The stannylvinyl cation that never was! New concentration- and temperature-dependent probe studies confirm an entirely free radical mechanism and O–Sn coordinative control of the hydrostannation of propargylically-oxygenated dialkyl acetylenes with stannanes and cat. Et3B.

Watson, H. A., Manaviazar, S., Steeds, H. G., & Hale, K. (2020). The stannylvinyl cation that never was! New concentration- and temperature-dependent probe studies confirm an entirely free radical mechanism and O–Sn coordinative control of the hydrostannation of propargylically-oxygenated dialkyl acetylenes with stannanes and cat. Et3B. *Tetrahedron*. https://doi.org/10.1016/j.tet.2020.131061

Published in: *Tetrahedron*

**Document Version:**
Publisher's PDF, also known as Version of record

**Queen's University Belfast - Research Portal:**
Link to publication record in Queen's University Belfast Research Portal

**Publisher rights**
Copyright 2020 the authors.
This is an open access article published under a Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution and reproduction in any medium, provided the author and source are cited.

**General rights**
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

**Take down policy**
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.
The stannylvinyl cation that never was! New concentration- and temperature-dependent probe studies confirm an entirely free radical mechanism and O–Sn coordinative control of the hydrostannation of propargylically-oxygenated dialkyl acetylenes with stannanes and cat. Et₃B

Hamish A. Watson, Soraya Manaviazar, Hannah G. Steeds, Karl J. Hale *

The School of Chemistry and Chemical Engineering, Queen’s University Belfast, Stranmillis Road, Belfast BT9 5AG, Northern Ireland, United Kingdom

Article info

Article history:
Received 30 October 2019
Received in revised form 7 February 2020
Accepted 18 February 2020
Available online 25 February 2020

Dedicated with friendship, respect, and admiration to one of the true maestros of modern-day UK synthetic organic chemistry: Professor Stephen G. Davies, Waynflete Professor of Chemistry at the University of Oxford, and winner of the 2011 RSC Perkin Prize for Organic Chemistry, the 1997 RSC Tilden Prize and Medal, and the 1989 RSC Bader Award.

Keywords:
O-Directed free radical hydrostannation
Ph₃SnH/Cat. Et₃B
O–Sn coordinative control
a-Cyclopropyl-β-Stannylvinyl radical
Stannylvinyl cations

ABSTRACT

O-Directed free radical hydrostannation of the β-cyclopropyl propargyl alcohol 57 with stannanes and cat. Et₃B in THF/H₂O or PhMe/MeOH failed to deliver any of the expected products of α-stannylvinyl cation capture. Instead only α-stannyl-β-cyclopropylvinyl radical intermediates were detected, which underwent fast H-atom abstraction and/or cyclopropane ring-opening as a result of eliminative β-scission. A second alkylnol probe 23 was also studied in this O-directed free radical hydrostannation process. It gave rise to an α:β stannyl radical addition regiochemistry that changed markedly in favor of the α-adduct (26) when the reaction was conducted at high stannane concentrations. This outcome confirmed that O–Sn coordinative control must be responsible for the strong α-regiochemical preference of hydrostannations run at higher stannane concentrations, since a non-coordinative, electronically-controlled, stannyl radical addition would always give rise to a fixed and identical ratio of α:β-regioisomers. The formation of 27 further confirmed the exclusively free radical nature of these reactions.

© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

The Ph₃SnH/cat. Et₃B/O₂ variant of the O-directed hydrostannation [1–3] of propargyloxy alkyl acetylenes is a reaction of outstanding utility for the highly stereocontrolled creation of (Z)-trisubstituted alkenes of general structure 4, when allied with IeSn exchange [4] and typical Pd(0)-catalyzed cross coupling procedures such as the Baldwin/Lee variant [5–7] of the Stille cross-coupling, the Suzuki reaction [4], the Negishi and Sonogashira cross couplings [4], and Pd-catalyzed carbonylation [4] (Scheme 1).

Given the superb performance of this room temperature (rt) hydrostannation process, there has been substantive interest in understanding the key events that control its impeccably high (Z)-stereoselectivity and its remarkable α-regioselectivity, which always positions the tin substituent proximal to the original propargyloxy group (Scheme 1) [1,9]. One particularly important finding has been that the reaction must be conducted at quite high substrate concentrations with excess Ph₃SnH in order to observe very...
high levels of stereo- and regiocontrol. While occasionally β-regioisomeric adducts are very rarely encountered in these processes, these are generally only ever observed as very minor products at quite low stannane concentrations, and when they are met, they usually always possess an alkene geometry where the β-Sn substituent is positioned syn with respect to the original propargyloxy group, presumably because of the profound O-directing effect that operates in these reactions [1].

With regard to the mechanism [1,9] of the rt O-directed hydrostannation with Ph3SnH/cat. Et3B/O2 (Scheme 2, mechanism 1), and contrary to all suggestions otherwise [10], such reactions are entirely free radical in their nature [1,9], proceeding by way of an O-coordinated triphenylstannyl radical which preferentially adds to the α-carbon of the acetylene due to its extremely close proximity to the internally coordinated Ph3Sn radical.

It is thought that the initial O-coordination event [11] between the Ph3SnH and the propargyloxy substituent not only serves to weaken the Sn–H bond of 5, it also helps to facilitate formation of the O-complexed Sn-radical 6, while also electronically stabilizing that radical, and magnifying steric crowding around the central Sn atom, to give it much greater persistence in solution than would otherwise be found for the corresponding uncomplexed Ph3Sn radical. It is entirely possible that the O–Sn complexation within 6 synergistically enhances both the nucleophilicity and electrophilicity of this radical, to help promote its addition to the α-acetylenic carbon to give 7, in a phenomenon that we have recently termed "Internal Ligand Enhanced Radicalophility" [1], which we consider to be electronically analogous to a captodative effect.

Following internal Sn-radical addition [1,2,9,11], a rapidly inverting pair of α-stannylylvinyl radicals (Z)-7 and (E)-7 is thought to form, in which the (Z)-invertermor is usually energetically preferred, due to it experiencing much greater hyperconjugative stabilization [1,9,12–14] from the β-Sn-substituent than its (E)-stannylvinyl radical counterpart (E)-7. The (Z)-7 radical also does not suffer from the high A [1,3] strain that is typically present in (E)-7. These two effects also likely operate in the transition states for H-atom abstraction from the Ph3SnH, which will be far less sterically encumbered and more favourable for (Z)-7 than they will be for (E)-7, with the result that the (Z)-configured vinylstannanes (Z)-2 always emerge as the predominant products.

Although an O-coordinated β-addition can potentially lead to (Z)-8 being formed, attainment of this transition state will generally be far less favorable than attainment of the transition state for α-addition, due to the β-acetylenic carbon being much further removed from the O-coordinated Sn radical than its α-carbon counterpart. Once formed, the (Z)-8 β-adducts may potentially experience more persistent O–Sn through-space interactions, post-addition, than their (Z)-7 α-stannylated counterparts, and this internal semi-coordination might just be sufficient to electronically weaken the vinylc C–Sn bonds in these intermediates, to help promote their rapid β-scission back into 6. Naturally, such an event would tend to greatly favor formation of the (Z)-7 α-adducts and their so-derived products (Z)-2 due to these adducts now lacking this O–Sn coordinate interaction.

In support of such mechanistic thinking have been a large number of X-ray crystallographic analyses [1,3] of α-vinylstannanes of general structure (Z)-2 where R = H, which have each revealed that there is no significant internal O–Sn coordinate interaction between the allylic-OH and the Sn atom. As well as this, X-ray crystallographic studies of the (Z)-configured vinyl triarylstannanes [10] have each revealed that there is a strong internal O-coordinative interaction between the allylic-OH group and the central Sn atom in these β-adducts, and it is only to be expected that the presence of an additional alkyl group on the β-
carbon atom might enhance such an interaction, by virtue of the alkyl group sterically butressing the Ph3Sn substituent towards the allylic OH.

Other evidence in support of the O–Sn coordinative model [1,9,11,12,14] of α-regiocontrol comes from the Alabugin team’s DFT and NBO (natural bond orbital) calculations [12] on the propargylically-oxygenated aryl acetylene 13 (Scheme 3) which have indicated that the intermolecular nOO→σSn−C O–Sn radical complexation event is highly favourable and exothermic to the tune of ΔE = −2.5 kcal mol⁻¹; nOO→NSn O–Sn radical complexation is also highly beneficial (ΔE = −3.8 kcal mol⁻¹). Alabugin and coworkers’ calculations [12] further reveal that when the O-coordinated Sn-radical adds to the α-acetylenic carbon of 13, the process is spontaneous and strongly exergonic (ΔE = −16.4 kcal mol⁻¹), it having only a quite low activation energy barrier of Eₐ = +4.2 kcal mol⁻¹.

According to the Hammond postulate, high exothermicity for a chemical process is generally indicative of an early reactant-like transition state, which, in this instance, would only help to further confirm that O–Sn coordination is playing a very substantive role in helping to direct the triphenylstannyl radical to the α-position. Significantly, Alabugin’s calculations [12] do not show any marked O–Sn coordinative interaction persisting within the (Z)-α-stannylvinyl radical adduct 14, which is illuminatory, since this would be predicted to be destabilizing, if it did occur. Alabugin’s observations [12] thus completely align with our own X-ray crystallographic studies [1,9a] on a range of vinyl triphenylstannanes of general structure (Z)-2.

Prior to this highly informative molecular modeling of 2015 by the Alabugin team [12,13], and their accompanying tandem radical cyclization studies (Scheme 4) [12], the strongest experimental support for an entirely free radical, predominantly O-directed, mechanism for these reactions (mechanism 1) [1,2,9] came from our own 2005 rt work [9] on the free radical hydrostannation of predominantly O-directed support for an entirely free radical, mode of stannyl radical addition [12].

Further evidence for mechanism 1 being the primary avenue of hydrostannation has also come from an elegant competition experiment devised by the Alabugin group [12], where a 1:1 26:27 would always remain fixed and constant.

It is clear, therefore, from our 2005 work [9a], which has been augmented here (see the Results and Discussion section), that higher stannane concentrations very strongly promote O–Sn complexation, and the operation of O-coordinative regiocontrol, and this event very markedly favors formation of the α-addition product 26 while much lower stannane and substrate concentrations start to strongly promote the mechanistic transition towards the non-coordinative, intermolecular mode of tin radical addition (Scheme 6, mechanism 2) which, at rt, ultimately favors a predominance of the β-cyclization product 27 due to this mechanism operating exclusively under electronic control.

Further evidence for mechanism 1 being the primary avenue of hydrostannation has also come from an elegant competition experiment devised by the Alabugin group [12], where a 1:1...
A mixture of the two acetylenes 28 and 29 was submitted to high temperature free radical hydrostannation with Bu3SnH/cat AIBN in PhMe-d8 at 110°C; a set of conditions that led to the propargylically-oxygenated acetylene 28 reacting selectively and with total exclusivity (Scheme 7). This result confirmed our earlier O-directed postulate that: “H-atom abstraction occurs more readily from the stannane of complex 5 (see Scheme 2 herein) than from Ph3SnH itself” [9a].

A near identical outcome was observed by Curran and McFadden [18] in a later experiment run with Bu3SnH, catalytic AIBN and a 1:1 mixture of (but-2-ynyloxy)(tert-butyl)-dimethylsilane and hex-3-yne in C6D6 at 80°C. However, in their particular case, the enhanced reactivity and exclusive \( \alpha \)-regiocontrol observed for the propargyloxy acetylene (93:7) were attributed to an electronically-controlled, intermolecular, stannyl radical addition of the type depicted in mechanism 2 (Scheme 6) [18], despite this being significantly at odds with a large body of prior evidence, gathered by ourselves [9a] and Alabugin [12], which all favored the operation of mechanism 1.

Now although our hydrostannation work [9] on the probe 23 (Scheme 5) provided very strong and convincing experimental support for the O-directed mechanism 1 strongly dominating the hydrostannation outcome at higher stannane concentrations [1,9,14] (Scheme 2), and the electronically-controlled addition mechanism 2 only playing a minor role in these reactions, still, another electronically-controlled mechanistic thesis (Scheme 8) was advanced [10] over the period 2013–2014 (mechanism 3), by a team who claimed to have gathered strong experimental support for the intermediacy of stannylvinyl cation intermediates in these hydrostannation reactions. These had specifically been invoked [10] to explain the extraordinarily high regio- and stereochemical control that typically manifests itself. However, as we shall soon see, all of the experimental evidence that this team has so far proffered [10], to support their new mechanistic position, has not actually supported it at all. Rather, it has universally opposed their new theory. A fact that will soon become apparent from a detailed reading of the current paper. A paper that has been written to counter [14] a recent reinstatement of mechanism 3 by a 2019 review article on hydrostannation [19].

So, by way of necessary background to the main topic of this paper, namely, the full and hopefully final refutal [1,12,14,18] of mechanism 3 [10,19], we will now describe the new mechanistic proposals of the reference 10 team (mechanism 3) [10] in some considerable detail, and then go on to discuss the numerous
discrepancies that now render this mechanism untenable.

Now in this newly advanced mechanism 3 (Scheme 8) [10], it has been suggested that the α- and β-stannylvinyl radicals 33a and 33b need not actually arise through an O-directed stannyl radical addition mechanism of the type that is presented in Scheme 2 (mechanism 1). Rather, it was indicated that the (Z)-35 products could equally well arise through a non-regiocontrolled, non-O-directed, tin radical addition to either acetylenic carbon of 31, which would afford a pair of α- and β-stannylvinyl radicals 34a and 34b. It was then postulated that both radicals would spontaneously undergo rapid and irreversible single electron transfer (SET) to the small amounts of O2 that would be present in the reaction medium to produce a pair of stannylvinyl cations 34a and 34b that, presumably, would be intimately associated with superoxide ion in the form of two solvated ion pairs, although this was never actually specified by the reference 10 team [10].

Significantly, though, further discussion did take place on the fate of the lone cations 34a and 34b. Specifically, it was argued [10] that the less stable of these two stannylvinyl cations (i.e. 34b) would spontaneously undergo a rapid and instantaneous 1,2-stannyl shift to give the more stable α-stannylvinyl cation 34a exclusively. It was then further proposed that the positive charge present on the vinylic carbon of 34b would subsequently be stabilized by a dynamic, reversible, partial bonding interaction with the adjacent tin substituent, and that formation of this partially bridged stannylvinyl ion 34a would help to explain the final (Z)-stereoselectivity observed. If an invertive pseudo-Sn2 reduction was invoked at the more electrophilic carbon of the partially bridged form of 34a, in a pathway where the tin hydride was serving as a netionic H- donor. Although never actually specified in these very precise terms, it is clear that this is what was actually intended, however, since an invertive hydride attack was suggested to occur on 34a to obtain the (Z)-vinylstannane (Z)-35 exclusively.

The above team then further postulated that a new uncoordinated stannyl R3Sn– ion (36) would consequently be created which, presumably, would be stabilized by its ionic interaction with the negatively charged superoxide anion. However, no specific comment was made on this point. Instead, readers were left to decide for themselves about whether a discrete solvated contact ion pair might actually be forming from these two reactive entities, but one thing is abundantly clear from the ensuing discussion: the resulting cation/anion partnership did not additively combine to form a stannylperoxy radical, R3Sn-O–O–, as one might naturally expect.

Instead, the superoxide ion was suggested to preferentially engage in a second SET that would return O2 and a new R3Sn radical 37, which would then instigate a fresh round of alkyne hydrostannation in the manner indicated in Scheme 8, until all of the starting alkyne 31 had been consumed.

So, conceptually, with their 2013 proposal [10], the mechanism 3 team had put forward a new, much lengthier, hybrid radical/ionic mechanism for alkyne hydrostannation in which O2 was serving as a net ionic H- donor. Although never actually specified, it was argued [10] which have even been formally characterized by ESR spectroscopy [24].

Moreover, trialkyltin and triaryltrim radicals are very well known to add irreversibly to O2 to produce stannylperoxy radical adducts [1] which have even been formally characterized by ESR spectroscopy [24].

Therefore, for us to see the vinylstannane product as a genuine intermediate in Scheme 5 mechanistic pathway. In this regard, the rate of SET of the stannylvinyl radicals 24 and 25 to O2 would have to occur more rapidly than the radical cyclization of 25 to give 27 which would potentially have an estimated rate of \( k = 3.14 \times 3.32 \times 10^9 \) sec\(^{-1}\) based upon Newcomb’s data for an analogous vinyl radical cyclization (see footnote 25) [25].

Therefore, for us to see the vinylstannane product 26 emerge as the major product of the hydrostannation of 23 (Scheme 5) at high stannane concentrations alongside 27, the \( k \) for the required ionic reduction of the hypothetical vinylstannane cation intermediate by Ph3SnH would probably have to be much greater than this tentative \( 3.32 \times 10^9 \) M\(^{-1}\) s\(^{-1}\) value. However, Ph3SnH is well known to be a rather poor ionic reducing agent for carbocations (see Scheme 9) [26] which renders the reference 10 assertions most unlikely.

In this regard, Mayr and coworkers [27] have specifically commented upon vinyl cations such as 38 having a very similar reactivity profile to diarylcarbenium ions like the (MeOC6H4)(Ph)C(H)\(^+\) cation 39 in their reactions with nucleophiles. Now this general observation is potentially of great mechanistic significance, since Mayr and Basso [26a] have specifically shown that the (MeOC6H4)(Ph)C(H)\(^+\) cation only reacts rather slowly with Ph3SnH...
in CH₂Cl₂ at −70 °C (k = 4.98 × 10⁻³ M⁻¹ s⁻¹). Moreover, Mayr et al. [26b] have further reported that the aforementioned ionic reduction has a k of 3.26 × 10⁴ M⁻¹ s⁻¹ at 20 °C (Scheme 9), which compares very favourably with their calculated value of 3.51 × 10⁴ M⁻¹ s⁻¹ at 20 °C [26b].

The above k is far slower than the anticipated rate of cyclization of the stannylvinyl radical 25 upon its own terminal trisubstituted alkene (Scheme 5), which would potentially have a k_cyclisation rate constant well in excess of the 3.32 × 10⁸ M⁻¹ s⁻¹ figure that we have conservatively estimated for the vinyl radical cyclization shown in footnote 25, due to the stannylvinyl radical 25 producing an even more stabilized secondary radical upon 5-exo-trig ring-closure.

Mayr’s ionic reduction k value of 3.26 × 10⁴ M⁻¹ s⁻¹ at 20 °C [26b] is obviously far smaller than the k for H-atom abstraction from Bu₃SnH by a typical vinylic radical at rt, which has now accurately been determined to be between 3.2 × 10⁹ M⁻¹ s⁻¹ and 3.7 × 10⁹ M⁻¹ s⁻¹ through laser flash photolysis by Ingold [28] and Galli [29]. Ph₃SnH is also known to be an even better H-atom donor than Bu₃SnH in H-atom abstraction reactions involving carbon-centred free radicals (e.g. t-Bu), with its k values typically being at least 4 times greater than the corresponding Bu₃SnH rate constant according to past literature [30].

So, given that the rate constant for ionic reduction of the hypothesized stannylvinyl cation by Ph₃SnH would probably need to be significantly greater than 3.32 × 10⁸ M⁻¹ s⁻¹, for us to observe a mixture enriched in 26 and 27 (Scheme 5), the Mayr-Basso [26] diarylcumuleneionic reduction rate constant data with Ph₃SnH (Scheme 9) does make mechanism 3 seem most unlikely.

Now apart from all of these experimental facts, which very strongly rule against mechanism 3 [10], there are two further unjustified claims that have been made by the mechanism 3 team with regard to their newly proposed controverting mechanism [10]. These are that mechanism 3 has been strongly experimentally supported: 1) by rt DFT calculations [10a] (see Schemes 8 and 10) and 2) by the 2.7–4.4-fold polar solvent rate acceleration effect that they claim to have observed for the hydrostannation of 47 in THF, THF/H₂O, acetone, and DMF relative to non-polar C₆H₆ (Scheme 11) [10c].

However, if we first of all examine the DFT calculations that accompany mechanism 3 in Scheme 8, it was reported by the mechanism 3 team [10a] that when R = H and R₁, R₂, and R₃ are all Me groups, and C₆H₆ is the reaction solvent, the O₂-mediated transitions of 33a to 34a and 33b to 34b are associated with ΔE (energy difference) values of +47.27 kcal mol⁻¹ and +45.2 kcal mol⁻¹, respectively, at 25 °C (see Scheme 8). However, both of these values are far too large and endergonic to allow such proposed electron transfers to O₂ to ever proceed at 25 °C, particularly if one further factors in the activation energy barriers (Eₐ) that would also need to be surmounted for 33a and 33b to successfully transit into 34a and 34b, respectively, unless, of course, one assumes that quantum mechanical (QM) electron tunneling is occurring. Yet, no experimental evidence has ever been presented by the mechanism 3 team for this possibility, nor has tunneling even been mentioned or discussed in any of their papers where this mechanism has been presented. Instead, it is simply stated [10a] that: “The vinyl radical oxidation mechanism accounts for all aspects of selectivity in the addition and presents barriers that are well within reach on the reaction surface”. Thus, it is clear that the ΔE values of +47.27 kcal mol⁻¹ and +45.2 kcal mol⁻¹ that were reported [10a] were actually considered to be viable and readily surmountable barriers, despite them being anything but viable or conducive to a

**Scheme 9.** According to Mayr and coworkers (2017) [26,27] the diaryl carbenium ion 39 has a very similar reactivity profile to the vinyl cation 38 towards nucleophiles. As a result, the k of 3.26 × 10⁴ M⁻¹ s⁻¹ at 20 °C provides a very good estimate of the likely rate constant for ionic reduction of a typical vinyl cation such as 38 [26] or a stannylvinyl cation (Scheme 8).

**Scheme 10.** The second set of disparate DFT calculations from the reference 10 team [10a] for the free radical hydrostannation of (R,S)-5,5,5-trifluoropent-3-yn-2-ol (41) with Me₃SnH.

**Scheme 11.** The reference 10d claim that polar solvents markedly accelerate the cat. ET₃B/O₂ initiated hydrostannation of alkyne 47. Clearly the above data [1] does not vigorously experimentally support an ionic reaction. Instead the data are much more aligned with mechanism 1 [1,2,9,12,14].
successful forward reaction at 25 °C via mechanism 3.

A further discrepancy with the reference 10a DFT calculations concerns the transition of 33x into 34x being +2.1 kcal mol⁻¹ higher in energy than the corresponding transition for 33β into 34β, when 34x is supposedly less inductively destabilized according to the team’s discussion in their paper. Such abberant data certainly does not lend much confidence to the claimed spontaneity of the β-stannylvinyl cationic migration that has been propounded in Scheme 8 [10a].

Similar problems also exist with the calculations that the mechanism 3 team have performed on (R,S)-5,5,5-trifluoroprop-2-yn-2-ol [41] with Me₃SnH (Scheme 10) [10a], which were intended to provide mechanistic insights into the O-directed free radical hydrostannation that had been conducted on this substrate with Bu₃SnH/AlBN in C₆H₆ at 80 °C [10a]. This is a reaction that gives rise to a sharply contrasting contra-regioselectivity to that observed with propargyloxy alkyl acetylenes (see footnote 31) [31].

With regard to the calculations of Scheme 10, the observed outcome was yet again rationalized with a modified stannylvinyl cation mechanism [10a]. As previously, it was once more asserted that a non-regioselective stannyl radical addition was occurring to the alkyne of 41, and that the resultant pair of stannylvinyl radicals would then undergo an O₂-mediated SET to give a pair of stannylvinyl cations 43x and 43β, which again would instantly equilibrate, in this instance, to the less inductively destabilized, partially bridged, stannylvinyl cation 43β exclusively. An ionic reduction with the tin hydride would then give the product (Z)-44. As previously, an identical SET role was postulated for the superoxide counter anion in helping to fashion the new stannyl radical 46 from the stannyl cation 45 that was suggested to be liberated during the ionic reduction step.

Unfortunately, a very close inspection of the DFT calculations that have been performed on 41 in C₆H₆ at 25 °C once more reveals very serious problems and discrepancies with the ΔE values that have been reported [10a], which again claim a lower relative energy (ΔE = +64.8 kcal mol⁻¹) for the more inductively destabilized cation 43x over its more stable cationic alternative 43β (ΔE = +68.7 kcal mol⁻¹) following O₂-mediated SET of the two stannylvinyl radicals 42x and 42β. Again these two values look to be in error, but nonetheless, we have to state this here as part of our renewed refutal [1] of this mechanism, now that this recent 2019 review article [19] has reinstated the stannylvinyl cation mechanistic theory [10].

Additionally, the extremely high energy barriers that would need to be surmounted for both of these radical oxidations to proceed would once more preclude either of them from ever occurring at rt or at 80 °C in C₆H₆.

Now before we depart fully from our analysis of the DFT calculations that have accompanied the newly proposed mechanism 3 [10a], we must draw attention to the tin hydride reduction steps that appeared in Fig. 2 of the 2013 Angewandte Chemie paper [10a].

Specifically, it was reported that the proposed ionic reduction of the stannylvinyl cations 34x and 34β with Me₃SnH (Scheme 8) presented energy barriers of ~9.1 kcal mol⁻¹ and ~12.8 kcal mol⁻¹, respectively [10a]. However, readers were not given any firm indication of what were the final energies of the reduced products in this particular calculation. This omission does, of course, render these calculations of limited value. However, if we add the energies that are reported to the minimum ΔE values of ~47.27 kcal mol⁻¹ and ~45.2 kcal mol⁻¹ that are quoted for stannylvinyl cation formation from 34x and 34β (Scheme 8) [10a], we must consider it highly probable that these are not the overall energy barriers that actually need to be surmounted to achieve these two transitions. It will be appreciated that simply to arrive at the claimed transition state for ionic nucleophilic reduction of 34x and 34β with Me₃SnH, would require a minimum energy input of ~56.37 kcal mol⁻¹ and ~58.0 kcal mol⁻¹, respectively, to be expended in each case, for the reactions to proceed. Again, these energy estimates look far too high and prohibitive to allow such processes to proceed readily at rt or 80 °C.

Clearly, when examined carefully with a more circumspect eye, the mechanism 3 team’s DFT calculations [10a] do not lend any genuine support to their mechanistic claims for how the acetylenes 31 (R = H, R₁ = R₂ = Me) (Scheme 8) and 41 (Scheme 10) are reacting with tin hydrides under free radical initiated conditions, contrary to suggestions otherwise. Indeed the claim [10a] that this new ionic pathway “presents barriers that are well within reach on the reaction surface” is just not credible. Rather, the ΔE values that are reported [10a] actually very strongly rule against the stannylvinyl cation mechanistic hypothesis [10].

However, as we have already indicated, we are now of the opinion [1] that these calculations have been erroneously performed. The modeling conclusions of the mechanism 3 team are also at variance with the later 2015 modeling that was done by Alabugin and coworkers [12], which led to a diametrically opposite set of conclusions and interpretations regarding the mechanism.

Now, as for the added experimental claim [10d] that a “pronounced solvent rate acceleration effect had been observed for the sub-stoichiometric Eₜ₆B initiated hydrostannation reactions that had been performed on the alkynyl 47 (Scheme 11), once more, this assertion does not stand up to careful examination [1].

In fact the published data [10d] did not provide any of the requisite experimental support needed to validate the proposed ionic mechanistic pathway of Scheme 8 [10a,b]. Thus, the 2.7-4.4-fold increases in reaction rate that were recorded, compared with the reaction rate in C₆H₆ [10a], were all far too miniscule [1] to be considered highly supportive of the ionic mechanism shown in Scheme 8 [10]. Instead the data exclusively points to a purely free radical mechanism operating in these reactions, of the type proposed in Scheme 2 [1,2,9,12,14]. Indeed, when dry THF is used as the reaction solvent for rate comparison [10d], as opposed to C₆H₆, Scheme 11 actually shows that there is a very pronounced decrease in reaction rate, or a near identical rate in solvents of massively increased polarity. Thus, the magnitudes of the claimed polar solvent rate accelerations cannot be considered to be supportive of mechanism 3.

And while we are on the topic of how reaction solvent can affect outcome, we must draw attention to the mechanism 3 team’s own hydrostannation work on the alkynyl 47 in THF/H₂O (Scheme 11) [10d], which afforded the (Z)-vinylstannane 48 exclusively in 75% yield, without the accompaniment of ketone or enol β-elimination products such as 51, 52 or 53 (Scheme 12). Naturally, these enol 50-derived products would likely have arisen (Scheme 12) had the ionic mechanism of Scheme 8 [10] been genuinely operating. Yet, no mention was ever made of having encountered such products by the mechanism 3 team [10d].

Additionally, our own added report [1] that not a single arylated tetrasubstituted vinylstannane has ever been encountered in any O-directed free radical hydrostannation conducted in C₆H₆ or PhMe further opposes [1] the stannylvinyl cation intermediates of mechanism 3 [10], since vinyl cations normally undergo Friedel-Crafts alklylation when they are generated in aromatic solvents such as C₆H₆ (see footnote 32 and the references therein) [32]. Moreover, the vast majority of O-directed hydrostannations that have been performed have primarily been conducted in C₆H₆ or PhMe [1]. The lack of enol ether products from propargyl alcohol substrates [1], and allenylstannane products from primary and secondary alkyl acetylene substrates further argues against the stannylvinyl cationic mechanism of reference 10 [10]. These collective findings had clearly not been considered by the mechanism
having recently been reinstated [1] as the most likely mechanism for this reaction in a 2019 Chemical Record article [1] which appeared a full 3 calendar months before the aforementioned ACS Catalysis review article [19] was even submitted to that journal.

Given the apparent lack of acceptance by some [10,18,19] of the O-directed mechanism that was proposed by us [2,9,11] for these entirely free radical hydrostannations in 2005 (mechanism 1, Scheme 2), and the continued propagation of the non-O-directed ionic mechanism 3 [19], despite our 2019 refutal [1], we recently resolved to reinvestigate our 2005 mechanistic work on the acetylenic alcohol 23 (vide infra Scheme 5) with a view to helping us reconfirm its general validity, and to further augment it, for the purpose of unambiguously ruling out mechanisms 2 [18] and 3 [10] as the primary determinants of hydrostannation reaction outcome, under the normal high stannane concentration conditions that we and others typically use to effect these reactions. Success in this endeavor would help to counter all suggestions that mechanism 1 was not playing a dominant role in these rt processes. This light touch reinvestigation has now duly been done, and our new results are presented in Scheme 13.

Naturally, they reconfirm our original mechanistic thinking of 2005, inasmuch as they show a dramatic 9-fold shift in product ratio towards the α-addition product 26 as we move from low to high stannane concentration. This unambiguously demonstrates that it must be the O-directed, entirely free radical, mechanism 1 that is gaining the upper-hand, over the competing non-directed, electronically-controlled, stannyl radical addition/H-atom abstraction pathway (mechanism 2) at higher stannane concentrations, and that mechanism 3 plays no role at all in the proceedings. Indeed, our rt data is very clear-cut, confirming that mechanism 2 can only ever start to gain hegemony over mechanism 1, when the stannane and substrate concentration are both very low, and when it does finally gain control, mechanism 2 does seemingly favor the β-product not the α. Significantly, as well, the product conversions and yields are always typically rather low when these reactions are conducted at low stannane and substrate concentration, with the starting alkylnol 23 always generally being returned in significant quantity under such circumstances. Our new results thus strongly reaffirm mechanism 1 as the primary arbiter of reaction outcome [1,2,9,11,12] in these hydrostannations, not the electronically-controlled mechanism 2 [18] which, although it does operate, it does so only to a very minor degree under the normal operational circumstances of these reactions, which have the stannane usually present in significant excess, in order to obtain a high product yield and high α-regioselectivity.

Our latest results also show here, for the first time, the profound effect that operating at low temperature can have on the regiochemical outcome of free radical hydrostannations with the probe 23. In this aspect, we have recently observed that if one runs these reactions at temperatures of between −5 and −10 °C, this significantly reinforces the observed α-regiocontrol of these Ph3Sn radical additions to 23, possibly because this promotes O−Sn complexation further, and/or it slows the overall rate of 5-exo-trig radical cyclization relative to the reverse β-stannyl radical elimination of 25 to give 54.

Indeed, if one works at a quite high stannane concentration in PhMe at −5 to −10 °C, one sees a very pronounced shift in the α:β product ratio, to 9:6.1, which now represents a 12-fold change in regiochemistry from the corresponding 20 °C reaction run at 0.025 M with just 1 equiv of Ph3SnH, which gave rise to an α:β product ratio of 1:2. Clearly, both of these regiochemical variations are only really compatible with an O-coordinative mechanism (mechanism 1, Scheme 2) starting to strongly dominate outcome at higher stannane concentrations and lower reaction temperatures.

Given these results, it is very tempting to speculate that lower
reaction temperatures might be enhancing internal O–Sn coordination within the β-stannylnvinyl radical adduct 25, which would be expected to promote the reverse elimination reaction very significantly. Following β-scission, the newly liberated, internally O-coordinated, Sn radical 54 would now be perfectly positioned to undergo α-selective Sn-radical addition preferentially, due to its closer proximity to the α-acetylenic carbon atom, and because of the lack of destabilizing internal O-coordination in the resulting α-stannylnvinyl radical adduct (Z)-24 [1,9,12,14]. Naturally, this would likely confer much greater longevity on (Z)-24 in solution, to enable H-atom abstraction to occur more readily, to give 26. Whatever effects are at play here, they are clearly very interesting, and add yet another layer of complexity to the truly fascinating mechanistic workings of these reactions.

Another important point that we would like to make is that even if one operates at low temperatures of between −5 and −10 °C, one can still see a marked change in α:β-selectivity as the stannane concentration changes from high to low, and once more, such an observation is wholly incompatible with an electronically-controlled addition mechanism 2 [18] exclusively dominating outcome, where no change in product regiochemistry would ever be expected under such circumstances. The same would be true for mechanism 3 [10].

Clearly, this newly-discovered effect of working at lower reaction temperatures to help prevent 5-exo-trig radical cyclization could be of considerable synthetic value, and it will be of great interest to examine how operating at much higher temperatures at low stannane concentrations will affect the outcome, to see if this could promote tandem radical cyclization in acceptable yields. However, such a study is well beyond the scope of the present mechanistic investigation, which is primarily concerned with re-examining how stannane concentration mechanistically affects these hydrostannations, including at lower reaction temperatures. One item of special note in the above experiments is how they indirectly confirm the reversibility of the stannyl radical addition step in these O-directed hydrostannations, since ordinarily one would only expect to see very tiny amounts of the stannylated β-adducts in most hydrostannation reactions run at rt with Ph3SnH/Cl2. This would change if we were to run these reactions at a high stannane concentration, and the very fact that we are able to successfully trap out these β-adducts in varying amounts with the probe 23, over a range of stannane concentrations, shows that under normal circumstances (where the stannane is present in significant excess) β-stannylnvinyl radicals of general structure (Z)-8 (Scheme 2) are ordinarily eliminating very rapidly, with a rate constant that is far in excess of $k = 3.14 - 3.32 \times 10^6$ sec$^{-1}$ (vide infra). The latter is the corrected estimate of the rate constant for a typical 5-exo-trig cyclization involving a vinylic radical (see footnote 25 herein) and slightly reduces Newcomb’s very valuable, originally published [25], value which used the k of an aryl radical H-atom abstraction from Bu3SnH ($k = 7.8 \times 10^8$ M$^{-1}$ s$^{-1}$ at 25–30 °C) [25b] to make its original estimate, as opposed to Ingold [28] and Galli’s [29] lower k determinations of $3.2 - 3.7 \times 10^5$ M$^{-1}$ s$^{-1}$ at rt for a similar vinyl radical H-atom abstraction; values which are now widely felt to be accurate by many in the field.

Concurrent with these efforts, we further resolved to test mechanism 3 with the small molecule probe 57 (Scheme 14), which was carefully designed to allow for the effective nucleophilic capture of the alleged stannylnvinyl cation 58 (R = Ph, Bu) by a set of nucleophiles (e.g. H2O or MeOH) with a known propensity to react rapidly with highly stabilized α-cyclopropyl vinyl cations when present in significant excess.

Significantly, the probe 57 would also potentially allow the postulated α-stannylnvinyl radical intermediate 64 (R = Ph, Bu) [1,2,9,14] (Scheme 15) to be readily detected, by offering it a facile β-scission pathway to follow, particularly at elevated temperatures. A pathway that would homolytically cleave the cyclopropane ring to give the stannyhomoallyl radical 65 (R = Ph, Bu), which could then H-atom abstract from the stannane to produce 66 (R = Ph, Bu) alongside 67. It was expected that the cyclopropane ring in 64 would cleave with particular facility in dilute solution at temperatures not far above 60 °C, given the previous literature reports of Crandall [36], Malacria [37] and Baines [38] in the α-cyclopropylvinyl radical ring-opening area, two of which [36,37] had previously confirmed that such ring-cleavages generally occur with great facility, when they are mediated by Bu3SnH at 80 °C [36,37].

Probe 57 (Schemes 14 and 15) could also give very precise information on whether the alleged SET (i.e. the conversion of 64 into 58) was actually proceeding as rapidly and instantaneously as the mechanism 3 team were seemingly suggesting which, based upon the mechanism that they had formulated in Scheme 8, would need...
to occur at a rate faster than H-atom atom transfer from a stannane to a quite reactive vinylic radical, or the 5-exo-trig cyclization of a vinyl radical upon an alkene (i.e. $k = 3.14 - 3.32 \times 10^6 \text{M}^{-1} \text{s}^{-1}$) [25] (based upon our work on 23), or the rate of formation of the stannyll homoallenyl radical 65, for mechanism 3 to hold true.

Moreover, if that very same irreversible single electron transfer event from the stannylvinyl radical 64 to the $\text{O}_2$ was indeed proceeding more rapidly than H-atom abstraction from the $\text{Ph}_3\text{SnH}$, as the mechanism 3 team have suggested [10], then this would inevitably mean that after the stannylyvinyl cation 58 (R = Ph) had formed, it would have no other choice but to react more rapidly with potent nucleophiles such as $\text{H}_2\text{O}$ or MeOH, present in excess, rather than undergo a much slower ionic reduction by the $\text{Ph}_3\text{SnH}$ ($k \approx 3.26 \times 10^4 \text{M}^{-1} \text{s}^{-1}$ at 20°C). [26] As a result, it would give rise to products such as 61, 62 and 59, or failing this, it would have to eliminate rapidly either by an E1 pathway, to give the $\beta$-cyclopropyl-stannylallene 68 (or its protodestannylated variant 69), or it would alternatively have to undergo a Stang-Muller elimination [39] to return the starting alkyne 57 (Scheme 16).

In fact, we reasoned that if the cation 58 was indeed a genuine reaction intermediate [10] in the chemical pathway to vinylstannane 67, it would almost certainly react very rapidly with added external nucleophiles such as $\text{H}_2\text{O}$ (or MeOH), due to this cation being quite long-lived and triply stabilized: a) the ester carbonyl; b) the $\beta$-(R)3Sn substituent; and c) the $\alpha$-cyclopropane ring.

We also envisaged that the above nucleophilic trapings would proceed by three main pathways (Scheme 14). In path A, the internal ester $\text{C}=\text{O}$ would attack the vinyl cation to give a six-membered enol lactone (63) following hydrolytic cleavage of the resulting positively charged oxonium ion. In path B, an external solvent nucleophile would attack the vinyl cation to give either 59 or the enol 60 which, in the latter case, would then rapidly $\beta$-eliminate to give the stannyl enone 62 or afford the protodestannylated aldol product 61. A third option, would be for the excess $\text{H}_2\text{O}$ or MeOH that was present to attack the (R)3Sn substituent to bring about a Stang-Muller eliminative cleavage [39] (Scheme 16), which would naturally return the starting acetylene 57 in copious amounts, which would, of course, lead to little, real, overall reaction progression. In fact, such nucleophile-induced eliminative cleavages have long been documented for $\beta$-stannylyvinyl cations by Stang and coworkers [39] and such behaviour is usually the norm for super-stable bis-silyl vinyl cations that are exposed to nucleophiles, according to Muller and coworkers [39c]. A priori, it would thus be expected that the stannylyvinyl cation 58 would behave in analogous fashion, if it was indeed a genuine and rapidly formed intermediate in these reactions [10].

With regard to the feasibility of achieving a direct $\alpha$-cyclopropyl vinyl cation trapping with $\text{H}_2\text{O}$, the classic work of Bergman [40] and Hanack [41] was uppermost in our minds, for it had collectively
shown that despite α-cyclopropyl vinyl cations benefitting from significant charge stabilization, as a result of hyperconjugation with the cyclopropane ring, such intermediates always still retain a very strong ability to react rapidly and efficiently with externally added nucleophiles such as H₂O or acetate ion (Schemes 17 and 18), virtually exclusively at the vinylic carbon bearing the positive charge. In this respect, the major products (>97%) of such cyclopropyl vinyl cation trapping reactions with nucleophiles such as H₂O, or acetate anion, are always the non-rearranged vinyl cyclopropane derivatives, accompanied by very small amounts of 1,2-rearranged cyclobutane derivatives (<1.8%) [40].

Of special significance, however, is the finding that α-cyclopropyl vinyl cations such as 72 show a very strong reluctance to undergo nucleophilic ring cleavage of their cyclopropane rings, even at elevated reaction temperatures. This because of the very high degree of charge stabilization within such systems. As a result, nucleophilically-captured allenes, where the cyclopropane ring has undergone nucleophilic ring-opening, never usually comprise more than 1.8% of a typical α-cyclopropyl cation reaction mixture, even under forcing circumstances [40].

It will thus be clear that ordinarily the nucleophilic ring-cleavage of α-cyclopropyl vinyl cations is a highly disfavored process, even with negatively charged nucleophiles, and it would likely be even more unfavorable with uncharged neutral nucleophiles such as tin hydrides or H₂O.

Consequently, if the probe 57 was subjected to O-directed free radical hydrostannation in aqueous THF, one could say, fairly confidently, that if one was to exclusively observe the reduced allenyltin derivative 66 in a substantive yield alongside the vinylstannane 67 (Scheme 19), without encountering H₂O-captured products such as 84, (Schemes 19 and 20), then simple ionic reductive cleavage of the α-stannylvinyl cation 58 was probably not the primary source of 66, because the pseudo-S2,1 and S2,2 reactions that would each lead to 66 would both be highly unfavorable processes (see Schemes 19 and 20). Moreover, even if they did occur, they would still only ever lead to 66 and 84 being formed simultaneously in very tiny quantities, and if one also did not observe the stannyl enone 62 nor the aldol 61 nor the lactone 63 (Scheme 14) in the resulting reaction mixtures, alongside alcohol 84, then one could most definitely rule out the claimed intermediacy of the hypothesized stannylvinyl cation 58 (R = Ph, Bu) [10].

Scheme 17. α-Cyclopropylvinyl iodides rapidly undergo solvolysis at their vinylic carbon due to the vinylic carboxation being highly stabilized by the cyclopropane ring [40,41]. So powerful is this electron-donating stabilizing effect that the cyclopropane ring shows very little tendency to undergo nucleophilic ring-opening by the H₂O. The cyclopropane ring also appears to hyperconjugatively accelerate the departure of the Ag-coordinated iodide in a truly breathtaking way, as demonstrated by the attempted solvolysis of vinyl iodide 70 under identical conditions.

One could also expect nucleophilic trapping of the cation 58 with H₂O to occur far more rapidly than the competing ionic reduction with Ph₃SnH, on the basis of Lodder’s [21] and Mayr’s [26,27] rate constant data for typical vinyl cation trappings with H₂O which have indicated that these typically proceed quite rapidly with k values of 1.3 × 10⁸ to 2.3 × 10⁹ M⁻¹ s⁻¹, which is significantly faster than the rate of ionic reduction of the vinyl cation equivalent 39 (Scheme 9) with Ph₃SnH, which has a k of 3.26 × 10⁸ M⁻¹ s⁻¹ in CH₂Cl₂ at 20 °C [26b].

One could thus safely conclude that, if they were formed exclusively, 66 and 67 must have originated from a common stannylvinyl radical precursor 64 (as shown in Scheme 15), which must have undergone competitive H-atom abstraction from the stannane alongside radical-induced β-scission of the cyclopropane ring followed by H-atom transfer.

Accordingly, we set out to investigate the hydrostannation of alkynol 57 with Ph₃SnH and Bu₃SnH under various initiating regimes, in a host of different solvents, over a range of different reaction temperatures (Scheme 21).

Initially, we examined the room temperature free radical hydrostannation of probe 57 in dry THF at approximately 1 M substrate concentration using a significant excess of Ph₃SnH (4 equiv) under our standard Et₃B (0.1 equiv)/O₂ initiating protocol (Scheme 21 Entry 1). The reaction proceeded very cleanly to deliver a single hydrostannation product 67 (R = Ph) in 77% yield with no evidence of any ring-opened α-stannyllane 66 (R = Ph). Such an observation is fully aligned with the prior work of Crandall et al.
who had previously found that when the vinyl iodide 85 was added to neat Bu3SnH at rt, it gave the reduced vinylcyclopropane 88 alongside a barely detectable amount of the ring-opened allene 89 (88:89 = 99:1) (Scheme 22). However, this ratio shifted quite dramatically towards the allene 89 at higher reaction temperatures and lower stannane concentrations. Malacria and Fensterbank [37] likewise found that the α-cyclopropylvinyl radical ring-opening of 90 was strongly favored by low Bu3SnH concentrations and high reaction temperature (Scheme 22), and so our work also aligns with their observations as well.

Given our findings in Entry 1, and our awareness of how α-cyclopropylvinyl radicals typically undergo radical-induced ring-opening to the corresponding homoallenyl radicals at elevated temperatures [36] who had previously found that when the vinyl iodide 85 was added to neat Bu3SnH at rt, it gave the reduced vinylcyclopropane 88 alongside a barely detectable amount of the ring-opened allene 89 (88:89 = 99:1) (Scheme 22), this ratio shifted quite dramatically towards the allene 89 at higher reaction temperatures and lower stannane concentrations. Malacria and Fensterbank [37] likewise found that the α-cyclopropylvinyl radical ring-opening of 90 was strongly favored by low Bu3SnH concentrations and high reaction temperature (Scheme 22), and so our work also aligns with their observations as well.

Given our findings in Entry 1, and our awareness of how α-cyclopropylvinyl radicals typically undergo radical-induced ring-opening to the corresponding homoallenyl radicals at elevated temperatures [36] who had previously found that when the vinyl iodide 85 was added to neat Bu3SnH at rt, it gave the reduced vinylcyclopropane 88 alongside a barely detectable amount of the ring-opened allene 89 (88:89 = 99:1) (Scheme 22), this ratio shifted quite dramatically towards the allene 89 at higher reaction temperatures and lower stannane concentrations. Malacria and Fensterbank [37] likewise found that the α-cyclopropylvinyl radical ring-opening of 90 was strongly favored by low Bu3SnH concentrations and high reaction temperature (Scheme 22), and so our work also aligns with their observations as well.

Given our findings in Entry 1, and our awareness of how α-cyclopropylvinyl radicals typically undergo radical-induced ring-opening to the corresponding homoallenyl radicals at elevated temperatures [36] who had previously found that when the vinyl iodide 85 was added to neat Bu3SnH at rt, it gave the reduced vinylcyclopropane 88 alongside a barely detectable amount of the ring-opened allene 89 (88:89 = 99:1) (Scheme 22), this ratio shifted quite dramatically towards the allene 89 at higher reaction temperatures and lower stannane concentrations. Malacria and Fensterbank [37] likewise found that the α-cyclopropylvinyl radical ring-opening of 90 was strongly favored by low Bu3SnH concentrations and high reaction temperature (Scheme 22), and so our work also aligns with their observations as well.

Given our findings in Entry 1, and our awareness of how α-cyclopropylvinyl radicals typically undergo radical-induced ring-opening to the corresponding homoallenyl radicals at elevated temperatures [36] who had previously found that when the vinyl iodide 85 was added to neat Bu3SnH at rt, it gave the reduced vinylcyclopropane 88 alongside a barely detectable amount of the ring-opened allene 89 (88:89 = 99:1) (Scheme 22), this ratio shifted quite dramatically towards the allene 89 at higher reaction temperatures and lower stannane concentrations. Malacria and Fensterbank [37] likewise found that the α-cyclopropylvinyl radical ring-opening of 90 was strongly favored by low Bu3SnH concentrations and high reaction temperature (Scheme 22), and so our work also aligns with their observations as well.

Given our findings in Entry 1, and our awareness of how α-cyclopropylvinyl radicals typically undergo radical-induced ring-opening to the corresponding homoallenyl radicals at elevated temperatures [36] who had previously found that when the vinyl iodide 85 was added to neat Bu3SnH at rt, it gave the reduced vinylcyclopropane 88 alongside a barely detectable amount of the ring-opened allene 89 (88:89 = 99:1) (Scheme 22), this ratio shifted quite dramatically towards the allene 89 at higher reaction temperatures and lower stannane concentrations. Malacria and Fensterbank [37] likewise found that the α-cyclopropylvinyl radical ring-opening of 90 was strongly favored by low Bu3SnH concentrations and high reaction temperature (Scheme 22), and so our work also aligns with their observations as well.
Malacria's [37] work, Scheme 21 Entry 2 conditions gave rise primarily to the vinylstannane led to a small amount of the ring-opened stannylallene from one another in 75% and 6% yield, respectively, following SiO2 chromatography. As one might expect from Crandall [36] and Malacria and Fensterbank [37] (Scheme 22), and quite convincingly further aligns with the prior observations of Scheme 21. Entry 3).

Having shown that radical-induced ring-opening of the stannylvinyl radical 64 to give 65 could indeed be achieved at 66 °C in dry THF at reflux (Scheme 21, Entries 1–3), and that the stannyl homoaallenyl radical 65 readily underwent H-atom abstraction to give 66, we next confirmed that 66 was indeed arising via an entirely free radical mechanistic pathway. We did this by examining the hydrostannation of 57 in aqueous THF under a variety of conditions (Scheme 21, Entries 4–12).

Conducting the reaction in THF:H2O (11:1) under conditions otherwise identical to Entry 1 very quickly demonstrated that the incorporation of 8% added H2O had little effect on the reaction outcome when 4 equiv of Ph3SnH was used at rt (Scheme 21, Entry 4).

A similar result was obtained when THF:H2O (4:1) was employed as the reaction solvent, and the amount of H2O was increased to 20% of the reaction volume (Scheme 21, Entry 5). In both cases, a near identical yield of the product vinylstannane 67 (R = Ph) was obtained exclusively in 75–83% yield. Importantly, as well, we did not observe any major rate acceleration as a result of adding highly polar H2O to the reaction medium; certainly not a rate acceleration of the magnitude that would lend strong support to the ionic mechanism 3 that has been proposed [10]. This stands in sharp contrast to the testimony of the mechanism 3 team [10d].

Likewise when we performed the hydrostannation of 57 with 4 equiv of Ph3SnH in THF:H2O (4:1) at 80 °C (Scheme 21, Entry 6), we saw a very similar outcome to that seen in dry THF, under identical circumstances. In this regard, a 15:1 mixture of 67:66 was obtained enriched in the vinylstannane 67 which was an outcome virtually the same as that seen in dry THF alone (67:66 = 14:6:1) (Scheme 21, Entry 2). Tellingly, and despite the presence of the competitor H2O nucleophile in the reaction medium, yet again, we could only detect 67 and 66, and pointedly, none of the nucleophilically ring-cleaved stannylallenyl primary alcohol product 84 was ever encountered.

Had an ionic/nucleophilic reduction pathway been demonstrated that it is an entirely free radical induced ring-opening that is operating here that has a modest activation energy barrier needing to be thermally overridden before the radical ring-opening event can proceed readily.

In this regard, our observations agree fully with the high level 2007 computational chemistry calculations performed by Guo et al. [42] for the conversion of 92 into 93 (Scheme 23), which revealed that an activation barrier of approximately +10.7 kcal mol⁻¹ needs to be overridden for the α-cyclopropyl vinyl radical 92 to be converted into the homoallenyl radical 93. However, when this barrier is actually surmounted, the overall transition of 92 into 93 is quite exergonic and facile to the tune of −4.3 kcal mol⁻¹. Naturally, given that the activation energy barrier for the reverse cyclization of 93 into 92 is significantly endergonic (+15 kcal mol⁻¹), it is little surprise to find that the re-cyclization is significantly disfavored.

1. H.A. Watson et al. / Tetrahedron 76 (2020) 131061

Scheme 22. Crandall [36] and Malacria’s [37] prior experimental findings on α-cyclopropylvinyl radical ring-opening, which is generally promoted by generating the radical at low stannane concentrations and high temperatures (80 °C).

Scheme 23. Guo and coworkers’ ONIUM calculations [42] of the energies involved in the transition of the α-cyclopropylvinyl radical 92 into the homoallenyl radical 93 at 298 K. A significant activation energy barrier E_a of +10.7 kcal mol⁻¹ has to be overridden for ring-opening to occur. However, after this has been surmounted, the overall transition is exergonic to the tune of −4.3 kcal mol⁻¹.
mechanically responsible for generating the reduced allenylstannane 66 from the hypothetical stannylnyl vinyl cation 58, it is inconceivable that none of the ring-cleaved alcohol 84 would also not have been competitively formed under such circumstances, if one assumes, of course, that a normally unfavorable nucleophilic cyclopropane ring-opening was genuinely competitive, as would have to be claimed by the mechanism 3 team [10] (vide infra).

This conspicuous fact, plus the added observation that the other much more likely products of nucleophilic H2O trapping of the alleged stannylnyl vinyl cation 58, namely, the stannyl enone 62, the aldol 61, and the lactone 63 were each not seen in any of our crude reaction mixtures, even when the H2O was present in excess (Scheme 21, Entries 7–12), unambiguously rules out a stannylnyl vinyl cationic intermediate in this reaction pathway. These clear-cut observations once more explicitly demonstrate that the stannylnyl vinyl radical (2)-64 must be the authentic and true progenitor of the products 67 and 66.

Now although the presence of up to 20% H2O in the THF did not adversely affect this hydrostannation reaction (the reaction outcomes typically being very similar to those in dry THF), we did notice that the product yields markedly diminished as the H2O content of the reaction mixture started to rise significantly, despite each of these reactions still looking as though they were complete by TLC analysis (Scheme 21, Entries 7–9).

If we now progress our discussion, and focus specifically on Scheme 21, Entry 10, it can again be seen that the alkyne 57 was converted into the hydrostannylated products 67 and 66 in very good yield (86%, ratio of 67:66 = 9:2:1) in THF/H2O (4:1) at 0.2 M substrate concentration using 2 equiv of Ph3SnH at rt for 7 h. The high overall product yield obtained from this reaction, despite a greatly reduced amount of stannane being used, again weighs heavily against the formation of a stannylnyl vinyl cation intermediate in this reaction, since such an \( \alpha \)-stannylnyl vinyl cation would almost certainly undergo significant facile Stang-Muller elimination back to the starting acetylene [39] if a strong nucleophile such as H2O was present in such excess [39]. Yet, virtually none of the starting alkylnol 57 remained after 7 h at rt.

The same is true for the rt hydrostannation conducted with a much greater quantity of Ph3SnH (4 equiv) in THF/H2O (4:1) at 1 M substrate concentration (Scheme 21, Entry 5), where complete product conversion occurred, with no starting acetylene 57 remaining at reaction end (see TLC in the ESI). Now if Stang-Muller elimination [39] was occurring (Scheme 16), as one might legitimately expect if a stannylnyl vinyl cation was genuinely involved in the reaction pathway, one would expect to see little reaction progression, and the starting alkyne 57 would always be returned; even if a massive excess of stannane was used, simply because such an eliminative pathway would constantly keep recurring until all of the excess stannane had been converted into Ph3SnOH. However, in Entry 5, we see the vinylstannane 67 (R = Ph) being formed in high yield (83%) with no starting material remaining.

Now when the hydrostannation of 57 was performed at lower Ph3SnH concentration (2 equiv), in a mixture of THF/H2O (4:1) at elevated temperature (50 °C) for 7 h (Scheme 21, Entry 11), the proportion of stannylallene 66 increased significantly; with a 1:3:1 ratio of 67:66:66 now being formed in a combined overall yield of 77%. As found by Crandall [36] and Malacria et al. [37] in the \( \alpha \)-cyclopropylnvinyl radical ring-opening reactions shown in Scheme 22, working at higher dilutions and higher reaction temperatures with lower quantities of stannane quite profoundly affected the reaction outcome. Thus, in the presence of less stannane, the intermediary stannylnyl radical 64 now had a much longer lifetime in the reaction mixture, and at elevated temperatures it was thus able to channel significantly down the path of radical ring-opening. However, because the Ph3SnH was still present in significant excess, stannylnylvinyl radical H-atom abstraction from the stannane competed significantly at 50 °C. Nonetheless, heating at a much higher reaction temperature (80 °C) with an identical quantity of Ph3SnH (2 equiv) (Scheme 21, Entry 12) did start to promote more of the radical-induced \( \beta \)-scission event, as one might expect from Guo’s theoretical analysis [42] of the ring-opening of the \( \alpha \)-cyclopropylnvinyl radical 92 into its ring-opened homo-allenyl radical 93, since this extra energy input allows the activation energy barrier to be more readily surmounted for the transition of radical 64 into its stannyl homoallenyl radical counterpart 65.

To further confirm these outcomes with Ph3SnH/cat. Et3B in THF/H2O (Scheme 21, Entries 4–12), we also duly examined the O-directed free radical hydrostannations of 57 in PhMe/MeOH and PhMe/EtOH (Scheme 21, Entries 13, and 14). In the former case, the outcome essentially mirrored that of Entry 1 including for the product yield, while for Entry 14 we saw a greatly increased amount of the reduced ring-opened stannylallene being formed, in much lower overall product yield. It would appear that the presence of EtOH in these reactions has a detrimental effect on reaction performance, which is a point worth noting for the future.

Not too surprisingly, based on our past work with Bu3SnH and cat. Et3B for the O-directed hydrostannation of propargyloxy alkyl acetylenes, we found this particular reagent combination to be far inferior for the room temperature O-directed free radical hydrostannation of 57 than Ph3SnH, with the yield of 67 (R = Bu) from the Bu3SnH reaction plummeting, it being some 30% lower than that obtained from the Ph3SnH mediated process, despite 4 equiv of high quality tin hydride being used at 1 M substrate concentration in both cases (compare Scheme 21, Entries 1 and 15), and the integrity of the Bu3SnH having been checked before it was used (see the General Information description in Part B of our ESI).

Moreover, our added finding that the stannylnyl radical induced cyclopropane ring-cleavage product 66 (R = Bu) massively predominated in the Bu3SnH mediated reactions at 80 °C, at higher dilution (0.1 M alkyne substrate concentration, 2 equiv Bu3SnH) (Scheme 21, Entries 17–21), further powerfully illustrated the much poorer ability of Bu3SnH to serve as a H-atom donor towards \( \alpha \)-stannylnyl radicals.

Indeed, the outcomes in Scheme 21 very clearly demonstrate the vastly inferior performance of Bu3SnH in the O-directed free radical hydrostannation reactions of alkyl acetylenes more generally, in stark contrast to various claims otherwise [10]. Only rarely does one ever obtain a comparable yield for the two processes for most substrates [1], and the vastly superior performance of Ph3SnH/cat. Et3B in most such O-directed free radical hydrostannation reactions is why we originally recommended [2] its preferential use over Bu3SnH/cat. Et3B in 2005 [2]. We have also typically not found that operating at higher reaction temperatures markedly improves reaction outcomes in more complex systems, despite various claims that it does [10].

Another point to note from our studies on the probe 57 is how the mode of initiation (either cat. Et3B/O2 or AIBN) makes little real difference to the outcome in the Bu3SnH reactions at elevated temperatures. The results of Scheme 21, Entries 17 and 21, particularly emphasize this point.

However, one interesting effect that did reveal itself in the Bu3SnH hydrostannation reactions mediated at elevated temperature, was the marked effect that solvent could have on the rate of stannylnyl radical H-atom abstraction; with the presence of highly polar H2O noticeably affecting the outcome in the THF/H2O systems, it guiding the outcome more towards the vinylstannane product 67 (R = Bu), unlike its less polar solvent counterparts THF, C6H6, and PhMe (Scheme 21, Entries 17–21).

While this polar solvent effect might well reflect a possible coordinative event between the Bu3SnH and the H2O causing a
lengthening and weakening the Sn–H bond, to facilitate H-atom abstraction by the stannylnal radical, these differences of outcome in the various solvents might simply be a reflection of how well the various solvents each solvate the respective transition states for cyclopropylvinyl radical β-scission and H-atom abstraction. The profound effect that a change in solvent can have on shifting the balance from competitive radical induced β-scission to H-atom abstraction is now well documented in the radical field, including by workers such as Walling [43] and Ingold [44] to name but a few. However, the manifestation of these polar effects here is really quite striking.

So, to finalize our discussion of our individual experimental results with the probe 57, the tabulated data of Scheme 21 very clearly shows that only two stannylated products ever emerge from these hydrostannation reactions, and these are compounds 67 and 66, even when powerful external nucleophiles such as H2O or alcohols are present in the reaction mixture, in far greater excess than the stannane.

Such an observation only satisfactorily aligns itself with the intermediacy of a stannylnal α-cyclopropylvinyl radical [36–38], not an α-stannylnal vinyl cation, and this outcome powerfully reconfirms the entirely free radical mechanism of the dialkyl acetylene hydrostannation reaction (mechanism 1) [1,2,5,11–15].

Although we are presently working towards elucidating the relative contributions of the key frontier molecular orbital interactions [45] that likely govern the cyclopropane ring-opening of stannylnal vinyl radical (Z)-64, our current thinking has the low lying Walsh 4e− (W4) LUMO of the cyclopropane strongly interacting with the adjacent stannylnal radical SOMO to promote an anti-bonding interaction within the C1−C2 bond of the cyclopropane, which would clearly favor its cleavage at higher temperatures (Scheme 24). Concurrently, we also envision that the high-energy 3e− (W2) HOMO of the cyclopropane will strongly interact with the vinyl radical SOMO to initiate the process of C=C double bond formation and creation of the new stannylallene 66. It could well be that the same high lying 3e− (W2) HOMO of the cyclopropane is also interacting with the vinylstannane π* LUMO, and once more, heating could be facilitating this destabilizing antibonding interaction. Yet again, this would be expected to lengthen and weaken the C1−C2 cyclopropane bond, while also shortening and strengthening the C2−C3 bond. Such frontier molecular orbital interactions [45] could equally well be determining reactivity in either a bent or a linear α-stannylnal vinyl radical.

While the above frontier orbital analysis is currently only tentative, and not based upon any natural bond orbital (NBO) modeling [12], it does potentially provide some insights into why stannylnal homoolynal radical formation does proceed quite readily from 64 when external heating is applied [42,46]. It also plausibly rationalizes why higher reaction temperatures, lower stannane concentrations, and the use of the much poorer H-atom donor Bu3SnH, each strongly favor divergence down the cyclopropyl vinyl radical β-scission path. Clearly external heating of the α-stannylnal vinyl radical 64 provides the requisite activation energy needed to induce the critical bond distortions and electronic transitions needed to bring about successful cyclopropane ring-opening, while lower stannane concentrations and use of the poorer H-atom donor Bu3SnH help to increase the lifetime of the stannylnal vinyl radical 64 (R = Bu) in solution to help promote its β-scission.

By way of contrast, the stannylnal cation mechanism fails to satisfactorily account for how lower substrate and tin hydride concentrations and higher reaction temperatures could possibly be favoring formation of the stannylallene 66 in entries 3 and 12, and 17−21 of Scheme 21, while a high stannane and substrate concentration massively favors formation of the vinylstannane product 67 in entries 2 and 15.

While our two-step, entirely free radical, mechanism does very nicely explain this observation, due to a lower stannane and alkylne concentration both greatly disfavoring H-atom abstraction by 64, and the latter event promoting more vinyl radical β-scission at higher reaction temperatures, the rival stannylnal cationic mechanism involving 58 does not provide any truly convincing explanation for why the ratio of 67:66 should change so dramatically as the stannane and probe 57 concentration changes, nor the quite dramatic effects of raising the reaction temperature!

Indeed, a comparison of entries 2 and 17 (Scheme 21) is really quite striking in this regard where opposite product ratio extremes are observed at 80 °C. Clearly, it is hard to imagine how the stannylnal cationic mechanism [10] could ever plausibly explain such concentration and temperature dependent effects so cogently.

Another powerful insight that has emerged from our study of the hydrostannation of 57 concerns the great reluctance with which the doubly branched sterically hindered (Z)-vinylstannane systems of structure 67 (R = Bu or Ph) undergo (Z)- to (E)-vinylstannane isomerization [1] under the reaction conditions that we have employed, even at elevated temperatures. The fact that cyclopropylicarbinyl radicals generally undergo rapid ring-opening (Ea = 5.9 kcal mol−1 with a k = 9.4 × 107 s−1 − 1.3 × 108 s−1) [25] once generated, yet no doubly-stannylnal ring-opened products are seen in our reactions, very strongly suggests that tin radical addition is not occurring readily to such vinylstannane systems, at least not at the olefinic carbon bearing the Sn, or if it is, eliminative β-scission must be occurring before isomerizing central C−C bond rotation can proceed in the initially formed adducts.

Likewise, it is not possible to rule out the possibility that tin radical addition is occurring with much greater facility at the other less hindered olefinic carbon adjacent to the cyclopropane, and that we are simply not observing (Z)- to (E)-isomerization due to the subsequent elimination being extremely fast [1], and there being a significant steric repulsive barrier opposing the 180° C−C bond rotation needed to allow eliminative isomerization.

Scheme 24. The possible key frontier molecular orbital interactions [45] that might be helping to promote thermally mediated β–scissive cleavage of the cyclopropane ring in the likely more populated Boltzmann conformer (Z)-64 at elevated temperature.
3. A summary of our main conclusions

So, to conclude, one can summarize the main key point of our present paper in the following highly simplified way. Basically, one of the fundamental principles of the stannylvinylic cation mechanism theory (mechanism 3) [10] is that the postulated O₂-mediated single electron transfer (SET) from the stannylvinylic radical 64 to O₂ must irreversibly lead to the stannylvinylic cation 58 at a rate faster than H-atom abstraction from the stannane by the stannylvinylic radical (Z)-64.

Such a definitive tenet implies that the above SET is possibly occurring with a rate constant that is significantly greater than the k of 3.2–3.7 x 10⁸ mol⁻¹ s⁻¹ for the H-atom abstraction from Bu₃SnH by a typical vinylcyclopropane radical at rt (although the k for Ph₃SnH would likely be at least 3–5 times greater, due to it being a far superior H-atom donor towards carbon-centred free radicals more generally [30]).

Now given that mechanism 3 [10] requires the postulated α-stannylbicyclopropylvinyl cation 58 (R = Ph) to form in its entirety, before the α-stannylbicyclopropylvinyl radical (Z)-64 (R=Ph) can abstract a H-atom from the stannane, this will inevitably mean that if it was genuinely being formed, the fully rearranged cation 58 would be more than capable of being readily trapped by the huge excess (5–271 equiv.) of H₂O that would be present in the reaction medium (see Scheme 21, Entries 4–12), before any ionic reduction by the much lower quantity of Ph₃SnH could possibly occur to give 67.

This is because the direct ionic nucleophilic reduction of 58 by the Ph₃SnH would simply not be able to satisfactorily compete with the much faster rate of cation trapping by the H₂O. This is due to the rate constant for the H₂O trapping of most typical vinyl cations typically being very fast and lying between 1.3 x 10²⁷ M⁻¹ s⁻¹ and 2.9 x 10²⁷ M⁻¹ s⁻¹ at 20 °C according to Lodder [21] and Mayr [27] (Scheme 9), which is significantly faster than the rate of ionic reduction of the well-known vinyl cation surrogates (p-MeOCH₂CH₂)₂C(=O)⁺ by Ph₃SnH [26] which, according to Mayr and coworkers [27], has essentially the same reactivity as a typical vinyl cation (e.g. 38) towards a wide range of nucleophiles, and would thus translate to a k = 3.26 x 10⁸ M⁻¹ s⁻¹ in CH₂Cl₂ at 20 °C (Scheme 9), which is much slower.

In light of the fact that the vinyl cation surrogates (p-MeOCH₂CH₂)₂C(=O)⁺ reacts fairly slowly with Ph₃SnH at 20 °C, this must thus be immediately apparent that H₂O-trapped products will form far more readily than their ionically reduced counterparts given the k values of Lodder [21] and Mayr [27] for the corresponding trappings of the same carbeneium ion 39 (Scheme 9) by H₂O, and related vinyl cations [21,27]. The same would thus likely be true for the stannylvinylic cation 58, if it was a genuine intermediate in these hydrostannation reactions, and H₂O was present in far greater excess than the Ph₃SnH, as it is in Scheme 21, Entries 4–12; and the alleged Ph₃Sn⁺ cation was also able to withstand the presence of the H₂O, to continue the alleged O₂-mediated catalytic cycle of mechanism 3 [10].

If one continues further with this analysis, and one extrapolates the aforementioned ionic reduction rate constant data to Bu₃SnH, which, according to Mayr et al. [26b] reacts approximately 354 times faster than Ph₃SnH in the ionic reduction of the 4,4'-bis(dimethy lamino)benzhydrylum ion, this would translate to an estimated rate constant for the corresponding reduction of the (p-MeOCH₂CH₂)₂C(=O)⁺ cation of k = 1.15 x 10²³ M⁻¹ s⁻¹ at 20 °C. Assuming that this k value is similar to that for ionic reduction of the stannylvinylic cation 58, this would again not allow ionic reduction by Bu₃SnH to successfully outpace the H₂O trapping of 58 which, if it was more stable than the (p-MeOCH₂CH₂)₂C(=O)⁺ cation, would actually react even more slowly with tin hydrides based upon Mayr’s data on the ionic reduction of the highly stabilized 4,4'-bis(dimethy lamino)benzhydrylum ion with stannanes [26b].

So, Mayr’s highly valuable data [26b], when considered alongside our own experimental findings on the probe 57 in THF/H₂O (Scheme 21) [14], suggest very strongly that mechanism 3 cannot be a viable mechanism for these O-directed free radical hydrostannation reactions.

Thus, the fact that we do not see any H₂O trapped products such as 61, 62 or 84 in our reaction mixtures in Scheme 21 Entries 4–12 and 18–19 very clearly indicates that such highly stabilized stanny lvinylic cations are almost certainly not forming, and that the two observed reduction products 67 and 66 (R = Ph, Bu) are solely arising through an entirely free radical mechanism involving 64.

Now it is important to note here that it will not actually matter whether the k for stanny lvinylic radical H-atom abstraction from Bu₃SnH will be larger or smaller than the estimated k of 1.3-2.9 x 10⁴ mol⁻¹ s⁻¹ for H₂O trapping [21,27] by the putative stanny lvinylic cation 58, since according to the proposers of mechanism 3 [10], all of the stanny lvinylic radical 64 will immediately be converted into the stanny lvinylic cation 58 before the intermediary stanny lvinylic radical 64 will ever have any opportunity to homolytically H-atom abstract from the stannane.

Therefore, this key theoretical tenet and requirement of the stanny lvinylic cation mechanistic theory (mechanism 3), and the lack of any observed H₂O-trapped enol-derived side products such as 62 strongly rules against the intermediary of a stanny lvinylic cation in these hydrostannation reactions. Even moreso, given that the alleged stanny lvinylic cation 58 would be triply stabilized and have a sufficient lifetime to be even more readily captured by nucleophiles, based upon Bergman and Sherrerd’s [40], and Muller and Stang’s collective results [39]. So, again, the lack of observed enol-derived products in the aqueous THF hydrostannation runs, and the long known much faster rate of a stabilized vinyl cation trapping by H₂O [21,27], compared with the rate of ionic reduction of the vinyl cation surrogate 39 (Scheme 9) by Ph₃SnH [26], must inevitably mean that 66 is arising purely from the stanny lvinylic radical 64 by the mechanism shown in Schemes 15 and 2 viz. via mechanism 1.

The added observation that we did not observe the nucleophilically ring-opened primary stannylallenyl alcohol 84 from the direct SO₂ attack of H₂O on 58 (Scheme 20) or H₂O attack on its stannyl homoallenyl carbonation 83 (Scheme 19) in Scheme 21, Entries 4–12, further argues again against 66 arising from an analogous ionic reduction of 58 by the stannane. Consequently, this too counts as good hard experimental evidence against mechanism 3. The additional finding that we did not encounter any E1 elimination product 68 (Scheme 16) in our reaction mixtures further argues strongly against the possible formation of a ring-cleaved stannyl homoallenyl cation 83 (Scheme 19). Stanny llene 68 would almost certainly have co-arisen had the primary carbonation 83 been the predominant source of 66 (Scheme 16).

The finding that all of our hydrostannations progressed to completion in Scheme 21 at high stannane concentration further banks against the operation of a Stang-Muller eliminative nucleophilic attack [39] by H₂O on the hypothesized stanny lvinylic cation 58 (Scheme 16), despite this long being known to be the preferred mode of reaction of stanny lvinylic cations with even quite weak nucleophiles.

Thus, we believe that it is entirely reasonable for us to question the very existence of this much publicized stanny lvinylic cation intermediate [10] from the mechanism 3 team [10], and that we refer to it as “the stanny lvinylic cation that never was”, since so far, 7 years on, not a single piece of corroborative experimental evidence has ever been put forward by any team [10,19] to genuinely confirm its
existence (Scheme 8) in such O-directed free radical hydrostannation reactions, and based upon the data that we presently have at hand, we are in significant doubt about whether such evidence will ever be produced in the future.

As well as this, in the THF/H2O reaction runs that we examined (Scheme 21, Entries 18 and 19), it is mechanistically implausible that the reduced stannyllene 66 could ever arise in such large quantity (47–59% isolated yield) from pseudo-Sn2 or Sn1 cyclopropane ring-cleavages of the postulated stannylinyl cation 58 by Bu3SnH, without the co-formation of the primary stannyllalenyl alcohol 84 (R = Bu) (Scheme 21) in substantial quantity as well.

In this regard, Bergman and Sherrod’s 1971 results [40] (see Schemes 17 and 18) are quite unambiguous, for they have conclusively shown that the ring-opening of α-cyclopropyl vinyl cations with strong nucleophiles is generally a highly disfavored process. Indeed, their classic mechanistic work [40] of 1971 definitively reveals that nucleophiles always prefer to attack α-cyclopropylvinyl cations at the vinylic carbon bearing the positive charge, and they do this virtually exclusively.

As well as this, stannanes are well-known to be very poor ionic hydride donors towards carbocations [27], due to the Sn–H α-bonding orbital often being far too low in energy to be able to readily donate its electrons into the requisite unoccupied vinyl cationic p-orbital, which would be much higher in energy.

So, the above hydrostannation outcomes with the alkynol 57 in THF/H2O (Scheme 21) very powerfully rule against the intermediacy of stannylvinyl cations in these hydrostannation reactions, and when this new data is considered alongside our prior 2005 radical cyclization work on 23, and Alabugin’s 2015 results, this collective body of evidence very strongly points to mechanism 1 being the primary arbiter of hydrostannation outcome under the room temperature, high stannane concentration, conditions that are typically employed to mediate most such reactions with stannanes and cat Et3B.

While our rt hydrostannation studies on the alkynol probe 23 (Schemes 5 and 13) have quite clearly demonstrated that mechanism 2 [18] can operate in these reactions, at very low stannane and substrate concentrations, such experimental conditions generally give rise to very poor levels of α-regiocontrol. They also result in rather disappoointing product conversions and yields, in contrast to what is typically observed when such Ph3SnH mediated hydrostannation reactions are run at much higher stannane concentrations, which is our specific recommendation whenever deploying this reaction.

Yet another synthetically useful result that has emerged from our new 2019–2020 hydrostannation studies on the probe 23 is our finding that lower reaction temperatures significantly increase the amount of α-stannylated product 26, relative to 27 and 55. Importantly, as well, under these circumstances, one is still able to record a marked change in the α:β-product ratio if one varies the Ph3SnH concentration, in full accord with our previous experimental findings at rt.

Thus, our latest data on the alkynol 23 once more very strongly rules against mechanism 2 [18] playing a significant controlling role in the free radical hydrostannation of propargyloxy dialkyl acetylenes at quite high stannane concentrations.

The collective results reported here thus strongly align with the operation of mechanism 1 [1,2,9,12,14] under the normal, high stannane concentration, conditions that one typically employs in these hydrostannation reactions. Future work from our laboratory will examine further the effects of high and low temperature on alkyn hydrostannation reactions run under free radical initiated conditions, and hopefully this work will delineate further how temperature can modulate both reaction outcome and mechanism.

4. Experimental section

The augmentation of our 2005 work [9] with probe 23:

4.1. (4S,5R,E)-5-(tert-butyldimethylsilyloxy)-4,6-dimethyloct-6-yn-1-ol (23)

The following new experimental procedure is now considered superior and far more convenient for the preparation of the alkynol 23 [9a] and it totally avoids the use of pyrophoric n-BuLi under cryogenic conditions. It exploits our recently developed excellent new Carreira [47] terminal alkyne hydroxymethylation procedure which uses Zn(OTf)2/ Et3N/TMEDA [48] in PhMe at 60 °C with solid paraformaldehyde to accomplish this novel C–C bond-forming process reliably in good yield. The new improved procedure for securing 30 is as follows:

To a stirred solution of Zn(OTf)2 (16.42 g, 45.16 mmol) (1.9 equiv) in dry PhMe (100 mL) under N2 was added freshly distilled dry Et3N (6.63 mL, 47.54 mmol) (2 equiv) followed by TMEDA (7.13 mL, 47.54 mmol) (2 equiv) via syringe. The resulting suspension was then stirred vigorously at rt for 2 h before a solution of known alkynol 94 [9,49] (6 g, 23.77 mmol; see footnote 49 for the structure of 94) dissolved in dry PhMe (15 mL) was added via cannula. The flask was further rinsed with a second portion of dry PhMe (5 mL), and the ensuing solution added via cannula. The resulting mixture was then stirred for 20 min before solid (HCHO)n (3.57 g, 118.85 mmol, 5 equiv) was added in a single portion, after which the reaction mixture was heated at 60 °C for 4 days. The reaction was then quenched by diluting with EtOAc (300 mL) and saturated aqueous NH4Cl (150 mL). The layers were then separated and the aqueous layer further extracted with EtOAc (3 × 100 mL). The combined organic layers were now dried over MgSO4, filtered, and concentrated in vacuo. The crude residue was purified by SiO2 flash chromatography with Petrol/EtOAc as the eluent (gradient elution from 100:1 to 5:1 then 20:1 then 10:1) to afford the alkynol 23 (4.94 g, 74%) as a clear colorless oil. Its spectral properties matched closely with those reported previously [9].

1H NMR of 23 (600.13 MHz, CDCl3, 298 K) δ 5.39 (q of sextets, 1H, J = 1.2 Hz, 6.6 Hz, −(C(Me))Me = (C(Me))Me). 4.16 (d, 2H, J = 1.8 Hz, HOCH2CC−), 3.77 (d, 1H, J = 7.8 Hz, −CH(Me)−OTBS), 2.53 (complex m, 1H, −CH(Me)−), 1.81 (br s, 1H, HOCH2CC−), 1.57 (dq, 3H, J = 1.2 Hz, 6.6 Hz, −(C(Me))Me = (C(Me))Me), 1.53 (m, 3H, C(Me) = (C(Me))Me), 1.13 (d, 3H, J = 7.2 Hz, −CH(Me)−), 0.84 (s, 9H, t-Bu of OTBS), 0.004 (s, 3H, Me of OTBS), −0.07 (s, 3H, Me of TBS) ppm. 13C NMR of 23 (150.9 MHz, CDCl3, 298 K) δ 136.3 ((C(Me))Me = (C(Me))Me), 121.8 ((C(Me))Me = (C(Me))Me), 88.7 (HOCH2CC−), 81.9 (−C(OTBS)−), 79.8 (HOCH2CC−), 51.2 (HOCH2CC−), 31.5 ((C(Me))Me), 25.8 (3 x Me of t-Bu of OTBS), 18.2 (MeC of t-Bu of OTBS), 17.2 (−CH(Me)−), 12.9 ((C(Me))Me = (C(Me))Me), 11.1 ((C(Me))Me = (C(Me))Me), −4.8 and −5.2 (2 x Me of OTBS) ppm.

(2Z,4R,5R,6E)-5-(tert-butyldimethylsilyloxy)-4,6-dimethyloct-6-yn-1-ol (23)

*Ph3SnH (10 equiv), Et3B (0.1 equiv), PhMe (c of 23 = 1 M), 20–24 h*

Inside a glove bag filled with dry N3, Ph3SnH (1.49 g, 4.24 mmol)
(10 equiv) was accurately weighed out into an open-necked round-bottomed flask equipped with a magnetic stirring bar. Whilst still inside the glove bag, and while maintaining the N₂ atmosphere, the reaction vessel was fitted with a closed 3-way tap with a Quickfit male joint. The sealed flask was then removed from the N₂-filled glove bag and connected to a vacuum line with rubber hose via the 3-way tap, which was also fitted with an N₂-filled balloon. It was then sequentially evacuated and purged with N₂ from the balloon before the reaction flask was transferred to a hot-plate stirrer located inside a fume-cupboard. The contents of the reaction flask were then stirred under N₂ while a solution of alkynol [23] (119.9 mg, 0.424 mmol) in dry PhMe (0.42 mL) was added dropwise via cannula from a small septum-sealed pear-shaped flask fitted with an N₂-filled balloon. To this stirred slurry of the Ph₃SnH and [23] at 20 °C was then successively added Et₂Sb (0.04 mL, 1 M solution in hexane, 0.04 mmol) (0.1 equiv) dropwise over 5 s via syringe, followed by air (5 mL, from a syringe) 5 min later. The reagents were then stirred at 20 °C under N₂ for 24 h, after which, the reaction mixture was concentrated in vacuo. A tiny portion of the crude residue was taken and dissolved in CDC₁₃ and submitted for ¹H NMR spectroscopy to ascertain the crude ratio of the products. In this instance, this revealed that the α:β-addition ratio [26, 27/55] was 6.8:1. The remaining crude concentrated residue was then purified by gradient elution SiO₂ flash chromatography using initially 3:1 then 2:1 then 1:1 Petrol:CH₂Cl₂ to remove excess tin hydride, followed by 50:1 to 40:1 Petrol:EtOAc to afford the α-vinylstannane product [26] (175.5 mg, 65%) as a clear oil. Finally eluted with 30:1 Petrol:EtOAc furnished the uncyclized β-vinylstannane [55] (25.4 mg, 9%) as a slightly impure clear oil.

The 600 MHz ¹H NMR data of [26] in CDC₁₃ matched up well with our previously reported 500 MHz ¹H NMR spectral values in CDC₁₃ [9a]. The new confirmatory spectral data for [26] are as follows: ¹H NMR data of [26] (600.13 MHz, CDC₁₃, 298 K) δ 7.68–7.56 (m, 6H, Ph), 7.39–7.32 (m, 9H, PhH), 6.41 (dt, 1H, J = 10.2, 12.7 Hz, ²⁷⁰⁰Sn=H – 163.8 Hz, ²⁷⁰⁰Sn-H – 156.6 Hz, HOCH₂C(SnPh₃)=C(H)-), 5.18 (q quint, 1H, J = 1.2 Hz, 6.6 Hz, -(Me)-C(H)-), 4.30 (dd, 2H, J = 1.2 Hz, 6.0 Hz, ²⁷⁰⁰Sn=H – 154.0 Hz, ²⁷⁰⁰Sn-H – 151.6 Hz, -(CH₂OH)-), 3.60 (d, 1H, J = 4.8 Hz, -CH(OTBS)-), 2.23 (complex m, 1H, -(CHMe)-), 1.46 (dt, 3H, J = 12 Hz, 6.6 Hz, -(Me)=C(=MeH), 1.36 (t, 1H, J = 6.0 Hz, -CH₂OH), 0.92 (s, 3H, -(Me)=C(=MeH)), 0.86 (s, 9H, t-Bu), 0.71 (d, 3H, J = 6.6 Hz, -(CHMe)-), –0.02 (s, 3H, TBS-Me), –0.12 (s, 3H, TBS-Me) ppm. The new spectral and physical data for previously uncharacterized [55]: [x]D = –16.5 (c 0.41, CH₂Cl₂); IR (neat) 3431 (br s), 3065 (m), 2955 (s), 2928 (s), 2855 (s), 1461 (m), 1430 (s), 1388 (m), 1267 (s), 1047(s), 874 (m), 838 (s), 780 (s), 733 (s), 701 (s), 455 (m). ¹H NMR data for [55] (600.13 MHz, CDC₁₃, 298 K) δ 7.59–7.47 (m, 6H, Ph), 7.39–7.30 (m, 9H, PhH), 6.45 (dt, 1H, J = 10.2, 12.7 Hz, ²⁷⁰⁰Sn=H – 163.8 Hz, ²⁷⁰⁰Sn-H – 156.6 Hz, HOCH₂C(SnPh₃)=C(H)-), 5.18 (q quint, 1H, J = 1.2 Hz, 6.6 Hz, -(Me)-C(H)-), 4.30 (dd, 2H, J = 1.2 Hz, 6.0 Hz, ²⁷⁰⁰Sn=H – 154.0 Hz, ²⁷⁰⁰Sn-H – 151.6 Hz, -(CH₂OH)-), 3.60 (d, 1H, J = 4.8 Hz, -CH(OTBS)-), 2.23 (complex m, 1H, -(CHMe)-), 1.46 (dt, 3H, J = 12 Hz, 6.6 Hz, -(Me)=C(=MeH), 1.36 (t, 1H, J = 6.0 Hz, -CH₂OH), 0.92 (s, 3H, -(Me)=C(=MeH)), 0.86 (s, 9H, t-Bu), 0.71 (d, 3H, J = 6.6 Hz, -(CHMe)-), –0.02 (s, 3H, TBS-Me), –0.12 (s, 3H, TBS-Me) ppm.

Inside a glove bag filled with dry N₂, Ph₃SnH (0.22 g, 0.627 mmol) (1 equiv) was accurately weighed out into an open-necked round-bottomed flask equipped with a magnetic stirring bar. The reaction vessel was fitted with a closed 3-way tap with a Quickfit male joint while still inside the glove bag. The sealed flask was then removed from the glove bag and connected to a vacuum line and hose via its 3-way tap. The latter was also fitted with an N₂-filled balloon. The flask was then sequentially evacuated and purged with N₂ from the balloon before being transferred to a hot-plate stirrer located inside a fume-cupboard. The contents of the reaction flask were then stirred under N₂ while a solution of alkynol [23] (177 mg, 0.627 mmol) in dry PhMe (25.1 mL) was added dropwise via cannula from a small septum-sealed pear-shaped flask also fitted with an N₂-filled balloon. To this stirred mixture of the Ph₃SnH and [23] at 20 °C was then added Et₂Sb (0.06 mL, 1 M solution in hexane, 0.06 mmol) (0.1 equiv) dropwise via syringe, followed by air (5 mL, from a syringe), 5 min later. The reagents were then stirred at 20 °C for 24 h, after which, the reaction mixture was concentrated in vacuo and a ¹H NMR spectrum was recorded of a tiny portion of the crude residue in CDC₁₃ to ascertain the crude ratio of products. In this particular instance, this revealed that the α:β-addition ratio [26, 27/55] was 1:2. The remaining crude concentrated residue was then purified by gradient elution SiO₂ flash chromatography using 3:1 then 2:1 then 1:1 Petrol:CH₂Cl₂ to remove the excess tin residues, followed by 50:1 Petrol:EtOAc to afford the cyclized β-vinylstannane product [27] (116 mg, 29%) as a clear oil. Further elution with 40:1 Petrol:EtOAc furnished the α-vinylstannane [26] (84 mg, 21%) as a clear oil and finally 30:1 then 20:1 then 10:1 petro-:EtOAc allowed the starting alkynol [23] (49 mg, 28%) to be recovered as a clear oil. Because of the very similar TLC mobility of the starting alkynol [23] and the uncyclized β-vinylstannane [55], in this instance, we were unable to isolate it in pure condition following SiO₂ flash chromatographic purification.

New confirmatory spectral data for [27]: ¹H NMR (600.13 MHz, CDC₁₃, 298 K) δ 7.63–7.51 (m, 6H, Ph), 7.38–7.29 (m, 9H, PhH), 4.09 (dd, 2H, J = 1.8 Hz, 6.0 Hz, -CH₂OH), 3.76 (d, 1H, J = 5.4 Hz, -CH(OTBS)), 2.71 (m, 1H, -(CHMe)-), 1.45 (m, 2H, -(CHMe)-), 1.08 (t, 1H, J = 6.0 Hz, -CH₂OH), 1.05 (s, 3H, -(Et)=C(CH₃)), 0.92 (d, 3H, J = 7.2 Hz, -(CHMe)-), 0.90 (s, 9H, t-Bu of OTBS), 0.86 (t, 3H, J = 7.2 Hz, -(CHMe)-), 0.05 (s, 3H, Me of OTBS), 0.03 (s, 3H, Me of OTBS) ppm. This data matched extremely well with the previously published ¹H and ¹³C NMR spectra of [27] published in 2005 [9a].

4.1.3. Ph₃SnH (10 equiv), Et₂Sb (0.1 equiv), PhMe (c of 23 = 0.025 M), −5 to −10 °C, 3.5 h

Inside a glove bag filled with dry N₂, Ph₃SnH (0.52 g, 1.48 mmol) (10 equiv) was accurately weighed out into an open-necked round-bottomed flask equipped with a magnetic stirring bar. Whilst still inside the glove bag, and while maintaining the N₂ atmosphere, the reaction vessel was fitted with a closed 3-way tap with a Quickfit
male joint. The sealed flask was then removed from the N2-filled glove bag and connected to a vacuum line with rubber hose via the 3-way tap, which was also fitted with an N2-filled balloon. It was then sequentially evacuated and purged with N2 from the balloon before the reaction flask was transferred to a hot-plate stirrer located inside a fume-cupboard. The contents of the reaction flask were then stirred under N2 while a solution of allyl alcohol 23 (41.8 mg, 0.148 mmol) in dry PhMe (0.15 mL) was added dropwise via cannula from a small septum-sealed pear-shaped flask fitted with an N2-filled balloon. To this stirred slurry of the Ph3SnH and 23 at −5 to −10 °C was then successively added Et3B (0.015 mL, 1 M solution in hexane, 0.015 mmol) (0.1 equiv) dropwise over 5 s via syringe, followed by air (5 mL, from a syringe) 5 min later. The reactants were then stirred at −5 to −10 °C under N2 for 3.5 h, after which, the reaction mixture was concentrated in vacuo. A tiny portion of the crude residue was then dissolved in CDCl3 and submitted for 1H NMR spectroscopy to ascertain the crude ratio of the products. In this instance, this revealed that the χ:β-addition ratio (26:27/55) was 9:6:1. The remaining crude concentrated residue was then purified by gradient elution SiO2 flash chromatography using initially 3:1 then 2:1 then 1:1 Petrol:CH2Cl2 to remove excess tin residues, followed by 50:1 to 40:1 Petrol:EtOAc to afford the α-vinylstannane product 26 (47.8 mg, 51%) as a clear oil.

4.1.4. Ph3SnH (1 equiv), Et3B (0.1 equiv), PhMe (c of 23 = 0.025 M), −5 to −10 °C, 3.5 h

Inside a glove bag filled with dry N2, Ph3SnH (0.10 g, 0.285 mmol) (1 equiv) was accurately weighed out into an open-necked round-bottomed flask equipped with a magnetic stirring bar. The reaction vessel was fitted with a closed 3-way tap with a Quickfit male joint while still inside the glove bag. The sealed flask was then removed from the glove bag and connected to a vacuum line and hose via its 3-way tap. The latter was also fitted with an N2-filled balloon. The flask was then sequentially evacuated and purged with N2 from the balloon before being transferred to a hot-plate stirrer located inside a fume-cupboard. The contents of the reaction flask were then stirred under N2 while a solution of allyl alcohol 23 (80.5 mg, 0.285 mmol) in dry PhMe (11.4 mL) was added dropwise via cannula from a small septum-sealed pear-shaped flask also fitted with an N2-filled balloon. The flask was then sequentially evacuated and purged with N2 from the balloon before being transferred to a hot-plate stirrer and a 1H NMR spectrum was recorded of a tiny portion of the crude residue in CDCl3, to ascertain the crude ratio of products. In this particular instance, this revealed that the χ:β-addition ratio (26:27/55) was 1:9.1. The remaining crude concentrated residue was then purified by gradient elution SiO2 flash chromatography using 3:1 then 2:1 then 1:1 Petrol:CH2Cl2 to remove the excess tin residues, followed by 50:1 to 40:1 Petrol:EtOAc to afford the α-vinylstannane product 26 (45.9 mg, 25%) as a clear oil. Further elution with 30:1 then 20:1 then 10:1 petrol:EtOAc allowed the starting allyl alcohol 23 (36.5 mg, 45%) to be recovered as a clear oil. Because of the very similar TLC mobility of the starting allyl alcohol 23 and the uncyclized β-vinylstannane 55, in this instance, we were unable to isolate it in pure condition following SiO2 flash chromatographic purification.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank the Leverhulme Trust (Grant No RPG-2015-438) and the EPSRC (Grant GR/N20059/01) for their generous support of our hydrostannation work. HAW also thanks QUB and DEL for their provision of a Postgraduate Research Studentship.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131061.

References

[1] For a detailed review and Personal Account, entitled: “The O-Directed Free Radical Hydrostannation of Propargyloxy Dialkyl Acetylenes with Ph3SnH.cat. Et3B: A Refutal of the Stannylvinyl Cation Mechanism” see K.J. Hale, S. Manaviazar, H.A. Watson, Chem. Rec. 19 (2019) 238–310.
[2] P. Dimopoulos, A. Athlan, S. Manaviazar, J. George, M. Walters, L. Lazarides, A.E. Alley, K.J. Hale, Org. Lett. 7 (2005) 5369–5372.
[3] R. Willem, A. Delmotte, I. De Borger, M. Biesemans, M. Gielen, F. Kayser, E.R.T. Tiekink, J. Organomet. Chem. 480 (1994) 255–259.
[4] P. Dimopoulos, A. Athlan, S. Manaviazar, K.J. Hale, Org. Lett. 7 (2005) 5373–5376.
[5] S.P.H. Mee, V. Lee, J.E. Baldwin, Angew. Chem. Int. Ed. 43 (2004) 1132–1136.
[6] For a first rate review on the Baldwin-Lee cross coupling entitled: “Application of Copper(I) Salt and Fluorode Promoted Stille Coupling Reactions in the Synthesis of Bioactive Molecules” see: V. Lee Org. Biomol. Chem. 17 (2019) 9959–9123.
[7] Total synthesis of (−)-3R(+)–thionam C via O-directed free radical hydrostannation: (a) K.J. Hale, M. Grabski, S. Manaviazar, M. Maczka, Org. Lett. 16 (2014) 1164–1167; (b) K.J. Hale, S. Hatakeyama, F. Urabe, J. Ishihara, S. Manaviazar, M. Grabski, M. Maczka, Org. Lett. 16 (2014) 3536–3539; (c) For Professor Donohoe’s recent elegant total synthesis of (−)-3R(+)–thionam C, which provides citations to the total synthesis work done after 2014, see: S. Balecels, M.B. Haughey, J.C.L. Walker, L. Jose-Culliere, C. Towers, T.J. Donohoe Org. Lett. 20 (2018) 3583–3586; (d) For another fine total synthesis of (−)-3R(+)–thionam C which appeared after publication of the Donohoe total synthesis, and which describes the synthesis of other thionam family members, see: M. Kumar, L. Bromhead, Z. Anderson, A. Overy, J.W. Burton Chem. Eur J. 24 (2018) 16753–16756.
[8] For our double O-directed hydrostannation route to the C7-C(22)-sector of (−)-scutaphycin see: K.J. Hale, M. Maczka, A. Kaur, S. Manaviazar, Ostovar, M. Grabski Org. Lett. 16 (2014) 1168–1171.
[9] For our formal total synthesis of (−)-pumiliotoxin B via O-directed free radical hydrostannation, see: S. Manaviazar, K.J. Hale, A. LeFranc, Tetrahedron Lett. 52 (2011) 2080–2084; (b) For the total synthesis of (−)-pumiliotoxin B, see: N-H. Lin, L.E. Overman, M.H. Rabinowitz, L.A. Robinson, M.J. Sharp, J. Zablocki J. Am. Chem. Soc. 118 (1996) 9062–9072.
[10] P. Dimopoulos, J. George, D.A. Tocher, S. Manaviazar, K.J. Hale, Org. Lett. 7 (2005) 5377–5380 (b) Apart from the aforementioned paper proposing mechanism 1 for the O-Directed free radical hydrostannation of dialkyl acetylenes with Ph3SnH.cat. Et3B (see Scheme 2, herein), our 2005 paper was the very first in the field to suggest that a [−(−)-C−C−SnH3]− radical conjugative interaction might possibly be stabilizing the postulated β-triphenyl-stannylvinyl radical intermediates of these reactions. However, at the time we first made this proposal, we were unable either to computationally or experimentally support our very tentative suggestion and therefore, as an unreserved caveat to our very own proposal, we did specifically alert the community to a prior 1994 ab initio computational chemistry report from Lalitha and Chandrasekhar on related β-styrylvinyl radicals, where it was concluded that strong hyperconjugative stabilization was probably not that significant in such intermediates (see Lalitha, S.; Chandrasekhar, J. Proc. Indian. Acad. Sci. (Chem. Sci.) 1994, 106, 259–266). The Chandrasekhar work, which had been conducted with STO-3G and STO-3G* basis sets at the UMP2/6-31G* level, further based its mechanistic conclusions upon direct experimental comparisons with prior related ESR work that had been performed by Rhodes and Symons on α-β -(trimethylsilyl)vinyl radicals (see: Rhodes, C.J.; Symons, M. C.R. J. Chem. Soc. Faraday Trans. 2 1984, 84, 4495–4500), where it had been revealed that the more favourable mode of overlap in these systems was between the vinyl radical and the β-β-conjugation orbital. Given the close structural similarity of both sets of β-metalacrylnylvinyl radicals (where M = Si and Sn), we therefore qualified our tentative thinking with some words of cautionary note about what had previously been observed in β-styrylvinyl radical systems. While this did not in any way constitute a specific denial of the potential occurrence of hyperconjugative stabilization of β-stannylvinyl radical systems, it did make it clear that there was then no experimental
evidence then available to support such a suggestion and, if anything, there was actually a very good reason to think that it might not be significant. Since then, however, very powerful computational evidence has now been gathered by Professor Igor V. Alabugin and his team at FSU to support the idea that hyperconjugative delocalization (σSn-C=vinyl radical orbital) is contributing very significantly to stabilizing such β-stannylvinyl radicals to that of Sn-Sn = 27 kcal mol⁻¹. We refer readers to references 12 and 13 herein for details of these new NBO (natural bond orbital) calculations that have been performed by the Alabugin team, which now very strongly endorse our original 2005 thinking, which had first come about as a result of our experimental confirmation of the reversibility of these Ph-Sn radical additions (in references 2 and 9a), which inevitably must involve orbital interactions very similar to those involved in hyperconjugative stabilization. We thank a reviewer of our manuscript for requiring us to further clarify our original position on this matter, and we note that, in references 1 and 14, we had already endorsed the idea of β-Sn-C hyperconjugative interactions stabilizing the proposed stannylvinyl radicals (Z)-2 that had been invoked, following Professor Alabugin’s highly insightful computational work (reference 12) which, in our view, provided much needed mechanistic insights in this regard.

(a) R. Mertens, C. von Sonntag, Angew. Chem. Int. Ed. 52 (2013) 11334–11338;
(b) M. Alami, A. Hamze, O. Provot, ACS Catal. 9 (2019) 3437–3443;
(c) D.-S. Zhu, Z.-M. Mei, C.-S. Lu, W. Gao, Y.-T. Zhang, Y. Mu, Z.-M. Wang, Polyhedron 138 (2016) 7741–7749;
(d) M.-S. Oderinde, R.D.J. Froese, M.G. Organ, Angew. Chem. Int. Ed. 52 (2013) 11821–11826;
(e) C. von Sonntag, Angew. Chem. Int. Ed. 33 (1994) 1265–1268;
(f) E. S. Krijnen, J.-D. van Loon, G. Lodder, S. Steenken, J. Am. Chem. Soc. 137 (2015) 6349–6351;
[35] J.-A. Muller, Bull. Soc. Chim. Fr. 45 (1886) 438.
[36] J.K. Crandall, G.L. Tindell, A. Mannmade, Tetrahedron Lett. 23 (1982) 3769–3772.
[37] E. Mainetti, L. Fensterbank, M. Malacria, Synlett (2002) 923–926.
[38] K.K. Milnes, S.E. Gottschling, K.M. Baines, Org. Biomol. Chem. 2 (2004) 3530–3534.
[39] (a) L. Williamson, P.J. Stang, A.M. Arif, J. Am. Chem. Soc. 115 (1993) 2590–2597;
(b) F.J. Stang, V.V. Zhdankin, R. Tykwinski, N.S. Zefirov, Tetrahedron Lett. 33 (1992) 1419–1422;
(c) T. Muller, R. Meyer, D. Lennartz, H.-U. Siehl, Angew. Chem. Int. Ed. 39 (2000) 3074–3077.
[40] (a) S.A. Sherrod, R.G. Bergman, J. Am. Chem. Soc. 93 (1971) 1925–1940;
(b) S.A. Sherrod, R.G. Bergman, J. Am. Chem. Soc. 91 (1969) 2115–2117.
[41] (a) M. Hanack, T. Bassler, J. Am. Chem. Soc. 91 (1969) 2117–2118;
(b) For an excellent review on stabilized vinyl cations, which discusses the special stability of \( \alpha \)-cyclopropylvinyl cations, see: M. Hanack Acc. Chem. Res. 9 (1976) 364–371.
[42] J. Shi, M. Zhang, Y. Fu, L. Liu, Q.-X. Guo, Tetrahedron 63 (2007) 12681–12688.
[43] C. Walling, P. Wagner, J. Am. Chem. Soc. 85 (1963) 2333–2334.
[44] D.V. Avila, C.E. Brown, K.U. Ingold, J. Lusztyk, J. Am. Chem. Soc. 115 (1993) 466–470.
[45] A. Rauk, in: Orbital Interaction Theory of Organic Chemistry, John Wiley and Sons, New York, 1998, p. 58.
[46] For a recent, truly excellent, paper where the intermediacy of an \( \alpha \)-cyclopropylvinyl radical was detected by cyclopropane ring-opening at room temperature, see: X. Lin, Z. Gan, J. Lu, Z. Su, C. Hu, Y. Zhang, Y. Wu, L. Gao, Z. Song Chem. Commun. 52 (2016) 6189–6192.
[47] (a) D.E. Frantz, R. Fassler, E.M. Carreira, J. Am. Chem. Soc. 122 (2000) 1806–1807;
(b) D. Boyall, F. Lopez, H. Sasaki, D. Frantz, E.M. Carreira, Org. Lett. 2 (2000) 4233–4236;
(c) D. Boyall, D.E. Frantz, E.M. Carreira, Org. Lett. 4 (2002) 2605–2606.
[48] K.J. Hale, Z. Xiong, L. Wang, S. Manaviazar, R. Mackle, Org. Lett. 17 (2015) 198–201.
[49] The structure of known alkyne 94 (9) is as follows: It was prepared from 95 according to the experimental procedures previously set out in reference 9.

\begin{center}
\includegraphics[width=0.5\textwidth]{image.png}
\end{center}