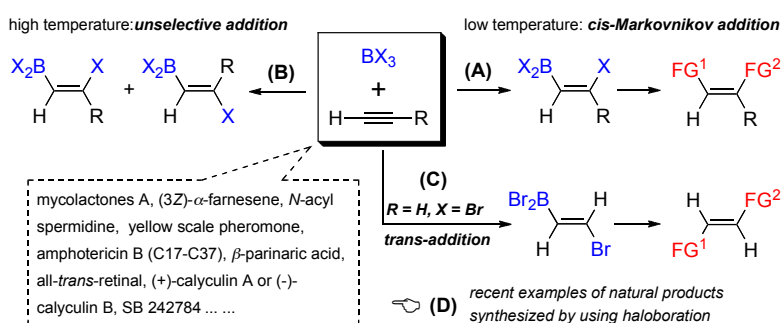


アルキンに対するハロボレーション反応の理論解析

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Introduction

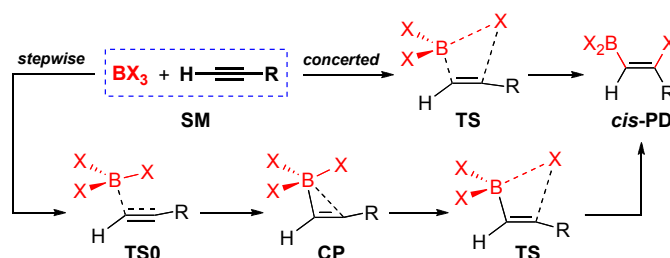
Haloboration of alkyne is an important reaction in synthetic organic chemistry to afford regio/stereo-defined C=C double bonds which can be further functionalized at both halogen- and boron-sites to provide a wide range of multi-functionalized alkenes (Scheme 1).¹ Thus, since the first discovery by Lappert and Prokai in 1964,² this methodology has attracted continuous interests from chemists and has been successfully applied in synthesis of a variety of natural products, bioactive compounds and pharmaceuticals. However, till now details of the mechanism of this reaction are far from being settled, despite such information would be helpful in improving the reactivity and selectivity of the reactions, as well as in designing more efficient alkyne metalation. Here we would like to report the first systematical computational and theoretical studies on the mechanism for the haloboration of alkynes, addressing the questions such as the reactivity, origin of the regio/stereoselectivity, etc.



Scheme 1

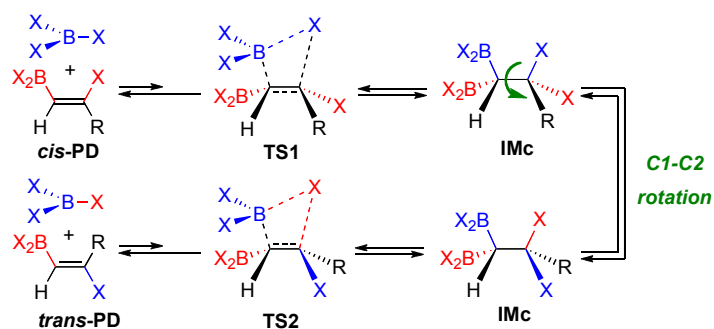
Result and discussion

Experimental observations showed that this reaction proceeds regio-/stereo-specifically at lower temperature whereas the stereo-selectivity dramatically decreases or even totally converts cis into trans isomer at higher temperature in some cases (Scheme 1). In calculation, acetylene and propyne as representative alkynes, and boron halides as representative haloboration reagents were employed and all calculation were done at B3LYP/6-31+G* level. The present results have addressed some important aspects. Firstly, the addition reaction undergoes through two different pathways, the concerted or the stepwise route, depending on the reaction conditions, including alkyne substrate, boron reagents and solvent, etc. (Scheme 2). In both cases, this reaction in general proceeds through four-centered transition states that are pivotal for determining the reactivity and regio-/stereo-selectivity.



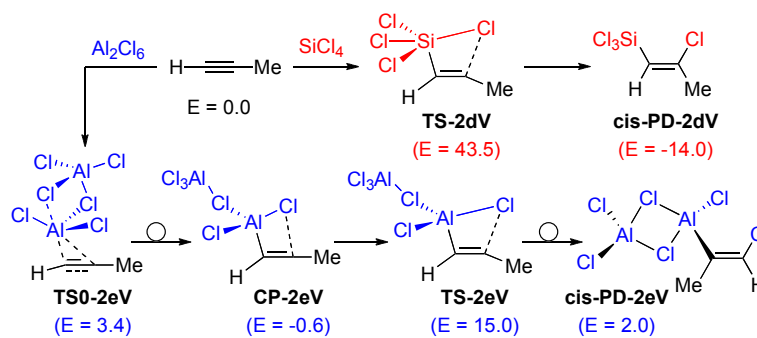
Scheme 2

Secondly, the decrease or conversion of stereo-selectivity at higher temperature is considered as a result of boron halide-mediated conformational isomerization of the product, cis-alkenes (PD) via an addition-elimination routine (Scheme 3). This process usually showed a relatively high E_a value, which is in good agreement with the experimental fact that (i) the isomerization requires a higher temperature than (the first) haloboration and (ii) boron halides with lower Lewis acidity may suppress the conversion. For case of bromoboration of acetylene, regularly used conditions including a large excess of BBr_3 , high temperature and long reaction time, or prolonged heating during repeated distillation for separation, should accelerate the isomerization to give trans-PD eventually.



Scheme 3

Finally, DFT calculations of the hypothetical direct haloalumination and halosilation of propyne to compare with the case of haloboration showed that neither process is favorable, strongly intimating that haloboration of alkynes is a unique elemento-metalation, proceeding readily under mild conditions owing to the kinetic and thermodynamic characteristics of boron halides (Scheme 4).



Scheme 4

Conclusion

In this work, we have examined in detail the mechanism for haloboration of alkynes by means of DFT

studies, results of which well match and explain the experimental findings. Knowledge obtained here on the reaction route, region-/stereo-selectivity and comparison with other metalations should be valuable for further investigations of reaction mechanisms, as well as in development and applications of elemento-metalation of unsaturated compounds. Work to clarify other heterometalation reaction pathways and mechanisms, both theoretically and experimentally, is in progress.

Reference

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