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OXIRANYLLITHIUM REAGENTS: GENERATION FROM ORGANOTIN PRECURSORS, ADDITION TO ALDEHYDES AND KETONES, AND DIMERIZATION TO α,α'-DIALKOXYOLEFINS[1]

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Abstract: Oxiranyllithium compounds can be generated from organotin precursors by tin-lithium exchange with butyllithium in THF at -90°C. In the presence of TMEDA, they react with aldehydes and ketones to give epoxy alcohols in good yields. In the absence of TMEDA, they dimerize to α,α'-dialkoxyolefins.

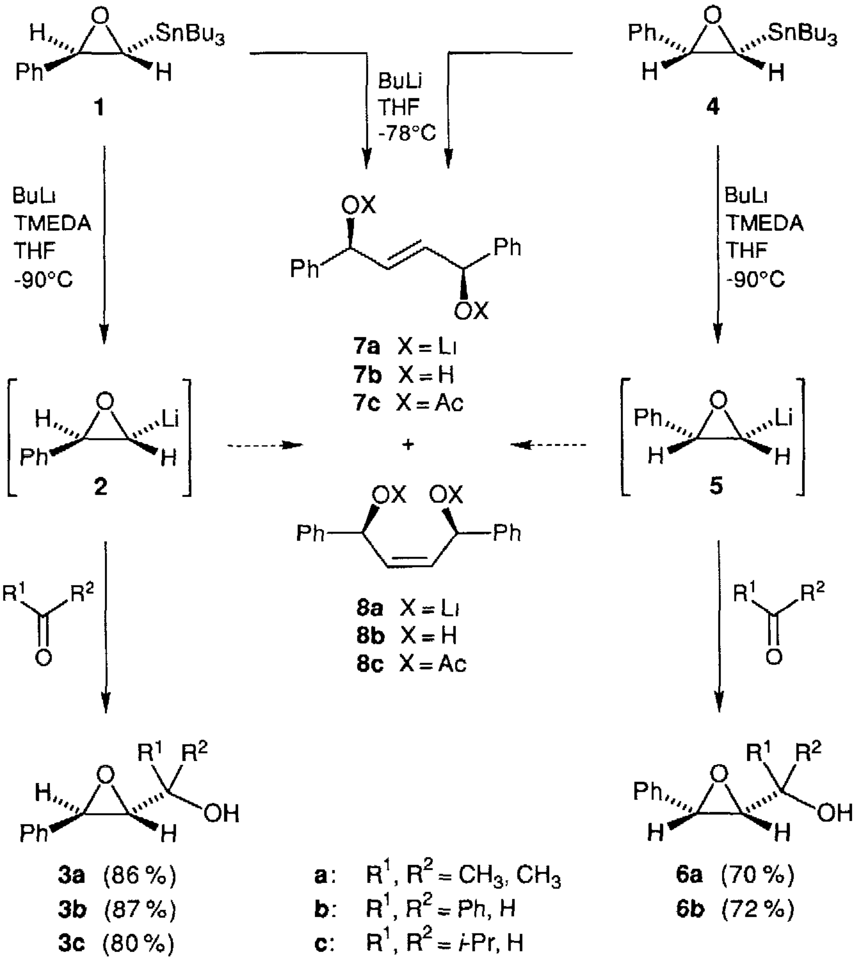
Epoxides can be deprotonated at the oxirane ring by strong bases.[3] The resulting oxiranyl anions are highly reactive species which readily undergo ring-opening via α-elimination to form alkoxycarbenes. Because of their diverse reactivity profiles, metalated oxiranes are of interest both from a mechanistic point of view[3,4] and as potential reagents for organic synthesis.[3,5] Eisch and Galle[5a] were the first to show that oxiranes containing a carbanion-stabilizing substituent can be selectively metalated at the activated carbon atom and coupled with electrophiles to give substituted epoxides.[5] However, a feasible method for generating non-stabilized oxiranyl anions and their conversion to substituted epoxides by reaction with electrophiles has not been reported. We have found that non-stabilized oxiranyllithium compounds can be readily prepared from oxiranyltin precursors by transmetalation with butyllithium in THF at -90°C in the presence of N,N,N',N'-tetramethylethylenediamine (TMEDA). Under these conditions, the metalated oxiranes can be trapped with aldehydes or ketones to give epoxy alcohols in good yields

Oxiranyltin derivatives are easily prepared by epoxidation of the corresponding alkenyltin compounds.[5b,6] Radical addition of tributyltin hydride to phenylacetylene[7] and subsequent reaction with 3-chloroperbenzoic acid (CH_2Cl_2, aq. $NaHCO_3$) provided a 4:1 mixture of *trans* and *cis* epoxides **1** and **4** in ca. 50 % yield which could be separated by flash chromatography on silica gel or neutral alumina.

Upon treatment with *n*-butyllithium in THF, the oxiranyltin **1** underwent rapid tin-lithium exchange which was complete in less than 5 min at -90°C. After quenching with acetic acid or acetone, tetrabutyltin was isolated in essentially quantitative yield. Phenyloxirane and the epoxy alcohol **3a**, the expected products derived from the oxiranyllithium intermediate **2**, were isolated in much lower yields varying between 20-50%.[8] The reason for the unsatisfactory yields was found to be a competing dimerization of the lithium compound **2** leading to the (*E*)- and (*Z*)-olefins **7a** and **8a** (Scheme 1). In another experiment, in which the reaction mixture was stirred for 4 h at -75°C after transmetalation with butyllithium and then treated with acetic anhydride (-75° →25°C), the dimer-derived diacetates **7c** and **8c** were obtained in 75% yield (**7c**/**8c** = 3:2).

A reasonable pathway leading to products **7** and **8** can be postulated proceeding via addition of the oxiranyllithium compound **2** to an α-alkoxycarbene derived from **2** by α-elimination.[3,5ab] The reaction is remarkably stereoselective: starting from (*rac*)-**1**, the racemic (*E*)-olefin **7** was formed with a preference of 4:1 over the corresponding *meso* form, whereas of the two diastereomeric (*Z*)-olefins, only the *meso* isomer **8** was observed.[9] Analogous results were obtained with the *cis*-compound (*rac*)-**4**, although the yields of (*Z*)-olefin **8** were distinctly lower in this case (32% of **7c**, 6% of **8c**).

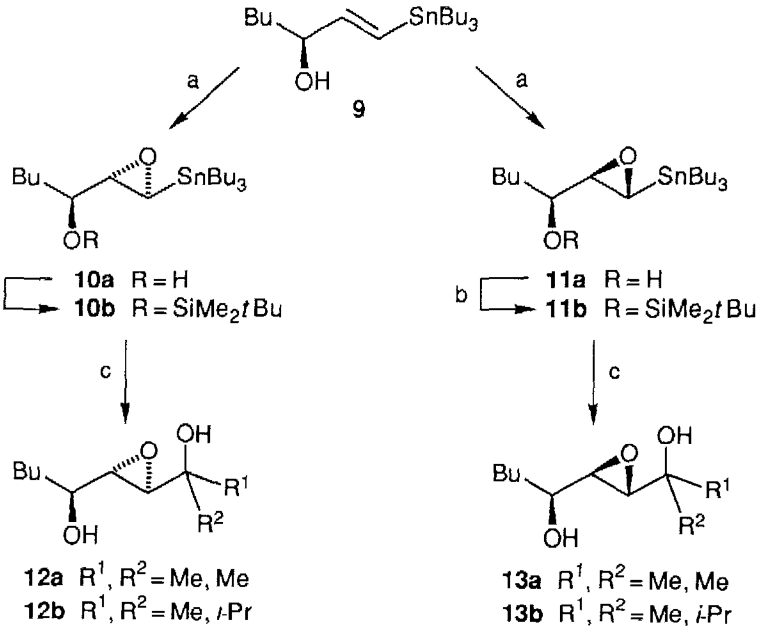
Scheme 1



The formation of dialkoxy-olefins **7** and **8** is effectively inhibited by TMEDA. Transmetalation of **1** with butyllithium in the presence of 2 equivalents of TMEDA followed by addition of acetone afforded the epoxy alcohol **3a** in 86% yield (Scheme 1). Only traces of **7** and **8** were observed under these conditions. Benzaldehyde and isobutyraldehyde also reacted cleanly to form the corresponding epoxy alcohols **3b** and **3c**, which were obtained as mixtures of diastereomers (diastereoselectivity (ds) = 2:1 in both cases).[10] The same reaction sequence starting from the *cis*-oxiranyltin **4** led to the epoxy alcohols **6a** and **6b**; the corresponding *trans*-isomers **3a** and **3b** could not be detected. Apparently, the oxiranyllithium intermediates **2** and **5** are configurationally stable under the reaction conditions. The observed stereochemical course of the transmetalation-addition sequence is in accord with the expectation that both steps should occur with retention of configuration at the oxirane ring.[5,11]

Scheme 2 shows some additional examples. Hydroxyalkenyltin compounds, such as (*rac*)-**9**, are readily available by hydrostannylation of propargyl alcohols[6b] or by addition of 2-trialkylstannyl-ethenyllithium[12] to aldehydes.[6b] Via Sharpless epoxidation,[6b,13] they can be converted to optically active epoxides. Whereas epoxidation of (*rac*)-**9** with 3-chloroperbenzoic acid afforded a 1:1 mixture of racemic epoxides **10a** and **11a**, kinetic resolution by the Sharpless method selectively led to (-)-**10a** (45% yield based on (*rac*)-**9**, >90%ee, **10a**:**11a** >10:1).[14] Prior to transmetalation with butyllithium, epoxy alcohols **10a** and **11a** were protected as silylethers.[15] Tin-lithium exchange and subsequent addition of acetone or isobutyraldehyde gave the expected products (**12a**: 57%; **12b**. 58%, ds = 3:2; **13a**: 77%; **13b** 85%, ds = 3:2). The lower yields of **12a** and **12b** can be attributed to competing formation of dialkoxy-olefins (see above).

Scheme 2



(a) MCPBA (2.5 equiv), NaHCO$_3$ (2.5 equiv), CH$_2$Cl$_2$, H$_2$O, 23°C; (*rac*)-**10a**: 33%, (*rac*)-**11a**: 35%. Kinetic resolution (*rac*)-**9**→(–)-**10a**: see text. (b) *t*-BuMe$_2$SiCl, NEt$_3$, DMAP (5 mol%), DMF, 23°C.[15,16] (c) 1. BuLi, TMEDA, THF, -90°C; 2. $R^1R^2C=O$ (see Experimental Procedure)

In summary, we have shown that non-stabilized oxiranyllithium reagents can be generated from readily available oxiranyltin precursors. Reaction with aldehydes and ketones leads to epoxy alcohols in good yields, providing a new route to this synthetically useful class of compounds. Moreover, the unexpected formation of dihydroxyalkenes should also be of value for the preparation of α,α'-difunctionalized olefins.

Experimental Procedure: To a cooled (-90°C) solution of **1** (414 mg; 1.01 mmol) and TMEDA (300µl; 2.02 mmol) in 5 ml of anhydrous THF under N$_2$ was added *n*-BuLi (1.71M in hexane; 0 76 ml; 1.30 mmol) over 1 min After 5 min, acetone (120µl; 1.63 mmol) was added in one portion. The mixture was stirred for an additional 10 min at -90°C, poured onto aqueous phospate buffer (pH 7), and extracted with Et$_2$O. The combined extracts were dried (Na$_2$SO$_4$) and concentrated. Flash chromatography of the crude product with Et$_2$O/pentane 2:1 (2 cm×14 cm silica gel column) gave 154 mg of **3a** (R_f = 0.16; 86% yield) as a colorless oil.[17]

References and Notes

1. Part of the diploma theses of *P L.* (1986), *F S.* (1985), and *H. L.* (1988); presented at the Fall Meeting of the Swiss Chemical Society, October 21, 1988 in Bern. We thank *Oliver Sennhauser* for his experimental contributions.
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8. During the course of this work, two analogous studies were published· in the reaction of 1,2-epoxydecyltrimethyltin with BuLi followed by addition of butanal, Molander *et al* [5c] obtained the corresponding epoxy alcohol in 17% yield. Eisch and Galle[5b] reported that treatment of Bu_3Sn-substituted oxiranes with excess *t*-BuLi or PhLi led to alkoxycarbenes which reacted with *t*-BuLi or PhLi to afford olefins.
9. The relative configuration of **7c** and **8c** was determined by epoxidation with MCPBA. ^1H and ^{13}C NMR spectroscopy showed that the corresponding epoxides were symmetric Therefore **7** must have C_2-symmetry and **8** C_s-symmetry. The structure of **7c** was additionally confirmed by comparison with a sample of (*rac*)-**7** and the corresponding *meso*-isomer prepared from (*E*)-Bu_3Sn-CH=CH-$SnBu_3$[12] and PhCHO.
10. Preliminary attempts to trap **2** with alkyl halides or epoxides have not been successful.
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14. $Ti(OiPr)_4$ (0.1 equiv), (L)-diisopropyl tartrate (0.18 equiv), *t*-BuOOH (0 7 equiv), 3Å mol sieves, CH_2Cl_2, -20°C; **10a**: $[\alpha]_D^{23} = -24.3$ (c=1, $CHCl_3$), the enantiomeric excess was determined by ^1H NMR spectroscopy with $Eu(tfc)_3$. The configurational assignment for **10a** is based on analogy with literature examples.[6b,13] Kinetic resolution of Bu_3Sn-substituted allylic alcohols via Sharpless epoxidation has also been described by Sato *et al* [6b]
15. During silylation, competing nucleophilic epoxide opening by chloride ions at the Bu_3Sn-substituted position was observed. The resulting chlorohydrins (10-25% yield) are readily converted to the desired products by treatment with DBU (CH_2Cl_2, 25°C). In this way, **10b** and **11b** can be obtained in total yields of 80-85%.
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17. Selected NMR data ($CDCl_3$). **1**· $\delta(^1H) = 0.8-1.7$ (m, 27 H), 2.75 (d, J = 3.6 Hz, 0.84 H; $^{117}Sn/^{119}Sn$-satellites: 2 dd, $J_{HH} = 3.6$, $J_{SnH} = 95/102$ Hz, 0.16 H), 3.72 (d, J = 3.6 Hz, 1 H), 7.2-7.4 (m, 5 H). **4**: $\delta(^1H) = 0.5-1.6$ (m, 27 H), 3.08 (d, J = 5 1 Hz, 0.84 H; 2 dd, $J_{HH} = 5.1$, $J_{SnH} = 87/97$ Hz, 0.16 H), 4.21 (d, J = 5.1 Hz, 1 H), 7.2-7 4 (m, 5 H). **3a**: $\delta(^1H) = 1$ 30, 1.38 (2 s, 2×3 H), 1.87 (s, 1 H), 3.00, 3.94 (2 d, J = 2.2 Hz, 2×1 H), 7.25-7.4 (m, 5 H). **6a**: $\delta(^1H) = 1.04$, 1.25 (2 s, 2×3 H), 1.33 (s, 1H), 3.16, 4 15 (2 d, J = 4.4 Hz, 2×1 H), 7.2-7.5 (m, 5 H). **7c**: $\delta(^1H) = 2.09$ (s, 6 H), 5.91, 6 30 (AA'BB'-system· 2 "dd", J = 3.0, 1.4 Hz, 2×2 H), 7.2-7.4 (m, 10 H); AcO-signal of the *meso*-isomer[9] at 2.08. $\delta(^{13}C) = 130.8$ (HC=CH), 75.0 (CH-OAc). **8c**: $\delta(^1H) = 2.09$ (s, 6 H), 5.84, 6.69 (AA'BB'-system: 2 "dd", J = 5.7, 1.8 Hz, and additional weak signals at 5.80, 5.88, 6.65, 6.73, 2×2 H), 7.2-7 .4 (m, 10 H). $\delta(^{13}C) = 130.7$ (HC=CH), 71.9 (CH-OAc).

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