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An easy one-step procedure for the synthesis of novel β-functionalised tellurides

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ABSTRACT

Novel β-hydroxy-,β-amino- and β-mercapto- dialkyl- and phenyl-alkyl tellurides have been achieved through regioselective ring opening reactions of oxiranes, aziridines and thiiranes with different Te-nucleophiles, including tellurosilanes. Tellurium-125 NMR chemical shifts of selected compounds have been measured.

1. Introduction

Organotellurium compounds,[1] are able to generate nucleophilic, electrophilic or radicophilic species that often react in a chemo-, regio- and stereo-selective manner. For these properties, they have been employed in different functional group conversions,[2] in the formation of new carbon-carbon bonds,[3] in the synthesis of natural products[4] and in materials science.[5] Furthermore, several tellurium-containing organic molecules have been studied for their biological properties as thioredoxin reductase modulators, glutathione peroxidase mimics and cancer cell growth inhibitors.[6]

A number of differently functionalised organotellurium compounds, including suitable amino- and hydroxy-substituted systems, have been reported as useful synthetic intermediates in organic transformations.[7]

Several methods for the synthesis of diaryl tellurides and ditellurides have emerged over recent years,[8] nonetheless the corresponding symmetric dialkyl analogues have received less attention. They are commonly synthesised through the reaction of tellurolates or silyl tellurides[9] with haloalkanes[1,10] or alkyl tosylates.[11] Other methods involve the reactivity of elemental tellurium with organolithium compounds[1,12] or Grignard reagents.[1] β-Halo tellurides or ditellurides can be synthesised from alkenes or alkynes and $TeCl_4$ or $TeBr_4$.[13] Unsymmetrical β-amino tellurides can be accessed through reaction of alkyl- or aryl- tellurolates with mesylates,[14] 2-haloamines or by ring opening of 2-oxazolines and 2-oxazolidinones.[15] A few examples of ring opening reactions of epoxides and aziridines with organic tellurolates (RTe^-) towards unsymmetrical β-hydroxy- and β-amino- tellurides are also reported.[7d,10,16]

During our studies towards the synthesis of novel sulfur- and selenium- containing molecules,[17] we explored the reactivity of three membered heterocycles with chalcogen-containing silyl-nucleophiles disclosing convenient procedures for the synthesis of sulfides and selenides through a ring opening-based protocol. Indeed, thiosilanes and selenosilanes such as HMDST and HMDSS (Me_3Si-S-$SiMe_3$ and Me_3Si-Se-$SiMe_3$, respectively) were efficiently reacted with epoxides, thiiranes and aziridines leading to a straightforward formation of β-functionalised thiols, selenides and diselenides.[18] These bidentate molecules can find application in

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organic synthesis, as ligands, catalysts or intermediates, and in biology. We recently reported our preliminary findings on the GPx-like catalytic activity of selected organoselenium compounds.[19]

As an extension of our interest in the synthesis of chalcogen-containing molecules, we evaluated whether new β-functionalised tellurides could be achieved through ring opening reactions of three membered heterocycles with a suitable tellurium nucleophile. To the best of our knowledge, only a few reports dealing with the synthesis of β-functionalised symmetric tellurides through nucleophilic reactions on tosylates, halides, and β-lactones are available in the literature.[11,20] We report herein an easy and versatile procedure for the preparation of novel tellurium-containing β-substituted organic small molecules *via* ring opening of oxiranes, aziridines and thiiranes.

2. Results and discussion

Aiming to access β-functionalised dialkyl tellurides, on the basis of our previous findings in silicon-mediated reactions, we initially considered the possibility to synthesise these chalcogen-containing compounds exploiting the reactivity of strained heterocycles with a suitable tellurosilane such as $(Me_3Si)_2Te$. We began our studies with the synthesis of bis(trimethylsilyl)telluride, the tellurium containing analogue of HMDST and HMDSS, from Li_2Te (or Na_2Te) and Me_3SiCl following literature reported procedures.[21,22] This tellurosilane proved to be rather unstable and, as already observed by other authors,[21b] a partial decomposition was observed over 24 h, even though it was stored in the dark under inert atmosphere at low temperature (−20 °C). Nevertheless, the reactivity of bis(-trimethylsilyl)telluride with epoxides was investigated under conditions used for the ring opening of oxiranes with HMDST and HMDSS towards thiols,[18a] selenides and diselenides[18b] (room temperature or 0 °C, 20% TBAF). Unfortunately, only traces of desired β-hydroxydialkyl tellurides were detected, most likely due to a rapid decomposition of the tellurosilane. The reaction was also performed under milder conditions; however, neither lower temperatures nor the use of a minor amount of TBAF led to the formation of the desired tellurides in useful yields.

The difficulties encountered in handling $(Me_3Si)_2Te$, coupled with the volatility and the pungent odour of the decomposition products, prompted us to explore the reactivity of a different Te nucleophilic species. Thus, the ring opening reaction of epoxides was carried out in the presence of Li_2Te, generated *in situ* by the reaction of elemental tellurium with $LiBEt_3H$. Pleasingly, under these conditions, treatment of 2-methyloxirane **1a** led to 1,1′-tellurobis(propan-2-ol) **2a** as a mixture of diastereoisomers, arising from a clean regioselective attack of the tellurium nucleophile on the less hindered side of the oxirane (Scheme 1).

In order to evaluate the generality of this procedure, a series of substituted epoxides was reacted under the same conditions as reported in Table 1 (entries 1–5). The reactivity proved general, leading to the regioselective formation of differently substituted β-hydroxy tellurides. The methodology can also be applied to useful but labile compounds such as glycidol derivatives. Glycidyl benzyl- and allyl- ethers **1b-c** were opened affording tellurides **2b-c** without cleavage of the protecting group. β-Hydroxy tellurides were isolated in rather good yields, even though partial decomposition on silica gel was evidenced during purification. Nevertheless, it is worthwhile to remember that these compounds are the result of three different consecutive reactions. In fact, the *in situ* generated dianion Te^{2-} reacts with the epoxide, then a subsequent S_N2 type reaction of the [$AlkTe^-$] intermediate on a second equivalent of the electrophile leads to the β-dialkyl tellurides **2**. When the non racemic epoxide (*R*)-**1b** was employed, the ring opening took place with complete retention of stereochemistry, and the corresponding diastereoenriched telluride (2*S*,2′*S*)-**2b** was achieved. Furthermore, the di-substituted oxirane **1d**, limonene oxide, which arises from a natural product, gave the corresponding β-hydroxy tellurides **2d**, albeit in lower yields with respect to the mono-substituted ones.

In order to evaluate whether the yield of the process could be increased by using different reducing agents, Na/naphthalene and Na/DMF were reacted with elemental tellurium to generate Te^{2-} but, upon *in situ* treatment with epoxides, β-hydroxy tellurides were formed in lower yields with respect to $LiEt_3BH$ conditions.

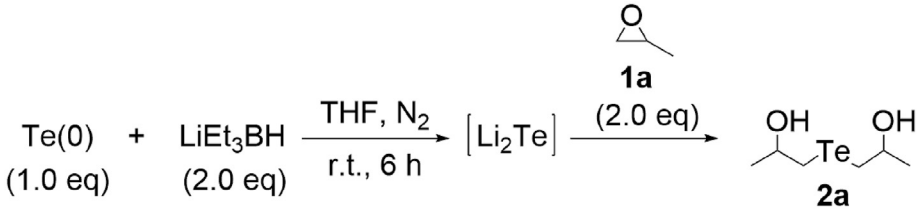
With the aim to explore the scope and the limitations of the procedure, *N*-protected aziridines synthesised from natural amino acids were reacted with Li_2Te under the same conditions. This investigation led to an easy and direct access to enantioenriched *N*-Tosyl or *N*-Boc β-amino tellurides **4a-c** and **4d** following a regioselective and stereospecific ring opening pathway. Examples of such reactivity are listed in Table 1 (entries 6–9).

Having evaluated the reactivity of oxiranes and aziridines with Li_2Te, we sought to apply this methodology to thiiranes, aiming to synthesise sulfur-containing organotellurium compounds.

To the best of our knowledge, no example dealing with the ring opening of episulfides with Te-nucleophiles has been reported to date. Thus, thiiranes **5a** and **5b** were reacted under the described conditions leading to 3,7-disubstituted 1,2,5-dithiatellurepanes **6a,b**, together with a minor amount of β-mercapto tellurides **7a,b** (Scheme 2).

In analogy with what was observed in the reaction of silyl chalcogenides (HMDST and HMDSS) with episulfides,[18c] the formation of dithiatellurepanes **6** occurred through the oxidation of the thiol groups of tellurides **7**. However, it was observed that dithiatellurepanes **6**, as well as β-functionalised tellurides **2** and **4** were labile on exposure to air and partially decomposed during purification on silica gel.

Aiming to extend this study to different tellurium nucleophiles, we evaluated the reactivity of thiiranes with $PhTe^-$, *in situ* generated through the reduction of diphenyl ditelluride with $NaBH_4$, as reported in Scheme 3. The ring opening reactions were conducted under two sets of conditions: i) conditions **A**: addition of the thiirane to $PhTe^-$ at 0 °C, followed by warming to room temperature for 3 h; ii) conditions **B**: addition of the thiirane to $PhTe^-$ at 0 °C, followed after 30 min by addition of citric acid (50%, H_2O



Scheme 1. Synthesis of β-hydroxy tellurides from epoxides.