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* a Fast, Chemoselective and Biomolecule-Compatible Reaction

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Copper-Catalyzed Sulfimidation in Aqueous Media: a Fast, Chemoselective and Biomolecule-Compatible Reaction

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Performing transition metal-catalyzed reactions in cells and living systems has equipped scientists with a toolbox to study biological processes and release drugs on demand. Thus far, an impressive scope of reactions has been performed in these settings, but many are yet to be introduced. Nitrene transfer presents a rather unexplored new-to-nature reaction. The reaction products are frequently encountered motifs in pharmaceuticals, presenting opportunities for the controlled, intracellular synthesis of drugs. Hence, we explored the transition metal-catalyzed sulfimidation reaction in water for future in vivo application. Two Cu(I) complexes containing trispyrazolylborate ligands (Tp′) were selected, and the catalytic system was evaluated with the aid of three fitness factors. The excellent nitrene transfer reactivity and high chemoselectivity of the catalysts, coupled with good biomolecule compatibility, successfully enabled the sulfimidation of thioethers in aqueous media. We envision that this copper-catalyzed sulfimidation reaction could be an interesting starting point to unlock the potential of nitrene transfer catalysis in vivo.

Introduction

Catalysis proves a powerful tool to achieve otherwise synthetically challenging, or even impossible, transformations and is therefore naturally employed in various areas of chemistry. Transition metal-catalyzed reactions have even found successful applications in cells (in vitro) and living systems (in vivo) recently. Such applications range from cell surface labelling (photocatalytic) azide reduction, and ring-closing metathesis reactions, to the activation of prodrugs, e.g., live cell imaging or treatment, chemists have devoted much research to translate transition metal-catalyzed reactions from organic solvents to aqueous media.

Key examples of these transformations are the copper-catalyzed azide-alkyne cycloadditions, and the ruthenium-catalyzed alkylation, (photocatalytic) azide reduction, and ring-closing metathesis reactions. This scope of reactions is still rapidly expanding. For example, Mascareñas and co-workers showed the application of carbene transfer catalysis in mammalian cells. They performed copper-catalyzed N–H carbene insertions to afford bioactive benzoquinoxalines, which can alter the mitochondrial functions of cells, from simple ortho-aminooarylamines and α-keto diazocarbenes.

Although carbene transfer catalysis has been performed intracellularly, nitrene transfer catalysis to nonnatural substrates, such as prodrugs, has yet to be reported in biological settings to the best of our knowledge. Nonetheless, several promising studies in water as the reaction medium have been performed, mainly focused on C–H insertions and aziridination reactions. Sulfimidation reactions are somewhat less explored in water, while its new-to-nature reaction products, e.g., sulfimides (RN=S=RR′), only one report of a naturally occurring sulfimide moiety has been presented to date and their oxidized analogues, sulfoximines (RN=S(=O)RR′), are also fre-

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Figure 1. Graphical representation of this study, in which we set out to explore the transition metal-catalyzed sulfimidation reaction of thioethers in aqueous media and evaluate the potential of the catalytic system for future in vivo application with the focus on three fitness factors: reactivity, selectivity and stability.
quently encountered motifs in pharmaceuticals. For example, \((N\text{-arylsulfonyl})\text{sulfimide}-\text{based drugs (ArSO}_2\text{N}=\text{SR'}, with R'= alkyl and R''= aryl) were reported to inhibit osteoclastogenesis and bind to proteins (e.g., p53), causing inhibition of melanoma cell migration.\)\(^{26,27}\) Hence, performing sulfimidation reactions in biological settings presents opportunities for the controlled and demand synthesis of drugs. Motivated by this potential application, we set out to explore transition metal-catalyzed sulfimidation reactions in water for future in vivo application.

Compared to the highly controlled and adaptable conditions achieved in a flask, the conditions in cells and living systems are fairly different: water, oxygen, 37 °C (for mammalian cells), and pH 7. Moreover, the reaction components are typically present at low concentrations due to practical limitations such as solubility or non-specific toxicity, or the intrinsic metabolism of the biological system.\(^{28,29}\) Nonetheless, the catalytic reaction must still proceed at reasonable rates to ensure product formation.\(^{30,31}\) Furthermore, the inherent complexity of the cellular environment demands exquisite chemoselectivity.\(^{32}\) In the presence of various functionalities, the catalyst and reagents must react selectively with each other. Finally, an ideal catalyst should display high compatibility with salts and biomolecules bearing (coordinating) functional groups, such as thiols or basic amines.\(^{33}\)

To successfully apply a catalytic system in biological settings, the above-mentioned criteria, i.e., reactivity, selectivity, and stability, also known as ‘fitness factors,’\(^{32}\) have to be considered. In this study, we evaluate transition metal-catalyzed sulfimidation reactions under biologically relevant (water, oxygen, 37 °C, pH 7) and biomimetic conditions (in the presence of salts and biomolecules) with the aid of these explorative fitness factors (Figure 1).

### Results and Discussion

#### Reactivity

We initially sought a suitable transition metal catalyst for our studies. We came across a series of \(\text{Tp}^n\text{Cu}(\text{NCMe}) complexes \) (\(\text{Tp}^n\) = trispyrazolylborate ligand), which presented excellent reactivity and selectivity in olefin aziridination and cyclopropanation reactions in aqueous and micellar media, employing diazo compounds and iminoiodianes (\(\text{PhINTs, R} = \text{tosyl or nosyl}) as the respective \(\text{CR}-\) and \(\text{NR}-\) sources.\(^{30,31}\) In a separate study, it was disclosed that those complexes with electron-poor ligands disfavor a reaction with oxygen, being stable toward \(\text{Cu(I)}\) to \(\text{Cu(II)}\) oxidation.\(^{34}\) Given that the undesired formation of reactive oxygen species (ROS) is one of the toxic side reactions typically associated with the application of copper-based catalysts, intrinsic inertness towards oxygen is highly desirable. Hence, similar complexes have been employed in mammalian cells, indeed without presenting significant toxicities.\(^{35}\)

For the above-mentioned reasons, we chose those \(\text{Tp}^n\text{Cu}\) complexes to explore the transition metal-catalyzed sulfimida-
which yields minor amounts of 2 from a (background) reaction with thioanisole.

With the optimized reaction conditions at hand, two other copper-based complexes were evaluated as potential catalysts: Tp(CF3)2BrCu(NCMe) and Tp(CF3)2BrCu(NCMe) (Table 1). These complexes bear CF3 groups, which may be helpful handles for characterization in complex reaction media while maintaining the electron-poor character of the Tp2 ligands (vide supra). Under the optimized reaction conditions, the Tp(CF3)2Br-based catalyst is less productive in the sulfimidation reaction of thioanisole to product 1 (8%, entry 4). In contrast, the Tp(CF3)2Br analog afforded 73% of 1 and only 2% of 2 (entry 5). This catalyst was therefore utilized in further studies.

Intracellular transition metal-catalyzed reactions need to proceed with reasonable rates to ensure product formation before the reaction components are metabolized. To have an idea of the reaction progress of the copper-catalyzed sulfimidation reaction under the applied biologically relevant conditions, we obtained kinetic profiles (Figure 2) for the formation of 1 with both catalysts at room temperature (see the Supporting Information for more details; Table S3). Based on these kinetic profiles, we observed that the Tp(CF3)2Br-based catalyst reached the maximum yield after 40 minutes, whereas the Tp(CF3)2Br analog reached the maximum yield after 20 minutes.

Next, we evaluated the general suitability of both catalysts for the sulfimidation of thiocarbamates under biologically relevant conditions (Scheme 1 and Table S4). First, the influence of the nitrene precursor was investigated by using a more electron-withdrawing NR-source: PhINNs (Ns = nosis). The reaction proceeded equally well for both catalysts with either PhINNs or PhINTs as the NR-source, affording products 1 and 3 in good yields. The catalysts were also subjected to a series of thioanisole derivatives to examine the compatibility of the reaction with different arene substituents. Substrates with electron-donating (–OMe, –Me) and -withdrawing (–F, –Cl, –Br, –Ac, –CN, –NO2) substituents at the para-position of the arene ring were tolerated. Products 4 and 5, and 6–11, respectively, were obtained in good yields. Substitutions at the ortho- and meta-positions were also tolerated (12–13). Furthermore, two more classes of sulfides were investigated. Diphenylsulfane was cleanly converted to 14 in 58% and 76% yield with the Tp(CF3)2Br and Tp(CF3)2Br-based catalysts, respectively. Notably, the former displayed some activity towards (methylsulfinyl)benzene affording 15, albeit with poor yield. Lastly, we explored the transformational potential of the copper-catalyzed sulfimidation reaction for potential intracellular drug synthesis applications. (4-(Benzyloxy)phenyl)methylsulfane was employed as a substrate to access (N-arylsulfonyl)sulfinamide-based drug 16. This compound has been studied in the context of cancer treatment and inhibits melanoma cell migration (vide supra). Both catalysts selectively provided the drug after clean conversion of the substrate with moderate to good yields (up to 48%).

Figure 2. Kinetic profiles for the formation of 1 in water, catalyzed by Tp(CF3)2BrCu(NCMe) (blue) and Tp(CF3)2BrCu(NCMe) (red). Conditions: 1.0 mM NR-source. Yields are quantified by 1H NMR integration using 1,3,5-tri-tert-butylbenzene as an external standard and are versus PhINTs. Reactions were performed in duplicate, yields are averaged.

Scheme 1. Substrate scope A for the sulfimidation reaction catalyzed by Tp(CF3)2BrCu(NCMe) complexes. Conditions: 1.0 mM NR-source. Yields are quantified by 1H NMR integration using 1,3,5-tri-tert-butylbenzene as an external standard and are versus PhINTs.
Chemoselectivity

A myriad of chemical functional groups can be found in the cellular environment. To afford the formation of the desired product, the reaction compounds must be somewhat inert towards these functionalities and react selectively with each other. In other words, the catalytic system must possess excellent chemoselectivity. To investigate the chemoselectivity of the copper-based catalysts for nitrene transfer reactions, we first performed intermolecular competition experiments (Table 2). Nitrene transfer catalysis is not limited to thioethers. Nitrenes and their transition metal complexes can also add to double bonds and insert into C–H bonds; both are functionalities present in nature, generating aziridines and amines, respectively. Hence, the copper-catalyzed sulfidation reaction of thiourea was performed in the presence of styrene or ethylbenzene as representative substrates. After 2 h, we observed 85–90% selectivity for sulfidation in the presence of styrene and >99% selectivity in the presence of ethylbenzene. In the absence of thiourea, styrene aziridination is strongly favored over C–H amination of ethylbenzene (>99%) but is less productive than the sulfidation reaction.

Next, we examined the intramolecular chemoselectivity for the sulfidation reaction in the presence of alkenes and weak C–H bonds (Scheme 2, Table S4). Those with a bond dissociation energy (BDE) of ≤85 kcal mol⁻¹ or 85 < (BDE) ≤ 95 kcal mol⁻¹ are highlighted in purple and blue, respectively. Alkene fragments prone to aziridination are highlighted in red. The same conditions as for the intermolecular competition experiments were employed in these studies.

Based on ¹H NMR spectroscopy, no transformations of the relatively stronger C–H bonds (highlighted in blue) were observed. Substitution of the methyl group in thiourea for ethyl or iso-propyl afforded 17 and 18 selectively and in moderate to good yields (Scheme 2, Table S4). Side reactions with the relatively weaker α-CH₃ bonds of benzylic(phenyl)sulfane and phenethyl(phenyl)sulfane (highlighted in purple) were not observed either. Both substrates were selectively converted to 19 and 20 in moderate yields. The corresponding ¹H NMR spectra after reactions performed with alkene functionalized substrates, phenyl(vinyl) sulfane and allyl(phenyl)sulfane (highlighted in red), did not indicate aziridine formation. The former substrate led to the clean formation of 21, albeit with poor yields. The latter substrate afforded product 22 in moderate yields via a [2,3]-sigmatropic rearrangement of the initially formed S-allyl-sulfimide, as reported in literature. This rearrangement does, however, support the initial S-amination of allyl(phenyl)sulfane (product 22*). Also, no reaction with the

Table 2. Intermolecular competition experiments to investigate the chemoselectivity for sulfidation in the presence of C–C and weak C–H bonds.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate A</th>
<th>Substrate B</th>
<th>Yield Prod₁ (%)</th>
<th>Yield Prod₂ (%)</th>
<th>Selectivity Prod₁ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Thiourea</td>
<td>Styrene</td>
<td>63</td>
<td>5</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>Thiourea</td>
<td>Ethylbenzene</td>
<td>33</td>
<td>0</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>Styrene</td>
<td>Ethylbenzene</td>
<td>28</td>
<td>0</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4</td>
<td>Thiourea</td>
<td>Styrene</td>
<td>73</td>
<td>2</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>Thiourea</td>
<td>Ethylbenzene</td>
<td>75</td>
<td>0</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>Styrene</td>
<td>Ethylbenzene</td>
<td>23</td>
<td>0</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

Conditions: 1.0 mM NR-source. [a] Yields and selectivities are quantified by ¹H NMR integration using 1,3,5-tri-tert-butylbenzene as an external standard and are versus PhINTs. Reactions were performed in duplicate, yields are averaged.

Scheme 2. Substrate scope B for the sulfidation reaction catalyzed by TP[Cu(NCMe)] and TP[Cu(NCMe)]$_2$. Grey: desired position for nitrene transfer (sulfidation); Blue: C–H bonds with 85 < (BDE) ≤ 95 kcal mol⁻¹; Purple: relatively weak C–H bonds (BDE ≤ 85 kcal mol⁻¹). Red: alkene prone for aziridination. Conditions: 1.0 mM NR-source. Yields are quantified by ¹H NMR integration using 1,3,5-tri-tert-butylbenzene as an external standard and are versus PhINTs.
relatively weak C–H bonds could be observed for these two substrates.

**Catalyst stability**

The chemical stability of the catalytic system is of equal importance as its reactivity and selectivity. An ideal catalyst for in vivo applications displays high compatibility with biomoelcules bearing (coordinating) functional groups, such as thiols or basic amines. In practice, however, catalyst stability tends to be one of the most critical challenges within the field of in vivo catalysis as such functional groups typically poison catalysts. A systematic evaluation of the catalyst performance in the presence of biomolecules is therefore indispensable and fundamental for further development of a catalytic system. To examine the compatibility of the copper-catalyzed sulfimidation reaction with various biomolecules, we employed an adapted version of the bio-additive-based screening protocol developed by the Glorius group (see the Supporting Information for more details, Table S5).

The copper-catalyzed nitrene transfer reaction to thioanisole with PhINTs as the NR-source was performed in the presence of sulfur- and basic amine-containing biomolecules, sugars, acids, and amino acids (1 equiv versus the catalyst, Figure 3). The presence of sugars, and amino acids did not affect the reaction outcome (~70–80% yield). The copper-catalyzed sulfimidation reaction also proceeded well in the presence of cytosine and adenosine, which belong to the basic-amine-containing class of biomolecules. The presence of histidine and adenine does, however, affect the catalytic system to varying extents. In the presence of histidine, the TpBr$_3$-based catalyst afforded only 18% product, whereas the TpH$_3$-analog still afforded product 1 in 63% yield. The yields varied to 15% and 40% yield, respectively, in the presence of adenine. Based on these results, the fluorinated catalyst thus seems affected to a lesser extent than the brominated one. A similar trend was observed when acids were introduced to the reaction mixture. For example, in the presence of ascorbic acid, the TpH$_3$Cu(NCMe) complex (53% yield) outperformed the TpBr$_3$Cu(NCMe) complex (37% yield). Finally, the effect of sulfur-containing biomolecules was evaluated. When employing the TpBr$_3$-based catalyst, the yield drops significantly in the presence of glutathione (GSH, 18%), whereas the biomolecules cysteine and methionine only have a moderate to negligible effect on the reaction outcome (42% and 64%, respectively). A similar trend was observed for the TpH$_3$ analog, which still affords product 1 in 36% yield in the presence of GSH. This class of sulfur-containing biomolecules thus has a negligible to significant effect on the catalytic systems. Nonetheless, the catalytic system seems compatible with most biomolecules. It is also worth mentioning that no C–H or S–H bond insertions were observed in the presence of (sulfur-containing) biomolecules.

In an effort to mimic the cellular environment, the copper-catalyzed sulfimidation reaction was performed in water containing 10% cell culture medium (i.e., DMEM) or cell lysates. Under these conditions, both catalysts still afford nitrene transfer to thioanisole, albeit with a significantly reduced product yield (Figure 3). Finally, the reaction was performed in PBS buffer as the reaction media. Although this medium affects the performance of the brominated catalyst (33% yield), the fluorinated one performs equally well as in water (72% yield).

**Catalyst solubility**

The reduced performance of the TpBr$_3$-based catalyst in PBS buffer may be explained by poor solubility of the catalyst in the presence of substantial salt concentrations, as we observed some precipitation throughout the reaction (which was not observed for the TpH$_3$ analog). With solubility being a critical physicochemical property for in vivo applications, we sought a general solution to overcome this issue.

Motivated by the previously reported application of the TpBr$_3$Cu(NCMe) complex in micellar catalysis, we investigated the potential use of liposomes. Liposomes are tunable spherical vesicles with both hydrophobic and hydrophilic domains due to the amphipathic nature of the phospholipids they are assembled from. Hence, hydrophobic compounds can be solubilized upon encapsulation within the hydrophobic domain: the lipid bilayer. This property has been beneficial for drug delivery applications, where the lipid bilayer ‘dissolves’ and protects its cargo.

Catalyst-liposome solutions were prepared in PBS buffer with the aid of passive loading and subsequently filtered to remove undissolved catalyst (Scheme 3A, see the Supporting Information).
Information for more details). Dynamic light scattering (DLS) measurements supported the self-assembly of the vesicles in the presence of Tp$^{3+}$Cu(NCMe) -liposome solutions via passive loading. (B) Catalysis experiment with a 10 mol % Tp$^{3+}$Cu(NCMe) -liposome solution. Reaction conditions: 1.0 mM PhINTs. The yield is quantified by $^1$H NMR integration using 1,3,5-tri-tert-butylbenzene as an external standard and is versus PhINTs.

Scheme 3. Tp$^{3+}$Cu(NCMe) encapsulation in liposomes to enhance its solubility in buffered medium. (A) Schematic representation of the formation of Tp$^{3+}$Cu(NCMe) -liposome solutions via passive loading. (B) Catalysis experiment with the encapsulated catalyst. We therefore selected this biomolecule for further initial studies on this topic. The sulfimidation reaction of thioanisole with PhINTs as the NR-source was performed with the Tp$^{3+}$Cu(NCMe)-liposome solutions in the absence or presence of histidine (1 equiv versus the catalyst; Table 4, entries 1 and 2). To monitor the effect of the presence of histidine, we used a higher catalyst loading to reach significant product formation as we wanted to keep the substrate concentration relatively low (1.5 equiv). Gratifyingly, similar yields were obtained in the presence and absence of histidine (~15%), indicating a positive effect of catalyst encapsulation. To support this hypothesis further, we reproduced the reactions with the non-encapsulated Tp$^{3+}$Cu(NCMe) complex in PBS buffer (entries 3 and 4). In the absence of the liposomes, a significant drop in the yield of 1 was observed in the presence of histidine (from 28% to 13%).

Also, increasing the catalyst loading to 23 mol % had a positive effect on the catalysis outcome at lower thioanisole concentration (5 mM); product 1 was formed in 36% yield (entry 4). No product formation was observed when the reaction was performed with ‘empty’ liposomes (entry 5), highlighting the indispensability of the copper-based catalyst. It should however be emphasized that the sulfimidation reaction performed with the encapsulated catalyst is significantly less productive than the copper-catalyzed reaction in the absence of liposomes. We propose the following potential reasons for this: 1) diffusion limitations of the reaction components, 2) coordination of phospholipid moieties to the Cu(I) center, or 3) side reactions between the nitrene intermediate and the phospholipid moieties.

Table 3. Catalytic sulfimidation with Tp$^{3+}$Cu(NCMe)-liposome solutions.

| Entry | Catalyst (μM) | Catalyst loading (mol%) | Thioanisole (equiv) | Yield 1 (%)$^a$ | Yield 2 (%)$^a$
|-------|---------------|--------------------------|---------------------|---------------|---------------
| 1     | 95            | 10                       | 1.5                 | 13            | 18            |
| 2     | 95            | 10                       | 5                   | 21            | 11            |
| 3     | 95            | 10                       | 10                  | 33            | 7             |
| 4     | 227           | 23                       | 5                   | 36            | 9             |
| 5     | –             | –                        | 10                  | < 1           | 8             |

Conditions: 1.0 mM NR-source. $^a$ Yields are quantified by $^1$H NMR integration using durene as an external standard. Reactions (blanks excepted) were at least performed in duplicate, yields are averaged. Yields of 1 are versus PhINTs and of 2 versus substrate.
Conclusions

In this study, we explored the copper-catalyzed sulfimidation reaction in aqueous media and evaluated its potential for future in vivo application with the aid of three fitness factors: reactivity, selectivity, and stability. Catalysts Tp³BrCu(NCMe) and Tp³BrCu(NCMe) presented good reactivity and chemoselectivity for the desired nitrene transfer reaction at low concentrations of catalyst (50–100 μM) and under biologically relevant conditions. Maximum yields are reached in short reaction times: 20–40 minutes, with minimal byproduct formation (<3%). Late stage sulfimination of (4-(benzyloxy)phenyl)(methyl)sulphonium afforded a reported drug molecule in good yields, providing proof of principle for potential intracellular drug synthesis applications. Furthermore, both catalysts proved compatible with most biomolecules selected from different classes. Even in the presence of coordinating biomolecules, such as GSH and histidine, the sulfimidation product was formed, whereby the Tp³BrCu(NCMe) complex seems more robust than Tp³BrCu(NCMe). Similar observations were made when the reaction was carried out in PBS buffer, cell culture medium, and in the presence of cell lysates, highlighting the potential of the Tp³Br-based catalyst for future in vivo application. Solubility limitations of the Tp³BrCu(NCMe) complex in buffered media could be countered via the encapsulation of the catalyst in liposomes, which were also observed to have a positive effect on the biomolecule compatibility of the catalyst. Overall, copper-catalyzed sulfimination is a fast, chemoselective, and biomolecule-compatible reaction, which could be an interesting starting point to unlock the potential of nitrene transfer catalysis in vivo.

Acknowledgements

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: copper · sulfimidation · nitrene transfer · chemoselectivity · biocompatibility

Table 4. Catalysis experiments with Tp³BrCu(NCMe)-liposome solutions and the Tp³BrCu(NCMe) complex in PBS buffer, in the absence and presence of histidine.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (μM)</th>
<th>Histidine (equiv)</th>
<th>Yield 1 (%)&lt;sup&gt;[a]&lt;/sup&gt;</th>
<th>Yield 2 (%)&lt;sup&gt;[a]&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tp³BrCu(NCMe)-liposome</td>
<td>–</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>Tp³BrCu(NCMe)-liposome</td>
<td>1</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>Tp³BrCu(NCMe)</td>
<td>–</td>
<td>28</td>
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<td>4</td>
<td>Tp³BrCu(NCMe)</td>
<td>13</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Conditions: 1.0 mM NMR-source. [a] Yields are quantified by 1H NMR integration with durene as an external standard. Reactions (blanks excepted) were at least performed in duplicate; yields are averaged. Yields of 1 are versus PhINTs and of 2 versus substrate.
When in solution, iminoiodinanes may be more prone to hydrolysis than when introduced as a solid, as has been previously reported. See: H. V. R. Dias, T. K. H. H. Goh, Chem. Sci. 2014, 5, 273–282.

This complex is the acetonitrile analog of the Tp2Cu(CO) complex previously reported. See: H. V. R. Dias, T. K. H. H. Goh, Polyhedron 2004, 23, 273–282.


