N,N-bis(Trimethylsilyl)alkenesulfenamides: Synthesis and Transaminations *via* *S*-Alkenylthiophthalimides. A General Route to Alkenesulfenamides and Alkenesulfonamides

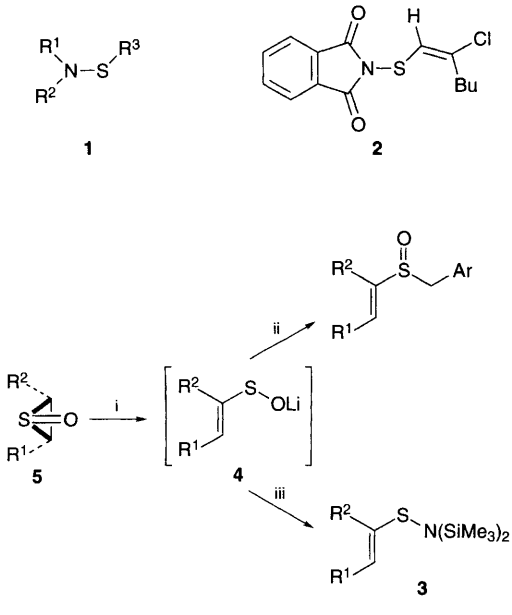
Adrian L. Schwan* and Mitchell D. Refvik

Guelph-Waterloo Centre for Graduate Work in Chemistry, Guelph Campus, Department of Chemistry and Biochemistry, University of Guelph, Guelph, Ontario, Canada, N1G 2W1

N,N-bis(Trimethylsilyl)alkenesulfenamides **3**, prepared by the reaction of *trans*-alkenesulfenates with TMSCl and LiHMDS, are modified to their corresponding *S*-alkenylthiophthalimides **6** which are then converted to alkenesulfenamides **7** bearing more general nitrogen functionality.

Sulfenamides **1**[1] are of interest to the fundamental chemist for their uses in organic synthesis[2] and to the applied chemist because of their numerous commercial applications.[1] A number of methods are available for the synthesis of arene-, alkane- or haloalkane-sulfenamides, but only two routes have been reported for the preparation of alkenesulfenamides (*e.g.* **2**).[3,4] Here, we report a new synthesis of *N,N*-bis(trimethylsilyl)alkenesulfenamides and describe a method for their conversion to other alkenesulfenamides bearing more general nitrogen functionality.

The synthesis of the *N,N*-bis(trimethylsilyl)alkenesulfenamides **3** was achieved by utilizing our method for the generation of exclusively *trans*-alkenesulfenate anions **4** through the regioselective deprotonation and stereoselective ring-opening of alkyl substituted thiirane *S*-oxides **5**.[5] Rather than capturing the sulfenates as vinyl sulfoxides (Scheme 1),[5] it was discovered that treatment of that sulfenate mixture with TMSCl, cyclohexene and additional LiHMDS (0.7–0.8 equiv.) affords clean mixtures of the *N,N*-bis(trimethylsilyl)-alkenesulfenamides.† The mixtures were chromatographed on alumina or distilled to afford pure alkenesulfenamide. If the sulfenamides are prepared for further reaction, purification is hardly necessary since the crude material is quite clean. The yields listed in Table 1 are for the conversion of thiirane *S*-oxide to alkenesulfenamide. Our yields compare favourably to those obtained for many other preparations of alkane- and arene-sulfenamides.[1] Moreover, considering that sulfenates **4** are generated in 60–80% yield from their corresponding thiirane *S*-oxide,[5] the conversion of sulfenate to sulfenamide is actually more efficient than indicated by the yields in Table 1.



Scheme 1 *Reagents*: i, LiHMDS; ii, $ArCH_2Br$ (ref. 5); iii, TMSCl, LiHMDS, cyclohexene (this work)

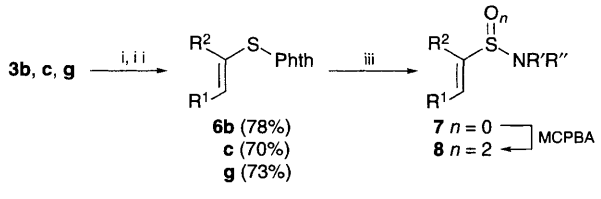
While the *N,N*-bis(trimethylsilyl)alkenesulfenamides **3** are interesting molecules and are likely to undergo a number of reactions,[6] it was our immediate goal to achieve transaminations on them and hence present a synthetic procedure for a larger family of alkenesulfenamides.‡ Direct transaminations with heat alone or in combination with various acid catalysts gave either recovered starting material or a complex mixture of decomposition products. It was decided at this point that the nitrogen bearing the silicon groups did not possess sufficient leaving ability and accordingly, had to be converted to a more accommodating functionality. Following the lead of Harpp and Back[7] and others,[4,8] the phthalimido group was chosen. Modification of sulfenamides **3b, c** and **g** to their corresponding thiophthalimides **6** was achieved through a desilylative treatment followed by triethylamine and 3 equiv. of phthaloyl dichloride.§ Three conversions were effected and are shown in Scheme 2; the isolated, purified yields were in the 70–78% range.

Transaminations with primary and secondary amines on compounds **6** were effected in benzene at room temperature or in ethanol at 80 °C in one sluggish instance. The initial purification step involved concentration of the reaction mixture and trituration of the residue into pentane. Concentration of the pentane solution provided crude alkenesulfenamides **7** in 80–100% yield and 85–95% purity with the exception of **7c** which formed in lower yield. Chromatography of the crude alkenesulfenamides **7** provided pure compounds, but the separation was accompanied by substantial loss of material.

Table 1 Synthesis of *N,N*-bis(trimethylsilyl)alkenesulfenamides **3** from thiirane *S*-oxides **5**[a]

	Product	R^1	R^2	Yield (%)[b]
1	**3a**	Me	H	43(58)[c,d]
2	**3b**	Bu^n	H	51
3	**3c**	$Ph[CH_2]_2$	H	57
4	**3d**	But-3-enyl	H	50
5	**3e**	$C_{11}H_{23}$	H	53
6	**3f**	Ph	Ph	34(46)[c,e]
7	**3g**	$-[CH_2]_4-$		63

[a] The reaction is the lower pathway of Scheme 1. [b] All yields are of isolated, purified material unless otherwise indicated. Satisfactory elemental analysis was obtained for all products except **3f**. [c] Yield in parentheses is a crude, ^1H NMR calibrated yield. [d] The volatility of this compound led to some losses during distillation. [e] This material partially decomposed during alumina chromatography.

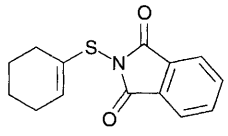


Scheme 2 (Phth = phthalimido); *Reagents*: i, TBAF, THF; ii, 3 equiv. phthalolyl dichloride, TEA; iii, NHR'R'', solvent

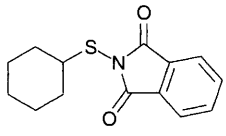
Table 2 Preparation of alkenesulfenamides **7** and alkenesulfonamides **8** by transaminations of *S*-alkenylthiophthalimides **6**[a]

Starting phthalimide	Amine (HNR′R″) R′	R″	Trans. cond.[b]	Sulfonamide (%), state[c]
6b	H	benzyl	A	**8a** (67), oil
6b	Me	benzyl	A	**b** (73), oil
6b	Ph	allyl	B	**c** (35), oil[d]
6c	$-[CH_2]_2O[CH_2]_2-$		A	**d** (63), 96–96.5
6g	$-CH_2C(CH_3)H-$		A[e]	**e** (60), oil
6g	H	cyclo-C_6H_{11}	A	**f** (67), 90–90.5

[a] Alkenesulfenamides **7** were identified by ^1H and ^{13}C NMR prior to oxidation. Alkenesulfonamides **8** were identified by ^1H and ^{13}C NMR, IR and elemental analysis. [b] Transamination conditions are A: benzene, room temp. 2 h; B: ethanol, reflux, 16 h. [c] The physical state of the sulfonamides is reported. The mp (°C) is noted for solids. [d] Compound **8c** solidifies at −20 °C but melts upon warming to room temp. [e] Two diastereoisomers were evident in the ^1H and ^{13}C NMR spectra of alkenesulfenamide **7e**.



6g



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After further investigation, it was realized that alkenesulfenamides **7** are not stable on silica gel nor neutral or basic alumina. Since the reactions were carried out on a 1–2 mmol scale and distillation was not a practical alternative, the crude alkenesulfenamides were isolated in a pure form after oxidation to their respective alkenesulfonamides **8** (3 equiv. MCPBA, K_2CO_3, 25 °C, 2–3 d). Hence the yields in Table 2 are a combination of both transamination and oxidation with MCPBA. Moderate yields for the oxidation are not unexpected since losses of 15–37% were encountered in the MCPBA oxidation of alkenesulfinamide to sulfonamide, a conversion that transfers only one oxygen.[9]

The reaction of **6g** with cyclohexylamine is particularly noteworthy. It contrasts the work of Boustany and Vander Kooi[10] who found that cyclohexylamine did not undergo nucleophilic attack with saturated thiophthalimide **9** at sulfur (transamination) under matching conditions. Rather, the reaction observed was attack at a phthalimido carbonyl followed by ring opening.[10] These distinctly different results indicate that our alkenyl systems seem to be more inclined to participate in transamination reactions than their saturated analogues.

We are currently pursuing other reactions of silylated sulfenamides **3** and their derivatives. For instance thiophthalimides **6** would be expected to undergo nucleophilic reactions similar to those reported for the related family of β-chloroalkenylthiophthalimides **2**.[4]

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Footnotes

† The role of cyclohexene is unknown. In its absence the reaction mixture is contaminated with dialkenyl disulfide (5–10%).

‡ It is conceivable that addition of TMSCl and an amide (LiNR′R″) other than LiHMDS to the sulfenate would lead to an alkenesulfenamide that bears the NR′R″ functionality and experiments to that end were performed. Silylated sulfenamides **3** were obtained as the major products under such conditions, presumably due to proton transfers that occur prior to S–N bond formation. Full details of these particular experiments will be presented in a full paper. Direct use of LiNR′R″ (R′, R″ = alkyl) for deprotonation of **5** provides two isomeric sulfenates (see Ref. 5) and eventually two inseparable isomeric sulfenamides.

§ General procedure: To a flame-dried flask under N_2 was added sulfenamide **3** (1–3 g, 3–11 mmol) and dry ether (200 ml). The flask was cooled to 0 °C and TBAF (2 equiv., 1 mol dm^{-3} in THF, freshly opened bottle) was added. The mixture was allowed to come to room temp. over 20 min and then was cooled to −78 °C for the addition of triethyl amine (6 equiv.) and phthaloyl dichloride (3 equiv.). The mixture was transferred to an ice bath for 1 h and then was stirred at room temp. for 2 h. The mixture was then suction filtered through Celite with the aid of EtOAc. The filtrate was transferred to a separatory funnel and saturated aq. NH_4Cl (80 ml) was added. The layers were separated and the aq. layer was extracted with EtOAc (2 × 30 ml). The combined organic extracts were washed with saturated aq Na_2CO_3 (4 × 60 ml), saturated aq. NH_4Cl (3 × 60 ml), water (2 × 60 ml) and brine (60 ml). The mixture was dried (Na_2SO_4). Filtration, concentration and chromatography (silica gel, 10% EtOAc in hexanes) afforded compounds **6** as stable solids which could be recrystallized from EtOAc/hexanes to afford analytically pure thiophthalimides.

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