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Trialkylsilyl substituent effect on ring expansion of chloroalkyl dithioketals. An easy method for the preparation of 2-trialkylsilyl-1,5-dithiacyclooct-2-enes

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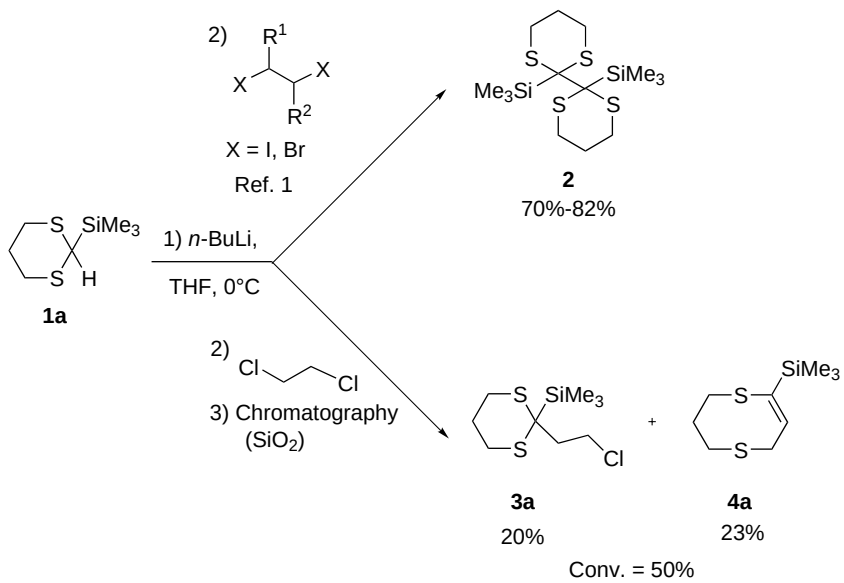
Abstract—Silylated 2- and 3-chloroalkyl dithioketals were prepared from corresponding 2-lithio dithioketals with 1,2- and 1,3-dihaloalkanes. The functionalized 1,3-dithianes underwent an easy ring expansion reaction into 1,5-dithiacyclooct-2-enes in the presence of basic alumina in refluxing petroleum ether. © 2001 Elsevier Science Ltd. All rights reserved.

Within a program on the synthesis of bis(acylsilanes) using 2-trimethylsilyl-1,3-dithiane **1a** as a building block, we observed recently that the reaction of the corresponding lithio derivative with 1,2-dibromo- or 1,2-diiodoethane led effectively to the dehydrodimer **2** (Scheme 1).[1] A halophilic nucleophilic attack was proposed to explain this result. Such a process should not occur with much less polarizable leaving groups. Indeed, 1,4-bis(dithiane) derivatives were prepared from the corresponding 1,2-bis(triflyloxy)ethane.[1] On the other hand, completely different behavior occurred when 1,2-dichloroethane was treated with **1a** under similar conditions: a monosubstitution product which further rearranged with ring expansion was observed. We report in this paper the study leading to the optimization of this ring expansion reaction.



Scheme 1.

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In a preliminary experiment, only the expected monosubstitution product **3a** and unreacted **1a** were observed in the crude reaction mixture. More interestingly, **3a** was partly converted into the new compound **4a** during silica gel chromatography (Scheme 1). The heterocycle **4a** was fully characterized by IR, MS and NMR (^{1}H, ^{13}C, homonuclear (COSY) and heteronuclear (HMQC, HMBC) correlations).

Medium ring 1,4- and 1,5-dithiacycloalkenes have long attracted the attention of synthetic chemists as they are generally resistant to attempts to prepare them via standard cyclization methodologies.[2] A brief survey of the literature reveals several approaches of ring expansions of cyclic thioketals: via a sulfoxide;[3] via alkylation of sulfur;[4] via protonation of a 2-alkenyl chain;[5] or via an intramolecular substitution of γ- or δ-halogen.[6] To the best of our knowledge, no ring expansion of this type was reported from silylated 2-(β- or γ-chloroalkyl)-1,3-dithianes.

The 2-(β-chloroethyl)-1,3-dithianes **3a**,[7] **3b** and the homologue **3c** were prepared in moderate to good yields by alkylation of the corresponding 2-trialkylsilyl-1,3-dithianes **1a**, **1b** with dihalogenated alkane according to a reported procedure.[8] The 2-(β-chloroethyl)-1,3-dithiane **5** was synthesized from the corresponding acetal and 1,3-propanedithiol.[9]

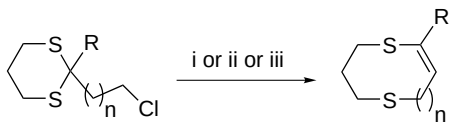
First, we performed a set of experiments to optimize the conditions of ring expansion (Scheme 2). It was found that refluxing a suspension of compound **3a** and basic alumina in petroleum ether (method ii)[10] afforded quantitative yield of 1,5-dithiacyclooct-2-ene **4a**[11] (Table 1, entry 2). It is worth noting that silica gel or alumina is needed for the ring expansion (Table 1, entries 1–3). The reaction also seemed to be general for silylated eight membered ring as indicated for the *t*-butyldimethylsilyl (TBS) derivative **4b** (Table 1, entry 4).

Unfortunately, the extension of these reaction to 1,6-dithiacyclonon-2-ene failed; the 2-(γ-chloropropyl)-1,3-dithiane,[9] which probably came from a protodesilylation reaction, was isolated in 38% yield (Table 1, entry 5). On the other hand, the presence of trialkylsilyl substituent is crucial. Indeed, 2-(β-chloroethyl)-1,3-dithiane **5** treated under the same conditions proved to be unreactive (Table 1, entry 6).

Extension of such a reaction to acyclic silylated dithioketal **6** is depicted in Scheme 3. This compound was prepared from trimethylsilyl bis(methylsulfanyl) methane[13] and 1,2-dichloroethane as described above.[8] The reaction of **6**[14] in the presence of alumina in boiling petroleum ether gave a mixture (80/20) of stereomers **7a**,**b**[15] in 95% yield (Scheme 3).

The stereochemistry of the double bond of compounds **4a**,**b** and **7a**,**b** was assigned from literature data (for **4a**,**b**) and by NOE experiments (for **7a**,**b**). For the eight-membered rings (**4a**,**b**), the *cis* isomer was produced exclusively, as might be expected (the eight-atom heterocycle is too small to accommodate a *trans* double bond).[6] For the *cis* isomer **7a**, an 8% NOE effect was observed between the trimethylsilyl group and the vinylic proton (Scheme 3). Moreover, irradiation of the allylic protons ($\delta = 3.48$ ppm in ^{1}H NMR) induced NOE on the vinylic methylthio group. The configuration of the *trans* isomer **7b** was assigned from the 2% NOE effect between the vinylic proton and the vinylic methylthio group (Scheme 3).

A possible mechanism for the reaction of dithioketals **3a**, **3b**, **6** is described in Scheme 4. We can postulate two different pathways. In path a, as previously proposed,[6] a sulfonium salt **9** is produced by an intramolecular alkylation of one of the thioketal sulfur atoms by the primary alkyl halide. This intermediate is converted into the final product by loss of hydrogen chloride either directly or via the opened salt **10**. One cannot exclude the path b, involving a C–S bond dissociation leading to the intermediate salt **11** (Scheme 4). The subsequent substitution of chlorine by the resulting thiolate would give the salt **10** which then could be converted into compounds **4a**,**b** and **7a**,**b** by the loss of hydrogen chloride. It is very important to



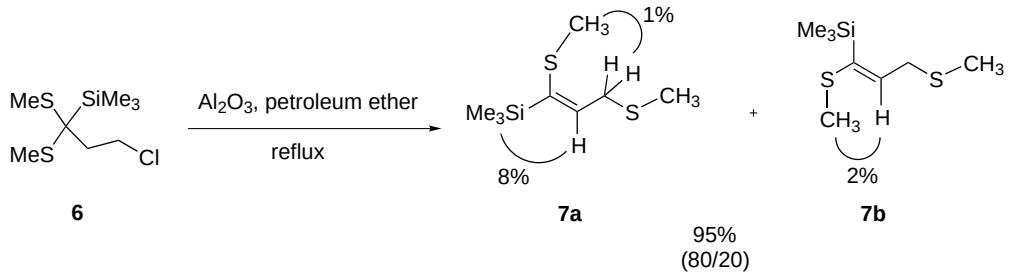
3a-c, 5 **4a, 4b**

Scheme 2. *Reagents and conditions*: (i) SiO_2, petroleum ether/ether (98/2), reflux; (ii) Al_2O_3, petroleum ether, reflux; (iii) petroleum ether, reflux.

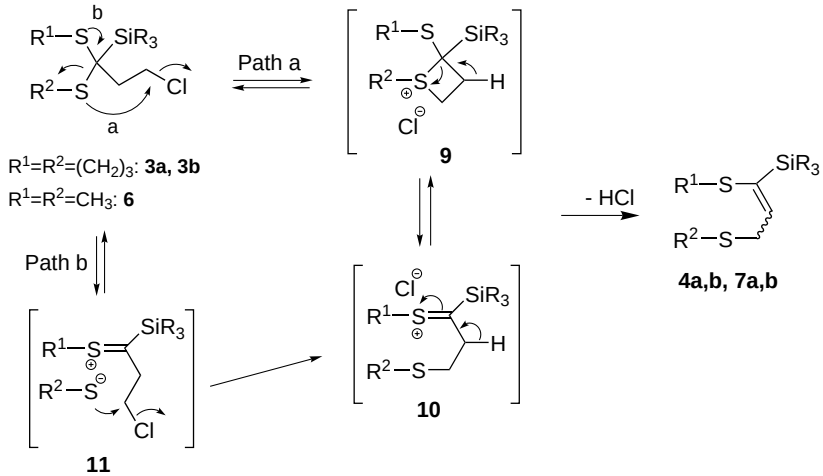
Table 1. Preparation of haloalkyl dithianes and ring expansion reactions

Entry	R	*n*	Haloalkyl dithiane	Method[a]	Dithiacycloalkene (%)
1	TMS	1	**3a**	i	**4a** (90)[b]
2			**3a**	ii	**4a** (100)
3			**3a**	iii	–
4	TBS	1	**3b**	ii	**4b** (98)
5	TMS	2	**3c**	ii	–[c]
6	H	1	**5**	ii	–[d]

[a] Method: (i) SiO_2, petroleum ether/ether (98/2), reflux; (ii) Al_2O_3, petroleum ether, reflux; (iii) petroleum ether, reflux.
[b] (2-Vinyl-[1,3]dithian-2-yl)trimethylsilane[12] was also obtained (10%).
[c] 2-(γ-Chloropropyl)-1,3-dithiane[9] was isolated in 38% yield.
[d] Conversion: 0%.



Scheme 3.



Scheme 4.

notice that sulfonium salts **9**, **10** and **11** are stabilized by the β-effect of silicon.[16] This may be the driving force of this effective rearrangement only observed for 2-silylated haloalkyl 1,3-dithioketals.

In summary, we described an easy, high-yielding method for the preparation of silylated 1,5-dithiacyclooct-2-enes **4a**,**b**. Extension of this reaction to acyclic derivative **6** was also performed. The influence of silyl substituent was clearly shown. In comparison with reported procedure for non-silylated compounds (excess of diisopropylethylamine, DMF, reflux),[6] very mild conditions (basic alumina, petroleum ether, reflux) are required for silylated analogues.

Acknowledgements

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7. *Spectral data for compound* ***3a***. White solid: mp 83–85°C. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.22 (s, 9H), 1.8–2.1 (m, 2H), 2.49 (ddd, 2H, $J=13.5$, 13.2, 2.7 Hz), 2.70 (t, 2H, $J=7.8$ Hz), 2.99 (ddd, 2H, $J=14.2$, 14.1, 3.8 Hz), 3.65 (t, 2H, $J=7.8$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): −2.8 ($SiMe_3$), 23.5 (CH_2), 24.7 (CH_2), 37.1 (C_4), 40.1 (CH_2), 42.1 (CH_2). IR (KBr, cm^{-1}): 2938, 1452, 1251. GC-MS (m/e): 256 (M+2), 254 (M^+), 219, 149 (100). HRMS: m/e calcd for $C_9H_{19}ClS_2Si$ 254.038, found 254.035.
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10. *General procedure for the synthesis of 1,5-dithiacycloalkenes* ***4a***, ***4b*** *and trimethylsilylpropenes* ***7a***, ***7b***: A boiling suspension of dithiane **3a**, **3b** or dithioketal **6** (1.0 mmol, 1 equiv.) and basic alumina (activity 90, 0.063–0.200 nm, 1.03 g) in petroleum ether (30 mL) was stirred overnight. After cooling at room temperature, the solid was filtered, washed with petroleum ether (15 mL). The resulting solution was evaporated in vacuo and the residue was purified by preparative TLC on silica gel (petroleum

ether/ether (98/2)) to give the heterocycles **4a**, **4b** (Scheme 2, Table 1) or the compounds **7a**, **7b** (Scheme 3).

11. *Spectral data for 1,5-dithiacyclooct-2-ene **4a***. Oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.19 (s, 9H), 2.1–2.3 (m, 2H), 2.66 (dd, 2H, $J=5.6$, 5.4 Hz), 2.86 (dd, 2H, $J=5.7$, 5.6 Hz), 3.64 (d, 2H, $J=8.3$ Hz), 6.23 (t, 1H, $J=8.3$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): −1.6 ($SiMe_3$), 27.2 (CH_2), 29.5 (CH_2), 34.8 (CH_2), 35.7 (CH_2), 138.3 (CH), 140.6 (C_4). IR (film, cm^{-1}): 2954, 1582, 1423. GC–MS (m/e): 218 (M^+), 145, 113, 73 (100).
12. (2-Vinyl-[1,3]dithian-2-yl)trimethylsilane was already prepared by lithiation and silylation of 2-ethylidene-1,3-dithiane: Dziadulewicz, E.; Hodgson, D.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3367–3374.
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14. *Spectral data for compound **6***. Oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.20 (s, 9H), 2.06 (s, 6H), 2.27 (t, 2H, $J=8.6$ Hz), 3.67 (t, 2H, $J=8.6$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): −1.2 ($SiMe_3$), 11.4 (CH_3), 40.8 (CH_2), 41.4 (CH_2), 45.8 (C_4). IR (film, cm^{-1}): 2956, 1435, 1250. GC–MS (m/e): 244 (M+2), 242 (M^+), 158, 73 (100).
15. *Spectral data for compounds **7a**,**b***. Mixture of stereomers (80/20). Oil. IR (film, cm^{-1}): 2961, 1580, 1437. GC–MS (m/e): 206 (M^+), 158, 143, 73 (100). *cis Isomer (major) **7a***: ^{1}H NMR ($CDCl_3$) δ (ppm): 0.21 (s, 9H), 2.06 (s, 3H), 2.21 (s, 3H), 3.48 (d, 2H, $J=7.3$ Hz), 6.16 (t, 1H, $J=7.3$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): −0.6 ($SiMe_3$), 14.6 (CH_3), 18.2 (CH_3), 32.3 (CH_2), 140.5 (C_4), 141.0 (CH). *trans Isomer (minor) **7b***: ^{1}H NMR ($CDCl_3$) δ (ppm): 0.21 (s, 9H), 2.09 (s, 3H), 2.24 (s, 3H), 3.34 (d, 2H, $J=7.6$ Hz), 5.60 (t, 1H, $J=7.6$ Hz). Selected ^{13}C NMR ($CDCl_3$) δ (ppm): −0.1 ($SiMe_3$), 35.2 (CH_2), 127.6 (CH).
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