTces R = Me (1)	50 <sup>c</sup>	94
2	$H = n - C_{14} H_{29} (2)$	$90^d$	70
3 <sup>e</sup>	R = <i>i</i> -Pr ( <b>3</b> )	$90^{d}$	84
4	<sup>⊝</sup> NTces R = F (4)	90 <sup>d</sup>	97
5 <sup>e</sup>		$90^d$	98
6 <sup>e</sup>	R = BPin (6)	90 <sup>d</sup>	86
7 <sup>e</sup>	<sup>⊖</sup> NTces <sup>⊕</sup> S Me Br 7	90 <sup>d</sup>	98
8	ONTCES OS N 8	90 <sup>d</sup>	75
9 <sup>e</sup>	<sup>⊖</sup> NTces ⊕S S B 9	90 <sup>d</sup>	71
10 <sup>f</sup>	CI CI CI CI CI CI CI CI CI CI	90 <sup>d</sup>	56
11	<sup>⊝</sup> NTces ⊕S 11	50 <sup>c</sup>	>98
12	12 <sup>O</sup> NTces	50 <sup>c</sup>	86
13	MeO MeO MHBoc	50 <sup>c</sup>	83
14	<sup>⊖</sup> NTces ⊕S 14	50 <sup>c</sup>	>98
15	15 <sup>O</sup> NTces ⊕S	90 <sup>d</sup>	73

<sup>a</sup> All experiments were conducted with 0.17 mmol of thioether in 2 mL of solvent (C = 0.085 mmol/min) using 37.5 mL PFA tubing (ID 1 mm). <sup>*b*</sup> Isolated yields. <sup>*c*</sup> Flow : 0.75 mL/min. <sup>*d*</sup> Flow : 0.42 mL/min. <sup>*e*</sup> 20 mol % of Fe(acac)<sub>3</sub>. <sup>*f*</sup> 2 cycles of 90 min using 2 x 20 mol % of Fe(acac)<sub>3</sub>.

The reaction conditions were particularly suitable to produce often difficult to access alkyl substituted sulfilimines.<sup>18</sup> The reaction of tetrahydrothiophene with TcesN<sub>3</sub> afforded sulfilimine **11** in a quantitative yield with a residence time of 50 min (entry 11). Long alkyl chains were also tolerated, as well as functional groups such as an ester and a Boc-protected amine (entries 12, 13). More sterically hindered cyclohexylmethyl sulfilimine **14** was also produced in a quantitative yield (entry 14). The reaction of an alkylthioether containing a terminal double bond produced the desired sulfilimine **15** in 73% yield, with no side-reaction on the double bond (entry 15).

It is also possible to use a chiral azide reagent, 2phenyltrichloroethoxyacyl azide **16** (PhTrocN<sub>3</sub>)<sup>19</sup> to produce a 1:1 mixture of diastereomers of sulfilimines **17** that can be separated (Scheme 1). This method is a straightforward facile process to access both enantiomers of the desired chiral molecule and should find many applications in pharmaceutical industries.

Scheme 1. Iron-Catalyzed Amination of Thioanisole with 2-Phenyltrichloroethoxyacyl azide.



The amination of sulfoxides was next studied. Using the Luzchem UV reactor with TcesN<sub>3</sub> and 10 mol % Fe(acac)<sub>3</sub>, the amination of phenyl methyl sulfoxide proceeded in only 6% yield with a residence time of 150 min. Gratifyingly, using the capillary cylinder photoreactor shown in Figure 2, the desired sulfoximine **18** was obtained in 87% yield while decreasing the residence time to 90 min (Table 2, entry 1). The scale-up of the reaction was very easy, and 1 gram (91% yield) of sulfoximine **18** could be synthetized in 90 min.<sup>20</sup> Under the same reaction conditions, the *p*-fluoro-substituted phenyl methyl sulfoximine **19** was isolated in 85% yield, while the use of 20 mol % of Fe(acac)<sub>3</sub>, afforded 95% of the desired product (entries 2, 3). Alkyl sulfoxides were highly reactive affording the desired sulfoximines in 87–97% yield (entries 4-6).

The amination of sulfoxides was found to be stereospecific. Starting with a 95:5 er of phenylmethyl sulfoxide, sulfoximine R-18 was isolated in 87% yield with the same enantiomeric ratio (Scheme 2). The Tces protecting group could be easily cleaved from sulfoximine **18** using zinc in acetic acid to afford free sulfoximine **23** in high yield. Table 2. Iron-Catalyzed Amination of Sulfoxides with  $\mbox{Tces}N_3.$ 





<sup>*a*</sup> All experiments were conducted with 0.17 mmol of thioether in 2 mL of solvent (C = 0.085 mmol/min) using 37.5 mL PFA tubing (ID 1 mm) and a flow rate of 0.42 mL/min. <sup>*b*</sup> Isolated yields. <sup>*c*</sup> 20 mol % of Fe(acac)<sub>3</sub>.

#### Scheme 2. Stereospecific Iron-Catalyzed Amination of Thioanisole Sulfoxide and Synthesis of the Free Sulfoxime.



The reaction optimization had revealed that both UVA light and Fe(acac)<sub>3</sub> were required for a productive process. In addition, the structure of the azide reagent strongly influenced the reaction outcome. While absorption of UVA light by Fe(acac)<sub>3</sub> was observed, none of the azide reagents explored demonstrated absorption at  $\lambda > 320$  nm.

In conclusion, we have developed an efficient continuous flow process to synthesize sulfilimines and sulfoximines in high yields using readily available azide reagent and catalyst. The reaction proceeds at room temperature with a residence time below 2 h using UVA light. A chiral reagent is also compatible with these reaction conditions to produce easily separable diastereomeric sulfilimines. The amination of sulfoxides is stereospecific and the Tces group is easy to cleave. The development of an enantioselective process using a chiral iron catalyst is currently under investigation.

# **ASSOCIATED CONTENT**

#### Supporting Information

Complete experimental and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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## REFERENCES

(1) (a) Vanacore, R.; Ham, A.-J. L.; Voehler, M.; Sanders, C. R.; Conrads, T. P.; Veenstra, T. D.; Sharpless, K. B.; Dawson, P. E.; Hudson, B. G. *Science* **2009**, *325*, 1230. (b) Weiss, S. J. *Nature Chem. Bio.* **2012**, *8*, 740. (c) Lücking, U. *Angew. Chem. Int. Ed.* **2013**, *52*, 9399. (d) Zhou, S.; Yan, T.; Li, Y.; Jia, Z.; Wang, B.; Zhao, Y.; Qiao, Y.; Xiong, L.; Li, Y.; Li, Z. *Org. Biomol. Chem.* **2014**, *12*, 6643. (e) Zhou, S.; Li, *Z. J. Phys. Chem. Biophys.* **2015**, *5*, 1

(2) Reviews: (a) Driver, T. G. *Org. Biomol. Chem.* **2010**, *8*, 3831. (b) Uchida, T.; Katsuki, T. *Chem. Rec.* **2014**, *14*, 117. (c) Bizet, V.; Hendriks, C. M. M.; Bolm, C. *Chem. Soc. Rev.* **2015**, *44*, 3378.

(3) For selected references using azides: (a) Bach, T.; Korber, C. *Tetrahedron Lett.* **1998**, *39*, 5015. (b) Bach, T.; Körber, C. *Eur. J. Org. Chem.* **1999**, *1999*, 1033. (c) Murakami, M.; Uchida, T.; Katsuki, T. *Tetrahedron Lett.* **2001**, *42*, 7071. (d) Tamura, Y.; Uchida, T.; Katsuki, T. *Tetrahedron Lett.* **2003**, *44*, 3301. (e) Uchida, T.; Tamura, Y.; Ohba, M.; Katsuki, T. *Tetrahedron Lett.* **2003**, *44*, 7965. (f) Liu, Y.; Che, C.-M. *Chem. Eur. J.* **2010**, *16*, 10494. (g) Farwell, C. C.; McIntosh, J. A.; Hyster, T. K.; Wang, Z. J.; Arnold, F. H. J. Am. Chem. Soc. **2014**, *136*, 8766.

(4) For selected references using alternative reagents: (a) Mancheño, O. G.; Bolm, C. Org. Lett. 2006, 8, 2349. (b) Mancheño, O. G.; Bolm, C. Chem. Eur. J. 2007, 13, 6674. (c) Mancheño, O. G.; Dallimore, J.; Plant, A.; Bolm, C. Org. Lett. 2009, 11, 2429. (d) Wang, J.; Frings, M.; Bolm, C. Angew. Chem. Int. Ed. 2013, 52, 8661. (e) Bizet, V.; Buglioni, L.; Bolm, C. Angew. Chem. Int. Ed. 2014, 53, 5639. (f) Bizet, V.; Bolm, C. Eur. J. Org. Chem. 2015, 2015, 2854. (g) Dannenberg, C. A.; Bizet, V.; Bolm, C. Synthesis 2015, 47, 1951. (h) Zenzola, M.; Doran, R.; Luisi, R.; Bull, J. A. J. Org. Chem. 2015, 80, 6391.

(5) This is the case for  $BocN_3$ , reported in the iron-catalyzed amination of sulfides and sulfoxides, see 3a and 3b for details.

(6) Selected examples and references therein: (a) Bentley, H.
R.; McDermott, E. E.; Pace, J.; Whitehead, J. K.; Moran, T. *Nature* 1949, *163*, 675. (b) Bentley, H. R.; McDermott, E. E.; Whitehead, J. K. Proc. R. Soc. London, Ser. B 1951, 138, 265. (c) Bauer, V. J.; Fanshawe, W. J.; Safir, S. R. *J. Org. Chem.* 1966, *31*, 3440. (d) Shiner, C. S.; Berks, A. H. *J. Org. Chem.* 1988, *53*, 5542. (e) Brandt, J.; Gais, H.-J. *Tetrahedron: Asymmetry* 1997, *8*, 909. (f) Gaillard, S.; Papamicaël, C.; Dupas, G.; Marsais, F.; Levacher, V. *Tetrahedron* 2005, *61*, 8138.

(7) During the course of writing this manuscript, the following paper appeared describing the amination of a sulfoxide in continuous flow with  $TMSN_3$  and sulfuric acid : Gutmann, B.; Elsner, P.; O'Kearney-McMullan, A.; Goundry, W.; Roberge, D. M.; Kappe, C. O. *Org. Process Res. Dev.* **2015**, *19*, 1062.

(8) (a) Bucher, G., Photochemical reactivity of azides. In *CRC* Handbook of Organic Photochemistry and Photobiology (2nd Edition), CRC Press LLC: 2004; pp 44-1. (b) Gritsan, N.; Platz, M., Photochemistry of azides: the azide/nitrene interface. In Organic Azides: Syntheses and Applications (eds S. Bräse and K. Banert), John Wiley & Sons Ltd.: 2010; pp 311. (c) Wentrup, C. Acc. Chem. Res. **2011**, 44, 393. (d) Kubicki, J.; Zhang, Y.; Xue, J.; Luk, H. L.; Platz, M. Phys. Chem. Chem. Phys. **2012**, *14*, 10377.

(9) Reviews: (a) Geyer, K.; Gustafsson, T.; Seeberger, P. H. *Synlett* **2009**, 2382. (b) Webb, D.; Jamison, T. F. *Chem. Sci.* **2010**, *1*, 675. (c) Hartman, R. L.; McMullen, J. P.; Jensen, K. F. *Angew. Chem., Int. Ed.* **2011**, *50*, 7502. (d) Hessel, V.; Kralisch, D.; Kockmann, N.; Noel, T.; Wang, Q. *ChemSusChem* **2013**, *6*, 746. (e) Newman, S. G.; Jensen, K. F. *Green Chem.* **2013**, *15*, 1456. (f) Brzozowski, M.; O'Brien, M.; Ley, S. V.; Polyzos, A. Acc. Chem. Res. **2015**, *48*, 349. (g) Finelli, F. G.; Miranda, L. S. M.; de Souza, R. O. M. A. *Chem. Commun.* **2015**, *51*, 3708. (h) Gutmann, B.; Cantillo, D.; Kappe, C. O. *Angew. Chem., Int. Ed.* **2015**, *54*, 6688.

(10) Selected recent references: (a) Kleinke, A. S.; Jamison, T.
F. Org. Lett. 2013, 15, 710. (b) Snead, D. R.; Jamison, T. F.
Chem. Sci. 2013, 4, 2822. (c) Gemoets, H. P. L.; Hessel, V.;
Noël, T. Org. Lett. 2014, 16, 5800. (d) Pinho, V. D.; Gutmann,
B.; Miranda, L. S. M.; de Souza, R. O. M. A.; Kappe, C. O. J.
Org. Chem. 2014, 79, 1555. (e) Wu, J.; Kozak, J. A.; Simeon, F.;

Hatton, T. A.; Jamison, T. F. Chem. Sci. 2014, 5, 1227. (f) Wu, J.; Yang, X. Q.; He, Z.; Mao, X. W.; Hatton, T. A.; Jamison, T. F. Angew. Chem., Int. Ed. 2014, 53, 8416. (g) Zhang, P.; Russell, M. G.; Jamison, T. F. Org. Process Res. Dev. 2014, 18, 1567. (h) Snead, D. R.; Jamison, T. F. Angew. Chem., Int. Ed. 2015, 54, 983. (i) Hsueh, N.; Clarkson, G. J.; Shipman, M. Org. Lett. 2015, 17, 3632. (h) Jong, T.; Bradley, M. Org. Lett. 2015, 17, 422. (j) Lau, S.-H.; Galván, A.; Merchant, R. R.; Batilocchio, C.; Souto, J. A.; Berry, M. B.; Ley, S. V. Org. Lett. 2015, 17, 3218. (k) Matthies, S.; McQuade, D. T.; Seeberger, P. H. Org. Lett. 2015, 17, 3670.

(11) (a) Gutierrez, A. C.; Jamison, T. F. Org. Lett. 2011, 13, 6414. (b) Oelgemoller, M.; Shvydkiv, O. Molecules 2011, 16, 7522. (c) Knowles, J. P.; Elliott, L. D.; Booker-Milburn, K. I. Beilstein J. Org. Chem. 2012, 8, 2025. (d) Shen, B.; Bedore, M. W.; Sniady, A.; Jamison, T. F. Chem. Commun. 2012, 48, 7444. (e) Tucker, J. W.; Zhang, Y.; Jamison, T. F.; Stephenson, C. R. J. Angew. Chem., Int. Ed. 2012, 51, 4144. (f) Zhang, A.; Kuwahara, Y.; Hotta, Y.; Tsuda, A. Asian J. Org. Chem. 2013, 2, 572. (g) Zhang, Y.; Blackman, M. L.; Leduc, A. B.; Jamison, T. F. Angew. Chem., Int. Ed. 2013, 52, 4251. (h) Caron, A.; Hernandez-Perez, A. C.; Collins, S. K. Org. Process Res. Dev. 2014, 18, 1571.

(12) UVA is the safest of the three spectra of the UV light, and blacklights blue are used in many applications including dermatology, forensics, night clubs, etc.

(13) See supporting information for the optimization table.

(14) Fe(acac)<sub>2</sub>: 19%. No reaction was observed with hexafluoroacac iron(III) catalyst. Lower yields (79%) were observed with the more sterically hindered Fe(dibm)<sub>3</sub> (dibm : diisobutyrylmethane), Lo, J. C.; Gui, J.; Yabe, Y.; Pan, C.-M.; Baran, P. S., *Nature* **2014**, *516*, 343.

(15) TcesN<sub>3</sub> was initially developed by X. Peter Zhang to perform cobalt-catalyzed aziridination reactions: Subbarayan, V.; Ruppel, J. V.; Zhu, S.; Perman, J. A.; Zhang, X. P. *Chem. Commun.* **2009**, 4266. TcesN<sub>3</sub> is readily available from trichloroethanol.

(16) TGA-DSC analysis of TcesN<sub>3</sub> is reported in the supporting information. TcesN<sub>3</sub> should not be heated above 70 °C, as moderately endothermic evaporation started to occur at that temperature. TcesN<sub>3</sub> displayed a strong endothermic decomposition at 130 °C.

(17) The cost of the material for this home made photoreactor was less than 75 US\$. See supporting information for details and other pictures.

(18) (a) Lebel, H.; Piras, H.; Bartholoméüs, J. Angew. Chem.
Int. Ed. 2014, 53, 7300. (b) Lebel, H.; Piras, H. J. Org. Chem.
2015, 80, 3572.

(19) TGA-DSC analysis of PhTrocN<sub>3</sub> is reported in the supporting information. PhTrocN<sub>3</sub> displayed a strong exothermic decomposition at 150 °C.

(20) The productivity of the reaction is of 830 mg/hour, which correspond to ~20 g/day. See supporting information for details.

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