Epoxides are widely recognized as extremely versatile synthetic intermediates because of their enhanced reactivity, which is attributable to the high degree of ring strain. The reactions of epoxides, which are mostly due to their electrophilic nature, involve cleavage of the three-membered ring and include a wide range of nucleophilic ring openings, acid- or base-catalyzed rearrangements, and isomerization reactions.

On the other hand, the reaction of an epoxide as a nucleophile, i.e., an oxiranyl anion, is less common. In spite of their potential in organic synthesis, metalated epoxides have not been prepared in any practical manner and have long been recognized as transient intermediates formed in the reactions of epoxides with strong bases. Even after their discovery, oxiranyl anions have received little attention from synthetic chemists, mainly because of their difficult preparation and instability. The usefulness of oxiranyl anions in organic synthesis lies in the direct carbon–carbon bond formation on an epoxide ring.

Considering this synthetic potential, we chose a sulfonyl-stabilized oxiranyl anion generated from an epoxy sulfone, which enabled a smooth and high yielding C–C bond formation by the treatment of a mixture of an epoxy sulfone and an alkyl triflate with n-BuLi at −100 °C. Subsequent 6-endo cyclization allowed the iterative synthesis of trans-fused polytetrahydropyrans following a biosynthesis-inspired strategy. This methodology was applied to the total synthesis of bioactive marine polycyclic ether natural products hemibrebetoxin B and gambierol.

The large and complex structures of marine policy ethers with MW >1,000 necessitate a highly efficient synthetic strategy with minimal manipulations. We have developed a new [X+2+Y] convergent approach, which involves the construction of two rings after oxiranyl anion coupling of epoxy sulfone and triflate fragments. The total synthesis of gymnocin-A is achieved by using five iterations of the [X+2+Y] convergent strategy.

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