Synthesis of polyfunctionalized thiophenes and enediynes *via* ring-opening reactions of 3-lithiated thieno[2,3-*b*](and [3,2-*b*])thiophenes, 3,4-dilithiated thieno[2,3-*b*]thiophenes and 3,6-dilithiated thieno[3,2-*b*]thiophenes

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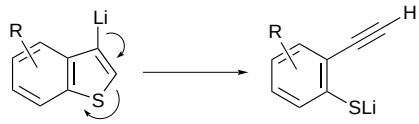
Solutions of the title lithiated thienothiophenes were synthesized from 2,5-disubstituted 3,4-dibromothieno[2,3-*b*]thiophenes or 3,6-dibromothieno[3,2-*b*]thiophenes *via* Br → Li exchange with 1.0 or 2.0 equiv. of BuLi (THF, −78 °C), respectively, and gave either polyfunctionalized thiophenes or polyfunctionalized enediynes (by a novel tandem ring-opening process in these cases) on being allowed to warm up to ambient temperature.

Previously we have reported that ethereal (Et_2O or THF) solutions of benzo[*b*]thiophen-3-yllithium[1–3] and its derivatives[2–4] (prepared from the corresponding 3-bromobenzo[*b*]-thiophene *via* Br → Li exchange with BuLi at −78 °C) undergo a ring-opening process, **1** → **2** (Scheme 1), as the solutions



1 **2**

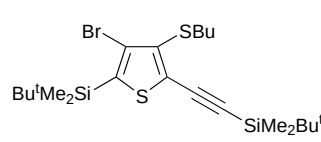
Scheme 1

are warmed up to give the lithium salt of an *o*-mercaptophenylacetylene, which can react further, *e.g.* by *S*-butylation with the bromobutane produced in the initial Br → Li exchange reaction or through metallation at the terminal alkyne position. Selenophen-3-yllithium[5–9] and 3-thienyllithium[2,6–12] behave similarly and yield enynes. We now report novel tandem ring-opening processes of 3,4-dilithiated thieno[2,3-*b*]thiophenes and 3,6-dilithiated thieno[3,2-*b*]thiophenes which afford novel enediynes. This work was prompted by intense current interest in enediynes as precursors to more complex molecular architectures.[13]

First we treated 2,3,5,6-tetrabromothieno[3,2-*b*]thiophene[14,15] successively with 2.0 equiv. of BuLi (THF, ambient temperature) and Bu^tMe_2SiCl, then the resulting solution of 3,6-dibromo-2,5-bis(*tert*-butyldimethylsilyl)thieno[3,2-*b*]thiophene[14] was cooled to −78 °C and a further 1.0 equiv. of BuLi was added. The resulting mixture was allowed to warm up slowly to ambient temperature, then it was quenched by addition of 20% aq. NH_4Cl. Following a standard work-up procedure (extraction of the crude product with Et_2O and flash chromatography on silica with light petroleum as eluent) we obtained 3-bromo-2-*tert*-butyldimethylsilyl-5-*tert*-butyldimethylsilylethynyl-4-butylsulfanylthiophene **3** (70% yield) as a yellow oil.‡ Other 2,5-disubstituted 3,6-dilithiothieno[3,2-*b*]-thiophenes[14] can be prepared and converted similarly into polyfunctionalized thiophenes analogous to compound **3**.

When thiophene **3** was treated successively with 1.0 equiv. of BuLi (THF, 0 °C) and MeI, it gave the enediyne **4** (89% yield) as a yellow oil, thus demonstrating that each thiolate anion, as it is generated in this two-stage process, can be captured by a different alkylating reagent.

Both ring-opening processes can be carried out in tandem. Thus, we converted 2,3,5,6-tetrabromothieno[3,2-*b*]thiophene



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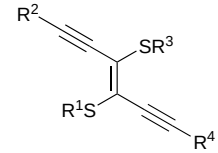
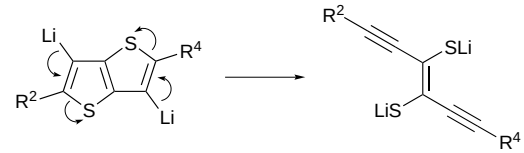


4 R^1 = Me, R^2 = R^4 = $SiMe_2Bu^t$, R^3 = Bu
5 R^1 = R^3 = Bu, R^2 = R^4 = $SiMe_2Bu^t$
6 R^1 = R^3 = Bu, R^2 = R^4 = H

into 3,6-dibromo-2,5-bis(*tert*-butyldimethylsilyl)thieno[3,2-*b*]-thiophene[14] *in situ*, as described before, then added a further 2.0 equiv. of BuLi (THF, 0 °C) prior to allowing the reaction mixture to warm up slowly to ambient temperature which, after work-up in the standard way, gave the enediyne **5** (70% yield) as a yellow oil. The extremely unstable enediyne **6** (73.5% yield) was prepared by removal of the Bu^tMe_2Si groups from compound **5** *via* treatment with Bu_4NF in THF. Starting from 2,3,5,6-tetrabromothieno[3,2-*b*]thiophene we have prepared a number of other enediynes using this strategy. Essentially the thienothiophene ring is a template to which a variety of functional groups can be attached prior to the tandem ring-opening process **7** → **8** (Scheme 2), *e.g. via* Br → Li exchange

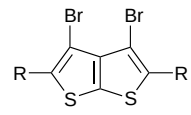


7 **8**

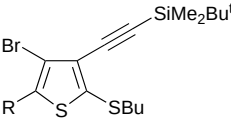
Scheme 2

techniques, by Pd^0-catalysed coupling reactions or through further modification of initial products such as by Wittig reactions of aldehydes.

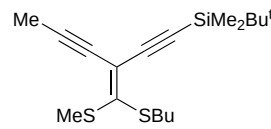
When 2,3,4,5-tetrabromothieno[2,3-*b*]thiophene[16] was treated successively with 3.4 equiv. of BuLi (THF, −65 °C) and 4.8 equiv. of Me_3SiCl, it gave 3,4-dibromo-2,5-bis(trimethylsilyl)thieno[2,3-*b*]thiophene **9** (51% yield) as a solid which decomposed when heated to 125 °C in a capillary tube. A similar attempt (2.6 equiv. BuLi, THF, but at 0 °C instead of



9 R = $SiMe_3$
10 R = $SiMe_2Bu^t$



11 R = $SiMe_2Bu^t$
12 R = H



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−65 °C; 2.4 equiv. of Bu^tMe_2SiCl) to synthesize 3,6-dibromo-2,5-bis(*tert*-butyldimethylsilyl)thieno[2,3-*b*]thiophene **10** gave this compound (mp 112–114 °C) in only 23% yield together with 3-bromo-2-*tert*-butyldimethylsilyl-4-*tert*-butyldimethylsilylethynyl-5-butylsulfanylthiophene **11** (33%), a pale yellow solid with mp 35–37 °C, and 4-bromo-3-*tert*-butyldimethylsilylethynyl-2-butylsulfanylthiophene **12** (18%) as a pale yellow oil (formed by loss of the 2-Bu^tMe_2Si group from compound **11**).

When treated successively with 2.0 equiv. of BuLi (THF, 0 °C) and an excess of MeI, the bromothiophene **11** was converted into 2-*tert*-butyldimethylsilylethynyl-1-butylsulfanyl-1-methylsulfanylpent-1-en-3-yne **13** (87% yield) as a yellow oil. In this reaction not only does the MeI capture the generated thiolate anion but it also displaces a Bu^tMe_2Si group.

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Footnotes and References

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‡ All new compounds (pure by TLC analysis) were characterised by recording their IR, ^{1}H NMR and low- and high-resolution mass spectra. In most cases they were unstable in air at ambient temperature and we were unable to obtain satisfactory elemental microanalytical results (for C, H and N).

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