

Figure 4. Aniline scope for deaminative chlorosulfonylation. Products isolated as sulfonamides with pyrrolidine as nucleophile. Reaction conditions = 0.500 mmol aniline/amino heterocycle, 0.500 mmol $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$, 0.500 mmol $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, 0.500 mmol CuCl , 2.5 mL MeCN , 1.0 mmol HCl (4.0 M in 1,4-dioxane), 5.00 mmol SO_2 (3.00 M in MeCN) at 40°C for 16 h; then 2.00 mmol pyrrolidine at 23°C for 1 h. ^aIsolated on a 0.1 mmol scale. ^bIsolated on 10 mmol scale. ^cWas isolated as sulfonyl chloride.

previously described.⁸ The reduction of KNO_3 with SO_2 proceeds at 85°C .⁸ Since the concentration of SO_2 at 85°C is sufficient to give high yields of sulfonic acids, but only results in low yields of sulfonyl chlorides, we hypothesize that the sulfonic acid formation from aryldiazoniums does not proceed by initial formation of the sulfonyl chloride with SO_2 , followed by hydrolysis with water, but rather by direct conversion of the diazonium salt to the sulfonic acid. Control experiments in the absence of HCl (or any other chloride source) delivered the sulfonic acid **44** in 42% yield (Tables S17–S18), which further supports that the deaminative sulfonic acid formation can proceed without passing through a sulfonyl chloride intermediate. Due to the absence of any copper species for the deaminative sulfonic acid synthesis, Sandmeyer chlorination as a potential side reaction is not observed even in the presence of

HCl . Based on quantum chemical calculations, we propose that the sulfonic acid formation from the diazonium salt proceeds via initial reduction of the diazonium salt by sulfite, formed from the previously described fragmentation of the meta-bisulfite.⁴² The sulfite radical anion can subsequently react with the diazenyl radical ($\text{Ar}-\text{N}_2^\cdot$) to form the sulfonic acid in a single step under the extrusion of dinitrogen (Figure S13). When the deaminative sulfonic acid synthesis was carried out in the presence of radical traps, the respective radical addition adduct was observed (Figures S6–S7).

When the deaminative sulfonylation was monitored by ^1H NMR spectroscopy, no formation of sulfonyl chloride or other intermediates was detected in significant concentrations apart from aniline starting material and sulfonic acid reaction product (Figure S8). A significant change of the ^1H chemical

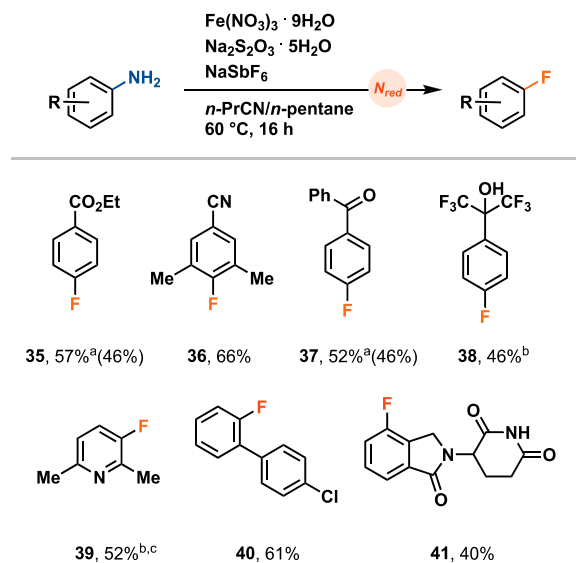


Figure 5. Aniline scope for the direct deaminative fluorination. Reaction conditions = 0.500 mmol aniline/amino heterocycle, 0.600 mmol $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$, 1.50 mmol NaSbF_6 , 1.00 mmol $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, 0.625 mL of $n\text{-PrCN}$, 0.625 mL of $n\text{-pentane}$, at 60°C for 16 h (a) isolated on 0.1 mmol scale (b) yield determined by ^1H NMR spectroscopy due to the volatility of compound (c) AgSbF_6 used instead of NaSbF_6 .

shift of the aromatic signals of the starting material and product was observed, which could result from a change in the degree of protonation of the aniline. Analysis of the reaction mixture by ^{17}O NMR spectroscopy before and after heating for 18 h showed the formation of sulfate, presumably as terminal reaction product from the nitrate reduction with SO_2 (Figure S10). By ^{14}N NMR spectroscopy, the formation of nitrite or other nitrogen species was not detected, which is consistent with the formation of NO_2 as a product of the nitrate reduction process (Figure S11). Direct conversion of electron-rich, electron-neutral, and electron-deficient anilines and amino heterocycles to the respective sulfonic acids was achieved with the KNO_3 , $\text{Na}_2\text{S}_2\text{O}_5$, and HCl -based protocol (Figure 6). Complex anilines were tolerated, of which the corresponding diazonium salts cannot be easily isolated or accumulated (47 and 50).⁸ Additionally, substrates that contain functional groups that are prone to oxidation and therefore do not tolerate nitrite,⁴⁵ such as tertiary amines, were successfully functionalized with the KNO_3 -based procedure (49). The simple reaction set up of mixing all solid reagents followed by addition of all liquid reagents at 25°C provides robust access to the sulfonic acids from anilines.

CONCLUSIONS

In conclusion, we have demonstrated that inexpensive $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (30.0€ per kg, Carl Roth) can generate NO_2 through nitrate reduction with thiosulfate at room temperature (25°C), which enables the use of the nitrate reduction strategy for the *in situ* generation of aryl diazonium salts below 85°C . The iron nitrate reduction was utilized for the deaminative chlorosulfonylation of a variety of structurally and electronically diverse anilines and amino heterocycles, giving access to multiple sulfur-based functional groups directly

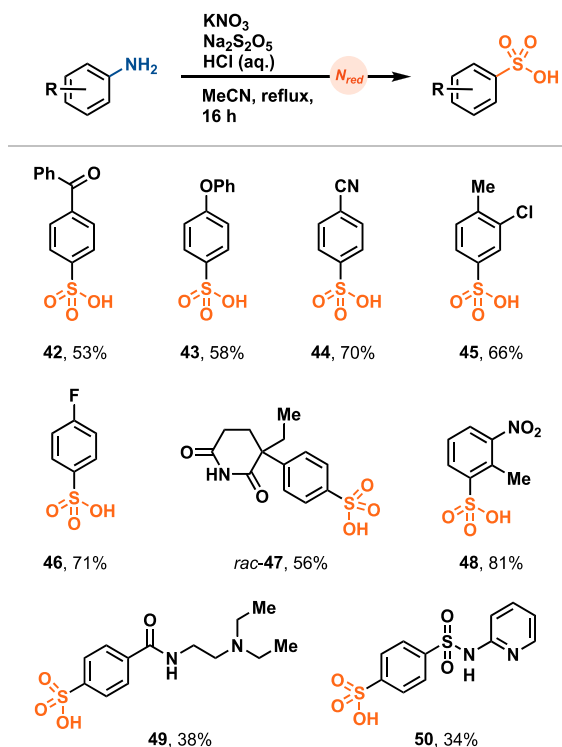


Figure 6. Aniline scope for direct deaminative sulfonic acid synthesis. Reaction conditions = 0.200 mmol aniline/amino heterocycle, 0.600 mmol KNO_3 , 0.500 mmol $\text{Na}_2\text{S}_2\text{O}_5$, 0.400 mmol HCl (aq. 9.25%), and 1.0 mL of MeCN , at 85°C for 16 h.

from the corresponding aromatic amines, without accumulation of the respective diazonium salt. The deaminative fluorination was presented as an additional application of Fe-mediated nitrate reduction. We envision that the iron nitrate reduction will also enable other deaminative functionalization reactions that require close to ambient temperature. Additionally, we described a deaminative sulfonic acid synthesis directly from anilines as a previously unknown transformation.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.4c17981>.

Experimental and computational procedures, spectroscopic data, NMR spectra of all products (PDF)

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