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The First Example of Oxiranyllithium and Oxiranyl Grignard Reagent Having a Carbanion Destabilizing Group: Generation, Property, and Some Synthetic Uses

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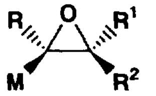
Abstract: The first generation of destabilized oxiranyllithium and oxiranyl Grignard reagent from sulfinyloxiranes with t-BuLi or EtMgCl is described. Treatment of α-methyl α,β-epoxy sulfoxide (sulfinyloxirane) with t-BuLi in THF at -100 °C gave oxiranyllithium having a carbanion destabilizing group. The oxiranyllithium reacted with several electrophiles to give new epoxides in good yields. Oxiranyl Grignard reagent could be generated by the reaction of the sulfinyloxirane having at least one aromatic group on its β-position with EtMgCl.

Oxiranyl anions **1** were formerly detected as fleeting intermediates in the reaction of epoxides with strong bases.[1] In 1976, Eisch and Galle reported the first example for trapping the oxiranyllithium **1** (R=$SiPh_3$, M=Li) with electrophiles to give several epoxy silane derivatives.[2] Since then, a few papers for the generation of oxiranyl anions and trapping them with electrophiles have been published (R=F, M=NBu_4;[3] R=$SiMe_3$, M=Li;[4] R=Ar, M=Li;[5] R=SO_2Ph, M=Li[6]). All these oxiranyl anions have an anion-stabilizing group (***stabilized oxiranyl anion***). ***Non-stabilized oxiranyl anion*** (**1**: R=H, M=Li) was prepared from oxiranyltin by Pfaltz.[7]



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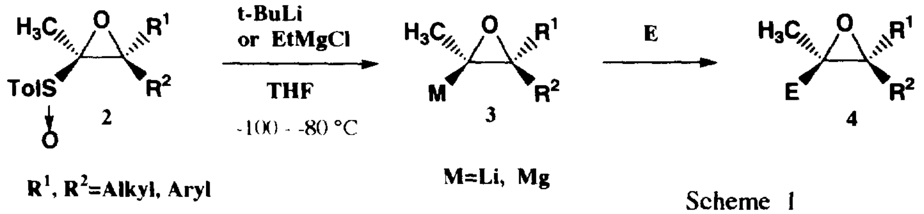
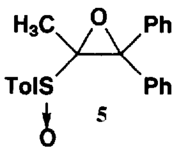
M=Li, NBu_4
R=SiR_3, F, Ar, SO_2Ph, H
R^1, R^2=H, Alkyl, Aryl

We previously reported a new synthesis of epoxides from sulfinyloxiranes by the ligand exchange reaction of sulfoxides with *n*-BuLi.[1j, k] In continuation of our study on the ligand exchange reaction of sulfoxides in organic synthesis,[8] we report herein the first generation of ***destabilized oxiranyl anion*** **3** from sulfinyloxiranes **2** with *t*-BuLi or EtMgCl, and trapping the oxiranyl anion **3** with several electrophiles (Scheme 1).



Scheme 1

To test the feasibility for generation of destabilized oxiranyl anion, we first selected two sulfinyloxiranes (**5** and **6**)[8a] and reacted them with *n*-BuLi, *t*-BuLi, and EtMgCl in THF at low temperature and quenched the reaction with CD_3OD.



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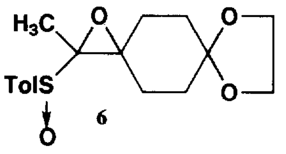

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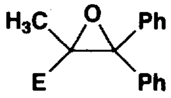
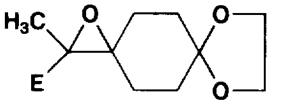
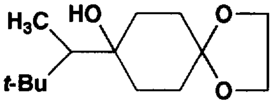


7a E=H
b E=D



8a E=H
b E=D



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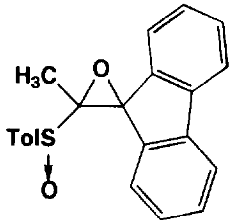
n-Butyllithium was added to a solution of sulfinyloxirane **5** in THF at -80 °C and after 1 min the reaction was quenched with CD_3OD to give only protonated epoxide **7a** in 73% yield. No deuterium incorporation was observed.[1k] Next, we carried out the reaction by using **6** and *t*-BuLi. A solution of **6** in THF was added to a solution of *t*-BuLi (2.5 equivalents) in THF at -100 °C and the reaction was immediately quenched with CD_3OD. This reaction gave desulfinylated epoxide in 95% yield and we found that it was deuterated **8b** (by ^1H NMR; deuterium incorporation was about 95%).[9] Careful inspection of the ^1H NMR showed the product contained about 9% of the alcohol **9**. From this experiment we were indeed able to generate the destabilized oxiranyl anion **3** (M=Li). Delaying the CD_3OD quench of the reaction (15 min) afforded increased yield (30%) of the alcohol **9**. This result implied that the destabilized oxiranyl anion **3** (M=Li) was unstable even at -100 °C. Formation of the alcohol **9** suggests that decomposition of the oxiranyl anion takes place through α-elimination of the carbanion to give carbenoid.[1c, d] A similar treatment of **5** with *t*-BuLi gave **7b** in over 95% yield. Trapping the oxiranyl anions with several electrophiles is discussed later.

Treatment of **6** with EtMgCl in THF at -80 °C gave over 70% yield of the recovered **6** and some decomposition products, in which a trace of **8a** was observed. In contrast to this result, reaction of **5** with EtMgCl (2 equivalents) at -80 °C for 1 min followed by quenching with CD_3OD gave deuterated epoxide **7b** in 70% yield (deuterium incorporation over 95%). We were somewhat surprised by this result; generation of oxiranyl Grignard reagent is possible by this method.[10] When a solution of **5** was added to a solution of EtMgCl (2.5 equivalents) at -100 °C yield of **7b** was increased to 85% and also deuterium incorporation increased to 98%.



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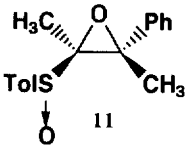

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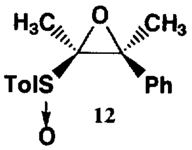

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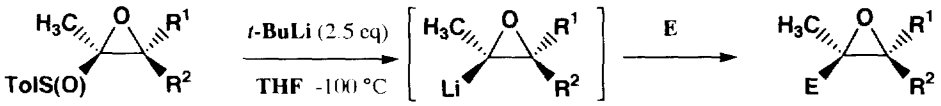
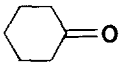
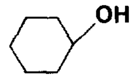
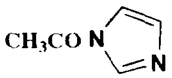
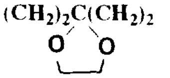
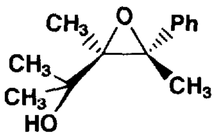
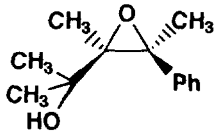
Table 1. Generation of Destabilized Oxiranyllithium and Trapping Them with Electrophiles



Entry	Sulfinyloxirane	Electrophile[a)]	Product (Yield/%)[b)]
1	**5** R^1=R^2=Ph	CH_3CH_2CHO	E=CH_3CH_2CHOH (80)
2			E=  (83)
3		$(CH_3)_3SiCl$	E= $(CH_3)_3Si$ (82)
4		EtOCOCl	E= EtOCO (87)
5		Et_2NCOCl	E= Et_2NCO (66)
6			E= CH_3CO (28)
7	**6** R^1=R^2=  $(CH_2)_2C(CH_2)_2$	PhCHO	E= PhCHOH (86)
8		CH_3COCH_3	E= $(CH_3)_2COH$ (82)
9		$(CH_3)_3SiCl$	E= $(CH_3)_3Si$ (42)
10	**11** R^1=Ph R^2=CH_3	CH_3COCH_3	 (81)
11	**12** R^1=CH_3 R^2=Ph	CH_3COCH_3	 (74)

a) All the reactions were carried out as follows. A solution of the sulfinyloxirane (0.3 mmol) in minimum amount of dry THF was added dropwise to a solution of *t*-BuLi (0.75 mmol) in THF (6 ml) at -100 °C. After 30 sec, the electrophile (0.8 mmol) was added and the reaction mixture was stirred at -100 °C for 10-30 min, then the reaction was quenched by adding aqueous NH_4Cl. b) Isolated purified yield after silica gel column chromatography.

To investigate the generation of oxiranyl Grignard reagent, sulfinyloxiranes **10-12** were reacted with EtMgCl at -80 °C. The sulfinyloxirane **10** derived from 9-fluorenone reacted with EtMgCl at -80 °C for 1 min to give desulfinylated epoxide in 51% yield. The reaction of the isomers of sulfinyloxiranes (**11** and **12**) derived from acetophenone is interesting. Treatment of sulfinyloxirane **11** with EtMgCl in THF at -80 °C for 5 min gave desulfinylated epoxide in 67% yield and no starting material **11** was observed on TLC. In contrast to this, in the same treatment of the isomer **12** with EtMgCl, the ligand exchange reaction took place only about 30 % (70% of the starting **12** was recovered). At any rate, from these results it was found that the sulfinyloxiranes having at least one aromatic substituent on their β-carbon gave oxiranyl Grignard reagent on treatment with EtMgCl.

Next, trapping the generated oxiranyl anions with electrophiles was investigated and the preliminary results are summarized in Table 1 (for experimental conditions, see footnote in Table 1). From the results shown in the Table, it is obvious that the generated destabilized oxiranyllithium has enough reactivity and can be trapped by several electrophiles to afford new epoxides in moderate to good yields. With regard to carbonyl compounds, both aldehydes and ketones react equally well with the oxiranyllithium (entries 1, 2, 7, 8, 10, and 11). Entries 10 and 11 show us the configurational stability of the destabilized oxiranyllithium. Generation of the oxiranyllithium from **11** and **12** at -100 °C with *t*-BuLi and trapping the anion with acetone afforded the adducts shown in Table 1 without any detectable isomers.

In contrast to the destabilized oxiranyllithium mentioned above, the oxiranyl Grignard reagents were found to be unreactive with electrophiles. For example, when **5** was treated with EtMgCl followed by propionaldehyde no detectable amount of the adduct was observed.

We are continuing to study the scope and limitation of this chemistry.

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References and Notes

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9. This reaction gave quantitative yield of *tert*-butyl *p*-tolyl sulfoxide as the product from the ligand exchange reaction of sulfoxide.
10. To the best of our knowledge this is the first example of oxiranyl Grignard reagent.

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