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[4] In references [2h] and [2i], we have described the use of alkenyl acetates as substrates and acyl donors in the presence of proper hydrogen donors.

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[9] The separation of the product from unreacted *p*-chlorophenyl acetate is difficult in some cases.[2c]

[10] When 5 mol % of acetic acid was added to the mixture given in entry 1 in Table 1, the optical purity of 1-phenylethanol changed only to 69.0 % *ee* in 30 min. However, the racemization was completed in 5 h by the subsequent addition of sodium carbonate (1 equiv).

[11] A related complex, $[\{2,5\text{-}Ph_2\text{-}3,4\text{-}tol_2(\eta^5\text{-}C_4COH)\}Ru(CO)_2(O_2CCF_3)]$, is formed in the reaction of $[\{2,5\text{-}Ph_2\text{-}3,4\text{-}tol_2(\eta^4\text{-}C_4CO)Ru(CO)_2\}_2]$ and trifluoroacetic acid: C. P. Casey, S. W. Singer, D. R. Powell, R. K. Hayashi, M. Kavana, *J. Am. Chem. Soc.* **2001**, *123*, 1090.

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Chiral Epoxides by Desymmetrizing Deprotonation of *meso*-Epoxides**

David M. Hodgson* and Emmanuel Gras

Epoxides are widely utilized as versatile synthetic intermediates, and the epoxide functional group is also found in a number of interesting natural products.[1] Therefore, the development of efficient (especially asymmetric) methods for the elaboration of epoxides is an important ongoing challenge.[2] In contrast to chemistry exploiting the electrophilic nature of epoxides, the utility of epoxides as nucleophiles (via oxiranyl anions, eg **1**-Li), first studied by Eisch and Galle,[3] is less developed.[4] A current requirement with this latter strategy is that the epoxide must possess an activating substituent (electron-withdrawing, trialkylsilyl, or trialkylstannyl group) attached to the epoxide ring. Electron-withdrawing and trialkylsilyl substituents facilitate the formation of oxiranyl anions by promoting deprotonation (usually lithiation) and prolonging the solution lifetime of these otherwise very labile intermediates. Trialkylstannyl- and sulfinyl-substituted epoxides react with organolithium species (by transmetalation and desulfinylation, respectively) rapidly enough at low temperatures, such that the resultant unstabilized oxiranyl anions can exhibit synthetically useful nucleophilic (rather than carbene-type) reactivity with a range of electrophiles.[5] Such reactions demonstrate the value of oxiranyl-lithium species as important intermediates in the elaboration of epoxides, but they also indicate the potential limitation of requiring an activated epoxide precursor to carry out the chemistry.

Recently, we showed that direct lithiation of terminal epoxides, followed by electrophile trapping of the nonstabilized oxiranyl anion intermediates, was possible in the presence of a diamine ligand.[6] However, the reaction was restricted to silylation (with TMSCl; TMS = trimethylsilyl) present during generation of the oxiranyl anion) and deuteration (MeOD as an external electrophile). Here we report the first examples of unactivated epoxides undergoing direct deprotonation to give destabilized (alkyl-substituted) oxiranyl anions, and their subsequent trapping with a range of electrophiles (including C–C-bond formation). Furthermore, a new enantioselective approach to substituted epoxides is demonstrated: symmetry breaking by asymmetric lithiation[7, 8]–electrophile trapping, at an epoxide functionality fused to eight- and seven-membered rings.

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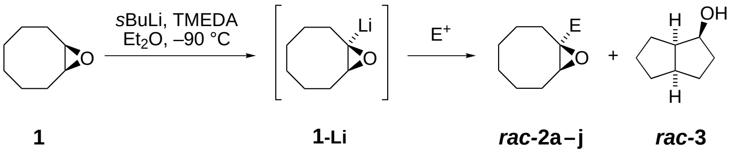
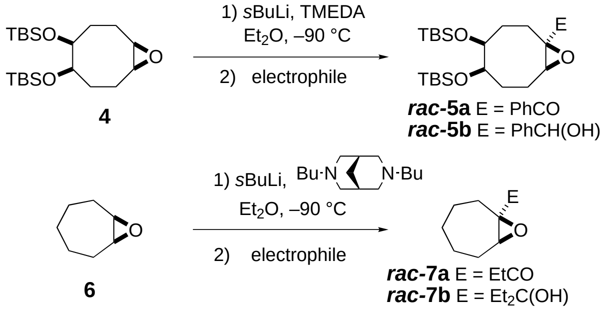
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

We first sought conditions for the efficient lithiation–deuterium (D) trapping of cyclooctene oxide (**1**; Scheme 1). As previously observed,[8c] in the absence of a diamine, the deprotonation of **1** by *s*BuLi (2.45 equiv) in Et$_2$O at −90 °C proceeded sluggishly. A reaction time of 1 h, followed by addition of CD$_3$OD, gave unreacted starting epoxide **1** (56 %), *rac*-**2a** (24 %), and the bicyclic alcohol *rac*-**3** (12 %). Thus, one third of the intermediate oxiranyl-lithium species **1**-Li had already undergone decomposition (by transannular C–H insertion)[8] under these conditions; this decomposition is an indication of its lability (in the absence of a diamine). However, reaction under otherwise identical conditions, but in the presence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA; 2.5 equiv) resulted in complete reaction of epoxide **1** to give *rac*-**2a** (78 %), along with only 5 % of the bicyclic alcohol *rac*-**3**. Thus, the added ligand appears to both accelerate deprotonation and reduce the rate of decomposition of the oxiranyl anion. Reducing the excess of base used in the deprotonation was obviously desirable, and using *s*BuLi (1.25 equiv) and TMEDA (1.3 equiv) gave 98 % D incorporation in cyclooctene oxide **1** after 3 h, with no byproducts. This encouraging result led us to examine the reaction of **1**-Li, generated under these conditions, with other electrophiles. Significantly, introduction of a wide array of functionality at an unactivated epoxide carbon atom was found to be possible (Scheme 1).



Scheme 1. Lithiation–electrophile trapping of cyclooctene oxide (**1**). a) E = D, 98 % (using CD$_3$OD); b) E = PhCH(OH) (*d.r.* 1:1[9]) 80 % (using PhCHO); c) E = PhCO, 56 % (using PhCONMe$_2$); d) E = EtCH(OH), 48 % (using EtCHO); e) E = Et$_2$C(OH), 60 % (using Et$_2$CO); f) E = EtCO, 45 % (using EtCONMe$_2$); g) E = EtOCO, 40 % (using EtOCOCl, 10 equiv); h) E = Bu$_3$Sn, 56 % (using Bu$_3$SnCl); i) E = Me$_3$Si, 38 % (using Me$_3$SiCl in situ), 60 % (using Me$_3$SiCl in situ and 3,7-dibutyl-3,7-diazabicyclo[3.3.1]nonane (DBB)[10] as ligand); j) E = Me, 60 % (using MeI).

A preliminary examination of lithiation–electrophile trapping with other epoxides was then undertaken. The methodology was successfully extended to a substituted cyclooctene-oxide substrate **4**[11] leading to *rac*-**5a** (84 %) and *rac*-**5b** (85 %; Scheme 2). Using DBB as the ligand, the reaction involving cycloheptene oxide (**6**) yielded the corresponding functionalized epoxides *rac*-**7a** (54 %) and *rac*-**7b** (52 %; Scheme 2).



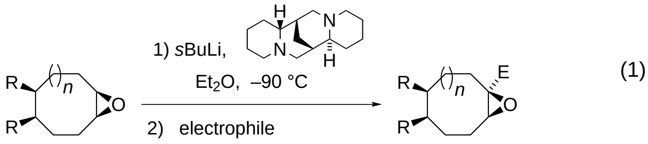
Scheme 2. Synthesis of substituted cyclooctene and cycloheptene oxides (**4** and **6**).

However, attempted lithiation–deuteration of cyclohexene oxide and cyclopentene oxide with either TMEDA or DBB as the ligand was unsuccessful (the presumed intermediate oxiranyl-lithium species underwent typical carbenoid rearrangements and reductive alkylation).[12] Electrophile trapping of the oxiranyl anion from an acyclic system was studied using *cis*-5-decene oxide, and (with DBB as the ligand) complete deuteration and partial silylation (using TMSCl in situ) were successful, albeit in low yields (30 % and 18 %, respectively).

As previous studies carried out in this laboratory have shown that the use of a chiral, nonracemic diamine (such as (−)-sparteine)[7] allows asymmetric deprotonation–rearrangement of epoxides,[8, 11] we explored enantioselective epoxide functionalization. Using (−)-sparteine as the ligand resulted in electrophile incorporation, in good yields and *ee* values (Table 1). As observed during the asymmetric rearrangements of epoxides,[8, 11] better *ee* values were achieved when *i*PrLi was used instead of *s*BuLi (Table 1, entries 4 and 5).

While many powerful methods have been developed for the asymmetric desymmetrization of *meso*-epoxides,[13] the present work illustrates a different approach, in which a chemical transformation occurs selectively at one of the enantiotopic epoxide termini, but the useful epoxide functional group is retained in the product, resulting in a new method for chiral

Table 1. Enantioselective electrophile trapping—symmetry breaking of *meso*-epoxides.[a]



Entry	*n*	R	E	Yield [%]	*ee* value [%][b]
1	1	H	TMS	72	74
2	1	H	SnBu$_3$	60	79[c]
3	1	H	PhCH(OH)	80	76[d]
4	1	H	PhCO	68 (77)[e]	77 (86)[e]
5	1	H	Et$_2$C(OH)	75 (63)[e]	77 (86)[e]
6	1	H	EtCH(OH)	74	76[f]
7	1	H	EtCO	67	78
8	1	H	EtOCO	58	81
9	1	OTBS	PhCH(OH)	79	77[d,g]
10	1	OTBS	PhCO	84	74[g]
11	0	H	Et$_2$C(OH)	48	73
12	0	H	EtCO	57	74

[a] Absolute configuration of predominant enantiomer [as shown in Equation (1)] is assigned by analogy with the known sense of asymmetric induction in the deprotonation–rearrangement of the *meso*-epoxides with (−)-sparteine.[8, 11] [b] Determined by chiral GC (Chrompack-CP-Chiralsil-DEX-CB column) unless otherwise indicated. [c] Determined after reaction with *n*BuLi and trapping with 3-pentanone.[5a] [d] Determined after MnO$_2$ oxidation. [e] *i*PrLi was used instead of *s*BuLi. [f] Determined after Dess–Martin oxidation. [g] Determined by chiral HPLC (Daicel Chiralpak OD column).

epoxide synthesis. A study of other ligands to expand the scope of the process and enhance asymmetric induction, as well as synthetic applications, is currently underway.

Experimental Section

Typical procedure for lithiation–electrophile trapping of cyclooctene oxide (**1**) in the presence of a diamine:

The diamine (2.6 mmol) was added dropwise to a solution of RLi (1.4 M, 2.5 mmol) in Et_2O (8 mL) at −90 °C. This mixture was stirred for 1 h at −90 °C. A solution of cyclooctene oxide (**1**; 2.0 mmol) in Et_2O (2 mL), precooled to −90 °C, was then added rapidly by cannula to the solution of ligand/RLi and the reaction mixture was then stirred at −90 °C for 3 h. Neat electrophile (3.0 mmol) was added dropwise, and the mixture was then allowed to warm to room temperature over 5 h. After quenching with aqueous H_3PO_4 (0.5 M, 25 mL), the organic phase was washed with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The aqueous layers were extracted twice with Et_2O (25 mL) and the combined organic phases were dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (SiO_2, Et_2O, petrol) gave the substituted epoxide.

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Synthesis and Structural Characterization of Organometallic Cyclynes: Novel Nanoscale, Carbon-Rich Topologies[**]

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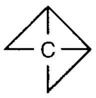
Uwe H. F. Bunz[*]

Dedicated to Professor Günther E. Szeimies

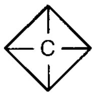
"Carbon-rich" defines an exciting area that spans the world of large arenes to that of highly alkynylated structures including carbon wires, peralkynylated π perimeters, graphdiyne segments, dehydroannulenes, and cyclophane derivatives.[1–9] Carbon-rich organometallic compounds are less explored than their organic counterparts, a tribute to the considerably increased effort in their synthetic access.[10–14] Aesthetic structures, exciting topologies on the nanometer scale, and their modular synthesis, however, make carbon-rich organometallic compounds attractive. Rewards are expected in materials properties that differ from their organic counterparts, such as electroactivity and potential nonlinear optics (NLO) activity. In addition, large carbon-rich organometallic molecules are often surprisingly soluble and form single crystals, which allows their structural characterization in the solid state,[13] a feature that is often elusive for their organic counterparts.

Herein we report the synthesis and structural characterization of three novel organometallic cyclynes[10] with an expanded bicyclo[1.1.0]butane (**A**) and a [2.1.0.0^{1,3}]pentane (**B**) topology. In these structures, the C–C single bonds of the small rings are replaced by alkyne or butadiyne bridges, while the carbon atoms are substituted by benzene rings, cyclobutadiene(cyclopentadienylcobalt) units, or ferrocene centers. Key steps in the synthesis of these targets are the selective *ortho*-metalation of organometallic acetals,[14] and the conversion of aldehydes into alkynes by the Ohira method.[15]


A



B



C

Pd-catalyzed coupling of **1**[14] to the iodide **2a** furnishes **3** in 23% (Scheme 1). The moderate yield of **3** is a result of the two *meta*-positioned alkyne groups in **2a** between which the iodide is sandwiched. Only the active Hartwig catalyst

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