Synthesis of primary-alkyl selenols and selenides from primary-alkyl thiols involving diphenyl sulfonium salts

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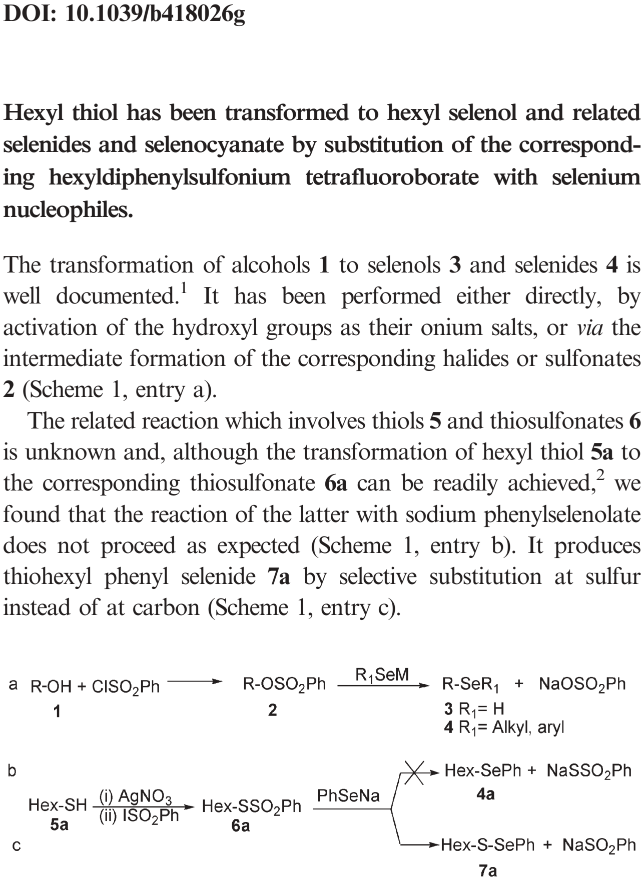
Hexyl thiol has been transformed to hexyl selenol and related selenides and selenocyanate by substitution of the corresponding hexyldiphenylsulfonium tetrafluoroborate with selenium nucleophiles.

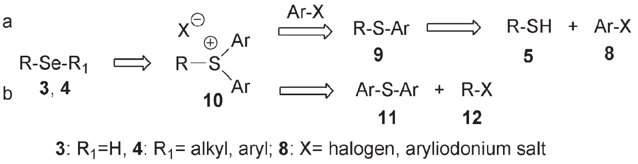
The transformation of alcohols **1** to selenols **3** and selenides **4** is well documented.[1] It has been performed either directly, by activation of the hydroxyl groups as their onium salts, or *via* the intermediate formation of the corresponding halides or sulfonates **2** (Scheme 1, entry a).

The related reaction which involves thiols **5** and thiosulfonates **6** is unknown and, although the transformation of hexyl thiol **5a** to the corresponding thiosulfonate **6a** can be readily achieved,[2] we found that the reaction of the latter with sodium phenylselenolate does not proceed as expected (Scheme 1, entry b). It produces thiohexyl phenyl selenide **7a** by selective substitution at sulfur instead of at carbon (Scheme 1, entry c).



Scheme 1 Reaction of hexyl phenylthiosulfonate with sodium phenylselenolate.

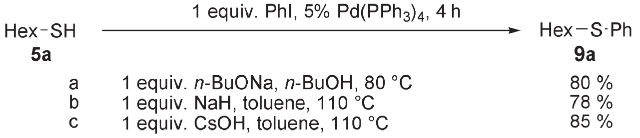
In order to bypass this inconvenience, we decided to activate the primary-alkyl thiol **5** as its corresponding diarylsulfonium salt **10** on which the substitution was expected to occur selectively at the alkyl chain (Scheme 2).†



Scheme 2 Planned synthesis of selenols and selenides involving alkyldiphenylsulfonium salts.

Although alkyldiarylsulfonium salts **10** are known compounds, they are usually prepared on reaction of diaryl sulfides **11** with (i) alcohols in protic media, (ii) their sulfonates or the corresponding alkyl halides in the presence of Lewis acid catalysts.[3,4]

Arylation of thiols **5**, required in our synthesis (Scheme 2), is usually achieved[5] by iodobenzene in *n*-butanol using palladium as a catalyst and sodium butoxide as a base (1 equiv. PhI, 5% Pd(PPh$_3$)$_4$, reflux, 4 h, Scheme 3, entry a).



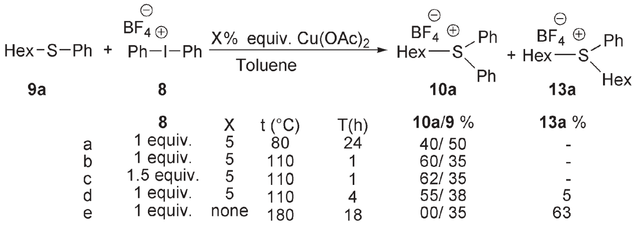
		9a
a	1 equiv. *n*-BuONa, *n*-BuOH, 80 °C	80 %
b	1 equiv. NaH, toluene, 110 °C	78 %
c	1 equiv. CsOH, toluene, 110 °C	85 %

Scheme 3 Palladium catalyzed arylation of hexyl thiol.

We found it more convenient, although the reaction takes place at higher temperature, to perform the arylation of hexyl thiol **5a** using sodium hydride or, better, caesium hydroxide in toluene (110 °C, 4 h, 78 and 85% yield respectively, Scheme 3, entries b and c) since the next step, which involves the arylation of the resulting sulfide, can be achieved in the same solvent.

We planned to synthesize hexyldiphenylsulfonium salts **10** from hexyl phenyl sulfide **9a** and diphenyl iodonium tetrafluoroborate **8**.‡[6] This reaction, which has been already performed on diaryl sulfides using a catalytic amount of copper(II) acetate, could not be extended, according to the authors, to alkyl aryl sulfides.[6]

Our first attempts, using hexyl phenyl sulfide, were nevertheless encouraging, although the arylation proceeded too slowly at 80 °C in toluene using 5% of copper acetate as catalyst (Scheme 4, entry a). The reaction does not take place in the absence of copper acetate and lowering its amount to 1% is detrimental. The reaction proved to be faster when carried out at higher temperature (110 °C, Scheme 4, entries b and c) but the yield of **10a** did not improve on prolonged heating, due to the competing formation of the dihexylphenylsulfonium salt **13a** which cannot be separated from **10a** (Scheme 4, entry d, compare with entry b).



	8	X	t (°C)	T(h)	10a/9 %	13a %
a	1 equiv.	5	80	24	40/ 50	-
b	1 equiv.	5	110	1	60/ 35	-
c	1.5 equiv.	5	110	1	62/ 35	-
d	1 equiv.	5	110	4	55/ 38	5
e	1 equiv.	none	180	18	00/ 35	63

Scheme 4 Diphenyl iodonium promoted alkylation of hexyl phenyl sulfide.

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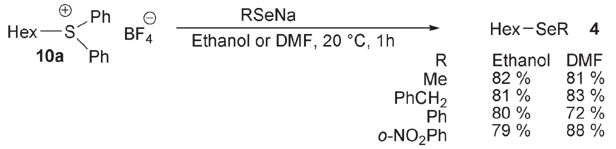
The synthesis of dihexylphenylsulfonium tetrafluoroborate **13a** can be selectively achieved by heating, without copper salts, **9a** and **8** for a prolonged period at high temperature (180 °C, 18 h, Scheme 4, entry e). Its formation can be rationalized by a competing nucleophilic attack of the unreacted sulfide **9a** on either the sulfonium salt **10a** or any other electrophilic species possessing an hexyl substituent. We have found that heating equimolar amounts of hexyldiphenylsulfonium tetrafluoroborate **10a** and hexyl phenyl sulfide, for 1 hour at 110 °C in toluene, provides diphenyl sulfide and dihexylphenylsulfonium tetrafluoroborate **13a** (10% yield each).§

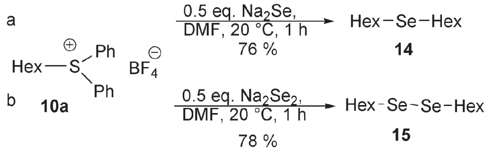
Finally, the synthesis of a series of organoselenium compounds has been efficiently achieved from hexyldiphenylsulfonium tetrafluoroborate **10a** by selective substitution of the diphenyl sulfide moiety by various nucleophilic selenium reagents (Scheme 5).



Scheme 5 Substitution of hexyldiphenylsulfonium tetrafluoroborate with selenium nucleophiles.

Thus hexyldiphenylsulfonium tetrafluoroborate **10a** reacts at room temperature with sodium methyl-, benzyl-, phenyl- or nitrophenylselenolates to produce the corresponding selenides in very good yield whether the reaction is carried out in ethanol or DMF (20 °C, 1 h, 70–80% yield, Scheme 5).¶

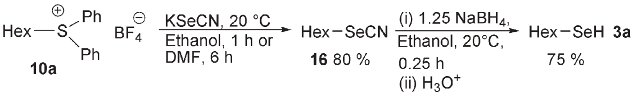
The sulfonium salt **10a** also reacts with the reagents generated from selenium and either sodium borohydride (2 equiv., 6 equiv. EtOH, in DMF)[7] or sodium hydride (1.1 equiv. in DMF)[8] to produce selectively dihexyl selenide **14** (76%, Scheme 6, entry a) or dihexyl diselenide **15** (78%, Scheme 6, entry b) respectively.



Scheme 6 Synthesis of dihexyl selenide and of dihexyl diselenide from hexyldiphenylsulfonium tetrafluoroborate.

Hexyldiphenylsulfonium tetrafluoroborate **10a** reacts also with potassium selenocyanate in DMF, as well as in ethanol in which the reaction proved to be faster.

Hexyl selenocyanate **16** has been, in turn, efficiently reduced to the corresponding sodium hexylselenolate on reaction with sodium borohydride (1.25 equiv. NaBH$_4$, ethanol, 20 °C, 0.25 h)[9] to give hexyl selenol **3a** after acid hydrolysis (Scheme 7).



Scheme 7 Synthesis of hexyl selenol from hexyldiphenylsulfonium tetrafluoroborate.

In conclusion, we have disclosed the transformation of hexyl thiol to hexyl selenocyanate, hexyl selenol, dihexyl diselenide and a series of hexyl selenides. Hexyldiphenylsulfonium tetrafluoroborate is the key intermediate in these transformations and diphenyl sulfide proved to be an extremely valuable leaving group. Generalization of this reaction is on the way.

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Notes and references

† Such selectivity should not be expected in the case of trialkylsulfonium salts bearing different alkyl groups on sulfur.

‡ Diphenyl iodonium tetrafluoroborate was prepared from diphenyl iodonium chloride and silver (II) oxide followed by treatment with an aqueous solution of tetrafluoroboric acid (−15 °C, 0.2 h, 60% yield). Diphenyl iodonium chloride was synthesized from benzene on sequential reaction with (i) potassium iodate in acetic anhydride, (ii) sulfuric acid in acetic acid and (iii) hydrolysis using an aqueous solution of ammonium chloride (90% yield).

§ Hexyldiphenylsulfonium tetrafluoroborate **10a** remains unchanged on heating at 110 °C for 24 h.

¶ Nucleophilic substitutions of alkyldiarylsulfonium salts are rare. See reference 4. Related reactions involving trialkylsulfonium salts will be disclosed soon.

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