**Homogeneous Catalysis**

**Dibenzothiophenesulfilimines: A Convenient Approach to Intermolecular Rhodium-Catalysed C–H Amidation**

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**Abstract:** A sulfilimine-based Group 9 transition-metal-catalysed C–H amidation procedure is reported. Dibenzothiophene-based sulfilimines were shown to constitute a class of novel amidation reagents which enable the transfer of a wide range of N-sulfonyl and N-acyl moieties. It was demonstrated that sulfilimines, which are easily accessible from cheap reagents, are safe-to-handle and represent broadly applicable amidation reagents. The dibenzothiophene can be recycled after use. The C–H amidation was shown to proceed with high selectivity and gave the mono-amidated products, mostly in good to excellent yields.

Nitrogen-containing groups constitute key structural motifs in a great number of natural products and synthetically relevant structures. The introduction of the nitrogen moiety can be effected by means of cross-coupling strategies such as the palladium-catalysed Buchwald–Hartwig amination,[1] or the copper-mediated Ullmann,[2] or Chan Lam-type[3] couplings. While this approach is highly efficient and widely applicable, it necessitates a pre-functionalisation of the substrate and, due to the generation of stoichiometric amounts of by-products, entails the disadvantage of a low atom economy.[4]

Direct amidation of C–H bonds provides a complementary strategy for the introduction of nitrogen-possessing moieties, a strategy not relying on the inherent reactivity of functional groups but rather enabling a metal-catalysed activation of relatively inert C–H bonds. It is possible to use amines without pre-functionalisation or amides as amino sources, but this requires the presence of stoichiometric amounts of external oxidants and thus significantly limits the functional group tolerance of the procedure. To circumvent this drawback, a number of pre-activated amidating reagents have been developed, bearing polarised N–X bonds that can be oxidatively cleaved by metal catalysts.[5] Commonly employed amidation reagents include for instance imidiodiones,[6] hydroxylamines,[7] amidobenzodioxolones[8] or organic azides.[9]

Previous studies have shown that the photolytic cleavage of the S–N bond in sulfilimines leads to the intermediate generation of nitrenes that can be trapped by alkenes or phosphines.[10] Furthermore, a variety of heterocycles have been synthesised employing sulfilimine-based reagents as key intermediates in gold-catalysed transformations.[11] Donor-substituted sulfoximines have lately been shown to serve as methyl nitrene precursors in ruthenium-catalysed [2+2+2+1] cycloaddition reactions that furnish highly substituted pyrroles in good to excellent yields.[12] Very recently, it has been shown that sulfilimines can serve as nitrene precursors in intramolecular metal-free, light-mediated C–H amidation reactions enabling the mild and efficient synthesis of carbazoles.[13]

In the light of these studies, we envisioned sulfilimines to be potent, bench-stable and convenient intermolecular nitrene transfer reagents in C–H amidation reactions. To evaluate the steric and electronic properties required to efficiently transfer the nitrogen moiety, we screened several N-tosyl-substituted sulfilimines 1a–1d and sulfoximines 1e–1f as well as the N-methyl-substituted sulfoximine 1g highlighted by Yamamoto et al.[12] The [Cp*RhCl₂]-catalysed C–H amidation of 2-phenylpyridine (2-ppy) was chosen as a model system (Scheme 1).

While all other sulfilimines and sulfoximines showed no conversion of 2-ppy, only the dibenzothiophene (DBT)-based sulfilimine 1a proved to be a suitable nitrene surrogate for this transformation. This highlights the intricate interplay of electronic effects leading to a labile S–N bond while maintaining a sufficiently high nucleophilicity of the nitrogen towards the transition-metal centre. Interestingly, this is in accord with recent reports highlighting the extraordinary electronic structure of DBT-based reagents as electrophilic alkylnyl or aryl transfer reagents.[14]

Then we studied the scope of this catalysis reaction with respect to different metals. We found the general amidation method to be easily conducted by employing Group 9 transition-metal catalysts in the oxidation state +III. Cobalt, rhodium

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and iridium were all able to catalyse the amidation of 2-phenylpyridine with N-tosyl dibenzothiophene sulfilimine (DBTNTs 1a) in the presence of AgSbF₆ and a base under relatively mild conditions (Table 1). Note that while the rhodium-catalysed reaction resulted in the highest isolated yield of 2a, it was also possible to use a high valent cobalt(III) species as a catalyst. This highlights the versatility of the presented reagent, considering that the utilisation of the significantly cheaper first-row transition metal was shown to lead to unsatisfactory results in some C–H activation procedures. \[15\]

The scope of C–H activation reactions is often limited with respect to the directing groups enabling the necessary coordination geometry for an efficient subsequent activation step. We amidated a range of different precursors 2a–f with DBTNTs to evaluate the performance of our procedure with different directing groups (Scheme 2). The reactions were carried out at 80 °C over a period of 36 h, employing 4 mol% catalyst loading of \([\text{Cp*RhCl}_2]\), 16 mol% of AgSbF₆ and 10 mol% of KOAc. The given systems performed with fair to excellent yields of 46% to 98%. The performance does, however, drop with weaker directing groups. Isobutyrophenone could only be amidated with a poor yield of 14% (2f). As our system was stable towards harsher conditions, we were able to show for example 2d that switching to 1,1,2,2-tetrachloroethane (TCE) and heating to 120 °C can be used to overcome the limitations of poor directing groups to achieve an excellent yield (93%). Furthermore, we studied whether the use of DBTNTs as nitrene surrogate impairs the activation of more challenging sp² or even sp³ C–H bonds. In this context, 2g–j were chosen as representative examples of different bonding situations. In comparison to known syntheses of such systems, \[16\] we observed comparable or even superior yields in all cases.

The accessibility and ease of handling of the transfer reagents is an important factor for useful C–H amidation protocols. The N-tosyl dibenzothiophene sulfilimine can be easily synthesised by condensation of commercially available chloramine-T with dibenzothiophene, followed by an aqueous work-up without the necessity of chromatographic purification. We utilised a simple three-step one-pot procedure to access a range of differently substituted dibenzothiophene sulfilimines in good yields from very affordable starting materials. Commercially available dibenzothiophene oxide can be converted to the sulfilimine with the corresponding amides after activation of the sulfoxide with trifluoroacetic anhydride (TFAA) (Scheme 3). \[17\] The dibenzothiophene oxide can also be easily prepared from cheap dibenzothiophene by treatment with hy-

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**Table 1.** Activity of different Group 9 transition-metal catalysts in the C–H amidation of 2-ppy with DBTNTs 1a.

| Entry | Catalyst | Solvent | [Cat.](equiv) | AgSbF₆(equiv) | t[h] | Yield [%] |
|-------|----------|---------|---------------|---------------|------|----------|
| 1     | \([\text{Cp*Co(CO)}_2]_2\) | DCE     | 0.05          | 0.10          | 36   | 82       |
| 2     | \([\text{Cp*RhCl}_2]\)   | DCE     | 0.04          | 0.16          | 36   | 94       |
| 3     | \([\text{Cp*IrCl}_2]\)  | TCE     | 0.04          | 0.16          | 52   | 43       |

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drogen peroxide or meta-chloroperbenzoic acid.\[18\] To further underline the efficiency of the C–H amidation, we attempted to re-isolate the only by-product that is formed in the reaction, dibenzothiophene, and were able to isolate 86% of the employed amount after column chromatography of the Rh-catalysed reaction of 2-ppy and DBTNTs.

We then transferred differently substituted nitrene precursors 3a–e under the conditions used above. Good to excellent yields were accomplished for the transfer of nitrenes derived from sulfonic acid amides and benzoic acid amide (72–91%) (Scheme 4). Electron poor nitrene precursors were transferred with the best yields. The tert-butyloxy carbonyl-substituted nitrene proved to be challenging and gave the amidated product 2n in a rather low yield of 27% due to incomplete conversion of 2-ppy.

In the case of the transfer of a trifluoromethyl amide moiety, the Rh-based system was shown to be very ineffective and produced a poor yield of 11%. However, the applicability of our developed system towards the use of other Group 9 metals proved to be useful, and we were able to accomplish a yield of 62% for the transfer of trifluoracetamide to give 2o employing the respective iridium analogue (Table 2). Cobalt can, thus, be employed in simple syntheses while rhodium is successful in a broad range of transfers. Iridium catalysts can enable the introduction of more challenging amide groups.

In summary, we have developed a convenient and safe method for the transfer of nitrenes for C–H amidation. The C–H amidation of several C–H bond targets succeeded in predominantly good to excellent yields. Rhodium(III) was suitable for a wide range of substrates. However, in cases where rhodium was shown to give unsatisfactory results, it was demonstrated that the method could be extended to the two other Group 9 transition metals, cobalt and iridium, which, in some cases, gave significantly better results. Especially the applicability of the cheap [Cp*Co(CO)I]2 further improves the economy of the method with regard to large-scale applications. The method was shown to be very convenient due to the reagents being bench-stable, non-explosive and easy to handle. The only by-product that is formed, dibenzothiophene, can easily be recycled. Mechanistic investigations and studies towards a broader reaction scope are ongoing.

## Conflict of interest

The authors declare no conflict of interest.

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**Table 2. Activity of different Group 9 transition-metal catalysts in the C–H amidation of 2-ppy with trifluoroacetyl-substituted dibenzothiophene sulfilimine 3e.**

| Entry | Catalyst | Solvent | [Cat] (equiv) | AgSbF6 (equiv) | t (h) | Yield [%] |
|-------|----------|---------|--------------|---------------|------|-----------|
| 1     | [Cp*Co(CO)I]2 | DCE     | 0.05         | 0.10          | 36   | 0         |
| 2     | [Cp*RhCl3]2 | DCE     | 0.04         | 0.16          | 36   | 11        |
| 3     | [Cp*IrCl3]2 | DCE     | 0.04         | 0.16          | 36   | 62        |

**Scheme 4.** Overview of the N-sulfonyl and N-acyl moieties that can be transferred from dibenzothiophene-based sulfilimines.

**Scheme 3.** Synthesis of N-sulfonyl and N-acyl dibenzothiophene sulfilimines. (a) NaHCO3, instead of NaOH.

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