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Facile Preparation of Unsymmetric Carbodiimides via *in Situ* Tin(II)-Mediated Heterocumulene Metathesis

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There is considerable interest in the development of metal-mediated oxo- and nitrene-transfer processes that can convert readily available reactants into commodity products.[1] Carbodiimides, $RN{=}C{=}NR'$, are one such product, as this class of compound is extremely important for the construction of a wide variety of chemical structures.[2] Surprisingly, however, one still finds that there is room for improved methods for their production. In particular, for unsymmetric carbodiimides ($R \neq R'$), there currently exists only two practical routes, and these involve either the extrusion of the elements of hydrogen sulfide from N,N′-disubstituted thioureas, RHNC(S)NHR′, or the aza-Wittig reaction of iminophosphoranes, e.g., $Ph_3P{=}NR$, with isocyanates, R′NCO.[2] Unfortunately, both of these methods suffer from the need to separately prepare the thiourea and iminophosphorane starting materials, and in the case of the former process, the use of noxious reagents such as yellow mercuric oxide,[3] phosgene,[4] sulfur dioxide,[5] or methanesulfonyl chloride,[6] which are not always general in scope for both alkyl- and aryl-substituted carbodiimides, has classically been required. Further, although it is known that group 5 and 6 imido complexes can catalyze the cross-metathesis of carbodiimides, this process as not yet yielded a viable method for the synthesis of unsymmetric carbodiimides.[7] Finally, there have been other sporadic reports of a metal-mediated heterocumulene metathesis process providing an isolated example of a carbodiimide product, but once again, none of these have ever been developed as practical synthetic methodology.[8] Recently, we have been developing the heterocumulene metathesis of metal bis(triorganosilyl)amides that proceeds according to $M{-}N(SiR_3)_2 + E{=}C{=}X$ ($X = O$ or NR, $E = O$, S and Se) $\rightarrow M{-}ESiR_3 + R_3SiN{=}C{=}X$, as a tool for the synthesis of metal triorganosilylchalcogenolates under mild conditions.[9] Given the high yields of the new heterocumulenes that were observed in these reactions, we naturally became interested in determining the value of this process as a practical route to unsymmetric carbodiimides. However, to achieve this objective, it was first necessary to map out the steric and electronic requirements of heterocumulene metathesis with respect to the metal center, the nature of the silylated amido ligand, and the heterocumulene. Herein, we now report the successful conclusions of these studies which have culminated in the development of a simple "one-pot" tin(II)-mediated synthesis of unsymmetric carbodiimides from readily available mono-trimethylsilyated amines, $(Me_3Si)RNH$,[10] and R′NCO. This new procedure should serve to expand both the scope and utility of carbodiimides, and of heterocumulene metathesis, as tools for organic synthesis.

Table 1. Isolated Yields of $R'N{=}C{=}NSiMe_3$ Obtained from the Reaction of **2** with R′NCO

entry	R′ [a]	yield (%)
1	*t*-Bu	75
2	Cy	82
3	1-Ad	95
4	Me_3Si	98
5	Ph	*b*
6	$2,6\text{-}Me_2C_6H_3$	60
7	$2,6\text{-}(i\text{-}Pr)_2C_6H_3$	94

[a] Cy = cyclohexyl, Ad = adamantyl. [b] Complex mixture of products.

Wannagat and co-workers[8a,b] have previously observed that sodium hexamethyldisilazide (**1**) cleanly reacts with 2 equiv of trimethylsilylisocyanate to produce 1,3-bis(trimethylsilyl)carbodiimide according to $NaN(SiMe_3)_2 + 2\ Me_3SiNCO \rightarrow Me_3SiN{=}C{=}NSiMe_3 + Na[NCO] + Me_3Si{-}O{-}SiMe_3$.[11] In this metathesis reaction, the second equivalent of Me_3SiNCO is required to sacrifically react with the initially formed $NaOSiMe_3$ in order to prevent it from reacting with the desired carbodiimide product. Unfortunately, it is due to this undesired side reaction that the Wannagat reaction cannot be extended as a general route for the synthesis of either $RN{=}C{=}NSiMe_3$ from **1** or $RN{=}C{=}NR'$ from other lithium monosilylamides, $LiNR(SiMe_3)$, and R′NCO.[12] In contrast, we have found that similar metathesis reactions of isocyanates with divalent tin bis(trimethylsilyl)amido compounds, and in particular, with the commercially available reagent, $Sn[N(SiMe_3)_2]_2$ (**2**),[13] always proceed in near quantitative yields as determined by ^1H NMR spectroscopy. These high yields are presumably due to the inertness of the formed dimeric tin(II) products, such as $[Sn(\mu\text{-}OSiMe_3)(OSiMe_3)]_2$,[9a] toward either the starting isocyanate reactant or the carbodiimide product. Thus, on a practical scale, as Table 1 reveals, a variety of $R'N{=}C{=}NSiMe_3$ derivatives can now be conveniently prepared by adding 2 equiv of R′NCO to a precooled (−78 °C) solution of **2**,[14] warming the reaction mixture to room temperature, filtering it through a short column of silica gel to remove the tin-containing

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[1] See, for example: (a) Barton, D. H., Martell, A. F., Sawyer, D. T., Eds.; *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*; Plenum Press: New York, 1993. (b) Ayers, W. M., Ed.; *Catalytic Activation of Carbon Dioxide*; ACS Symposium Series 363; American Chemical Society: Washington, DC, 1988. (d) Laplaza, C. E.; Cummins, C. C. *Science* **1995**, *268*, 861−863. (e) Du Bois, J.; Tomooka, C. S.; Hong, J.; Carreira, E. M. *Acc. Chem. Res.* **1997**, *30*, 364−372.

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[4] Ulrich, H.; Sayigh, A. A. R. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 704−712.

[5] Fujinami, T.; Otani, N.; Sakai, S. *Synthesis* **1977**, 889−890.

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[9] (a) Sita, L. R.; Babcock, J. R.; Xi, R. *J. Am. Chem. Soc.* **1996**, *118*, 10912−10913. (b) Weinert, C. S.; Guzei, I. A.; Rheingold, A. L.; Sita, L. R. *Organometallics* **1998**, *17*, 498−500. (c) Xi, R.; Sita, L. R. *Inorg. Acta Chim.* **1998**, *270*, 118−122. (d) Babcock, J. R.; Zehner, R. W.; Sita, L. R. *Chem. Mater.* **1998**, *10*, In press.

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[11] $LiN(SiMe_3)_2$ works equally well in this reaction.

[12] As determined by NMR spectroscopy, metathesis between $LiNR(SiMe_3)$ and R′NCO does appear to occur; however, only trace amounts of the carbodiimide product are obtained due to its apparent subsequent reaction with $LiOSiMe_3$.

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[14] A variety of aprotic solvents can be used (e.g., hexane, toluene, Et_2O, tetrahydrofuran, dichloromethane); however, pentane is preferred for volatile carbodiimide products.

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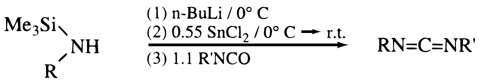
Scheme 1



material, and then isolating the product by distillation. Of the isocyanates utilized, only PhNCO failed to produce an appreciable amount of carbodiimide product, and in this case, following the course of the reaction by NMR spectroscopy revealed that secondary reactions were occurring to produce a complex mixture from which the product could not be separated. However, as can be seen, an increase in the steric bulk of the isocyanate appears to retard these secondary reactions as manifested in the higher yields obtained for 2,6-dimethyl- and 2,6-diisopropylphenyl isocyanate. Further, noting that the reaction of PhNCO with **2** was extremely rapid even at −78 °C, we prepared the more sterically hindered tin(II) reagent, $Sn[N(SiMe_2Ph)_2]_2$ (**3**),[15] and now found by NMR that reaction of this compound with PhNCO proceeded smoothly at 50 °C to provide the desired carbodiimide, $PhN{=}C{=}NSiMe_2Ph$, as the sole organic product.[16] Accordingly, by using either **2** or **3**, it should be possible to expand the range of mono-silylated carbodiimides that can be prepared by metathesis.

A key question that we wished to answer next was whether this heterocumulene metathesis could be extended for the productive synthesis of *nonsilylated* carbodiimides. To probe this, we first utilized the known monomeric tin(II) bisamide, $Sn[N(SiMe_3)(t\text{-}Bu)]_2$ (**4**),[13] and gratifyingly found that a 94−95% isolated yield of 1,3-bis(*tert*-butyl)carbodiimide could be obtained at room temperature either by reacting a pentane solution of **4** with 2 equiv of *t*-BuNCO or by reacting it with CO_2 (60 psi) in a pressure reaction vessel. On a NMR scale, **4** was also found to react cleanly with the range of isocyanates used in Table 1 to provide the corresponding unsymmetric carbodiimides, *t*-BuN═C═NR′, and this time, even in the case where R′ = Ph. Unfortunately, were the success of this methodology as a general synthetic tool to depend on the availability of well-characterized $Sn[N(SiMe_3)(R)]_2$ derivatives, it would fail as few other than **4** are known, and these all incorporate "bulky" R groups to aid in the kinetic stabilization of these monomeric tin(II) species.[17] Indeed, in an attempt to explore this chemistry further, we prepared the new derivative **5** where R = 2,6-diisopropylphenyl,[15] but this compound proved unreactive toward both isocyanates and CO_2, most likely as a result of too much kinetic stablization. Given these limitations, we next turned to determining whether high yields of unsymmetric carbodiimide products could be obtained if the tin(II) bisamides were simply prepared and reacted *in situ* according to Scheme 1. Fortunately, as Table 2 reveals, this idea worked exceedingly well. Thus, deprotonation of $(Me_3Si)RNH$ in diethyl ether (Et_2O) with *n*-butyllithium at 0 °C, followed by addition of slightly more than half an equivalent of tin dichloride, provided, in each case, an orange to orange-brown reaction mixture when warmed to room temperature. Addition of 1.1 equiv of an isocyanate at this stage then resulted in bleaching of this color with time, and after the usual workup, a range of carbodiimide products could be obtained in very good to excellent yields.[18] Surprisingly, however, as entry 12 in Table 2 shows, a notable exception was found for the *in situ* generation of **2** which failed to give as high of a yield of carbodiimide as that obtained by working with isolated **2**. Why this should be is not clear at this time; however, a possibility exists that complexation of **2** with lithium salts might be interfering with the course of the reaction.[19] We finally note that unsymmetric carbodiimides bearing small organic groups, such as *n*-butyl or isopropyl, can also be successfully prepared by having this group placed on either the amine starting component or the isocyanate (cf., entries 4 and 8 in Table 2).

Table 2. Isolated Yields of RN═C═NR′ Obtained According to Scheme 1

entry	R	R′	yield (%)
1	*t*-Bu	*t*-Bu	84
2	*t*-Bu	Cy	84
3	*t*-Bu	*i*-Pr	75
4	*t*-Bu	*n*-Bu	61
5	*t*-Bu	Ph	83
6	*t*-Bu	$2,6\text{-}Me_2C_6H_3$	83
7	*t*-Bu	$2,6\text{-}(i\text{-}Pr)_2C_6H_3$	97
8	*n*-Bu	*t*-Bu	72
9	Cy	*t*-Bu	86
10	Ph	*t*-Bu	60
11	*i*-Pr	*t*-Bu	80
12	Me_3Si	*t*-Bu	31
13	$2,6\text{-}(i\text{-}Pr)_2C_6H_3$	*t*-Bu	*a*
14	*i*-Pr	*i*-Pr	50

[a] No reaction.

In conclusion, we have developed a simple one-step synthesis of unsymmetric carbodiimides that is based on a facile in situ tin(II)-mediated heterocumulene metathesis process. Since this new methodology appears to offer complimentary advantages over existing routes, we are now in the process of defining the full extents and limitations of this chemistry as a tool for organic synthesis.

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(15) The preparation and crystal structure of this compound will be reported elsewhere.

(16) The controlled reactivity of **3** with para-substituted arylisocyanates, $X\text{-}C_6H_4NCO$ (X = OMe, Me, F, Cl, CF_3), has been used to conduct a Hammett study which revealed that the rate of heterocumulene metathesis is enhanced by electron-donating groups, and thus, these rates also parallel the nucleophilicities of these isocyanates.

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(18) *Representative procedure*: To a solution of 1.03 g (7.05 mmol) of *N*-*tert*-butyltrimethylsilylamine in 20 mL of Et_2O, precooled to 0 °C, was added 2.74 mL of *n*-butyllithium (2.57 M in hexanes). The reaction mixture was warmed to room temperature and stirred for 2 h, whereupon, it was transferred, via cannula, to a suspension of 0.67 g (3.88 mmol, 0.55 equiv) of tin(II) chloride in 20 mL of Et_2O that was cooled to 0 °C. The resultant orange mixture was allowed to warm to room temperature and stir for 2 h; at which time, it was cooled back down to 0 °C, and a solution of 0.77 g (7.75 mmol, 1.1 equiv) of *tert*-butyl isocyanate in 10 mL of Et_2O added. The mixture was warmed to room temperature and stirred for 12 h until the orange color faded. The volatiles were then removed under reduced pressure (200 mmHg); the crude mixture was taken up in a minimial amount of Et_2O and filtered through a 1 × 5 cm pad of silica gel on a glass frit. Removal of the volatiles provided the final crude product which was bulb-to-bulb distilled at 75 °C/35 mmHg to provide 0.918 g (5.92 mmol, 84%) of pure 1,3-bis(*tert*-butyl)carbodiimide as a colorless oil.

(19) Divalent tin(II) compounds have been observed in the solid state as LiCl complexes, see: Arif, A. M.; Cowley, A. H.; Elkins, T. M. *J. Organomet. Chem.* **1987**, *325*, C11−C13.