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Synthetic Routes to, Transformations of, and Rather Surprising Stabilities of (*N*-Methyl-*N*-phenylcarbamoyl)sulfenyl Chloride, ((*N*-Methyl-*N*-phenylcarbamoyl)dithio)carbonyl Chloride, and Related Compounds†

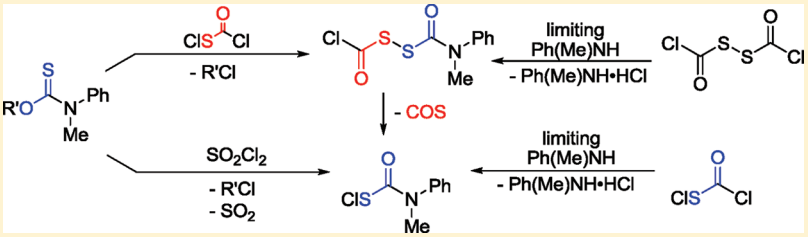
Alex M. Schrader,‡ Alayne L. Schroll,§ and George Barany*,‡

‡Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455, United States

§Saint Michael's College, Colchester, Vermont 05439, United States

Supporting Information

ABSTRACT:



The title compound classes, (carbamoyl)sulfenyl chlorides and ((carbamoyl)dithio)carbonyl chlorides, have been implicated previously as unstable, albeit trappable, intermediates in organosulfur chemistry. The present work reports for each of these functional groups: (i) several routes to prepare it in the *N*-methylaniline family; (ii) its direct structural characterization by several spectroscopic techniques; (iii) its rather unexpected stability and its ultimate fate when it decomposes; (iv) a series of further chemical transformations that give highly stable derivatives, each in turn subject to thorough characterization. Relevant kinetic and mechanistic experiments were carried out, including some with *p*-methyl- and 2,6-dimethyl-substituted *N*-methylanilines. Given that the title compounds can be isolated and are relatively stable, they may find applications in the preparation of thiolyzable and/or photolabile protecting groups for the sulfhydryl function of cysteine and for the development of new protein synthesis and modification reagents.

INTRODUCTION

A seminal 1970 review by Zumach and Kühle[1] made passing reference to both (carbamoyl)sulfenyl chlorides (**1**) and ((carbamoyl)dithio)carbonyl chlorides (**2**), each of which was implied to be an unstable, transient species that underwent facile loss of elemental sulfur[2] (and in the second case, carbonyl sulfide as well) to furnish carbamoyl chlorides (**3**) (Scheme 1). Nevertheless, each of the putative intermediates **1** and **2** was reported to form a characterizable adduct (**7** and **8**, respectively; Scheme 1) upon trapping with cyclohexene (for **1**) or methanol (for **2**). Primary references cited by Zumach and Kühle[1] were exclusively to unpublished studies from industrial laboratories, and a comprehensive, current literature search revealed a paucity of additional information on these species.[3−7] In contrast, the present paper reports not only the capability to generate the title functional groups by several complementary routes — as supported by thorough spectroscopic characterization as well as studies on several further transformations — it also documents their extraordinary (and rather surprising) stabilities. This work may have applications in the preparation of thiolyzable and/or photolabile protecting groups for the sulfhydryl of cysteine[8−10] and for the development of protein modification reagents.[11]

RESULTS AND DISCUSSION

Preparation of (*N*-Methyl-*N*-phenylcarbamoyl)sulfenyl Chloride (1). While the Zumach−Kühle review[1] alluded to a range of primary and secondary, aliphatic and aromatic carbamoyl moieties (legend to Scheme 1), we elected to study principally compounds based on *N*-methylaniline, especially because an extensive set of derivatives[13,14] were available in our laboratory that could be used as reference compounds in elucidating the subsequent chemistries. To facilitate and standardize spectroscopic characterization and comparisons, the described reactions (Scheme 2) were generally carried out in $CDCl_3$ solution, although for completeness, selected experiments were repeated in other aprotic solvents, specifically CD_3CN, dioxane-d_8, and benzene-d_6. Outcomes of such experiments were similar, although kinetics varied, consistent with the range of polarities for the solvents tested.

Several in situ routes produced **1** in the *N*-methylaniline family (Scheme 2). First, treatment at 25 °C of (*N*,*N*′-dimethyl-*N*,*N*′-diphenylcarbamoyl)sulfenamide (**5**)[13] with anhydrous hydrogen

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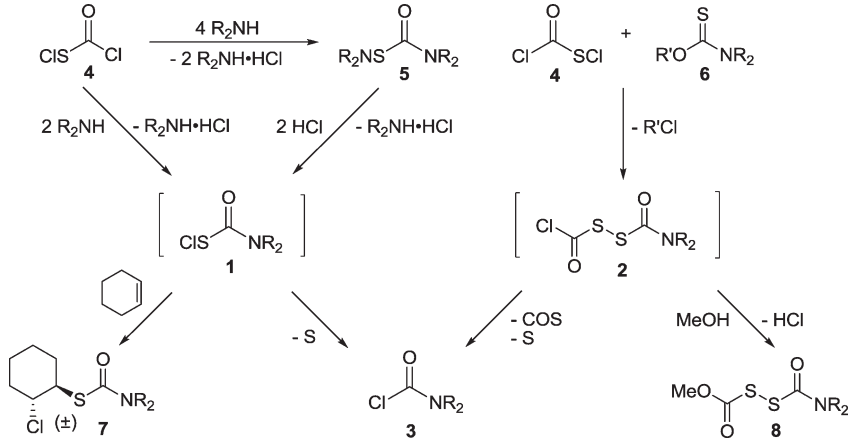
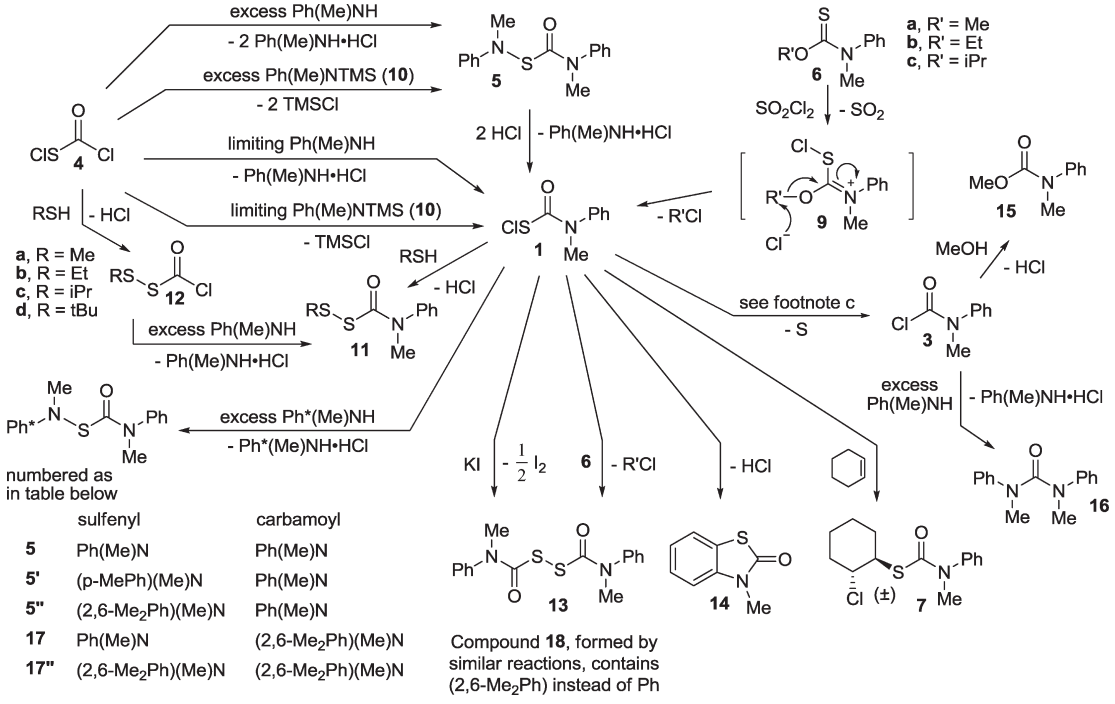
Scheme 1. Summary of Zumach–Kühle Observations and Conclusions [a]



[a] In ref 1 for chemistry on the left side of this scheme, R_2N = Me_2N, nPr_2N, morpholino, *i*PrNH, *t*BuNH, and PhNH; for chemistry on the right side, R_2N = Me_2N and R′ = *n*Bu. Intermediates **1** and **2** were both stated to be rather unstable [hence shown here within square brackets], a conclusion not supported by the presently reported studies for which R_2N = Ph(Me)N and related. Compound **7** is drawn with trans stereochemistry not due to specific spectroscopic evidence but rather based on general literature precedents.[12]

Scheme 2. Syntheses and Transformations Related to (Carbamoyl)sulfenyl Chloride 1 [a–c]



	sulfenyl	carbamoyl
5	Ph(Me)N	Ph(Me)N
5′	(p-MePh)(Me)N	Ph(Me)N
5″	(2,6-Me_2Ph)(Me)N	Ph(Me)N
17	Ph(Me)N	(2,6-Me_2Ph)(Me)N
17″	(2,6-Me_2Ph)(Me)N	(2,6-Me_2Ph)(Me)N

[a] The majority of these syntheses and transformations are new; previously known compounds are referenced in the text. Structure **9** is presumed based on NMR detection of a reaction intermediate (mixture of two configurations that have identical reactivities); it is therefore shown in square brackets to indicate its transient nature. Much of this chemistry was demonstrated not only for derivatives of unsubstituted *N*-methylaniline but also for appropriately substituted *N*-methylanilines. More specifically, phenyl (no further punctuation) was sometimes replaced by *p*-methylphenyl (prime = ′ series) or 2,6-dimethylphenyl (double prime = ″ series). [b] When this manuscript was under review, an anonymous referee suggested that cleavage of **13** with chlorine might generate **1** (see also ref 4). In fact (details in Experimental Section), reaction of **13** with sulfuryl chloride (a safer chlorine equivalent) led to direct formation of carbamoyl chloride **3** plus heterocycle **14** (in a 1:1 ratio), presumably because diacyl disulfanes are asymmetrically cleaved as has been noted for other examples summarized by Kühle (ref 15). [c] The decomposition of **1** to **3** occurred *only* when **1** had been generated by the chemistry in the upper right corner of this scheme. For all other methods to generate **1**, this compound was eventually converted to heterocycle **14**.

chloride [delivered either as gas bubbled through a $CDCl_3$ solution or from a 1 M stock solution in dioxane–$CDCl_3$ (3:7)] rapidly generated[16] the sulfenyl chloride **1**, along with a stoichiometric amount of *N*-methylaniline hydrochloride. Second,

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reactions[7] of *O*-alkyl *N*-methyl-*N*-phenylthiocarbamates (**6**)[13,17] with sulfuryl chloride (1 equiv) gave desired **1**, together with the appropriate alkyl chloride, within 1 h at 25 °C. While starting thiocarbamates **6** disappeared within moments of addition of sulfuryl chloride, short-lived intermediates did appear; these have been tentatively assigned structure **9** (Scheme 2). Interestingly, **9** existed in two more or less equally populated configurations for the methyl (**a**) and ethyl (**b**) series, albeit in a single configuration for isopropyl (**c**). Further conversion of **9** (both configurations, reacting at the same rates) to **1**, and concomitant alkyl chloride formation, occurred at 25 °C with $t_{1/2} \sim 8$ min for **6a** (R′ = methyl), $t_{1/2} \sim 10$ min for **6b** (R′ = ethyl), and $t_{1/2} \sim 3$ min for **6c** (R′ = isopropyl). These relative reactivities of methyl vs ethyl vs isopropyl were confirmed when all of the appropriate precursors (**6a**, **6b**, and **6c**) were combined into a single tube and reacted with SO_2Cl_2.

Further approaches to generate (carbamoyl)sulfenyl chloride **1**, while not recommended for preparative purposes, served to elucidate additional aspects of the chemistry, as well as to confirm spectroscopic assignments. Given that reaction of chlorocarbonylsulfenyl chloride (**4**)[1,13] with excess *N*-methylaniline leads rapidly and quantitatively to bis(substituted) compound **5**, it was of interest to note that when **4** was in excess (i.e., *N*-methylaniline was limiting), compound **1** was among the species formed. As might be expected, this mode of reaction was accompanied by formation of some **5** from substitution at the less reactive sulfenyl chloride function (above and beyond the preferred substitution at the carbonyl). Also, because *N*-methylaniline serves not only as the nucleophile but also as a base to absorb the hydrogen chloride coproduct, the corresponding hydrochloride salt was observed. To simplify stoichiometric calculations and provide more straightforward results, variant acylations were carried out when the substrate was the *N*-trimethylsilylated derivative[18−21] **10** of the secondary amine. As predicted from precedents in other systems,[22] these reactions resulted in quantitative formation of chlorotrimethylsilane (unreactive under these conditions) as the coproduct. Most relevant to the goals of this work, a 1:1 ratio of **4** plus **10** was transformed, essentially instantaneously at 25 °C, to **1** plus TMSCl (quantitative; does not react further), while reaction of **4** (1 equiv) plus **10** (2 equiv) gave the bis(substituted) adduct **5**, plus TMSCl (2 equiv). The fact that **5** was not detected from the 1:1 reaction suggests that a silylated amine is considerably more reactive toward the acyl chloride moiety of **4**, with respect to a significantly more sluggish reaction at the sulfenyl chloride moiety.

Trapping of Compound 1. (Carbamoyl)sulfenyl chloride **1**, generated by any of these methods, was trapped through quenches with *N*-methylaniline or simple alkanethiols, providing respectively the previously described (carbamoyl)sulfenamide **5**[13] or the appropriate alkyl (*N*-methyl-*N*-phenylcarbamoyl)disulfane (**11**).[23] Interestingly, when **1** was generated from SO_2Cl_2 plus **6**, *N*-methylaniline quenches conducted even before intermediate **9** had been fully converted (with simultaneous formation of alkyl chloride) gave only (carbamoyl)sulfenamide **5** and no alkyl group-containing products that might have corresponded to direct trapping of **9**. Of further interest, **1** did not react whatsoever with neat methanol at 25 °C, as evidenced by direct spectroscopic examination and confirmed by experiments in which the *N*-methylaniline quenches were repeated after an extended delay period. Because results on the delayed quenches were the same as for experiments with freshly made **1**, it was reasonable to conclude that methanol and **1** do not react readily. Finally, we reproduced the observation of Zumach−Kühle[1] that **1** can be trapped with cyclohexene to provide racemic **7** with presumed trans stereochemistry.[12] Compound **7** from the experiments in this work was evaluated by HPLC and gave a single peak consistent with a racemic pair of defined stereochemistry; two diastereomeric peaks would have been expected if both cis and trans addition had occurred.

Compelling further evidence consistent with structure **1** was provided by reductive dimerizations carried out on solutions of **1** in $CDCl_3$. To achieve the required transformation, the organic phase was washed with aqueous potassium iodide[24,25] to quickly give primarily bis(*N*-methyl-*N*-phenylcarbamoyl)disulfane (**13**),[13,26] along with much smaller amounts of the trisulfane and tetrasulfane counterparts.[14] Disulfane **13** was also formed, in excellent yield and purity, when thiocarbamate **6c** (2 equiv) was reacted with SO_2Cl_2 (1 equiv) in a process that undoubtedly goes through **1** as an intermediate. Thus, compound **1** formed from reaction of the first equivalent of **6c** is assumed to react with the second equivalent of **6c** to produce **13** (lower middle of Scheme 2; note that similar results, albeit with somewhat lower yields and purities, were also observed when starting with substrates **6a** and **6b**). These routes to **13** scale up readily and provide an original and efficient alternative pathway to a compound that was made previously by using *N*-methylaniline to quench bis(chlorocarbonyl)disulfane (structure **20**, introduced later in this text and in Scheme 3; a multistep route to **20** is described in ref 13).

When (carbamoyl)sulfenyl chloride **1** was simply maintained under ambient conditions in the absence of a trapping agent, it underwent a clean intramolecular aromatic substitution/cyclization to provide 3-methyl-2(3*H*)-benzothiazolone (**14**), a known heterocycle that was made previously by careful reaction[1,13] of *N*-methylaniline with chlorocarbonylsulfenyl chloride (**4**) or by unrelated chemistry.[28,29] At 25 °C, formation of **14** occurred with $t_{1/2} \sim 24$ h when **1** was generated from **4** plus **10** (final concentrations 0.1 M), with $t_{1/2} \sim 1$ h when the same method was used but at higher concentration (i.e., 1 M), with $t_{1/2} \sim 4$ h when **1** was made by reaction of SO_2Cl_2 plus **6**, and with $t_{1/2} \sim 30$ min when hydrogen chloride (acting as a catalyst) was present, as in those studies where (carbamoyl)sulfenamide **5** was the precursor. Within experimental error, such rates vary linearly with concentration. For example, when **1** was prepared from **6c** plus SO_2Cl_2, the rate of conversion of **1** to **14** decreased approximately 10-fold upon 10-fold dilution of the reaction mixture.

For further clarity, **1** was trapped by *N*-methylaniline derivatives that have additional substituents in the aromatic ring, i.e., *p*-methyl-*N*-methylaniline and *N*,2,6-trimethylaniline.[30−32] Such reactions provided the novel mixed sulfenamides **5′** and **5″**, in which the sulfenyl component was contributed regioselectively by the modified *N*-methylaniline (Scheme 2).

Stability of Compound 1. The stability of **1** was readily assessed both by direct spectroscopic examination over an extended time frame and by substantially delayed quenches. After correction for the already described relatively slow formation of heterocycle **14**, the title compound was remarkably stable, as evidenced by observation of the same quench patterns as many as 3 days later, at 25 °C. Attempts to isolate **1** by simple evaporation under reduced pressure, immediately after it had been generated from **6** plus SO_2Cl_2, resulted in its direct and quantitative decomposition to carbamoyl chloride **3**,[13] along with elemental sulfur. Compound **3** was recognized spectroscopically, and also by its very sluggish trappings[33] by either methanol to provide urethane **15**,[13] or by *N*-methylaniline to provide symmetrical urea **16**.[13] As a technical point, the ^{1}H chemical shifts of

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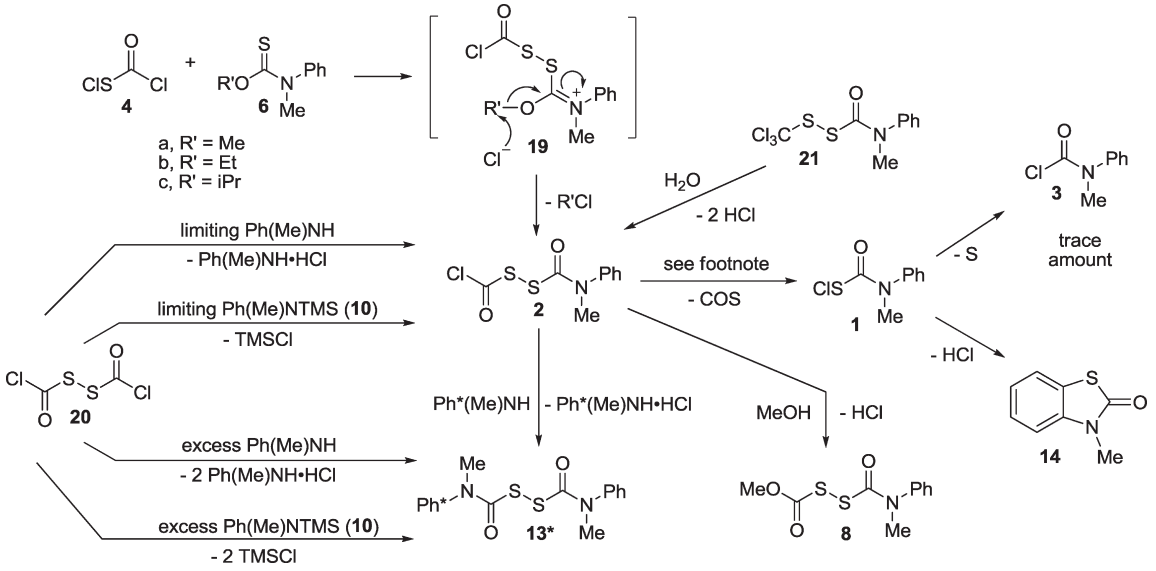
Scheme 3. Syntheses and Transformations Related to ((Carbamoyl)dithio)carbonyl Chloride 2[a]



[a] Conventions used are the same as in Scheme 2. The further decomposition of **2** to **1** occurred when it was generated from **6** plus **4** or from heating the reaction mixture that started from **21**, but *not* when **20** was the starting material, even upon heating. The further decomposition of **1** to **3**, a rather minor pathway to begin with, was seen exclusively in experiments that started with **6** plus **4**.

1 and **3** were the same, although **3** gave a broader singlet; the further trappings were necessary to establish unambiguously that **1** had been transformed to **3**. In contrast, when **1** was generated from (i) **4** (excess) plus *N*-methylaniline (limiting) (Scheme 2, upper left), (ii) equimolar amounts of **4** and silylated amine **10** (Scheme 2, upper left), or (iii) HCl cleavage of **5** (Scheme 2, upper middle), subsequent evaporation did *not* result in the formation of **3**. Instead, these latter experiments demonstrated exclusively the rapid and complete conversion of (carbamoyl)-sulfenyl chloride **1** to heterocycle **14**.

With the goal to create a system in which the (carbamoyl)-sulfenyl chloride functionality might have a longer lifetime, some of the aforementioned chemistry was repeated with the usual *N*-methylaniline group replaced by an *N*,2,6-trimethylaniline group. The presence of methyl substituents at both ortho positions in putative (*N*,2,6-trimethyl-*N*-phenylcarbamoyl)sulfenyl chloride (**1″**) was expected to preclude this intermediate from cyclization, a contrast to the already described transformation of unblocked **1** to **14**. In practice, synthesis of **1″** was achieved through treatment of chlorocarbonylsulfenyl chloride (**4**) with limiting *N*,2,6-trimethylaniline, as well as through S−N bond cleavage of the novel (carbamoyl)sulfenamide **17″** by HCl gas (Scheme 2). Whereas **1** prepared by the HCl acidolysis method cyclized to **14** completely within 2 h at 25 °C, **1″** prepared in an analogous fashion remained intact for at least 1 week. Confirmation of the proposed structure of **1″** was provided by trapping with alkanethiols, *N*-methylaniline, and *N*,2,6-trimethylaniline, yielding respectively disulfane **11″**, mixed (carbamoyl)sulfenamide **17**, and (carbamoyl)-sulfenamide **17″**. Furthermore, reductive dimerization of **1″** by aqueous potassium iodide treatment gave symmetrical bis-(carbamoyl)disulfane **18**. Upon drying and evaporation, **1″** made by any of the aforementioned procedures did not lose elemental sulfur, as proven through identical spectroscopic and quench data, as well as by direct elemental analysis.

In contrast to the results reported in the preceding paragraph, when **1″** was prepared by treatment of thiocarbamate **6b″** with SO_2Cl_2 (1 equiv), it decomposed rapidly ($t_{1/2} \sim 3$ min) to carbamoyl chloride **3″** plus elemental sulfur, even as the instantly formed intermediate **9b″** (single configuration by ^{1}H NMR) was still losing ethyl chloride to generate more **1″**. The fact that the stability of **1″** depends so markedly on the method by which it was formed is quite remarkable, but we cannot point to any component in the reaction mixtures that might respectively inhibit and/or catalyze its decomposition.

Preparation of ((*N*-Methyl-*N*-phenylcarbamoyl)dithio)-carbonyl Chloride (2). The title species **2** was accessed by several in situ routes (Scheme 3). The most straightforward (ease, clean, and unambiguous formation of desired product) of these was treatment of *O*-alkyl *N*-methyl-*N*-phenylthiocarbamates (**6**)[13,17] with chlorocarbonylsulfenyl chloride (**4**)[1,13] (1 equiv); this follows the Zumach−Kühle precedent[1] (Scheme 1) which in turn builds on work of Harris.[34] Desired **2** formed relatively rapidly and quantitatively, along with the appropriate alkyl chloride (complete within 40 min at 25 °C); an initial adduct formed within moments of addition and was assigned structure **19** (again, two configurations). Intermediate **19** was transformed to **2** plus alkyl chloride with $t_{1/2} \sim 1.5$ min for R′ = Me, $t_{1/2} \sim$ 40 min for R′ = Et, and $t_{1/2} \sim 1$ min for R′ = *i*Pr. This nonmonotonic trend in conversion rates as a function of alkyl group was confirmed in another experiment in which **6a**, **6b**, and **6c** were mixed and collectively treated with **4**; intermediate **19c** converted the fastest, followed closely by **19a**, and intermediate **19b** converted substantially slower. Most likely, for R′ = Me or Et, a limiting S_N2 displacement is followed, while for R′ = *i*Pr, the mechanism switches to S_N1. Alternatively, (dithio)carbonyl chloride **2** was made by reaction of bis(chlorocarbonyl)disulfane (**20**)[13,26] with limiting *N*-methylaniline to provide a mixture comprising **2**, unreacted **20**, and the bis(substituted) adduct **13**, a readily recognizable compound that had been made previously[13,14,26] by reaction of **20** with excess *N*-methylaniline, and in the present work (vida infra) by reductive dimerization of (carbamoyl)sulfenyl chloride **1**. In addition, compounds **2** and **13** were formed

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in similar amounts (3:2 molar ratio), along with TMSCl formed quantitatively, from reaction of equimolar amounts of *N*-trimethylsilyl-*N*-methylaniline (**10**)[18−21] plus bis(chlorocarbonyl)-disulfane (**20**).[13,26] Last, a stirred emulsion of (trichloromethyl)-(*N*-methyl-*N*-phenylcarbamoyl)disulfane (**21**)[13] (dissolved in $CDCl_3$) in the presence of aqueous sulfuric acid, emulating several precedents[1,13,26,27] for hydrolyzing a trichloromethylsulfenyl group to a chlorocarbonylsulfenyl group, gave a complex mixture with **2** as a significant component (∼45% conversion of **21** after 24 h at 55 °C). Lengthy additional heating resulted in a reaction mixture that comprised approximately equal amounts of unreacted starting **21** and heterocycle **14** ($t_{1/2}$ ∼ 7 days; ∼47% based on starting **21**). A likely explanation for this result is that all of intermediate **2** that had formed during the course of the reaction had decomposed to carbonyl sulfide plus (carbamoyl)-sulfenyl chloride **1**, which in turn converted almost entirely to heterocycle **14** according to a previously elucidated transformation.

Trapping of Compound 2. Irrespective of how generated, ((carbamoyl)dithio)carbonyl chloride **2** was readily trapped by quenches with methanol or *N*-methylaniline, providing respectively the previously described disulfanes **8**[13] and **13**.[13,14,26] For further clarity, **2** was trapped by substituted *N*-methylaniline derivatives to provide unsymmetrical bis(carbamoyl)disulfanes **13′** and **13″**. Just as the quenching of intermediate **9** gave the same results as the quenching of compound **1**, so did intermediate **19** and compound **2** display the same quenching patterns, i.e., no alkyl-containing quench products.

Stability of Compound 2. The stability of **2** was monitored primarily by repeated recording, at a variety of time points, of spectra of mixtures in which this species was a component. In addition, quenches with methanol or with *N*-methylaniline were carried out on a delayed basis. Results depended on the mode by which **2** had been generated (footnote to Scheme 3). Remarkably, even after 4 weeks under ambient conditions, **2** that had been prepared by monosubstitution of **20** remained essentially unchanged. Moreover, moderately pure **2** (∼95%, with the remainder **13**) could be isolated by flash chromatography, followed by simple evaporation of solvent. However, when **2** had been created from reaction of **4** plus **6**, decomposition to (carbamoyl)sulfenyl chloride **1** plus COS occurred (Me: $t_{1/2}$ ∼ 10 min; Et: $t_{1/2}$ ∼ 30 min; *i*Pr: $t_{1/2}$ ∼ 2 min), up to a saturation point, i.e., ratio of **2**:**1** = 2:1 for Me, 1:3 for Et, and 4:1 for *i*Pr, with no further **1** produced. Subsequently, for this set of experiments, **1** lost HCl to form heterocycle **14** ($t_{1/2}$ ∼ 10 h for all R). In addition, a modest level of bis(carbamoyl)disulfane **13** was noted, presumably from reaction of **1** with **6**, as hypothesized to explain other results discussed earlier.

SUMMARY AND CONCLUSIONS

This research has documented a number of ways (Schemes 2 and 3, respectively) to generate two types of species, i.e. (carbamoyl)sulfenyl chlorides **1** and ((carbamoyl)dithio)carbonyl chlorides **2**, that had hitherto been thought to be quite unstable. Instead, compelling spectroscopic and chemical evidence in support of these structures was obtained. Numerous derivatives, some new and others matching materials known by alternative routes, were prepared and characterized. While both **1** and **2** proved to be unusually stable as a result of most, but not all, of the methods used to obtain them, the pathways of their decompositions were also elucidated: **2** loses COS to form **1**, which either loses hydrogen chloride to form heterocycle **14** or loses elemental sulfur to form carbamoyl chloride **3**. Analogues based on *N*-2,6-trimethylaniline, where heterocyclization to a product akin to **14** is impossible, provided additional insights. Reasons for the selective stabilities of **1** or **2** as a function of their precursors, and/or the conditions of the reactions that convert those precursors to **1** or **2**, remain mysteries.

EXPERIMENTAL SECTION

General. Most methods and materials used were described in our previous publications,[13,14] although many of the spectroscopic and analytical methods are substantially more effective. Labile acid and sulfenyl chlorides were converted to the corresponding amides and sulfenamides by adding the compounds to a sufficient excess of *N*-methylaniline or a related amine, 2 M in $CHCl_3$ at 4 °C, unless otherwise specified; after 15 min reaction, extractive workups were carried out as described previously.[13] ^{1}H NMR spectra were recorded in $CDCl_3$ (or any indicated solvent) at 300 MHz (some) or 500 MHz (mostly, and assumed if not specified otherwise). ^{13}C NMR spectra were recorded in $CDCl_3$ on the same instruments at 75 or 125 MHz, with $CDCl_3$ normalized to δ 77.0 ppm. IR spectra were recorded in CH_2Cl_2 or $CHCl_3$ solutions. Electrospray ionization was used in most cases to acquire high resolution mass spectra. A spectrometer coupled with a gas chromatograph or solids probe was used to acquire chemical ionization (with methane and ammonia) high resolution mass spectra for chlorine-containing compounds. Elemental analyses were obtained by combustion analysis (for C,H,N,S) and by ion chromatography (for Cl). HPLC data was acquired using a dual solvent system with UV/vis detection, equipped with a 250 × 4.6 mm reversed phase (C18) column (5 μm particle size). Solvent was methanol−water (4:1, unless otherwise specified), with 1 mL/min flow rate. All solvent evaporation procedures were conducted under aspirator vacuum.

(*N*-Methyl-*N*-phenylcarbamoyl)sulfenyl Chloride (1) (Scheme 2). *Method A.* Neat SO_2Cl_2 (180 μL, 2.2 mmol) was added to a solution of *O*-methyl thiocarbamate **6a** (372 mg, 2.0 mmol) in $CDCl_3$ (2.0 mL). Reaction progress at 25 °C was tracked by repeat ^{1}H NMR scans of the mixture, as well as *N*-methylaniline quenches at appropriate time points. Within moments of addition, peaks attributed to intermediate **9a** were noted: ^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 5 H), 4.70 and 4.48 (two singlets of equal heights, representing two configurations, 3 H total), 4.04 and 3.59 (two singlets of equal height, 3 H total); ^{13}C NMR (125 MHz) diagnostic peaks at δ 63.1, 62.8, 45.5, 42.2. Then, with $t_{1/2}$ ∼ 8 min, title compound **1** appeared: ^{1}H NMR δ 7.65−7.35 (m, 5 H), 3.38 (s, 3 H); ^{13}C NMR δ 164.0, 138.6, 130.4, 130.1, 128.8, 38.9; along with MeCl formed at the same rate: ^{1}H NMR δ 3.01 (s, 3 H); ^{13}C NMR δ 25.8. An *N*-methylaniline quench after 5 min showed (carbamoyl)sulfenamide **5** as the major product [90% yield; diagnostic ^{1}H NMR signals at δ 3.38 (s, 3 H) and 3.27 (s, 3 H), as reported previously[13]]. After 3 days, heterocycle **14** [diagnostic signal at δ 3.45 (s, 3 H)] and carbamoyl chloride **3** [δ 3.38 (broad s, 3 H)] both formed, in a 4:1 ratio. A similar experiment, with CH_2Cl_2 as solvent and with the reaction being followed by IR, led to assignment of the main peaks due to **1**: 3054 (m), 1732 (vs) cm^{-1}.

Similar experiments were carried out starting with *O*-ethyl thiocarbamate **6b** (390 mg, 2.0 mmol) or *O*-isopropyl thiocarbamate **6c** (418 mg, 2.0 mmol). Results were similar, except for the kinetics (summarized in text). The intermediates were **9b** [^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 5 H), 5.15 and 4.98 (two q of equal heights, representing two configurations, J = 7.0 Hz, 2 H total), 3.98 and 3.55 (two singlets, 3 H total), 1.62 and 1.32 (t, J = 7.0 Hz, 3 H total); ^{13}C NMR (125 MHz) diagnostic peaks at δ 176.8, 176.6, 74.7, 74.3, 45.1, 42.1, 14.1, 13.8] and **9c** [^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 5 H), 6.02 (septet, J = 6.5 Hz, 1 H), 3.98 (s, 3 H), 1.32 (d, J = 6.5 Hz, 6 H); ^{13}C NMR (125 MHz) diagnostic peaks at δ 86.1, 44.9, 21.9]. Coproduct peaks were noted as follows: EtCl

[^{1}H NMR δ 3.57 (q, J = 7.2 Hz, 2 H), 1.48 (t, J = 7.2 Hz, 3 H); ^{13}C NMR δ 39.8, 18.7] and *i*PrCl [^{1}H NMR δ 4.19 (septet, J = 6.5 Hz, 1 H), 1.50 (d, J = 6.5 Hz, 6 H); ^{13}C NMR δ 53.8, 27.3]. After 3 days, the ratio of **14** to **3** was 3:1 in the case of series **b**, and 4:1 in the case of series **c**.

To confirm the surprising trend involving rates by which intermediate **9** converts to (carbamoyl)sulfenyl chloride **1** as a function of the R group (i.e., *i*Pr > Me > Et), a mixture of **6a** (90 mg, 0.5 mmol), **6b** (97 mg, 0.5 mmol), and **6c** (104 mg, 0.5 mmol) in $CDCl_3$ (1.5 mL) was treated with neat SO_2Cl_2 (138 μL, 1.7 mmol), and reaction progress was tracked by ^{1}H NMR. At 2 min, **9c** was in a 1:1 ratio with *i*PrCl; at 8 min, **9a** was in a 1:1 ratio with MeCl; and at 12 min, **9b** was in a 1:1 ratio with EtCl. Note that the kinetics of reaction with SO_2Cl_2 when **6a**, **6b**, and **6c** were admixed are close to, but not identical to, those determined when each of these pure compounds was reacted separately with SO_2Cl_2.

The effect of concentration on the rate of decomposition of **1** to **14** was studied by diluting the reaction mixture of **6b** plus SO_2Cl_2. To create 0.50 or 0.25 M mixtures, neat SO_2Cl_2 (45 or 22 μL, 0.55 or 0.27 mmol) was added to a solution of **6b** (98 mg or 49 mg, 0.50 or 0.25 mmol) in $CDCl_3$ (1.0 mL for both experiments). A 0.1 M mixture was created by adding SO_2Cl_2 (19 μL, 0.23 mmol) to **6b** (39 mg, 0.20 mmol) in $CDCl_3$ (2 mL). Reactions were tracked by ^{1}H NMR, and 1:1 ratios of **1** to **14** were seen at ~8 h for the 0.50 M mixture, ~12 h for the 0.25 M mixture and ~32 h for the 0.1 M mixture.

The reaction of *O*-ethyl thiocarbamate **6b** with SO_2Cl_2 (previously described quantities) was also conducted in the same manner, varying only the solvent: CD_3CN, benzene-d_6, and dioxane-d_8. Relevant chemical shifts are reported in the Supporting Information (Supporting Table 1). Results were the same as in $CDCl_3$, in terms of product distributions, stabilities, decompositions, and trappings, but there were differences in terms of kinetics. More precisely, initial adduct **9b** formed essentially instantly in all cases, but the rates of concomitant formation of **1** and ethyl chloride were increased ~5-fold in CD_3CN ($t_{1/2}$ ~ 2 min), slowed ~5-fold in benzene-d_6 ($t_{1/2}$ ~ 45 min), and slowed ~20-fold in dioxane-d_8 ($t_{1/2}$ ~ 3.5 h).

Method B. A commercially available solution of hydrogen chloride (4.0 M) in dioxane was diluted into $CDCl_3$ to create a 1.0 M solution [HCl (4.7 mmol) in dioxane (1.4 mL) and $CDCl_3$ (3.3 mL)] which was added to a solution of (carbamoyl)sulfenamide **5** (605 mg, 2.2 mmol) in $CDCl_3$ (23 mL), under N_2 at 25 °C. ^{1}H NMR examination after 15 min revealed a 1:1 mixture of starting **5** and product **1**, with no further decomposition products noted. At 1 h, the ratio of **5** to **1** was 1:7, and heterocycle **14** comprised ~5% of the mixture. At 6 h, starting **5** was no longer apparent and the ratio of **1** to **14** was 1:1. After 24 h, ^{1}H NMR showed only heterocycle **14**, along with *N*-methylaniline hydrochloride [diagnostic signal at δ 3.03 (s, 3 H)].

Method C. Hydrogen chloride gas was bubbled at a moderate rate through a solution of (carbamoyl)sulfenamide **5** (136 mg, 0.5 mmol) in $CDCl_3$ (5 mL), under N_2, at 25 °C for 1 min. A ^{1}H NMR (500 MHz) spectrum taken 20 min later revealed that starting **5** was entirely consumed, while **1** and **14** were present in a 3:1 ratio and *N*-methylaniline hydrochloride had formed quantitatively. A time point at 1 h showed a 1:3 ratio of **1** to **14**, and after 2 h, only **14** and the amine salt were noted.

Method D. A 2 M solution of *N*-methylaniline (0.5 mL, 2.0 equiv) in $CDCl_3$ (2.0 mL) was added slowly to a solution of chlorocarbonylsulfenyl chloride (**4**) (42 μL, 0.5 mmol) in $CDCl_3$ (0.5 mL) at 4 °C and then allowed to warm to 25 °C. ^{1}H NMR examination after 30 min revealed the presence of **1** and heterocycle **14** in a 2:1 ratio, while after 1 h, these species were in equal quantities, and after 8 h, **1** had disappeared entirely and only **14** plus a trace amount of disubstituted compound **5** were noted. At all time points, a quantitative amount of *N*-methylaniline hydrochloride (1 equiv) was present.

Method E. A solution of silylated amine **10** (180 mg, 1.0 mmol) in $CDCl_3$ (0.5 mL) was added over 1 min to a solution of chlorocarbonylsulfenyl chloride (**4**) (83 μL, 1.0 mmol) in $CDCl_3$ (0.5 mL) at 4 °C and then allowed to warm to 25 °C. Complete conversion of **10** was observed by ^{1}H NMR within 3 min after addition was finished, to provide **1** (~95%) and **5** (~5%) along with TMSCl (quantitative). Further time points revealed that **1** decomposed to **14** with a $t_{1/2}$ ~ 1 h, at 25 °C. When a similar experiment was carried out at a final concentration of 0.1 M, the initial reaction was again very fast, and the decomposition of **1** to **14** was substantially slower ($t_{1/2}$ ~ 24 h).

Further Reactions To Quench or Trap (Carbamoyl)sulfenyl Chloride 1 (Scheme 2). Once **1** had been generated by any of the described methods (Scheme 2), the followup transformations described herein were carried out to support the structural conclusions of this work. While results were consistent across-the-board, somewhat purer products were obtained when the starting material for generation of **1** was the *O*-isopropyl thiocarbamate **6c** and when quenching reactions were conducted at 4 °C within 5 min of the initial reaction. In a few cases, i.e., for species **5′**, **5″**, and **7**, the indicated novel products were isolated and characterized further. For the vast remainder of these studies, products from the quenches matched reference compounds made previously and/or in this work by alternative routes. For such latter cases, mixtures obtained after quenching reactions were spiked with known amounts of the relevant reference compounds to confirm identifications of reaction products.

Method A. An aliquot of a reaction mixture containing **1** (typically ~0.5 mmol scale; concentration ~0.5 M) in $CDCl_3$ was added quickly to the appropriate volume of a 2 M solution of an alkanethiol RSH (R = Me, Et, *i*Pr, *t*Bu) in $CHCl_3$, so that the thiol was in slight excess (1.2 equiv). After 1 h at 25 °C, these quenched reactions were evaporated, providing the appropriate carbamoyl disulfide **11** (see later for reference compounds and their properties). In a typical experiment, one-quarter portions of the reaction of **6c** with SO_2Cl_2 (previously described quantities) were quenched after 1 min with each of the four alkanethiols (0.6 mmol per experiment) to provide the appropriate **11a**−**d** in ~95% purity upon concentration. More specifically, **11a** was a brown oil (101 mg, 95%), **11b** was a brown oil (108 mg, 95%), **11c** was a white powder (113 mg, 93%) with mp 45−49 °C, and **11d** was a white powder (119 mg, 93%) with mp 38−41 °C. Note that the melting points of **11c** and **11d** were essentially identical to authentic materials made as described later. Quenching conducted after 20 min gave the same results, with a slight reduction in the purities of **11** to ~90%, the rest being mostly **14** and **3**.

Method B. Mixtures containing **1** (0.5−2 mmol; concentration 0.5−1.0 M) in $CDCl_3$ were added to methanol (equal volume), with the thought that **1** might react with the solvent, but in fact no substitution was noted. In one experiment, **1** was made from **6c** and SO_2Cl_2 (previously described quantities) and "quenched" into CD_3OD (equal volume) after 5 min, and the mixture was followed by ^{1}H NMR. At the 2-h point, only **1**, **3** (not converted to **15**), and **14** were observed, in a ratio of 12:1:4. At the 4-h point, an aliquot of the mixture was reacted with *N*-methylaniline to produce **5** (from trapping unreacted **1**), **14** (from the continuing intramolecular cyclization of **1**), and **3** (from decomposition of **1**; note that it did not react further with methanol to give **15**) in a ratio of 6:4:1. Extractive workup and concentration at this point gave a tan powder (384 mg, 86%), showing the same ratio of compounds.

In another experiment, the same reaction of **6c** and SO_2Cl_2 was added to CD_3OD after 5 min and left for 3 days. Concentration at that point gave only heterocycle **14** and carbamoyl chloride **3** in the usual 4:1 ratio (305 mg, 92%).

Method C. Mixtures containing **1** (~2 mmol; concentration ~1 M) in $CHCl_3$ were added to the appropriate volume of a 2 M solution of cyclohexene (1.2 equiv) in $CHCl_3$, for 1 h reaction at 25 °C. Then concentration and purification by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)] were performed. This process, applied to the reaction of **6c** and SO_2Cl_2 (previously described quantities), gave **7**

(a new compound) as a clear, colorless oil (325 mg, 65%), with diastereomeric purity indicated by HPLC (MeOH/H_2O = 9:1, t_r = 7.51 min.); ^{1}H NMR (500 MHz) δ 7.5−7.2 (m, 5 H), 4.1−4.0 (m, 1 H), 3.8−3.7 (m, 1 H), 3.32 (s, 3 H), 2.3−2.1 (m, 2 H), 1.80−1.69 (m, 2 H), 1.58−1.20 (m, 4 H); ^{13}C NMR (75 MHz) δ 167.4, 141.8, 129.4, 128.3, 128.2, 61.9, 50.0, 38.3, 33.7, 30.3, 24.0, 22.7; HRMS (ESI): m/z [M + Na^+] calcd for $C_{14}H_{18}ClNOS$: 306.0690; found: 306.0695; IR 3053 (s), 2986 (m), 1653 (s) cm^{-1}.

Method D. Mixtures containing **1** (∼2 mmol; concentration ∼1 M) in $CHCl_3$ were added, with stirring, to the appropriate volume of a 0.5 M aqueous solution of potassium iodide (5 equiv). After being stirred for 10 min, the resultant mixture was washed with 1 M aqueous sodium thiosulfate (3 × 1 volume) until it was colorless. Extractive workup and concentration gave a white powder that was predominantly disulfane **13**[13,26] but included traces of its tri- and tetrasulfane counterparts.[14] For example, when **6c** was reacted with SO_2Cl_2 (previously described quantities) to produce **1**, followed 5 min later by the aforementioned iodide treatment, **13** represented 90% of the product mixture (265 mg, 79%); mp 225−230 °C (lit.[13] mp 240−243 °C).

Method E. Mixtures containing **1** (0.5−2 mmol; concentration 0.5−1.0 M) in $CHCl_3$ were added to a 2 M solution of *N*,2,6-trimethylaniline (2.2 equiv) in $CHCl_3$ at 4 °C. The derivatization reaction was complete after 15 min. The case when **1** was generated by reaction of **6c** and SO_2Cl_2 (previously described quantities), followed by normal workup procedures, purification by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)], and crystallization under hexanes (6 mL, −20 °C) for 1 week, resulted in formation of **5″** as white needles (408 mg, 68%); mp 93−95 °C; ^{1}H NMR (500 MHz) δ 7.5−6.9 (m, 8 H), 3.29 (s, 3 H), 3.17 (s, 3 H), 2.41 (broad s, 6 H); ^{13}C NMR (75 MHz) δ 171.9, 148.7, 140.6, 136.6, 129.4, 128.6, 128.4, 128.0, 126.0, 47.2, 38.2, 19.0 (2 C); HRMS (ESI): m/z [M + Na^+] calcd for $C_{17}H_{20}N_2OS$: 323.1189; found: 323.1194; IR 3053 (s), 2986 (w), 1668 (m) cm^{-1}.

Method F. In a manner similar to method E, starting from **6c** and SO_2Cl_2 (previously described quantities), followed by an *N*-methyl-*p*-toluidine quench, gave after workup and purification by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)] compound **5′** as a viscous, brown oil (418 mg, 73%): ^{1}H NMR (300 MHz) δ 7.5−7.1 (m, 5 H), 3.35 (s, 3 H), 3.26 (s, 3 H), 2.24 (s, 3 H); ^{13}C NMR (125 MHz) δ 170.0, 147.7, 130.4, 129.5, 129.1, 128.7, 127.8, 122.2, 115.6, 44.6, 37.7, 20.2; HRMS (ESI): m/z [M + Na^+] calcd for $C_{16}H_{18}N_2OS$: 309.1032; found: 309.1028; IR 3027 (w), 2937 (m), 1679 (vs) cm^{-1}.

Method G. To test the quenching profile of intermediate **9**, the mixture after 1 min of the reaction between **6b** and SO_2Cl_2 (previously described quantities; a time when the original reaction mixture comprised primarily **9b**, with little of either starting material **6b** or product **1**) was treated with *N*-methylaniline (2.2 equiv, from a 2 M stock solution in $CDCl_3$). A ^{1}H NMR spectrum recorded 3 min after the quenching (no workup) showed the presence of (carbamoyl)sulfenamide **5** in 95% purity (the rest being **13**), along with the stoichiometric amount of EtCl. No change was seen thereafter. Extractive workup and concentration at this point gave the mixture as an off-white powder (445 mg, 85%); mp 66−70 °C (lit.[13] mp 71−72 °C).

Method H. Following a quenching procedure that Böhme et al.[35] used successfully on chlorocarbonyldisulfanyl chloride, a portion (0.5 mmol) of the reaction mixture of **6c** and SO_2Cl_2 (previously described quantities) was added, 3 min after it had reacted to form **1** plus *i*PrCl, to a solution of 1,3,5-trimethoxybenzene (117 mg, 0.7 mmol) in $CDCl_3$ (0.5 mL) at 25 °C. ^{1}H NMR after 24 h indicated that there was no reaction, showing only peaks corresponding to *i*PrCl, as well as **14** and **3** (ratio 4:1; these are decomposition products of **1**, which was no longer present), and the unreacted starting material, 1,3,5-trimethoxybenzene (diagnostic peak at δ 3.75; confirmed by doping).

Reaction of Bis(*N*-methyl-*N*-phenylcarbamoyl)disulfane (13) with Sulfuryl Chloride (Scheme 2, footnote b). A solution of bis(carbamoyl)disulfane **13** (166 mg, 0.5 mmol) and SO_2Cl_2 (45 μL, 0.55 mmol) in $CDCl_3$ (2.5 mL) was followed by ^{1}H NMR at 25 °C. Within minutes of addition, carbamoyl chloride **3** and heterocycle **14** were observed in a 1:1 ratio; this ratio was unchanged throughout the duration of the reaction and was also found once the end point was reached (no starting **13** remaining). The transformation of **13** to the aforementioned products proceeded with $t_{1/2}$ ∼ 45 min. As a practical matter, intermediate time points required careful scrutiny because of the similar chemical shifts of starting **13** (sharp singlet) and product **3** (broad singlet).

(*N*,2,6-Trimethyl-*N*-phenylcarbamoyl)sulfenyl Chloride (1″). *Method A (preferred).* Hydrogen chloride gas was bubbled at a moderate rate through a solution of sulfenamide **17″** (164 mg, 0.5 mmol) in $CDCl_3$ (5 mL), under N_2, at 25 °C for 1 min. ^{1}H NMR revealed that formation of **1″** and the amine hydrochloride was complete within 10 min, and extractive workup and concentration gave **1″** as a brown oil (106 mg, 93%); ^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 3 H), 3.26 (s, 3 H), 2.28 (s, 6 H); ^{13}C NMR (75 MHz) δ 164.2, 139.1, 130.7, 129.3, 129.0, 36.0, 17.4 (2 C); HRMS (CI) m/z [M + H^+] calcd for $C_{10}H_{12}ClNOS$: 230.0401; found: 230.0419; IR 3025 (w), 2926 (s), 2696 (s), 1696 (s) cm^{-1}; Anal. Calcd for $C_{10}H_{12}ClNOS$: C, 52.28; H, 5.27; N, 6.10; S, 13.96; Cl, 15.43. Found: C, 52.70; H, 5.46; N, 5.94; S, 14.12; Cl, 15.48.

Method B. A 2 M solution of *N*,2,6-trimethylaniline (0.5 mL, 2.0 equiv) in $CDCl_3$ was added slowly to a solution of chlorocarbonylsulfenyl chloride (**4**) (42 μL, 0.5 mmol) in $CDCl_3$ (0.5 mL) at 4 °C and then allowed to warm to 25 °C. Tracking by ^{1}H NMR revealed reaction completion within 10 min and formation of a trace amount of disubstituted compound **17″**. The usual workup gave **1″** as a brown oil (196 mg, 84%).

Method C. Neat SO_2Cl_2 (180 μL, 2.2 mmol) was added to a solution of *O*-ethyl thiocarbamate **6″** (223 mg, 2.0 mmol) in $CDCl_3$ (2.0 mL). Reaction progress at 25 °C was tracked by repeat ^{1}H NMR scans of the mixture, as well as *N*,2,6-trimethylaniline quenches at appropriate time points. Within moments of addition, peaks attributed to intermediate **9″** were noted: ^{1}H NMR (500 MHz) δ 5.07 (q, J = 7.0 Hz, 2 H), 3.97 (s, 3 H), 2.31 (s, 6 H), 1.39 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz) diagnostic peaks at δ 74.4, 42.8, 17.3 (2 C), 14.3. Then, with $t_{1/2}$ ∼ 3 min, title compound **1″** appeared, along with EtCl formed at the same rate. An *N*,2,6-trimethylaniline quench after 30 min showed (carbamoyl)sulfenamide **5″** as only a minor product (5%), with carbamoyl chloride **3″** comprising the rest [diagnostic signal at δ 3.25 (s, 3 H)]. After 2 h, the mixture was concentrated, giving **3″** as a tan powder (347 mg, 88%); mp 73−76 °C (lit.[36] mp 78−79 °C).

Quenches and Trappings of 1″. This section refers to quenches of experiments where (carbamoyl)sulfenyl chloride **1″** was generated in situ and followed closely the procedures already outlined for unsubstituted **1** (including confirmation of products by doping). As indicated above, it was also possible to isolate and characterize **1″** (methods A and B) and that material could be reacted in similar fashion.

Method A. Quenching mixtures containing **1″**, 5 min after they were made from **6b″** plus SO_2Cl_2 (previously described quantities) with 2 M solutions of the alkanethiols (1.2 equiv) in $CDCl_3$, 1 h reaction at 25 °C, gave (after concentratrion) mixtures with **11a″**−**d″** as ∼35%, with the rest being **3″**, which forms rapidly under the reaction conditions. The MeSH quench gave, after concentration, a brown oil (102 mg), EtSH quench also gave a brown oil (102 mg), *i*PrSH quench gave a white powder (106 mg), and *t*BuSH quench also gave a white powder (109 mg).

Method B. Reaction of **1″** with aqueous KI using the previously described procedure gave **18** quantitatively based on **1″**; however, due to the partial decomposition of **1″** to **3″** by the time the KI reaction was run, the same amount of **3″** (which does not react with KI) was carried over. For reaction of **6b″** and SO_2Cl_2 (previously described quantities), trapping with KI after 5 min gave a mixture that comprised **18** and **3″**

in a 3:7 ratio. When the KI procedure was applied to the reaction mixture of *N*,2,6-trimethylaniline and excess **4** (previously described quantities), filtration, extractive workup, and concentration gave a white powder (70 mg, 72%), mp 187−193 °C, of which **18** comprised ∼80% by ^{1}H NMR, with two further species (∼10% each) [^{1}H NMR respectively δ 3.20 (s), 2.32 (s) and δ 3.13 (s), 2.22 (s)], also present.

Method C. Quenching mixtures containing **1″** (0.5−2.0 mmol) with the appropriate amount of *N*-methylaniline also produced expected results, giving **17**. The reaction of **6b″** and SO_2Cl_2 (previously described quantities) was quenched after 3 min, giving a mixture that comprised **17** and **3″** in a 1:1 ratio, along with *N*-methylaniline hydrochloride commensurate with the amount of **17** formed. Extractive workup and concentration gave the mixture as a tan powder (448 mg, 90%).

Method D. A solution of pure **1″** (115 mg, 0.5 mmol) in $CHCl_3$ (0.5 mL) was added to CD_3OD (equal volume), and the mixture was maintained for 24 h at 25 °C, with no changes in its ^{1}H NMR spectrum. At this point, the mixture was added to a 2 M solution of *N*-methylaniline (118 mL, 2.2 equiv) in $CDCl_3$, and **17** was observed as the sole product. Extractive workup and concentration gave mixed (carbamoyl)sulfenamide **17** as the expected tan powder (137 mg, 92%); mp 144−148 °C.

((*N*-Methyl-*N*-phenylcarbamoyl)dithio)carbonyl Chloride (2). *Method A.* Neat chlorocarbonylsulfenyl chloride (**4**) (184 μL, 2.2 mmol) was added to a solution of *O*-methyl thiocarbamate **6a** (373 mg, 2.0 mmol) in $CDCl_3$ (2.0 mL). Reaction progress at 25 °C was tracked by repeat ^{1}H NMR scans as well as *N*-methylaniline quenches at appropriate time points. Within moments of addition, peaks attributed to intermediate **19a** were noted: ^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 5 H), 4.48 (more prevalent) and 4.70 (two singlets, ratio 6:5, 3 H total), 4.04 and 3.59 (two singlets, ratio 6:5, 3 H total); ^{13}C NMR (125 MHz) diagnostic peaks at δ 62.8, 61.6, 46.5, 45.5. Then, with $t_{1/2}$ ∼ 1.5 min, title compound **2** appeared: ^{1}H NMR δ 7.5−7.3 (m, 5 H), 3.40 (s, 3 H); ^{13}C NMR δ 171.4, 164.6, 130.1, 129.9, 128.7, 113.7, 39.6, along with MeCl formed at the same rate. An *N*-methylaniline quench after 10 min showed disulfane **13** and (carbamoyl)sulfenamide **5** in equimolar quantities [93% yield; diagnostic ^{1}H NMR signals of **13** at δ 3.36 (s, 3 H) as reported previously[13]]; this result reflects relatively rapid formation of compound **2** and decomposition of approximately half of that compound **2** to (carbamoyl)sulfenyl chloride **1** plus COS over the 10-min time span. An *N*-methylaniline quench was carried out 2 days after the original reaction and lasted for an additional 24 h to allow any carbamoyl chloride **3** to react to form urea **16**. This experiment showed **13** and **14** in a 2:1 ratio, with urea **16** comprising a further ∼3% of the mixture. This result was interpreted to mean that decomposition of compound **2** had stopped and that compound **1**, formed by decomposition of **2** earlier in the process, had by now entirely cyclized to **14**. To confirm this, the 2-day reaction mixture was evaporated directly to provide a brown oil (422 mg, 92%) which comprised stable **2** and heterocycle **14** in a 2:1 ratio.

Similar experiments were carried out starting with *O*-ethyl thiocarbamate **6b** (390 mg, 2.0 mmol) or *O*-isopropyl thiocarbamate **6c** (418 mg, 2.0 mmol). Results were similar, except for the kinetics (summarized in text). The intermediates were **19b** [^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 5 H), 5.21 and 5.01 (two quartets of equal heights, representing two configurations, J = 6.0 Hz, 2 H total), 4.00 and 3.55 (two singlets, 3 H total), 1.63 and 1.33 (t, J = 6.0 Hz, 3 H total); ^{13}C NMR (125 MHz) diagnostic peaks at δ 176.8, 176.7, 74.5, 74.2, 45.0, 42.0, 14.1, 13.8] and **19c** [^{1}H NMR (500 MHz) δ 7.5−7.1 (m, 5 H), 6.17 and 6.02 (two septets, J = 6.0 Hz, 1 H total), 3.99 and 3.54 (two singlets, 3 H total), 1.68 and 1.42 (two doublets, J = 6.0 Hz, 6 H total); ^{13}C NMR (125 MHz) diagnostic peaks at δ 86.1, 80.7, 44.9, 43.6, 22.3, 21.9]. EtCl and *i*PrCl were the respective coproducts of these transformations. The 3-day reaction mixtures were evaporated to give brown oils [starting with **6b**, 344 mg (91%) comprising **2** and **14** in a 1:3 ratio, with a small amount (2%) of **3**; starting with **6c**, 455 mg (95%) comprising **2** and **14** in a 4:1 ratio, with **3** not observed].

To confirm the surprising trend involving the rates by which intermediate **19** is converted to (dithio)carbonyl chloride **2** as a function of R group (i.e., *i*Pr > Me > Et), a mixture of **6a** (90 mg, 0.5 mmol), **6b** (97 mg, 0.5 mmol), and **6c** (104 mg, 0.5 mmol), together in $CDCl_3$ (1.5 mL) was treated with neat **4** (142 μL, 1.7 mmol), and reaction progress was tracked by ^{1}H NMR. At 3 min, **19c** was not seen (complete conversion to **2** plus *i*PrCl), **19a** was in a 1:1 ratio with MeCl, and **19b** was mostly unconverted. At 16 min, **19a** and **19c** were gone, the amounts of *i*PrCl and MeCl were quantitative, and **19b** was in a 1:1 ratio with EtCl.

Method B. A mixture of concentrated H_2SO_4 (1.0 mL) and water (0.2 mL) was added to a solution of carbamoyl disulfide **21** (150 mg, 0.48 mmol) in $CDCl_3$ (2.4 mL), and the heterogeneous mixture was stirred vigorously at 55 °C for 24 h while HCl gas was released continuously. At this point, the $CDCl_3$ phase was removed and examined by ^{1}H NMR, revealing a mixture of product **2** and starting material **21** in a 9:11 ratio, with no other species present. However, after 7 days of additional heating, unreacted **21** and heterocycle **14** (from decomposition of **2** to **1** plus COS, and subsequent cyclization of **1**) were present in a 1:1 ratio, with no discernible **2**. Concentration at this point gave a tan powder (95 mg, 82%) which was a 1:1 mixture of **21** and **14**.

Method C (preparative). A solution of *N*-methylaniline (1.29 g, 12 mmol, 2.0 equiv) in $CHCl_3$ (6.0 mL) was added slowly to a solution of bis(chlorocarbonyl)disulfane (**20**) (1.15 g, 6.0 mmol) in $CHCl_3$ (6.0 mL) at 4 °C. After 15-min reaction, the mixture was concentrated, and flash chromatography [SiO_2, eluted with hexanes:EtOAc (1:1)] provided **2** as a clear viscous colorless oil [672 mg, 43%; mostly separated from starting **20** and bis(carbamoyl)disulfane **13**]; HRMS (CI): m/z [M + H$^+$] calcd for $C_9H_8ClNO_2S_2$: 261.9758; found: 261.9754; IR 3055 (s), 2983 (m), 1779 (w), 1687 (s) cm^{-1}; Anal. Calcd for $C_9H_8ClNO_2S_2$: C, 41.30; H, 3.08; N, 5.35; S, 24.50; Cl, 13.54. Found: C, 41.69; H, 3.22; N, 5.27; S, 26.27; Cl, 12.05. The aforementioned data are admittedly different from ideal, and this is attributed to the presence of **13** (∼5%) that had not been entirely removed during the chromatography step.

Method D. A solution of silylated amine **10** (181 mg, 1.0 mmol) in $CDCl_3$ (0.5 mL) was added slowly to a solution of bis(chlorocarbonyl)disulfane (**20**) (191 mg, 1.0 mmol) in $CDCl_3$ (0.5 mL) at 4 °C. ^{1}H NMR examination within 3 min revealed that the reaction was complete (starting **10** consumed; stoichiometric amount of TMSCl formed), with products **2** and **13** present in a 3:2 molar ratio. The relative amount of **2** remained unchanged after even a day at 25 °C. Concentration of the reaction mixture after 15 min revealed the presence of **2** and **13** in the same ratio and accounting for essentially all of the material (287 mg, 95%).

Quenches and Trappings of Compound 2. Quenches of all mixtures containing **2** were carried out in the same way as that performed for mixtures containing **1** or **1″**. In situ reactions described next were used only for diagnostic purposes and not to isolate products. All quenches were confirmed by doping with authentic products, prepared as described later. Note that **2**, once isolated, reacts with the various trapping reagents to provide the appropriate products in high yields and purities.

Method A. Mixtures containing **2** (0.5−2.0 mmol; concentration 0.5−1.0 M) in $CDCl_3$ solution were added to a 2 M solution (2.2 equiv) of *N*,2,6-trimethylaniline at 4 °C, to ultimately provide unsymmetrical disulfane **13″**. When the reaction mixture of **6c** and **4** (previously described quantities) was quenched after 30 min, (carbamoyl)disulfane **13″** was observed alongside (carbamoyl)sulfenamide **5″** in a 4:1 ratio; this result was interpreted to indicate that about 20% of ((carbamoyl)-dithio)carbonyl chloride **2** had decomposed to sulfenyl chloride **1**, which would react further to give **5″**. Also, *N*,2,6-trimethylaniline hydrochloride [diagnostic ^{1}H NMR (500 MHz) signals at δ 3.07 (t, J = 5.5 Hz, 3 H),

2.67 (s, 6 H)] was observed in the immediate reaction mixture. Extractive workup and concentration gave the 4:1 mixture of **13″** and **5″** (but without the amine hydrochloride) as a white powder (626 mg, 90%); mp 126−131 °C.

Method B. Trapping in the same fashion as method A was conducted but using *N*-methyl-*p*-toluidine. When the reaction mixture of **6c** and **4** (previously described quantities) was quenched after 2 min, **13′** comprised nearly all of the mixture, and the corresponding amount of *N*-methyl-*p*-toluidine hydrochloride [diagnostic ^{1}H NMR signals at δ 2.86 (s, 3 H), 2.27 (s, 3 H)] was present. Extractive workup and concentration gave **13′** as a white powder (588 mg, 85%); mp 126−130 °C.

Method C. When mixtures containing **2** (0.2−2.0 mmol; concentration 0.2−2.0 M) in $CDCl_3$ solution were added quickly to excess methanol (equal volume) at 25 °C, ((methoxycarbonyl)dithio)carbamoyl derivative **8** formed, as observed 1 h later upon evaporation. For example, when compound **21** (0.2 mmol) was partially hydrolyzed with H_2O/H_2SO_4 at 55 °C for 24 h (method B to form **2**), a methanol quench showed a 9:11 ratio of derivative **8** to unreacted starting **21**. Concentration gave a tan powder (46 mg, 79%) with the same ratio of **8** to **21**.

Method D. To test the quenching profile of intermediate **19**, the mixture after 1 min of the reaction between **6b** and chlorocarbonylsulfenyl chloride (**4**) (previously described quantities; a time when the original reaction mixture comprised primarily **19b**, with little of either starting material **6b** or product **2**) was treated with *N*-methylaniline (2.2 equiv, from a 2 M stock solution in $CDCl_3$). A ^{1}H NMR spectrum recorded 3 min after the quenching (no workup) showed the presence of disulfane **13** in 90% purity (the rest being **5**), along with the stoichiometric amount of EtCl. No change was seen thereafter. Extractive workup and concentration at this point gave the mixture as an off-white powder (541 mg, 86%); mp 221−225 °C (lit.[13] mp 240−243 °C).

(*N*,*N*′-Dimethyl-*N*,*N*′-diphenylcarbamoyl)sulfenamide (5). Neat chlorocarbonylsulfenyl chloride (**4**) (42 μL, 0.5 mmol) was added to a solution of silylated amine **10** (180 mg, 1.0 mmol) in $CDCl_3$ (1.0 mL) at 4 °C. ^{1}H NMR of the reaction mixture, recorded within 3 min, showed that **10** was no longer present, and that **5** (0.5 equiv) plus TMSCl (1 equiv) had formed nearly quantitatively. Concentration gave title product **5** as an off-white powder (256 mg, 94%); mp 68−70 °C (lit.[13] mp 71−72 °C).

***O*-Methyl *N*-Methyl-*N*-phenylthiocarbamate (6a).** Material made by quenching methoxythiocarbonyl chloride with *N*-methylaniline, followed by the standard quantitative aqueous extractive workup,[13] was still good and usable 30 years later, having been stored under ambient conditions; ^{1}H NMR[17] (300 MHz, 50 °C) δ 7.5−7.2 (m, 5 H), 3.95 (broad s, 3 H), 3.64 (broad s, 3 H); with negligible MeS(C═O) isomer,[13] diagnostic δ 3.33 (s, 3 H), 2.26 (s, 3 H). Further characterization of this compound was reported previously.[13]

***O*-Ethyl *N*-Methyl-*N*-phenylthiocarbamate (6b).** *N*-Methylaniline (14.3 mL, 0.13 mol) was added to a solution of bis(ethoxy(thiocarbonyl)) sulfide[36] (28.0 g, 0.13 mol) in $CHCl_3$ (200 mL). After 2 days at 25 °C, extractive workup provided **6b** as a yellow oil (21.2 g, 82%); ^{1}H NMR[17] (300 MHz, 50 °C) δ 7.5−7.1 (m, 5 H), 4.50 (q, J = 7.2 Hz, 2 H), 3.58 (s, 3 H), 1.22 (theoretical triplet appearing as broad singlet, 3 H). Further characterization of this compound was reported previously.[13]

***O*-Isopropyl *N*-Methyl-*N*-phenylthiocarbamate (6c).** *N*-Methylaniline (20 mL, 185 mmol) was added to a solution of bis(isopropoxy(thiocarbonyl)) sulfide[14] (10.8 g, 45 mmol) in $CHCl_3$ (185 mL) at 25 °C. After 2 days, extractive workup gave the crude product, which was then placed under petroleum ether for 24 h at −20 °C, giving **6c** as white crystals (7.4 g, 78%); mp 72−74 °C (lit.[14] mp 67−70 °C); ^{1}H NMR[13] (300 MHz, 50 °C) δ 7.5−7.1 (m, 5 H), 5.56 (septet, J = 6.0 Hz, 1 H), 3.60 (s, 3 H), 1.20 (poorly resolved doublet, J = 6.0 Hz, 6 H).

***O*-Ethyl *N*,2,6-Trimethyl-*N*-phenylthiocarbamate (6b″).** A solution of ethoxythiocarbonyl chloride[13] (3.55 g, 28.5 mmol) in $CHCl_3$ (28.5 mL) was added to a solution of *N*,2,6-trimethylaniline (8.1 g, 60 mmol, 2.1 equiv) in $CHCl_3$ (30 mL). Extractive workup gave **6b″** as a brown oil (4.58 g, 69%). The compound showed two conformations,[17] in a 2:1 ratio (major listed first, then minor); ^{1}H NMR (500 MHz) (major) δ 7.2−7.0 (m, 3 H), 4.47 (q, J = 7.0 Hz, 2 H), 3.48 (s, 3 H), 2.13 (s, 6 H), 1.33 (t, J = 7.0 Hz, 3 H); (minor) δ 7.2−7.0 (m, 3 H), 4.59 (q, J = 7.0 Hz, 2 H), 3.24 (s, 3 H), 2.21 (s, 6 H), 1.43 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz) (major) δ 188.3, 141.4, 134.0, 128.1, 127.5, 67.1, 41.0, 17.3, 14.1; (minor) δ 187.9, 142.9, 134.5, 128.5, 127.7, 67.4, 36.7, 17.4, 14.2; HRMS (ESI): m/z [M + Na$^+$] calcd for $C_{12}H_{17}NOS$: 246.0923; found: 246.0926; IR 3017 (m), 2980 (s), 2927 (m), 1675 (m) cm^{-1}. This procedure was carried out both in 1983 and in 2010; the older material that had been stored under ambient conditions was still usable for reactions carried out in 2010.

***N*-Trimethylsilyl-*N*-methylaniline (10).** Modifying a procedure outlined briefly by Cullis et al.,[21] a solution of *N*-methylaniline (2.0 g, 19.0 mmol) and *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (5.0 g, 19.5 mmol) in dry acetonitrile (26 mL) was refluxed at 105 °C for 24 h. Subsequent solvent removal and vacuum distillation provided the title product as a pale yellow oil (2.04 g, 60%), bp 32−33 °C (0.7 mm) [lit.[21] 59−61 °C (1.9 mm); lit.[18] 77 °C (5.5 mm); lit.[19] 91 °C (14 mm)]. When the limiting reagent was the silylating agent, as in the original publication, it was difficult to separate fully unreacted *N*-methylaniline from the title product.

Alkyl (*N*-Methyl-*N*-phenylcarbamoyl)disulfanes (11). In a typical procedure, a solution of ((isopropyl)dithio)carbonyl chloride (**12c**) (339 mg, 2.0 mmol) in $CHCl_3$ (1.0 mL) was added to a solution of *N*-methylaniline (470 mg, 2.2 equiv) in $CHCl_3$ (2.2 mL). Extractive workup, followed by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)] and crystallization under hexanes (5 mL) at −20 °C for 24 h, gave **11c** as a white powder (344 mg, 62%); mp 49−51 °C (lit.[13] mp 54−55 °C); ^{1}H NMR (300 MHz) δ 7.5−7.3 (m, 5 H), 3.37 (s, 3 H), 3.05 (septet, J = 6.6 Hz, 1 H), 1.27 (d, J = 7.0 Hz, 6 H); ^{13}C NMR (75 MHz) δ 166.8, 141.3, 129.6, 128.8, 128.4, 41.1, 39.3, 22.1 (2 C); HRMS (ESI): m/z [M + Na$^+$] calcd for $C_{11}H_{15}NOS_2$: 264.0487; found: 264.0480; IR 3018 (s), 2965 (m), 1673 (vs) cm^{-1}. Applying the same procedure with *t*Bu reagent **12d** (368 mg, 2.0 mmol) provided **11d** as white needles (357 mg, 70%); mp 40−42 °C; ^{1}H NMR (300 MHz) δ 7.5−7.2 (m, 5 H), 3.33 (s, 3 H), 1.26 (s, 9 H); ^{13}C NMR (75 MHz) 165.5, 140.6, 128.9, 128.1, 127.7, 47.0, 38.6, 28.8 (3 C); HRMS (ESI): m/z [M + Na$^+$] calcd for $C_{12}H_{17}NOS_2$: 278.0644; found: 278.0636; IR 3061 (w), 2960 (s), 1684 (vs) cm^{-1}.

Alkyl (*N*,2,6-Trimethyl-*N*-phenylcarbamoyl)disulfanes (11″). A solution of ((methyl)dithio)carbonyl chloride (**12a**) (283 mg, 2.0 mmol) in $CHCl_3$ (1.0 mL) was added to a solution of *N*,2,6-trimethylaniline (593 mg, 2.2 equiv) in $CHCl_3$ (2.2 mL). Extractive workup, followed by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)], provided **11a″** as a white powder (386 mg, 80%); mp 68−70 °C; ^{1}H NMR (500 MHz) δ 7.3−7.1 (m, 3 H), 3.25 (s, 3 H), 2.38 (s, 3 H), 2.24 (s, 6 H); ^{13}C NMR (75 MHz) 166.4, 137.8, 137.5, 129.4, 128.9, 36.1, 23.3, 17.6 (2 C); HRMS (ESI): m/z [M + Na$^+$] calcd for $C_{11}H_{15}NOS_2$: 264.0487; found: 264.0494; IR 3018 (s), 1671 (s) cm^{-1}. The same procedure, including purification, using Et derivative **12b** (312 mg, 2.0 mmol) provided **11b″** as a brown oil (418 mg, 82%); ^{1}H NMR (300 MHz) δ 7.3−7.1 (m, 3 H), 3.24 (s, 3 H), 2.70 (q, J = 7.5 Hz, 2 H), 2.25 (s, 6 H), 1.26 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz) δ 166.5, 137.8, 137.4, 129.3, 128.8, 36.1, 32.7, 17.5, 13.6; HRMS (ESI): m/z [M + Na$^+$] calcd for $C_{12}H_{17}NOS_2$: 278.0644; found: 278.0640; IR 3029 (w), 2984 (w), 1674 (s) cm^{-1}. Use of *i*Pr derivative **12c** (339 mg, 2.0 mmol) provided **11c″** as a viscous, brown oil after purification (446 mg, 83%); ^{1}H NMR (500 MHz) δ 7.3−7.1 (m, 3 H), 3.20 (s, 3 H), 2.99 (septet, J = 6.5 Hz, 1 H), 2.23 (s, 6 H), 1.23 (d, J = 6.5 Hz, 6 H); ^{13}C NMR (75 MHz) δ 166.6, 137.8, 137.4, 129.2, 128.8, 41.0, 36.1, 22.0 (2 C), 17.5 (2 C); HRMS (ESI): m/z [M + Na$^+$] calcd for $C_{13}H_{19}NOS_2$: 292.0800;

found: 292.0804; IR 3022 (w), 2959 (s), 2922 (s), 2862 (m), 1687 (vs) cm^{-1}. Finally, using *t*Bu derivative **12d** (369 mg, 2.0 mmol), followed by purification and then recrystallization under hexanes at −20 °C over 24 h, gave **11d″** as white needles (418 mg, 74%); mp 92−94 °C; ^{1}H NMR (300 MHz) δ 7.3−7.1 (m, 3 H), 3.24 (s, 3 H), 2.28 (s, 6 H), 1.28 (s, 9 H); ^{13}C NMR (75 MHz) δ 166.6, 138.1, 137.5, 129.2, 128.9, 47.7, 36.4, 29.5 (3 C), 17.6 (2 C); HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{14}H_{21}NOS_2$: 306.0957; found: 306.0962; IR 3023 (w), 2959 (m), 1685 (s) cm^{-1}; Anal. Calcd for $C_{14}H_{21}NOS_2$: C, 59.32; H, 7.47; N, 4.94; S, 22.62. Found: C, 59.22; H, 7.40; N, 4.84; S, 22.47.

((Alkyl)dithio)carbonyl Chlorides (12). While these compounds (R = Me, Et, *i*Pr,[39] *t*Bu[40]) have all been described previously, including purifications by distillation,[1,38] the small-scale procedures for **12c** and **12d** that follow were newly developed to suit the needs of this research. A solution of chlorocarbonylsulfenyl chloride (**4**) (200 μL, 2.4 mmol) in $CHCl_3$ (2.4 mL) was added to a solution of *i*PrSH (198 mg, 2.6 mmol) in $CHCl_3$ (2.4 mL). After 1 h at 25 °C, the mixture was concentrated, providing **12c** as a clear, colorless oil (375 mg, 92%); ^{1}H NMR (500 MHz) δ 3.24 (septet, *J* = 7.0 Hz, 1 H), 1.36 (d, *J* = 7.0 Hz, 6 H); ^{13}C NMR (75 MHz) 167.0, 42.6, 22.3 (2 C); GC-MS: (60 m × 0.25 mm ID, DB-5, 50 °C for 1 min, then increase by 15 °C per min until 320 °C; t_R = 6.50 min); HRMS (CI): *m*/*z* [M + NH_4^+] calcd for $C_4H_7ClOS_2$: 187.9965; found: 187.9973; IR 2973 (s), 2927 (m), 2866 (m), 1782 (vs) cm^{-1}. The same procedure was used with *t*BuSH (234 mg, 2.6 mmol), providing **12d** as a translucent, brown oil (411 mg, 93%); ^{1}H NMR (300 MHz) δ 1.38 (s, 9 H); ^{13}C NMR (75 MHz) 167.2, 34.4, 29.6 (3 C); GC-MS: (same conditions as for **12c**; t_R = 6.98 min); HRMS (CI): *m*/*z* [M + NH_4^+] calcd for $C_5H_9ClOS_2$: 202.0122; found: 202.0126; IR 2965 (s), 1785 (vs) cm^{-1}.

Bis(*N*-methyl-*N*-phenylcarbamoyl)disulfane (13). *Method A.* A solution of SO_2Cl_2 (42 μL, 0.5 mmol) in $CDCl_3$ (0.5 mL) was added over 1 min to a solution of *O*-isopropyl thiocarbamate **6c** (209 mg, 1.0 mmol) in $CDCl_3$ (0.5 mL) at 25 °C. ^{1}H NMR data at 10 min showed completion of the reaction to produce **13** (quantitative, with all starting material consumed and converted to *i*PrCl). Direct concentration gave **13** as a white powder, ∼98% pure by ^{1}H NMR (156 mg, 94%); mp 227−231 °C (lit.[13] mp 240−243 °C); ^{1}H NMR (500 MHz) 7.5−7.2 (m, 10 H), 3.36 (s, 6 H).

Method B. Neat bis(chlorocarbonyl)disulfane (**20**)[13] (95 mg, 0.5 mmol) was added to a solution of silylated amine **10** (181 mg, 1.0 mmol) in $CDCl_3$ (1.0 mL). A ^{1}H NMR spectrum of the reaction mixture recorded after 3 min showed that **10** had reacted completely, while **13** (0.5 equiv) and TMSCl (1 equiv) had formed. Concentration at this stage gave **13** as an off-white powder (305 mg, 92%); mp 230−233 °C (lit.[13] mp 240−243 °C).

(*p*-Methyl-*N*-phenylcarbamoyl)(*N*-methyl-*N*-phenyl)disulfane (13′). A solution of ((carbamoyl)dithio)carbonyl chloride **2** (270 mg, 1.0 mmol) in $CHCl_3$ (1.0 mmol) was added to a solution of *N*-methyl-*p*-toluidine (264 mg, 2.2 mmol) in $CHCl_3$ (1.0 mL). The usual workup, followed by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)], provided **13′** as a white powder (311 mg, 90%); mp 127−130 °C; ^{1}H NMR (500 MHz) 7.5−7.2 (m, 9 H), 3.36 (s, 3 H), 3.33 (s, 3 H), 2.38 (s, 3 H); ^{13}C NMR (125 MHz) δ 166.7, 141.3, 129.6, 128.8, 128.3, 41.1, 39.2, 22.0; HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{17}H_{18}N_2O_2S_2$: 369.0702; found: 369.0703; IR 3019 (s), 2977 (w), 1683 (m), 1676 (m) cm^{-1}.

(*N*,2,6-Trimethyl-*N*-phenylcarbamoyl)(*N*-methyl-*N*-phenyl)disulfane (13″). A solution of ((carbamoyl)dithio)carbonyl chloride **2** (270 mg, 1.0 mmol) in $CHCl_3$ (1.0 mL) was added to a solution of *N*,2,6-trimethylaniline (297 mg, 2.2 mmol) in $CHCl_3$ (1.0 mL). Extractive workup and purification by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)] gave **13″** as a white powder (317 mg, 88%); mp 131−133 °C; ^{1}H NMR (500 MHz) 7.5−7.1 (m, 8 H), 3.35 (s, 3 H), 3.24 (s, 3 H), 2.34 (s, 6 H); ^{13}C NMR (75 MHz) δ 164.6, 163.2, 140.9, 138.1, 137.5, 129.7, 129.5, 128.9, 128.6, 128.4, 39.3, 36.2, 17.6 (2 C); HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{18}H_{20}N_2O_2S_2$: 383.0858; found: 383.0860; IR 3017 (m), 2939 (w), 1684 (s), 1676 (s) cm^{-1}.

(*N*,*N*′,2,6-Tetramethyl-*N*,*N*′-diphenylcarbamoyl)sulfenamide (17). A solution of pure (carbamoyl)sulfenyl chloride **1″** (115 mg, 0.5 mmol) in $CHCl_3$ (0.5 mL) was added to a solution of *N*-methylaniline (118 mL, 2.2 equiv) in $CHCl_3$ (0.5 mL). Extractive workup and purification by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)] gave **17** as a tan powder (130 mg, 86%); mp 76−78 °C; ^{1}H NMR (500 MHz) δ 7.3−6.8 (m, 8 H), 3.38 (s, 3 H), 3.17 (s, 3 H), 2.35 (broad d, *J* = 13.5 Hz, 6 H); ^{13}C NMR (75 MHz) δ 170.0, 150.2, 138.2, 136.5, 129.5, 129.0, 128.7, 119.5, 115.5, 44.7, 35.1, 17.7 (2 C); HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{17}H_{20}N_2OS$: 323.1189; found: 323.1195; IR 3019 (s), 1668 (m) cm^{-1}.

(*N*,*N*′,2,2′,6,6′-Hexamethyl-*N*,*N*′-diphenylcarbamoyl)sulfenamide (17″). A solution of chlorocarbonylsulfenyl chloride (**4**) (84 μL, 1.0 mmol) in $CHCl_3$ (2.0 mL) was added to a solution of *N*,2,6-trimethylaniline (594 mg, 4.4 equiv) in $CHCl_3$ (2.2 mL), followed by extractive workup and purification by flash chromatography [SiO_2, eluted with hexanes:EtOAc (6:1)] to give **17″** as short, white needles (233 mg, 71%); mp 146−149 °C; ^{1}H NMR (500 MHz) δ 7.5−7.2 (m, 6 H), 3.18 (s, 3 H), 3.16 (s, 3 H), 2.38 (broad s, 6 H), 2.21 (s, 6 H); ^{13}C NMR (75 MHz) δ 171.8, 148.6, 137.5, 137.0, 136.5, 129.0, 128.7, 128.5, 125.7, 47.2, 35.3, 19.0 (2 C), 17.6 (2 C); HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{19}H_{24}N_2OS$: 351.1502; found: 351.1510; IR 3054 (s), 2986 (m), 1671 (vs) cm^{-1}.

Bis(*N*,2,6-trimethyl-*N*-phenylcarbamoyl)disulfane (18). A solution of bis(chlorocarbonyl)disulfane (**20**) (761 mg, 4.0 mmol) in $CHCl_3$ (4.0 mL) was added to a solution of *N*,2,6-trimethylaniline (2.32 g, 4.3 equiv) in $CHCl_3$ (8.0 mL). Extractive workup gave **18** as a white powder (1.36 g, 88%); mp 195−197 °C; ^{1}H NMR (300 MHz) δ 7.3−7.1 (m, 6 H), 3.24 (s, 6 H), 2.35 (s, 12 H); ^{13}C NMR (75 MHz) δ 165.0 (2 C), 138.2 (2 C), 137.6 (4 C), 129.6 (4 C), 129.0 (4 C), 36.2 (2 C), 17.7 (4 C); HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{20}H_{24}N_2O_2S_2$: 411.1171; found: 411.1181; IR 3025 (w), 2965 (w), 2926 (w), 1674 (s) cm^{-1}.

(Trichloromethyl)(*N*-methyl-*N*-phenylcarbamoyl)disulfane (21). A solution of perchloromethyl mercaptan (0.6 g, 3.2 mmol) in CH_2Cl_2 (3 mL) was added to a solution of *O*-isopropyl *N*-methyl-*N*-phenylthiocarbamate (0.6 g, 2.7 mmol) in CH_2Cl_2 (2.7 mL), and the reaction proceeded for 15 min at 25 °C. Concentration gave the crude product (0.9 g, 2.8 mmol, quantitative), a portion (0.54 g, 1.7 mmol) of which was dissolved in hot hexanes (5.4 mL). White needles formed upon cooling (0.17 g total for two crops, 32%); mp 50−52 °C (lit.[13] mp 54−55 °C).

■ ASSOCIATED CONTENT

Supporting Information. A table of ^{1}H NMR shifts in various solvents, a description of chemical exchange in compound **6**, and copies of key NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: barany@umn.edu.

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DEDICATION

†Dedicated to Kate Bárány (April 29, 1929 to June 13, 2011), gifted teacher, renowned biophysical chemist, and champion for women in academia.

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(2) Reference 1 also draws the analogy to the well-known industrial-scale process for production of *N,N*-dialkylthiocarbamoyl chlorides, i.e., $^1/_2[R_2N(C{=}S)S]_2 + {}^1/_2Cl_2 \rightarrow [R_2N(C{=}S)SCl] \rightarrow R_2N(C{=}S)Cl + S$, to support their view that $R_2N(C{=}O)SCl$ should be unstable.

(3) (Carbamoyl)sulfenyl chloride $R_2N(C{=}O)SCl$ for $R_2N = iPr_2N$ was reported as an unstable intermediate in a complicated rearrangement/elimination that occurred upon oxidation of certain 3-chloroallyl thiocarbamates. See: Schuphan, I.; Casida, J. E. *Tetrahedron Lett.* **1979**, *10*, 841–844.

(4) Notwithstanding the caveat of ref 2, a full paper following up on ref 3 sketched how with $R_2N = iPr_2N$ that $^1/_2[R_2N(C{=}O)S]_2 + {}^1/_2Cl_2 \rightarrow [R_2N(C{=}O)SCl]$ (**1**), sufficiently stable to allow trapping with cyclohexene (compare to Scheme 1) prior to decomposing to $R_2N(C{=}O)Cl$ (**3**). Experimental details and spectral data were not reported. See: Schuphan, I.; Casida, J. E. *J. Agric. Food Chem.* **1979**, *27*, 1060–1066.

(5) A recently described one-pot synthesis of **3** by reaction of secondary amines with **4** undoubtedly goes through **1** as an intermediate (compare to Scheme 1). See: Adeppa, K.; Rupainwar, D. C.; Misra, K. *Can. J. Chem.* **2010**, *88*, 1277–1280.

(6) A handful of additional "hits" for $R_2N(C{=}O)SCl$ (**1**) in the patent literature turn out, upon close reading, to actually refer to $R_2N(C{=}S)Cl$ that had been erroneously indexed as **1**.

(7) From our own laboratories, tantalizing hints at the existence, trapping, and stabilities of **1** and **2** are found in footnote 14 and the text accompanying Scheme III of ref 14 (with brief accompanying experimentals for compounds **20** and **22** as numbered in that paper) and on pages 39 and 59 of the Ph.D. Thesis of Schroll, A. L. (1986), University of Minnesota.

(8) Schroll, A. L.; Barany, G. *J. Org. Chem.* **1989**, *54*, 244–247.

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(10) Kolano, C.; Sander, W. *Eur. J. Org. Chem.* **2003**, *6*, 1074–1079.

(11) Morin, T. J.; Kobertz, W. R. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 1478–1482 including Supporting Information which has relevant experimental procedures.

(12) The stereochemistry of addition of a variety of sulfenyl chlorides to alkenes is reviewed by: Kühle, E. *Synthesis* **1971**, 563–586.

(13) Barany, G.; Schroll, A. L.; Mott, A. W.; Halsrud, D. A. *J. Org. Chem.* **1983**, *48*, 4750–4761 and references cited therein.

(14) Schroll, A.; Barany, G. *J. Org. Chem.* **1986**, *51*, 1866–1881 and references cited therein.

(15) Review: Kühle, E. *Synthesis* **1970**, 561–580.

(16) Precedents for this chemoselective acidolytic cleavage of a sulfenamide bond are found in ref 1 and in: Schroll, A; Eastep, S. J.; Barany, G. *J. Org. Chem.* **1990**, *55*, 1475–1479 and references cited therein.

(17) Attention is called to the unusually broad ^{1}H NMR peaks of **6a**, **6b**, and **6c** as observed at 25 °C and 500 MHz for the present study, which contrast to the classical expected multiplicities when these same compounds were examined years earlier (refs 13 and 14) at lower magnetic field strength (i.e., 80 MHz). These new results are attributed to conformational averaging (medium exchange) on the NMR time scale; the fact that thiocarbamates can populate discrete cis and trans conformational states was first discussed by Bauman, R. A. *J. Org. Chem.* **1967**, *32*, 4129–4132. Consistent with this hypothesis, high-field ^{1}H NMR spectra of **6** run at higher temperature gave sharper peaks with the expected multiplicities (details in Supporting Information, pages S2−S5, with representative spectra on subsequent pages). Also, the ^{1}H NMR spectrum of the corresponding 2,6-dimethyl compounds, **6″**, showed the normal expected sharp peaks at 25 °C, indicating that cis and trans isomers of **6″** are likely to be in slow exchange.

(18) From *N*-methylaniline plus chlorotrimethylsilane in the presence of triethylamine, but without experimental details: Klebe, J. F.; Bush, J. B., Jr.; Lyons, J. E. *J. Am. Chem. Soc.* **1964**, *86*, 4400–4406.

(19) Prepared by using NaH to create anion of *N*-methylaniline and then alkylating with chlorotrimethylsilane: Rauchschwalbe, G.; Ahlbrecht, H. *Synthesis* **1974**, 663–665.

(20) Procedure similar to ref 18 with 65% yield: Smith, C. J.; Early, T. R.; Holmes, A. B.; Shute, R. E. *Chem. Commun. (Cambridge, U. K.)* **2004**, *17*, 1976–1977.

(21) From *N*-methylaniline plus *N,O*-bis(trimethylsilyl)trifluoroacetamide, and reproduced herein (other procedures proved difficult to carry out to completion), as reported in: Cullis, C. F.; Herron, D.; Hirschler, M. M. *Combust. Flame* **1985**, *59*, 151–165.

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(23) Authentic **11**, several of which were new compounds, were prepared by acylation of *N*-methylaniline by the corresponding (alkyldithio)carbonyl chlorides **12**, which in turn were derived from regiospecific reactions of thiols with chlorocarbonylsulfenyl chloride **4**, as previously described.[1,13,37]

(24) Precedent: Kharasch, N.; Wald, M. M. *Anal. Chem.* **1955**, *27*, 996–998.

(25) Precedent: Barany, G.; Mott, A. W. *J. Org. Chem.* **1984**, *49*, 1043–1051 and references cited therein.

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(33) While the overwhelming majority of mono- and bifunctional acid and sulfenyl chlorides react quickly with methanol or *N*-methylaniline (reactions under conditions described in Experimental Section are complete within 15 min), carbamoyl chloride **3** reacts at a very slow rate for reasons on which we can only speculate. To achieve complete conversion respectively to urethane **15** or symmetrical urea **16**, reaction times of 48 h at 50 °C were necessary.

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