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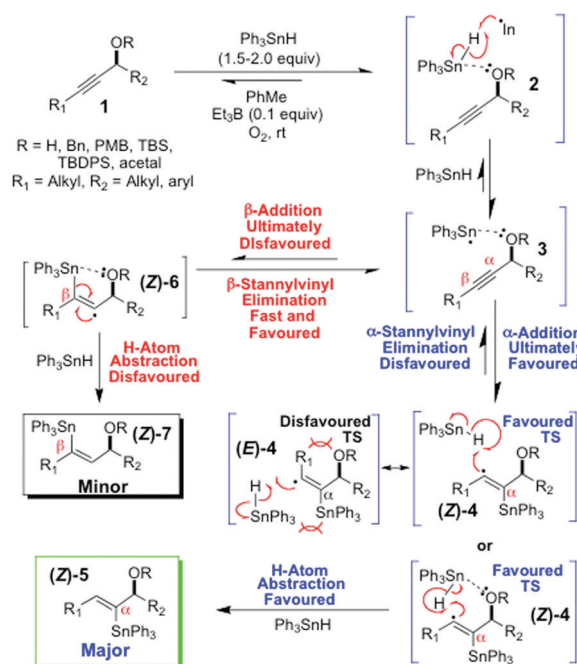
Fast ring-opening of an intermediary α -stannyl- β -cyclopropylvinyl radical does not support formation of an α -stannylvinyl cation in the O-directed free radical hydrostannation of dialkyl acetylenes†

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O-directed hydrostannation of β -cyclopropyl propargyl alcohol **22** with stannanes and cat. Et_3B in THF/ H_2O or PhMe/MeOH fails to deliver any detectable products of α -stannylvinyl cation capture. Instead only α -stannyl- β -cyclopropylvinyl radical intermediates can be detected, which undergo fast H-atom abstraction and/or cyclopropane ring-opening as a result of eliminative β -scission.

The O-directed, free radical hydrostannation of propargylic oxygenated alkyl acetylenes with Ph_3SnH /cat. Et_3B and O_2 in PhMe is a reaction of great synthetic worth for the highly stereocontrolled construction of (*Z*)-configured trisubstituted alkenes of high structural complexity.^{1,2} Given the superb performance of this reaction, in many extremely demanding settings,^{1,2} it is not at all surprising to find that there has been substantial interest in understanding the mechanistic origins of the high stereo- and regiocontrol that is typically observed.^{1–6}

Our picture of these reactions^{1–3} (Scheme 1, mechanism 1) has them proceeding by a totally free radical mechanism in which an O-coordinated triphenylstannyl radical **3**^{1,3} preferentially adds to the α -carbon of the acetylene to give an inverting pair of bent stannylvinyl radicals **4**, where lower hyperconjugative stabilisation in (*E*)-**4**, high internal $\text{A}^{1,3}$ -strain, and magnified steric repulsions collectively disfavour its H-atom abstraction from Ph_3SnH . As a result, the more hyperconjugatively stabilised (*Z*)-invertomer (*Z*)-**4** tends to preferentially react, since this does not experience such severe $\text{A}^{1,3}$ -strain, and it offers the least sterically hindered transition state for H-atom abstraction, which favours formation of the α -vinylstannane products (*Z*)-**5**. Although the initial O-directed addition can guide the O-coordinated tin radical to the β -acetylenic carbon of **3** to give (*Z*)-**6**, because this addition step is reversible, and the O-Sn complexation persists within the β -stannylvinyl radical adducts (*Z*)-**6**, this lengthens and weakens their C-Sn bonds, to inevitably



Scheme 1 The totally free radical O-directed mechanism for hydrostannation (mechanism 1), which operates at high Ph_3SnH concentrations, and is experimentally supported.^{1–4}

promote their rapid dissociation back into **3**. In contrast, the analogous elimination from the α -stannylvinyl radicals (*Z*)-**4** is far less facile, due to the internal O-Sn coordination not persisting within such systems,^{1,3} with the result that H-atom abstraction is far more favourable, and the α -vinylstannanes of structure (*Z*)-**5** typically predominate.

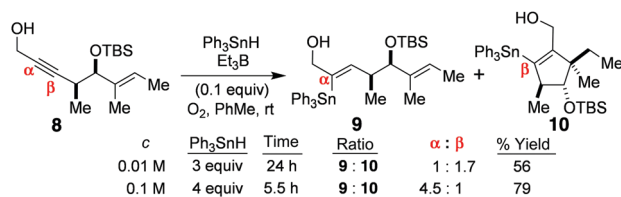
The above mechanistic analysis is one that has now been very strongly supported by X-ray crystallography,^{1,3} by Alabugin's computer-assisted DFT calculations,⁴ and by our own stannylvinyl radical trapping experiments with **8** (Scheme 2),³ which afforded a tandem β -addition/radical cyclisation product **10** at a range of stannane concentrations. Moreover, because the α : β addition step

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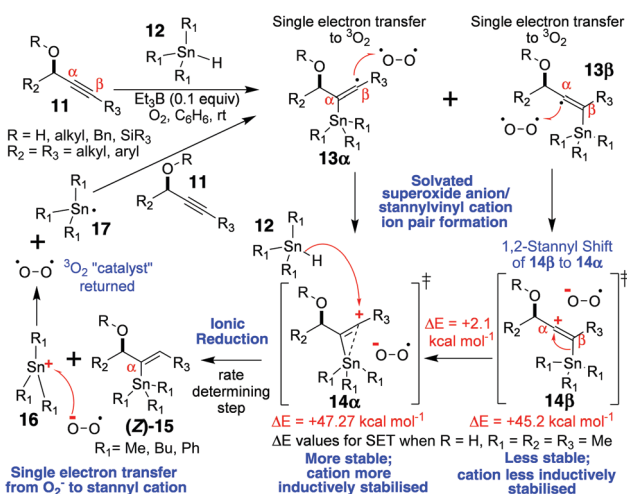


Scheme 2 The changing regiochemistry at increased Ph₃SnH concentrations, and the vinyl radical cyclisation product **10**.³

is reversible, and the regiochemistry changes significantly in favour of the O-directed α -addition product **9**, as the stannane concentration increases (due to this promoting O–Sn complexation), this indicates that alkyne ground state polarity and electronic control cannot be the primary or exclusive determinants of product regiochemistry in these systems, for if these were solely governing outcome, then the regiochemistry of **9** : **10** would never change as the stannane concentration altered; it would always remain constant. So, the O-directed free radical hydrostannation mechanism of Scheme 1 (mechanism 1) must be gaining the ascendancy over the non-directed, entirely free radical, addition/H-abstraction pathway (mechanism 2) as the Ph₃SnH concentration rises.^{1,3}

Now despite the solidity of this work,³ a new mechanism was proffered in 2013–2014⁵ (Scheme 3, mechanism 3); one where the α -vinylstannane products (**Z**)-**15** were suggested to arise, not through a coordinately-controlled regioselective tin radical addition, but rather, through a non-O-directed, non-regioselective tin radical addition at either alkyne carbon of **11**.

In this respect, it was proposed that it would be of little real consequence if a mixture of α - and β -stannylvinyl radicals **13 α** and **13 β** ever arose, for these would both simultaneously undergo rapid single electron transfer (SET) to O₂ present in the reaction medium, and this would lead to a pair of superoxide ion/ α - and β -stannylvinyl cation ion pairs **14 α** and **14 β** , where the β -stannylvinyl cation would spontaneously undergo a 1,2-stannyl shift, to afford the more inductively stabilised



Scheme 3 The non-directed stannylvinyl cation mechanism^{5a,b} for hydrostannation (mechanism 3) which is unsupported.

α -stannylvinyl cation ion pair **14 α** exclusively. It was further suggested that the α -stannylvinyl cation in **14 α** would thereafter enjoy extra stabilisation from a dynamic partial bridging interaction with the tin substituent. It was also postulated that this α -stannylvinyl cation would subsequently engage in an ionic reduction with the excess stannane that was present, and that this would then afford the observed α -vinylstannane product (**Z**)-**15**, along with a tin cation **16**, which itself would become involved in a second SET with the liberated superoxide ion, to return the O₂ and a new R₃Sn radical **17**, which would further propagate the reaction chain.

A major problem¹ with mechanism 3⁵ is that vinyl radicals are known to add to O₂ to form vinylperoxy radicals which then suffer a number of fates depending on the precise reaction conditions.¹ Mechanism 3 also does not satisfactorily explain why the $\alpha : \beta$ -product regiochemistry (**9** : **10**) changes as the stannane concentration increases, when the alkyne **8** is hydrostannated (Scheme 2).³ This is because the tenets of mechanism 3 require the β -stannylvinyl cation to always spontaneously rearrange to its α -isomer,⁵ due to this being more stable, and the reaction being exclusively electronically controlled. Naturally, this would give **9** as the sole product. Yet, this is not what is observed, as evidenced by Scheme 2.³ Mechanism 3⁵ is also incompatible with the observation of a β -stannylvinyl radical cyclisation product **10**. The DFT calculations^{5a} that accompany mechanism 3 also rule it out on simple thermodynamic grounds. In this regard, the postulated O₂-mediated SET conversions of **13 α** to **14 α** and **13 β** to **14 β** (where R = H, and R₁ = R₂ = R₃ = Me) are respectively associated with ΔE values of +47.27 kcal mol^{−1} and +45.2 kcal mol^{−1} for these two transitions in C₆H₆ at 25 °C (see Scheme 3). Such barriers are far too high to allow these conversions to proceed, as proposed, except through quantum mechanical tunnelling, but none of the traditional evidence needed to support such a mechanism has so far been provided by the proposers of mechanism 3. The fact also that the transition of **13 α** into **14 α** is higher in energy than the one for the transition of **13 β** into the more inductively destabilised **14 β** also seems discrepant. The conversion of **14 β** to **14 α** is also uphill to the tune of +2.1 kcal mol^{−1}.^{5a} Moreover, the rate accelerations that the mechanism 3 proposers have reported^{5c} for the hydrostannations of alkyne **18** in polar solvents, over 90 min (Scheme 4), are likewise far too small to be considered supportive of ionic mechanism 3.¹ Instead, they are much more aligned¹ with an entirely free radical, O-directed, mechanism of the type shown in Scheme 1 (mechanism 1).¹ Indeed, relative to THF, a net decrease in the

ϵ	Reaction Solvent	Yield	Observed	Not Observed
7.52	dry THF	82%	19	20
38.25	DMF	80%	19	21
21.01	THF/H ₂ O (5 equiv)	75%	19	21
	Me ₂ C=O	50%	19	21

In the reaction in THF/H₂O (5 equiv) **OTIPS** is observed, **OTIPS** is not observed, **OTIPS** is not observed.

The rate decreases in more polar solvents.

Scheme 4 The polar solvent rate data of ref. 5c that is claimed to support mechanism 3.

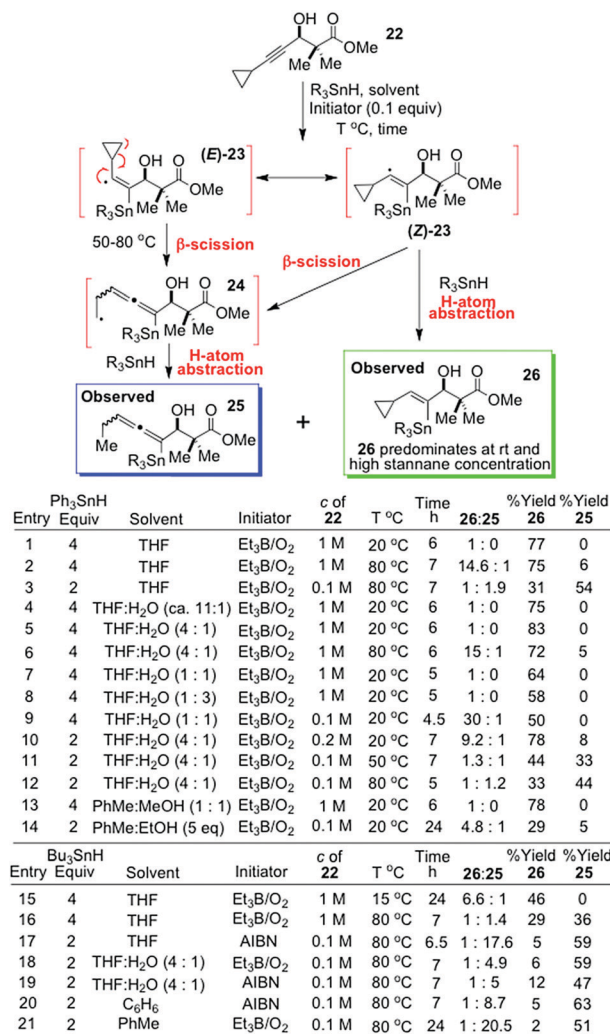
reaction rate^{5c} is observed for the hydrostannation of **18** in more polar solvents.

Now, despite the electronically-controlled stannylvinyl cationic ion pair hypothesis⁵ of Scheme 3 (mechanism 3) conflicting very strongly with the 2005 radical probe work of Scheme 2,^{1,3} and Alabugin's later 2015 experimental work and DFT calculations,⁴ which further confirmed an entirely free radical O-directed mechanism for these reactions (mechanism 1), still mechanism 3⁵ remains active and unwithdrawn from the literature, despite several criticisms,^{1,4,6} with the consequence that its mechanistic principles are still continuing to be widely disseminated within the community. This is best illustrated by a recent 2019 hydrostannation review,⁷ where exclusivity of discussion and mechanistic primacy were given to mechanism 3 over mechanism 1 to explain the conversion of **11** into (Z)-**15**. However, as we have seen, mechanism 3⁵ is at great odds with all experimental data gathered to date.^{1,3-5}

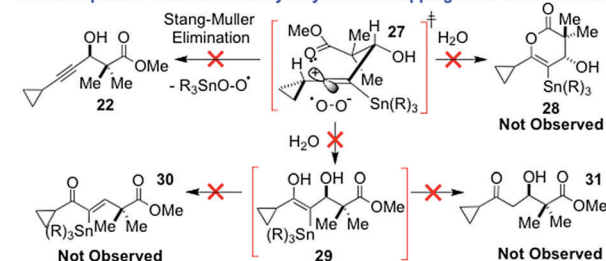
Given this continuing propagation of a mechanism⁵ that has been significantly criticised^{1,4,6} (mechanism 3⁵), over one that is much more reasonable and fully experimentally supported^{1,3,4} (mechanism 1¹⁻³), we felt it necessary to publish the results of our latest investigations into whether a stannylvinyl cation is a genuine intermediate in these reactions, since some in the field clearly seem unwilling to accept the unambiguous data that has been presented in Scheme 2^{1,3} and elsewhere,⁴ which all rule against it.

Therefore, to test mechanism 3 further (Scheme 5), we purposely designed a β -cyclopropyl propargylic alcohol probe **22** that we believed would give rise to an exceptionally stable, yet still quite reactive, stannylvinyl cation intermediate **27**, if it happened that mechanism 3 did hold true. It was reasoned that if **27** was indeed an authentic intermediate⁵ in the journey of **22** into vinylstannane **26**, then this super-stabilised vinyl cation **27** would almost certainly react competitively with H₂O and alcohols added to the reaction medium since it would be triply stabilised: (a) by neighbouring group participation from the ester carbonyl; (b) by hyperconjugation with the α -R₃Sn substituent; and (c) by hyperconjugation with the adjacent cyclopropane ring. It should thus have sufficient longevity in solution to undergo nucleophilic trapping by: (1) externally added nucleophiles present in excess (e.g. H₂O or MeOH) or (2) by the internal ester carbonyl to give a six-membered enol lactone (**28**), after subsequent nucleophilic attack on the resulting positively charged OMe group by the external nucleophile. A trapping of **27** with H₂O would, of course, lead to ketone or stannyl enone products such as **31** and **30** via **29** (Scheme 5), or potentially bring about a competitive Stang–Muller elimination⁸ through an attack of the H₂O on the R₃Sn grouping.^{8a} The latter would naturally return the starting acetylene **22** and lead to little overall reaction progression.

With regard to the feasibility of achieving an α -cyclopropyl vinyl cation trapping with H₂O, the classic work of Bergman⁹ and Hanack¹⁰ had previously shown that although α -cyclopropyl vinyl cations benefit from significant charge stabilization from the cyclopropane ring, they still retain the ability to react rapidly with external nucleophiles such as H₂O or acetate ion,



The Anticipated Products of Stannylvinyl Cation Trapping Were Not Observed



Scheme 5 Our various hydrostannations of the probe **22**.

either directly, or following internal 1,2-rearrangement. Muller's highly stable bis-silyl-vinyl cations, which have even been characterised by X-ray crystallography likewise react readily with nucleophiles, but by an eliminative nucleophilic attack on silicon to give an alkynylsilane.^{8b}

Most importantly as well, however, the probe **22** would inevitably afford the α -stannylvinyl radical precursor of the postulated cation **27** viz. radical **23**, and if, by due modification of the hydrostannation conditions, we could identify a set of experimental circumstances where **23** could be induced to predominantly undergo fast H-atom abstraction from the



stannane to give **26** while also undergoing concurrent vinyl radical eliminative β -scission of the cyclopropane ring to give the stannylhomoallenyl radical **24**,¹¹ and *vice versa*, where eliminative β -scission could be rendered more facile than concurrent stannylvinyl radical H-atom abstraction by **23**, then this would unambiguously confirm that the proposed H-atom transfer must actually be proceeding through the α -stannylvinyl radical, and that **26** was not arising from an ionic reduction of the stannylvinyl cation **27** by the tin hydride. In essence, it would support mechanism 1 and rule out mechanism 3.

With this in mind, great experimental effort went into identifying conditions that would give this experimental read-out, and a summary of that effort can be found in the tabulated hydrostannation data of Scheme 5, which very clearly shows that only two primary products ever emerge from the free radical hydrostannation reactions of **22**, and these are compounds **26** and **25**, even when reactive nucleophiles such as H₂O or alcohols are present in far greater excess than the stannane. Such observations only satisfactorily align with the intermediacy of a stannylcyclopropylvinyl radical,¹¹ not a stannylvinyl cation,⁵ and these outcomes powerfully reconfirm the entirely free radical mechanism^{1,3} of such dialkyl acetylene hydrostannations (mechanism 1).^{1–4,6}

Moreover, if one examines entry 10 in Scheme 5, one can see that the degree of conversion of the alkyne **22** into the hydrostannylated products **26** and **25** is very good indeed after 7 h at rt (86% overall yield, **26**:**25** = 9.2:1) in THF/H₂O (4:1) at 0.2 M substrate concentration using 2 equiv. of Ph₃SnH. The high yield observed indicates that a stannylvinyl cation of structure **27** cannot be a viable intermediate in these reactions, since such an α -stannylvinyl cation would almost certainly undergo significant facile elimination back to the starting acetylene^{8a} in the presence of a strong nucleophile such as H₂O or peroxide anion (Stang–Muller elimination⁸). However, only a minute amount of starting alkyne was ever present after 7 h at rt. In fact, when this same rt reaction was conducted with a much greater quantity of Ph₃SnH (4 equiv.) in THF/H₂O (4:1) at 1 M substrate concentration (entry 5), total product conversion occurred, with no starting acetylene **22** remaining at reaction end (see TLC in the ESI†). In this instance, **26** was obtained exclusively in 83% yield (entry 5). Additionally, no cyclopropyl ketone **31** or cyclopropyl stannyl enone β -elimination products such as **30** were ever detected in either of these two reactions from direct stannylvinyl cation capture by the excess H₂O present. This outcome weighs heavily against the intermediacy of stannylvinyl cations⁵ in such hydrostannations. Also, no 1,2-shifted cyclobutenols^{9,10} were ever detected, nor primary stannylallenyl alcohols arising from direct competitive nucleophilic ring-opening of the cyclopropane ring in **27** with H₂O.

The formation of only a minor quantity of the reduced allenyltin product **25** in entry 10, alongside the vinylstannane **26** is clearly only compatible with the intermediacy of a stannylvinyl radical intermediate **23** that primarily undergoes fast H-atom abstraction¹² from the stannane at rt, alongside competitive radical induced eliminative opening of the cyclopropane ring with accompanying H-atom abstraction (see Scheme 5), a process well

known for α -cyclopropylvinyl radicals.¹¹ This point is perhaps much better illustrated by entry 11 where, when the hydrostannation reaction was performed at 0.1 M substrate concentration and lower Ph₃SnH concentration (2 equiv.), in a mixture of THF/H₂O (4:1) at 50 °C for 7 h, the ratio of **26**:**25** now changed very dramatically to 1.3:1. Clearly, working at higher dilutions and higher reaction temperatures with lower quantities of stannane quite profoundly affects the behaviour of the intermediary stannylvinyl radical **23**, it now diverting it significantly down the pathway of competitive radical induced ring-opening, alongside stannylvinyl radical H-atom abstraction from the stannane. Indeed, heating at 80 °C with the same quantity of Ph₃SnH (entry 12) promotes even more of the radical-induced β -scission event,¹¹ as does performing the alkyne hydrostannation with Bu₃SnH (entries 16–21) which typically affords **25** and **26** in much lower yields than does Ph₃SnH.

So, to conclude, the combined observations recorded here, using a new type of vinyl radical clock,¹¹ once more fail to support^{1,3,4,6} the intermediacy of an α -stannylvinyl cation^{5,7} in the O-directed free radical hydrostannation of alkyl acetylenes.^{1–6} Instead, the tabulated data of Schemes 5 and 2 only support the operation of mechanisms 1 and 2 in these reactions with the former massively predominating under the excess stannane conditions that we typically employ.^{1–4}

Conflicts of interest

There are no conflicts to declare.

Notes and references

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