BREAKING BREDT'S RULE: ACCESSING ANTI-BREDT OLEFINS

Reported by Lynda Steen December 9, 2025

INTRODUCTION

In 1924, Julius Bredt reported that "a carbon double bond cannot occur at the branching positions of the carbon bridge."[1] This conclusion, now known as Bredt's Rule, was founded on Bredt's experimental findings and observations (Figure 1). Elimination to form a bridgehead double bond in the anhydride is not observed. However, when the anhydride is opened, elimination is observed. The difficulty in forming these double bonds is attributed to two main factors: a reduction in p-orbital overlap of the π bond and a distortion of the desired trigonal planar geometry of the sp^2 center.[2] With its establishment, Bredt's rule has served as a useful guide for evaluating proposed structures of compounds. In 1908, Bartelt proposed eight fenchene isomers, two of which contained a double bond at the bridgehead. Bredt contested these structures, and they are no longer accepted as plausible isomers.[3] However, since 1924, many have worked to break this rule and form anti-Bredt olefins (ABOs). This has been done by forming double bonds in rings able to accommodate the resulting strain or accessing ABOs as unstable intermediates.

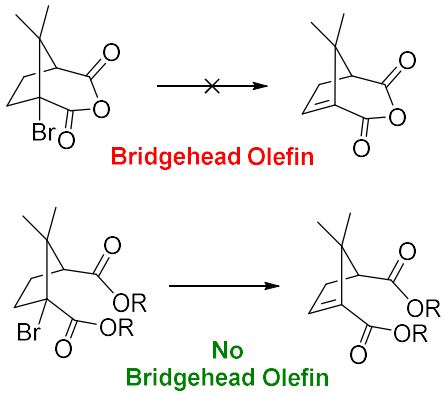

Figure 1. Experimental observations by Julius Bredt.

PURSUING ANTI-BREDT OLEFINS

Soon after Bredt's "Rule" was introduced, exceptions were discovered. Larger ring systems have increased flexibility, allowing for improved orbital overlap and increased planarity. Work to access smaller, more strained ABOs began soon after the rule was established. In the 1960s, Marshall and Wiseman used forcing elimination conditions to generate bridgehead olefins (Figure 2).[4,5] An additional method of accessing these strained systems employed carbene intermediates as introduced by Jones.[6]

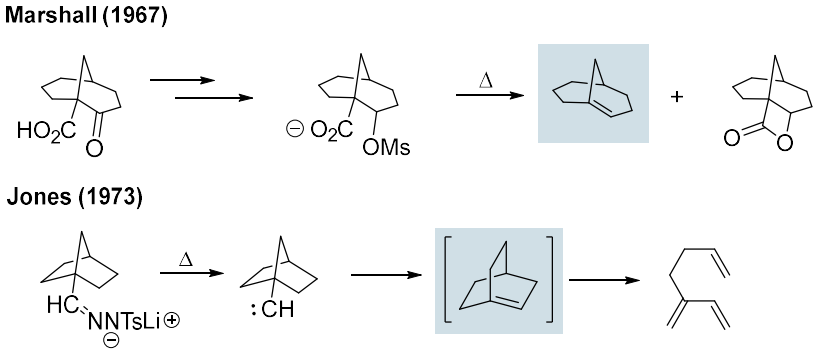

Figure 2. Early methods and examples of ABOs.

Accessing carbenes as intermediates allows for the generation of more strained ABOs owing to their high reactivity which enables expansion of smaller rings. This ability is possible owing to improved orbital overlap with the smaller ring and a relief of ring strain of the system.[6]

HEURISTIC AND COMPUTATIONAL RULES FOR PREDICTING STABILITY

As researchers continued to push the boundaries of Bredt's rule, criteria to predict the stability of ABOs were developed. Although empirical heuristic rules were developed early, computationally based rules were later established to determine the double bond strain of an ABO, using models to compare the strain to its saturated counterpart and assess stability.[7,8] By applying these heuristic and computational rules, researchers can determine compounds that are unlikely to be stable and subject them to further analysis. For example, neoveratrenone was initially proposed to contain a carbon double bond at the bridgehead. It was later further analyzed, and the structure was reassigned without a bridgehead double bond (Figure 3).[3]

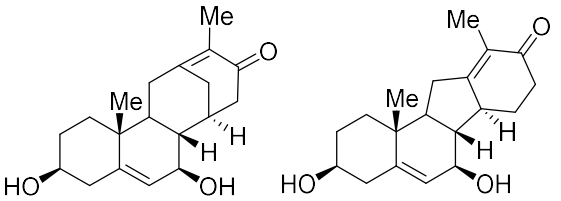

Figure 3. Initial proposed structure of neoveratrenone (left) and revised structure (right).

MODERN EFFORTS OF ACCESSING ANTI-BREDT OLEFINS

Whereas early efforts to form ABOs aimed to prove their viability, more recent efforts have pursued forming and trapping ABOs to generate products reminiscent of natural products or pharmaceutical agents. Bridgehead enones can be used as intermediates in forming various natural products, particularly those of the sesquiterpene and diterpene families. In 2019, Wang and Ma illustrated this objective using a base mediated β-elimination (Figure 4).[9] Garg recently greatly expanded the access to transient ABOs using β-halosilane elimination chemistry followed by trapping with various agents.[2] Highly strained ABOs were successfully trapped to generate complex products with reduced planarity and functional group handles for subsequent diversification (Figure 4).

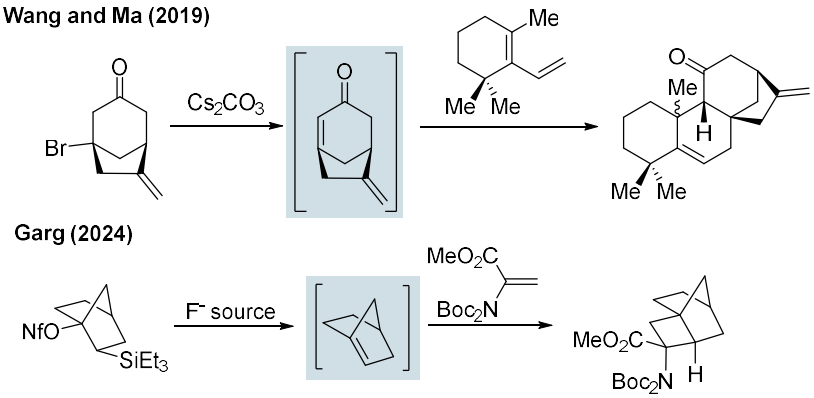

Figure 4. Modern efforts of expanding and applying access to ABOs.

REFERENCES

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