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A radical thia-Brook rearrangement†‡

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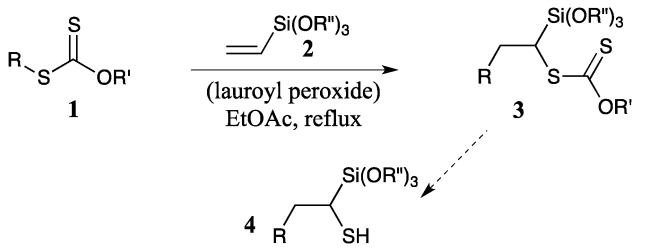
Geminal mercapto trialkyl- and trialkoxy-silanes undergo an efficient radical chain rearrangement, whereby the silyl group migrates from carbon to sulfur; the starting materials are readily obtained by exploiting the peroxide initiated radical addition of dithiocarbonates (xanthates) to trialkyl- or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

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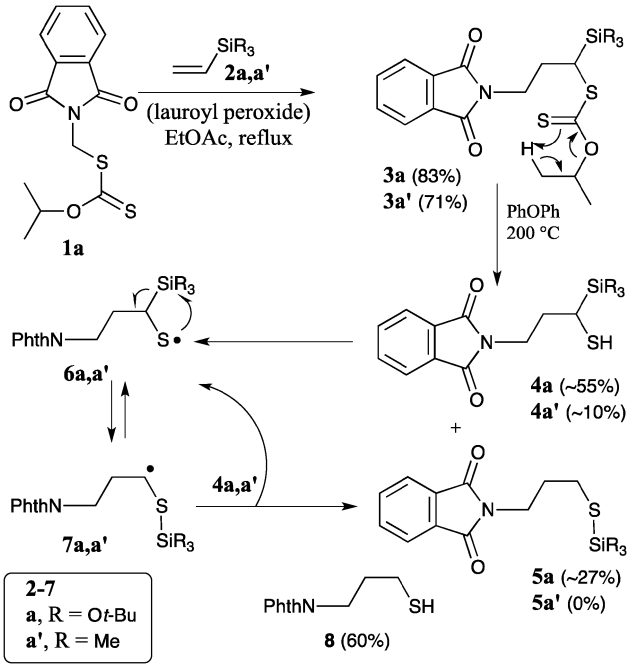
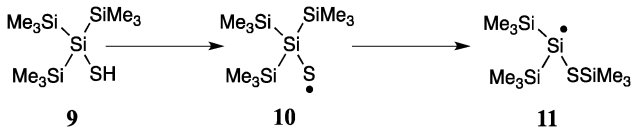
† This paper is dedicated with respect to the memory of Professor Adrian G. Brook (University of Toronto).

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



Scheme 2 An unexpected radical thia-Brook rearrangement.

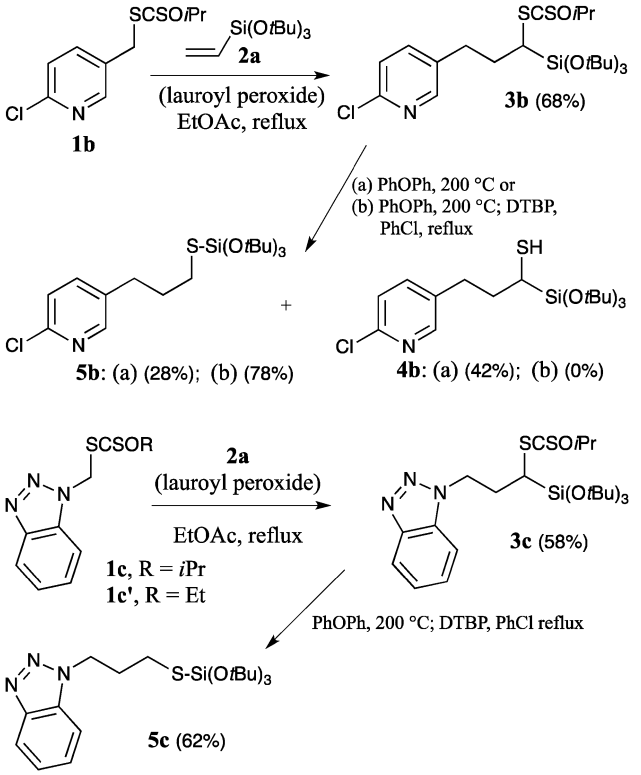


Scheme 3 Cleavage of a silicon–silicon bond by a thia-Brook rearrangement.

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**.

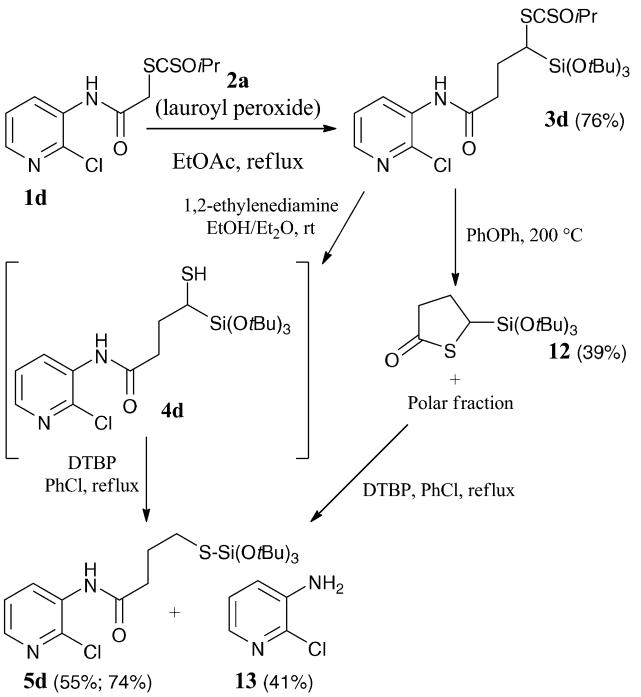
A similar sequence could be accomplished starting from the addition product of xanthate **1a** to vinyl trimethylsilane **2a′** (Scheme 2). Thus, thermolysis of **3a′** indeed furnished the corresponding rearranged derivative **5a′**, but this compound was too labile to chromatographic purification and 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.

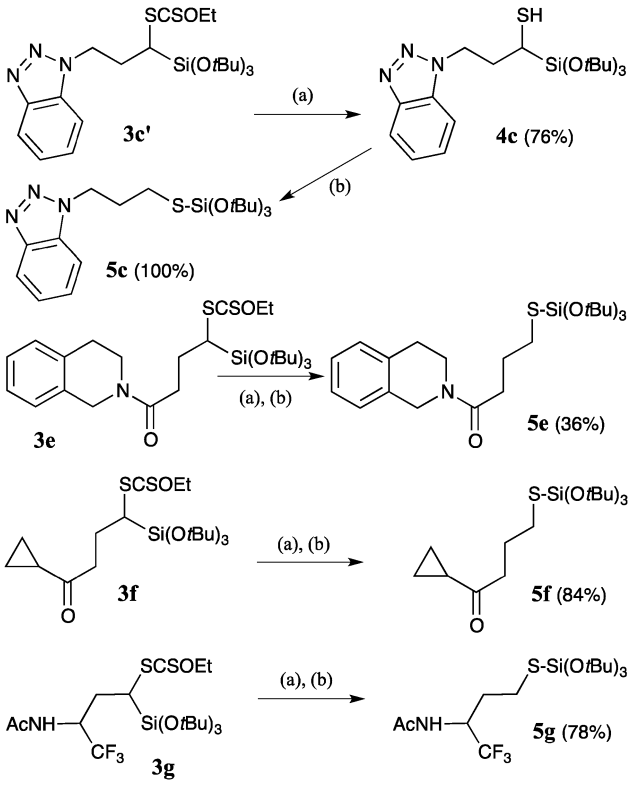


Scheme 4 Further examples of the radical thia-Brook rearrangement.

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.



Conditions: (a) 1,2-ethylenediamine, EtOH/Et_2O, rt; (b) DTBP, PhCl, reflux

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.

Notes and references

1 B. Quiclet-Sire, Y. Yanagisawa and S. Z. Zard, *Chem. Commun.*, 2014, **50**, 2324.
2 For reviews of the xanthate transfer, see: (*a*) S. Z. Zard, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 672; (*b*) B. Quiclet-Sire and S. Z. Zard, *Top. Curr. Chem.*, 2006, **264**, 201; (*c*) B. Quiclet-Sire and S. Z. Zard, *Chem. – Eur. J.*, 2006, **12**, 6002; (*d*) B. Quiclet-Sire and S. Z. Zard, *Pure Appl. Chem.*, 2011, **83**, 519; for an account of the discovery of the basic process, see: (*e*) S. Z. Zard, *Aust. J. Chem.*, 2006, **59**, 663.
3 (*a*) S. Fujita and S. Inagaki, *Chem. Mater.*, 2008, **20**, 891; (*b*) H. Zou, S. Wu and J. Shen, *Chem. Rev.*, 2008, **108**, 3893; (*c*) M. Llusar and C. Sanchez, *Chem. Mater.*, 2008, **20**, 782; (*d*) D. B. Cordes, P. D. Lickiss and F. Rataboul, *Chem. Rev.*, 2010, **110**, 2081; (*e*) S. Onclin, B. J. Ravoo and D. N. Reinhoudt, *Angew. Chem., Int. Ed.*, 2005, **44**, 6282; (*f*) A. Ulman, *Chem. Rev.*, 1996, **96**, 1533; (*g*) A. P. Wight and M. E. Davis, *Chem. Rev.*, 2002, **102**, 3589; (*h*) Z.-L. Lu, E. Lindner and H. A. Mayer, *Chem. Rev.*, 2002, **102**, 3543.
4 (*a*) F. Duus, in *Comprehensive Organic Chemistry*, ed. D. H. R. Barton and W. D. Ollis, Pergamon Press, Oxford, 1979, vol. 3, pp. 373–487; (*b*) S. Ramachandra Rao, *Xanthates and Related Compounds*, Marcel Dekker Inc., New York, 1971.
5 (*a*) C. E. Hoyle and C. N. Bowman, *Angew. Chem., Int. Ed.*, 2010, **49**, 1540; (*b*) A. K. Tucker-Schwartz, R. A. Farrell and R. L. Garrell, *J. Am. Chem. Soc.*, 2011, **133**, 11026; (*c*) E. L. Tyson, M. S. Ament and T. P. Yoon, *J. Org. Chem.*, 2013, **78**, 2046.
6 (*a*) L. Chugaev, *Chem. Ber.*, 1899, **32**, 3332; (*b*) H. R. Nace, *Org. React.*, 1962, **12**, 57.
7 (*a*) K. K. K. Goh, S. Kim and S. Zard, *J. Org. Chem.*, 2013, **78**, 12274; (*b*) B. Quiclet-Sire and S. Z. Zard, *Org. Lett.*, 2013, **15**, 5886.
8 (*a*) A. G. Brook, *Acc. Chem. Res.*, 1974, **7**, 77; for general reviews, see: (*b*) M. A. Brook, *Silicon in Organic, Organometallic, and Polymer Chemistry*, Wiley, New York, 1999; (*c*) H. Moser, *Tetrahedron*, 2001, **57**, 2065.
9 For general reviews on organosilanes in radical chemistry, see: (*a*) C. Chatgilialoglu, *Acc. Chem. Res.*, 1992, **25**, 188; (*b*) C. Chatgilialoglu, *Chem. – Eur. J.*, 2008, **14**, 2310; (*c*) C. Chatgilialoglu, *Organosilanes in Radical Chemistry*, Wiley, Chichester, 2003.
10 M. Ballestri, C. Chatgilialoglu and G. Seconi, *J. Organomet. Chem.*, 1991, **408**, C1.
11 A. R. Katritzky, M. A. C. Button and S. N. Denisenko, *Heterocylcles*, 2001, **54**, 301.

