Gold-Catalyzed Synthesis of Oxetan-3-ones from Propargylic Alcohols

Significance: The gold-catalyzed synthesis of oxetan-3-ones 3 from propargylic alcohols 1 is reported. A range of substituents (R1) are tolerated, including acid labile (OMOM, NHBoc) and reactive (N3, Br) groups. Tertiary propargylic alcohols 4 are also suitable substrates, although the electron-withdrawing ester is required to prevent the formation of undesired propargylic cations under the acidic reaction conditions. This methodology may also be used to prepare the volatile and expensive oxetan-3-one 7, which may be converted, without purification, into useful oxetane derivatives 8 and 9.

Comment: Oxetan-3-ones serve as highly useful synthetic intermediates, as a surrogate for the gem-dimethyl group, and as mimics in drug discovery. Despite this utility, they typically require multi-step, low-yielding syntheses. The current process delivers oxetan-3-ones in one step from simple and readily available starting materials under mild conditions. The intermediate α-oxo gold carbene is generated from a simple alkyne, by-passing the traditional method for carbenoid generation using hazardous α-diazo ketones. Importantly, the commercially available (but expensive) parent oxetan-3-one may be prepared in high yield from inexpensive propargyl alcohol.