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Ti-catalyzed heterometathetical condensation of *N*-sulfinylamines into sulfurdiimines

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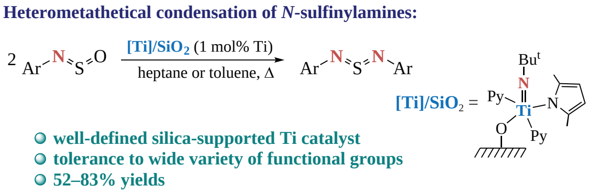
Well-defined silica-supported Ti imido complex (≡SiO)Ti(=NBu^t)(Me$_2$Pyr)(Py)$_2$ (Me$_2$Pyr = 2,5-dimethylpyrrolyl) catalyzes condensation of *N*-sulfinylanilines into sulfurdiimines *via* the oxo/imido heterometathesis providing a convenient synthetic route to functionalized sulfurdiimines.



Heterometathetical condensation of *N*-sulfinylamines:

- well-defined silica-supported Ti catalyst
- tolerance to wide variety of functional groups
- 52–83% yields

Keywords: imido complexes, titanium complexes, imides, metathesis, heterometathesis, *N*-sulfinylamine, sulfurdiimine.

Aza analogs of classic organic and inorganic sulfur-containing molecules or anions, where oxygen is isolobally replaced with an imido ‘NR’ fragment, is a burgeoning field of research.[1] *N*-Sulfinylamines RN=S=O and sulfurdiimines RN=S=NR′ isoelectronic to SO$_2$ are the illustrative examples of such compounds. *N*-Sulfinylamines have found a rich spectrum of applications in organic synthesis,[2] as well as in coordination chemistry where they serve as efficient reagents for the preparation of transition metal imides [M]=NR by imidation of oxo complexes [M]=O *via* a metathesis-like mechanism[3] (stoichiometric oxo/imido heterometathesis[4]). Applications of sulfurdiimines are less developed, although there are examples of their use in organic chemistry (such as preparation of heterocyclic compounds *via* cycloaddition reactions[5] and as intermediates in the synthesis of other sulfur-containing molecules[1(*a*),(*e*),2(*b*)]) and as ligands in coordination chemistry.[6] In part, this might be due to the lack of general protocols for their synthesis. Whereas *N*-sulfinylamines are readily available[2(*a*)] *via* treatment of the corresponding amines with SOCl$_2$[7(*a*)] or milder sulfinylating agents,[7(*b*)] the synthetic routes to sulfurdiimines are less general. They involve self-condensation of RN=S=O induced by stoichiometric amount of sodium[8(*a*),(*b*)] or bases (Figure 1, path *a*),[8(*c*)] application of lithiated *N*-trimethylsilylamines (path *b*),[8(*d*)] and treatment of amines with such reagents as S$_2$Cl$_2$[8(*e*)] (path *c*) or SF$_4$ (path *d*).[8(*f*)] The latter method requires handling of gaseous corrosive and highly toxic sulfur tetrafluoride, while strong bases may not be compatible with certain functionalities.

In recent years our group has been systematically investigating the catalytic oxo/imido heterometathesis,[4] a novel synthetic methodology mechanistically analogous to classical olefin metathesis where the organic ‘oxo’ substrates (*i.e.* those containing X=O bonds, such as aldehydes, ketones and certain carboxylic derivatives) are converted into the corresponding imino products using early transition metal oxo and imido complexes as catalysts and *N*-sulfinylamines as imidating agents (Figure 2). In the course of these studies we found that S=O moiety of *N*-sulfinylamines could also serve as an ‘oxo’ component of the reaction, *i.e.* it could be imidated by the second equivalent of RNSO resulting in a catalytic self-condensation of sulfinylamine into sulfurdiimine (see Figure 1, path *e*). The formation of sulfurdiimines was initially detected as side-reaction during the imidation of other compounds,[9] but already in the early works we showed that it could be used as preparative method.[9,10] A major advance in the development of catalytic oxo/imido heterometathesis was recently achieved by using well-defined silica-supported Ti imido catalysts[11] prepared *via* the Surface Organometallic Chemistry approach.[12] These grafted complexes demonstrated exceptional imido-transfer reactivity, whereas immobilization stabilized the intermediate Ti=O species from bimolecular deactivation (Figure 2, M = Ti). Using self-condensation of TolNSO as a model reaction we showed in a preliminary study that silica-supported Ti imides could also efficiently catalyze this transformation.[11(*b*)] Herein, we investigate the synthetic potential of this reaction for the preparation of a broader range of functionalized sulfurdiimines using currently the most active silica-supported Ti imido catalyst (≡SiO)Ti(=NBu^t)(Me$_2$Pyr)(Py)$_2$ ([Ti]/SiO$_2$, Me$_2$Pyr = 2,5-dimethylpyrrolyl; Scheme 1).

Heating TolNSO in refluxing heptane (98 °C) in the presence of 1 mol% [Ti]/SiO$_2$ (Ti content in the material 0.23 mmol Ti g^{-1})

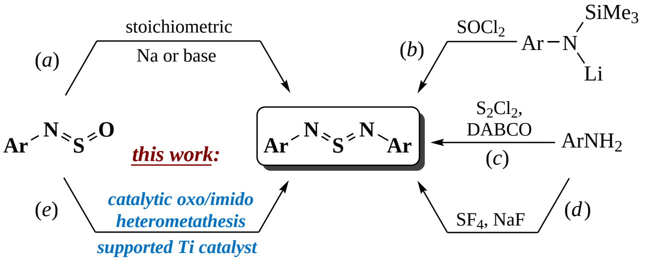


Figure 1 Main synthetic routes to sulfurdiimines.

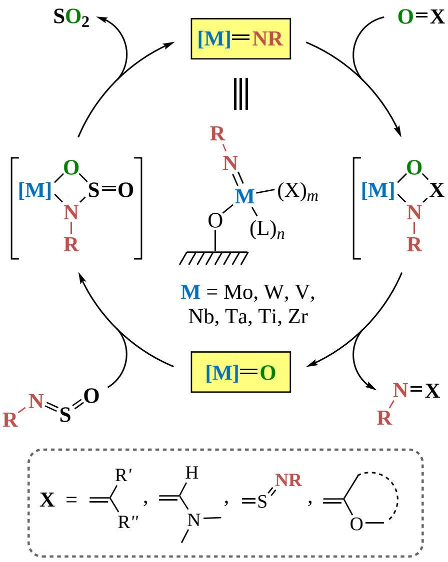
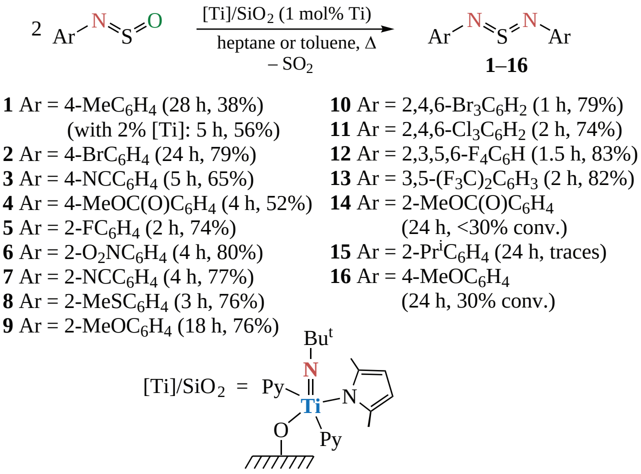


Figure 2 Oxo/imido heterometathesis catalytic cycle.

results in the formation of TolN=S=NTol **1** with half-conversion time within 2–4 h. After that the reaction however slows down significantly and reaches 60–80% conversion after 24 h with no further progress. Similar behavior was observed for some other substrates, but pure products can be isolated in most cases in good to moderate yields. The reaction proved particularly efficient (in terms of both rate and final conversion) for the preparation of products **10–13** from electron-deficient polyhalogenated sulfinylamines when the conversion reached ⩾95% within 1–2 h, even despite the significant steric hindrance in case of 2,4,6-tribromophenyl derivative. Other strong electron-withdrawing groups (such as CN, NO_2) also seem to generally favor the reaction. Nevertheless, reactants with *ortho*-positioned electron-donating groups reacted smoothly as well (*cf.* products **8**, **9**) albeit in some cases longer reaction time was necessary (*e.g.* **9**).[†] Higher reactivity of electron-deficient sulfinylamines is in contrast with the trends previously observed for other heterometathesis reactions, where electronic effects in RNSO were negligible and steric factors dominated.[10(*b*),11(*a*),14] However, these trends were found for sulfinylamines acting as imidating agents, while in this case they play a dual role of both imidating agent and oxo substrate and thus the electrophilic properties likely become crucial for their reactivity as oxo component (in line with the higher reactivity of electrophilic ketones). Several RNSO were found unreactive. Whereas in the cases **14**, **15** this can be ascribed to steric bulk, somewhat surprising is the poor reactivity of 4-$MeOC_6H_4NSO$ that is in contrast to the *ortho*-isomer (**16** *vs.* **9**). 1-Adamantyl-containing analog, *i.e.* AdNSO, remained unchanged under the reaction conditions.



1 Ar = 4-MeC_6H_4 (28 h, 38%)
(with 2% [Ti]: 5 h, 56%)
2 Ar = 4-BrC_6H_4 (24 h, 79%)
3 Ar = 4-NCC_6H_4 (5 h, 65%)
4 Ar = 4-$MeOC(O)C_6H_4$ (4 h, 52%)
5 Ar = 2-FC_6H_4 (2 h, 74%)
6 Ar = 2-$O_2NC_6H_4$ (4 h, 80%)
7 Ar = 2-NCC_6H_4 (4 h, 77%)
8 Ar = 2-$MeSC_6H_4$ (3 h, 76%)
9 Ar = 2-$MeOC_6H_4$ (18 h, 76%)
10 Ar = 2,4,6-$Br_3C_6H_2$ (1 h, 79%)
11 Ar = 2,4,6-$Cl_3C_6H_2$ (2 h, 74%)
12 Ar = 2,3,5,6-F_4C_6H (1.5 h, 83%)
13 Ar = 3,5-$(F_3C)_2C_6H_3$ (2 h, 82%)
14 Ar = 2-$MeOC(O)C_6H_4$
(24 h, <30% conv.)
15 Ar = 2-$Pr^iC_6H_4$ (24 h, traces)
16 Ar = 4-$MeOC_6H_4$
(24 h, 30% conv.)

Scheme 1

In order to better understand the factors that preclude reaching quantitative conversion in the case of certain substrates, we carried out a detailed monitoring of the condensation of TolNSO (see Online Supplementary Materials for details). It was found that in the beginning of the reaction it showed almost quantitative material balance (the formation of TolN=S=NTol followed the consumption of TolNSO), however at later stages the conversion of TolNSO started to exceed the formation of TolN=S=NTol. The amount of sulfurdiimine reached a plateau at *ca.* 80% conversion after 24 h while TolNSO kept being consumed. Concomitantly, a growth of an additional product was detected by GC. The latter was identified as azotoluene (TolN=NTol) using ^1H NMR and GC-FID (by comparison with an authentic sample) and by GC-MS. Its amount constituted *ca.* 2–3% after 24 h and increased to *ca.* 10–15% after several days of reflux when TolNSO was fully consumed. The *in situ* ^1H NMR experiments demonstrated that (1) azotoluene likely arose from the decomposition of sulfurdiimine, and (2) the catalyst was involved in this process. When TolN=S=NTol was heated in C_6D_6 at 100 °C in an NMR tube for 48 h, only trace amounts of azotoluene were observed. Then *ca.* 4 mol% of $[Ti]/SiO_2$ was added and after further 3 days of heating the formation of *ca.* 7% of TolN=NTol was detected in solution.[‡] Moreover, free pyridine and *p*-toluidine which could be present in the reaction media as a result of the catalyst decomposition cause the formation of neither sulfurdiimine nor azo-compound (prolonged heating of TolNSO in heptane with 10 mol% of both amines did not reveal any transformations). While elucidating the mechanism of the formation of azo by-product will require further investigation, this result is noteworthy as it likely uncovers a previously unknown catalyst decomposition pathway that may be relevant to all the oxo/imido heterometathesis reactions that utilize *N*-sulfinylamines as imidating agents.

It should be noted that whereas the formation of azo compounds likely results from an irreversible catalyst deactivation, the formation of sulfurdiimines is not detrimental for the imidation of other substrates because they can also be used as imidating agents instead of *N*-sulfinylamines.[§] This implies that sulfurdiimines are able to undergo stoichiometric exchange with oxo and imido complexes and thus the latter should also catalyze metathesis of sulfurdiimines. Indeed, when compounds **1** and **10** were heated together in C_6D_6 at 80 °C overnight, no changes were observed. However, when 5 mol% $[Ti]/SiO_2$ was added to the reaction mixture, a new product was

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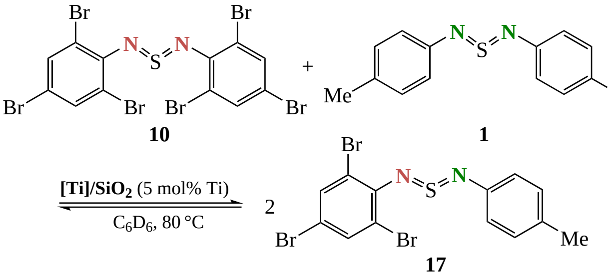
[†] We have very recently shown that $Ti(NEt_2)_4/SiO_2$ activated with anilines could be used as a simple and efficient equivalent of $[Ti]/SiO_2$ (that is more challenging to prepare) in different oxo/imido heterometathesis reactions.[13] Using compounds **10** and **12** as illustrative examples, we confirmed that this system could also be applied for the synthesis of sulfurdiimines reported here. Compounds **10** and **12** were prepared in 74 and 86% yields using 1 mol% $Ti(NEt_2)_4/SiO_2$ *in situ* activated with 2 mol% $TolNH_2$, with reaction time being only slightly longer than for $[Ti]/SiO_2$.

[‡] It should be noted that the formation of minor unidentified by-products was also observed by GC in the reactions with other RNSO, which may explain the lower final conversion in certain cases. This implies that longer reaction time is not desirable and that for preparative purposes it could be more beneficial to slightly increase the catalyst loading. This was confirmed by repeating the synthesis of TolN=S=NTol with 2 mol% $[Ti]/SiO_2$ that gave 56% yield after 5 h of reflux (see Scheme 1).

[§] This is particularly useful in case of thermolabile RNSO where the corresponding RNSNR typically are more stable.[14]



1/**10**/**17** =	*ca.* 1 : 1 : 2 (1 day) *ca.* 1 : 1 : 3.5 (4 days)

Scheme 2

formed with an ^{1}H NMR spectrum compatible with the unsymmetrical sulfurdiimine **17** (Scheme 2). Although the examples of such exchange catalyzed by alkali metals (presumably *via* a radical mechanism) are known,[8(*b*)] to our knowledge this is the first example of transition metal mediated catalytic metathesis of sulfurdiimines, which expands the family of catalytic ‘imide/imide’ heterometathesis reactions that previously included metathesis of imines and carbodiimides.[4] The mechanism of this process is likely similar to that postulated for related carbodiimide metathesis catalyzed by W and V imides[15] involving surface metallacyclic trisimidosulfito intermediates $(\equiv \mathrm{SiO})\mathrm{Ti}\{\kappa^2\text{-}\mathrm{RN{-}S({=}NR){-}NR}\}(\mathrm{Me_2Pyr})(\mathrm{Py})_x$. It should be noted that in the molecular chemistry of group 4 transition metal imides in some cases such complexes were found to be stable enough to be isolated and characterized by XRD and spectroscopic techniques.[16] Perhaps the relatively low yield of sulfurdiimines **1** and **16** is also due to the formation of such stable to retrocyclization surface species.

In summary, we investigated the Ti-catalyzed heterometathetical self-condensation of *N*-sulfinylamines and found it to be a convenient method for the preparation of functionalized sulfurdiimines, especially those containing electron-withdrawing groups (*e.g.* polyhalogenated). We also demonstrated the first example of catalytic sulfurdiimine metathesis mediated by transition metal imido complex, and identified a potential catalyst decomposition pathway that involves the formation of azo compounds and may play an important role in oxo/imido heterometathesis reactions utilizing *N*-sulfinylamines as a source of imido group.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.06.028.

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