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A radical thia-Brook rearrangement†‡

Béatrice Quiclet-Sire* and Samir Z. Zard*

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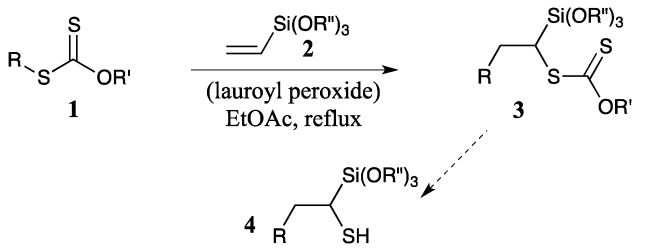
Geminal mercapto trialkyl- and trialkoxy-silanes undergo an efficient radical chain rearrangement, whereby the silyl group migrates from carbon to sulfur; the starting materials are readily obtained by exploiting the peroxide initiated radical addition of dithiocarbonates (xanthates) to trialkyl- or trialkoxy-vinylsilanes.

We recently found that various xanthates readily add to vinyl trialkoxysilanes allowing access to numerous functional trialkoxysilane derivatives **3** (Scheme 1).[1] This peroxide initiated radical chain addition is flexible, modular, and experimentally very simple to implement.[2] Trialkoxysilanes are of key importance in numerous areas: material sciences, sol gels and organogelators, surface modification and monolayer formation, especially on metal oxides and silica surfaces, supported catalysts *etc.*[3] In the course of this work we stumbled upon an unexpected and very efficient radical thia-Brook rearrangement we now describe.

While the xanthate group in adduct **3** may be reductively removed if needed, it is in fact a protected form of the corresponding thiol **4**.[4] The presence of the thiol would indeed offer some further interesting possibilities, either by itself as a cross-linking handle (*via* the disulfide) or as a springboard for a host of transformations through ionic (*e.g.* alkylation) or radical (*e.g.* addition to alkenes, the so-called "thiol click reaction"[5]) processes. With these considerations in mind, we attempted to generate the thiol through the Chugaev reaction[6,7] by simply heating adduct **3a** in diphenyl ether at 200 °C. The thermolysis takes place under neutral conditions that should not affect groups sensitive to nucleophilic attack, such as the phthalimido group present in **3a**.

In the event, heating xanthate **3a** in diphenyl ether at 200 °C for 1 h furnished after purification two inseparable products, one of which was indeed the expected thiol **4a** but the other turned out to be rearranged trialkoxysilane **5a**, as determined by analysis of the NMR spectrum of the mixture. We noticed, furthermore, that, while the combined yield of **4a** and **5a** was generally good, their relative yield varied significantly with the exact experimental conditions. In one experiment, the ratio of **4a** : **5a** by NMR was approximately 2 : 1 in a combined yield of 82% (reaction time 1 h).



Scheme 1 A possible route to geminal mercapto trialkoxysilanes.

The unexpected formation of rearranged trialkoxysilane **5a** may be rationalised by the mechanism displayed in Scheme 2 and proceeding through a radical thia-Brook rearrangement.[8] In one experiment, we succeeded in isolating a pure sample of thiol **4a** in 53% yield and, indeed, exposing it to di-*t*-butyl peroxide (DTBP) in refluxing chlorobenzene for 1 h afforded a quantitative yield of rearranged silane **5a**. This mechanism also accounts for the variability in the relative yield of **4a** and **5a** initially observed, since the efficiency of the chain reaction leading to the latter depends on the presence of adventitious radical initiators (oxygen, traces of metallic salts, *etc.*).

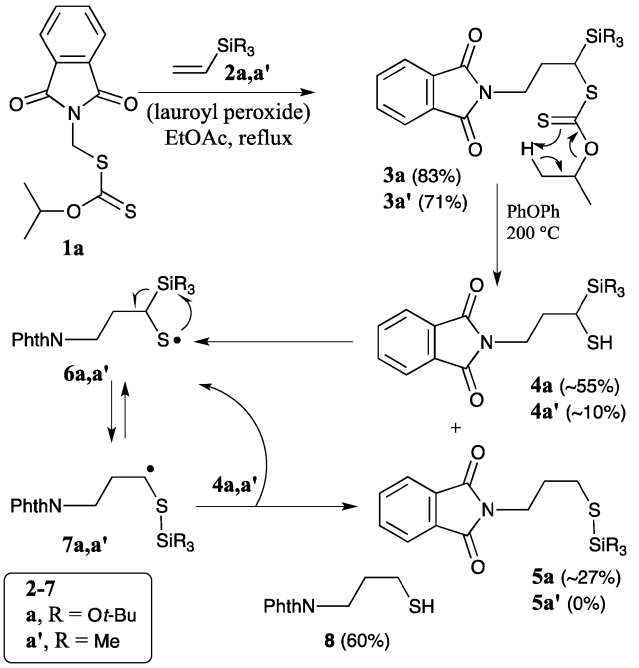
Whereas the radical Brook rearrangement involving silicon migration from carbon to oxygen is well documented,[9] only one instance of a radical thia-Brook rearrangement has been reported as far as we know.[10] It involves the cleavage of a silicon–silicon bond in going from sulfur radical **10** to silicon radical **11** (Scheme 3). This step was incorporated in a radical sequence allowing the use of thiol **9** in ingenious tin-free reductive dehalogenations and Barton–McCombie deoxygenations.

Rupture of a carbon–silicon bond in a thia-Brook rearrangement, as in the present case, appears to be unprecedented.

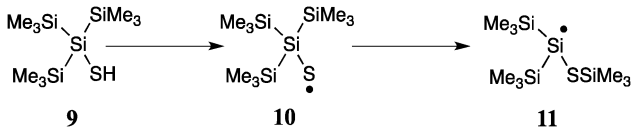
Laboratoire de Synthèse Organique, CNRS UMR 7652, Ecole Polytechnique, F-91128 Palaiseau, France. E-mail: beatrice.sire@polytechnique.edu, samir.zard@polytechnique.edu; Fax: +33 169335972; Tel: +33 169335971

† This paper is dedicated with respect to the memory of Professor Adrian G. Brook (University of Toronto).

‡ Electronic supplementary information (ESI) available. See DOI: 10.1039/c4cc01683a



Scheme 2 An unexpected radical thia-Brook rearrangement.

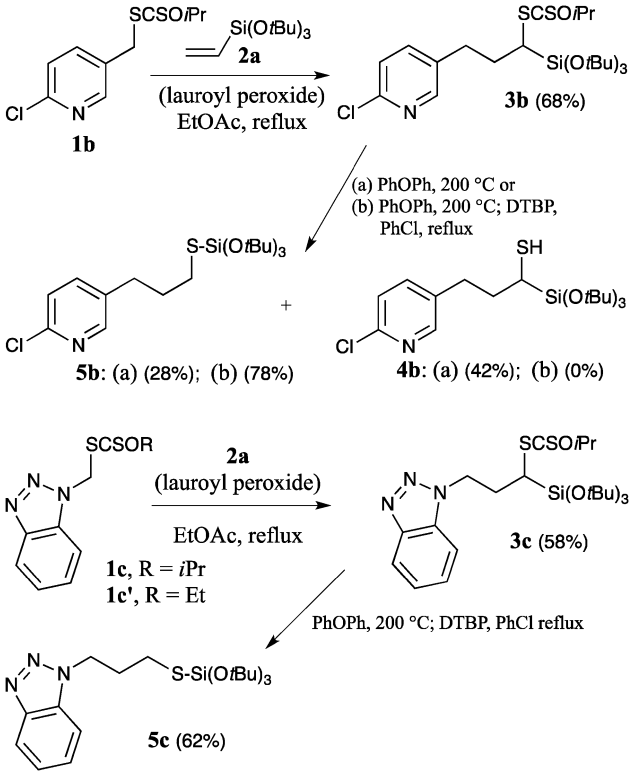


Scheme 3 Cleavage of a silicon–silicon bond by a thia-Brook rearrangement.

The driving force may be the formation of a carbon radical **7a** stabilised by a sulfur atom, with the possible equilibrium between intermediates **6a** and **7a** being finally driven by the irreversible hydrogen abstraction from another thiol molecule **4a**.

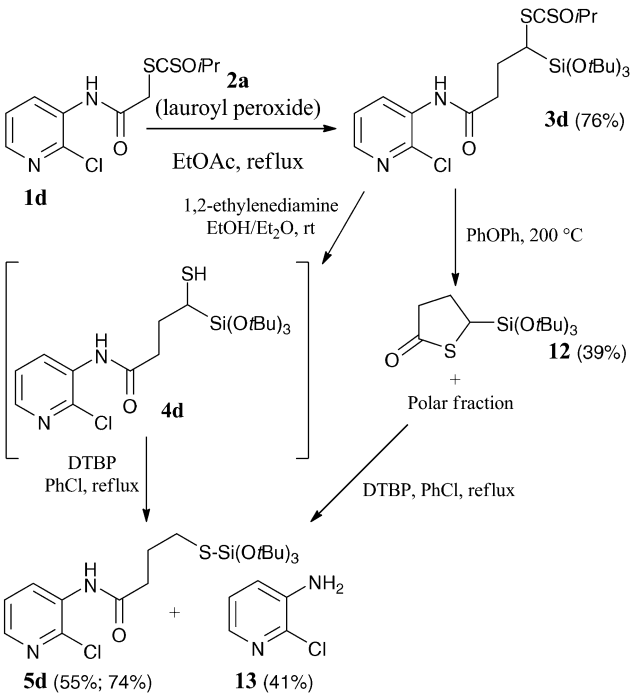
A similar sequence could be accomplished starting from the addition product of xanthate **1a** to vinyl trimethylsilane **2a′** (Scheme 2). Thus, thermolysis of **3a′** indeed furnished the corresponding rearranged derivative **5a′**, but this compound was too labile to chromatographic purification and decomposed to the free thiol **8**, which was isolated in 60% yield. A small amount of un-rearranged thiol **4a′** (*ca.* 10%) was also observed by NMR of the crude reaction mixture. In view of the hydrolytic lability of trimethylsilyl derivatives, the remainder of the study was conducted with the tri(*t*-butoxy)silyl derivatives.

Our next task was to examine the scope of the reaction. Addition of chloropyridinyl xanthates **1b** to vinyl tri(*t*-butoxy)-silane **2a** afforded adduct **3b** in 68% yield (Scheme 4). Thermolysis for 1 h gave a mixture of thiol **4b** (42%) and thia-Brook product **5b** (28%). Repetition of the experiment and exposure of the crude product from the thermolysis to DTBP in refluxing chlorobenzene for 2 h furnished **5b** in a better yield (78%). In the case of adduct **3c**, derived from xanthate **1c**, no attempt was made to separate the intermediate thiol. The crude mixture was treated directly with DTBP in refluxing chlorobenzene to furnish the rearranged material **5c** in 62% yield.

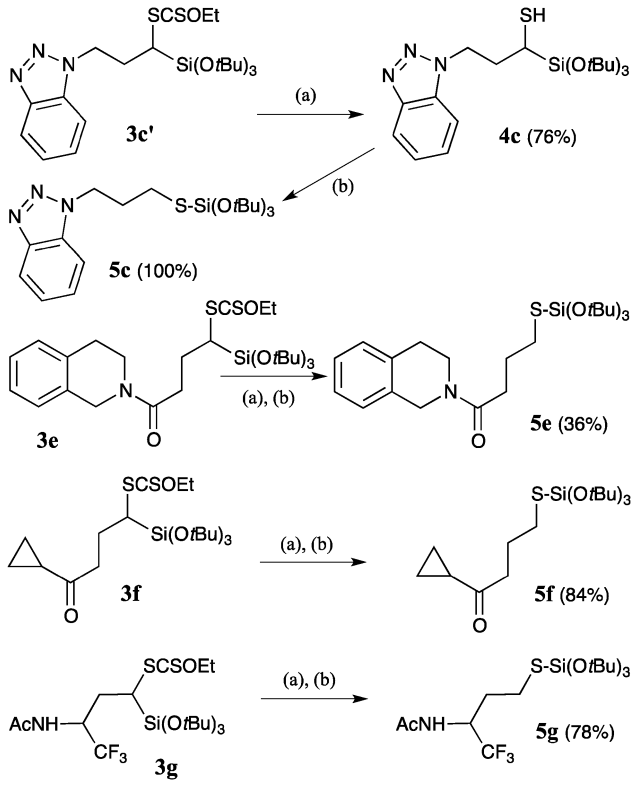


Scheme 4 Further examples of the radical thia-Brook rearrangement.

An unexpected problem was encountered with substrate **3d**, prepared using xanthate **1d** (Scheme 5). The thermolysis step gave, after chromatographic purification, thiolactone **12** (39%) and a polar mixture of compounds. This mixture was simply



Scheme 5 Unexpected formation of a thialactone.



Scheme 6 Additional examples of the radical thia-Brook rearrangement.

subjected to the action of DTBP in refluxing chlorobenzene. Purification then afforded aminopyridine **13** (41%) and the radical thia-Brook rearrangement product **5d** (55%). Aminopyridine **13** is the leaving group in the formation thiolactone **12**. This latter compound would be difficult to obtain by more conventional routes and is interesting in its own right, for example as a cross-linking agent in material science; however, in the present context, its formation by attack of the thiol sulfur on the activated amide is clearly in competition with the desired radical thia-Brook rearrangement.

To circumvent this complication, we resorted to a more traditional cleavage of the xanthate group by aminolysis with 1,2-ethylenediamine.[4] Thus, treatment with xanthate **3d** with 1,2-ethylenediamine in a 1 : 1 (v/v) mixture of ethanol and ether at room temperature gave the crude thiol **4d**, which was not purified but directly heated in refluxing chlorobenzene with DTBP. This gave the expected rearranged product **5d** in good yield. No thiolactone **12** or the corresponding aminopyridine **13** were observed under these conditions. Because of the lower temperature (heating in refluxing chlorobenzene at 130 °C *vs.* thermolysis in diphenyl ether at 200 °C) and, especially, the presence of the DTBP initiator, the radical chain process overcomes the intramolecular ionic ring-closure leading to thiolactone **12**.

The *O*-isopropyl group in the xanthate is now not needed any more and can be replaced by the simpler *O*-ethyl analogue. Thus, adduct **3c′**, obtained in 52% yield by the radical addition of benzotriazole xanthate **1c′**[11] to vinyl tri(*t*-butoxy)silane **2a**, was cleaved by 1,2-ethylenediamine into thiol **4c** (76% yield) and the latter rearranged quantitatively into tri(*t*-butoxy)silyl sulfide **5c** by heating in refluxing chlorobenzene in the presence of DTBP initiator (Scheme 6).

In the same manner, but without purification of the intermediate thiols, xanthates **3e–g**[1] underwent conversion into the corresponding radical thia-Brook rearrangement products **5e–g** (Scheme 6). The possibility of introducing a *geminal* trifluoromethyl acetamido motif is worthy of note.

In summary, we have described a hitherto unknown migration of a silicon group from carbon to sulfur by a radical chain mechanism, a process that may be viewed as a formal radical thia-Brook rearrangement. This provides a route to a plethora of otherwise inaccessible functionalised silyl sulfides **5**. The possibility of capturing intermediate carbon radical **7** (Scheme 2) before hydrogen atom abstraction from the thiol has occurred, for example by cyclisation to a suitably located internal alkene, could also be of some synthetic interest. Studies along these lines are underway.

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