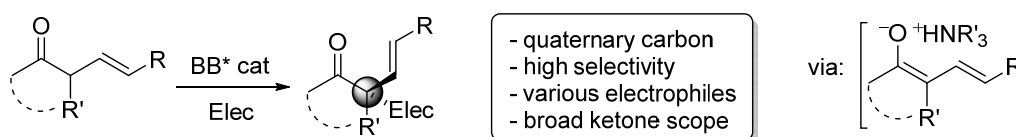


DFT STUDY OF THE REACTIVITY OF TRANSIENTLY GENERATED CYCLIC DIENOLATES VERSUS THE ACYCLIC COUNTERPARTS IN ADDITION REACTIONS

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Manuel de Lardizabal 3, 2018 San Sebastián, Spain

Ketone dienolates are interesting substrates because they can lead to adduct with strategically positioned C=C double bond for further chemical elaboration. Among the possible catalytic approaches, a catalytic and enantioselective α -functionalization of unactivated α -tertiary cyclic ketones was explored to get α -quaternary cycloalkanone products, providing important scaffolds for natural products. The method is based on the site-selective activation of α -alkenyl cycloalkanones by bifunctional Brønsted base/H-bond catalysts [1] that yields reactive dienolate intermediates, able to react smoothly with Michael acceptors to afford the corresponding α -quaternary cycloalkanone adducts in high site-, regio- and stereoselectivity (Scheme 1). The reaction of low active α -substitued dienolate with 1,1-bis(phenylsulfonyl)ethylene, a highly reactive acceptor lacking substitution at β -position, was studied experimentally and computationally.[2] Through DFT studies we investigated the reactivity associated with cyclic α -alkenyl ketones compared to acyclic counterparts, computing the reactions between ketones and bis-sulphone in the presence of a model catalyst, which is not influenced by the steric constraints of the real catalysts. Furthermore, calculations of electronic parameters highlighted that pure intrinsic electronic properties are not completely dictating the degree of reactivity. Finally, we performed DFT calculations to elucidate the origin of the stereoselectivity and the nature of the H-bond network between the enolate, bis-sulfone and the catalyst, confirming the experimental results.



Scheme 1: Catalytic and enantioselective α -functionalization of unactivated α -tertiary cyclic ketones.

[1] Campano, T. E.; Iriarte, I.; Olaizola, O.; Etxabe, J.; Mielgo, A.; Ganboa, I.; Odriozola, J. M.; Oiarbide, M.; Palomo, C. *Che. Eur. J.* **2018**, *25*, Accepted Article

[2] Manuscript under preparation