

Two-carbon extension of *N,N*-disubstituted amides with bis(trimethylsilyl)thioetene affording *N,N*-disubstituted 3-oxothioamides

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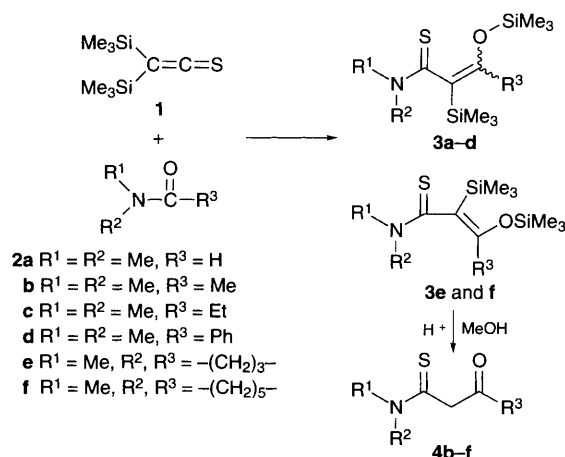
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N,N-Disubstituted alkanamides cleanly react with bis(trimethylsilyl)thioetene to form *N,N*-disubstituted 2-trimethylsilyl-3-trimethylsilyloxyalk-2-enethioamides, which upon acid hydrolysis give *N,N*-disubstituted 3-oxoalkanethioamides

Thioketenes are a versatile class of building blocks that allow numerous synthetic reactions.¹ Since most of them are quite reactive, in many cases, they are generated *in situ* and immediately treated with reactants without isolation. Unprotected thioetene in particular is extremely reactive and hard to handle in synthetic applications. Rather surprising in this context is the lack of reports in the literature of synthetic application of bis(trimethylsilyl)thioetene **1** which can be stored under ambient conditions and is a potentially useful synthetic equivalent of unprotected thioetene. We describe here a new and unique reaction of **1** with *N,N*-disubstituted amides **2**, which forms, after acid hydrolysis, 3-oxothioamides **4**; the overall reaction is an addition of amide-acyl and -amino moieties across the C=C bond of unprotected thioetene.

When *N,N*-disubstituted amides (**2**, 2.5 mmol) were treated with bis(trimethylsilyl)thioetene (**1**, 2.5 mmol) without solvent, 1:1 adducts **3** were formed in fair to excellent yield (Scheme 1).[‡] ¹H, and ¹³C NMR, MS and elemental analysis data of the products were all fully consistent with the proposed structures.[§] The structure of **3e** was further confirmed by X-ray crystallography, Fig. 1.[¶]

This reaction appears very general. As regards the reactivity, the sterically least demanding *N,N*-dimethylformamide **2a** reacted vigorously. The reaction of *N,N*-dimethylbenzamide **2d** however required heating at 100 °C over 6 d for completion. The low reactivity of **2d** as compared with aliphatic amides **2b**, **2c** is, besides the steric reason, due at least partly to the carbonyl oxygen being less nucleophilic, and is compatible with the proposed mechanism. Lactams **2e** and **2f** also reacted under mild conditions to afford seven- and nine-membered cyclic adducts, respectively. These products **3** were readily desilylated



Scheme 1

upon acid methanolysis to give 3-oxothioamides of **4** which can be readily desulfurated to 3-oxoamides by published procedures.³ Thus the overall process constitutes an unusual formal addition of amides across the C=C bond of unprotected thioetene.

Although a detailed mechanistic study is yet to be done, the reaction can be best explained by the path outlined in Scheme 2. The initial [2 + 2] adduct cleaves heterolitically followed by migration of a silyl group to the oxygen resulting in the formation of the thioketenes **5**, which subsequently undergo intramolecular nucleophilic 1,3-migration of the amino group to the thiocarbonyl carbon to form **3**. We have been unable to date to detect any evidence for the intermediacy of thioetene **5** in

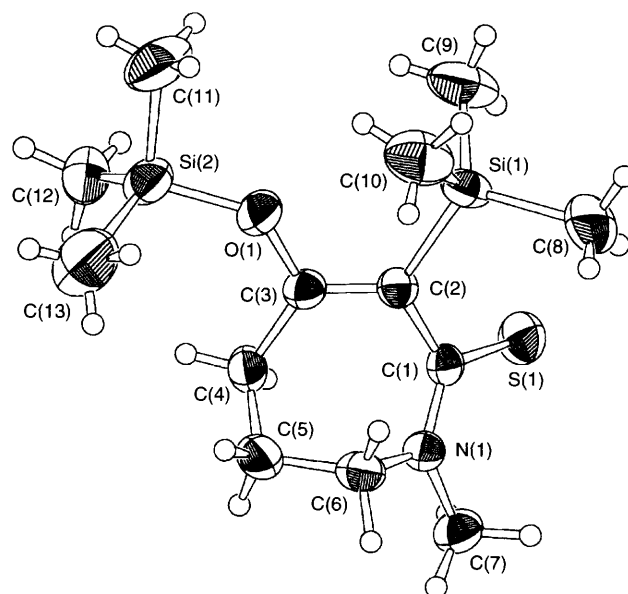
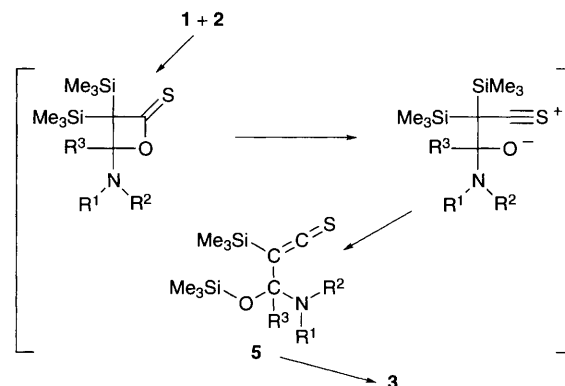


Fig. 1 ORTEP drawing of **3e** with 40% probability thermal ellipsoids. As the thioamide group is fixed in a plane the whole molecule is in a boat form.



Scheme 2

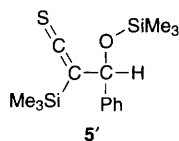


Fig. 2

any reactions that successfully form **3** in good yields. However, strong evidence came from the related study on the reaction of aldehydes; treatment of benzaldehyde with **1** (100 °C, 4 d) did indeed form an adduct **5'** (Fig. 2) analogous to **5**.

To confirm the possibility of other mechanisms, di-*tert*-butylthioetene⁴ was treated with **2a**, the most reactive amide. However, the starting materials were recovered unreacted even under forcing conditions [application of a high pressure (800 MPa) at 100 °C over 20 h]. Accordingly, one can envisage that the formation of the Si–O bond is integral for the occurrence of the reaction.

Footnotes

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‡ **3a**: 93%, reacted at room temp. (r.t.), 1 h, mp 80 °C (sublimation at 72 °C, 66 Pa), a mixture of two isomers; **3b**: 85%, r.t., 2 d, mp 75.0–75.9 °C (sublim. 60 °C, 66 Pa); **3c**: 85%, 40 °C, 7 d, bp 115 °C, 132 Pa; **3d**: 88%, 100 °C, 6 d, mp 111.8–112.9 °C (sublim. 115 °C, 106 Pa); **3e**: 92%, r.t., 4 d, mp 104–117 °C (sublim. 85 °C, 66 Pa); **3f**: 88%, r.t., 4 d, bp 138 °C, 106 Pa.

§ Selected spectroscopic data for **3e**: Yellow crystals, mp 104–117 °C; *m/z* 301 (11) [M⁺], 286 (100%) [M⁺ – CH₃]; δ_H (Brucker AC200, CDCl₃, 400 K) 3.67 (t, *J* 6.6 Hz, 2 H, NCH₂CH₂), 3.50 (s, 3 H, NCH₃), 2.29 (t, 2 H, *J* 6.6 Hz, =CCH₂CH₂), 2.09 (quintet, 2 H, *J* 6.6 Hz, =CCH₂CH₂CH₂N), 0.268 [s, 9 H, Si(CH₃)₃] and 0.246 [s, 9 H, Si(CH₃)₃]; δ_C (CDCl₃, 300 K) 201.74 (C=S), 157.49 (OC=CSi), 123.54 (OC=CSi), 52.28 (NCH₂CH₂),

41.37 (NCH₃), 30.46, 29.66 (CH₂CH₂), 1.14 [Si(CH₃)₃] and 0.53 [Si(CH₃)₃]; For **4e**: Colourless crystals, mp 72.0–74.7 °C (from methanol or sublim. 66 °C, 132 Pa); *m/z* 157 (100%) [M⁺], 114 (32); δ_H (CDCl₃, 300 K) 4.05 [s, 2 H, C(O)CH₂C(S)], 3.83 (t, *J* 6.2 Hz, 2 H, NCH₂), 3.54 (s, 3 H, NCH₃), 2.56 [t, *J* 7.14 Hz, 2 H, C(O)CH₂CH₂] and 2.09 (t × t, *J* 6.2, 7.14 Hz, 2 H, CH₂CH₂CH₂); δ_C 202.55 (C=S), 195.69 (C=O), 60.94 [C(O)-CH₂C(S)], 53.06 (NCH₂CH₂), 44.04 (NCH₃), 40.24 [C(O)CH₂CH₂], 24.23 (CH₂CH₂CH₂).

¶ Crystal data for **3e**: yellow block, 0.3 × 0.3 × 0.5 mm³; FW = 301.60; monoclinic, space group *P*2₁/*n*; *a* = 11.627(9), *b* = 9.895(12), *c* = 16.028(6) Å, β = 93.08(5)°, *V* = 1841(3) Å³, *Z* = 4; *D*_{calc} = 1.09 g cm⁻³; μ(Mo-Kα) = 2.98 cm⁻¹; RIGAKU AFC7R diffractometer; 302 K, Mo-Kα radiation (λ = 0.71073 Å); 3.0° < 2θ < 55.0°, ω-scan; 2486 unique reflections [*I* > 2.0σ(*I*)]; empirical absorption correction. The structure was solved by a direct method (SIR88) and refined by a full-matrix least-squares procedure to yield the final residuals of *R* = 0.052 and *R*_w = 0.064. All the hydrogen atoms were located in differential Fourier maps. Terminal hydrogen atoms at C(7) and C(10) exhibit positional disorder. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/123.

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