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

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

Hamish A. Watson,† Soraya Manaviziar, Hannah G. Steeds and Karl J. Hale*†

O-Directed hydrostannation of β-cyclopropyl propargyl alcohol 22 with stannanes and cat. Et3B in THF/H2O or PhMe/MeOH fails to deliver any detectable products of α-stannylvinyl cation capture. Instead only α-stannyl-β-cyclopropylvinyl radical intermediates can be detected, which undergo fast H-atom abstraction and/or cyclopropane ring-opening as a result of eliminative β-scission.

The O-directed, free radical hydrostannation of propargylyloxygenated alkyl acetylenes with Ph3SnH/cat. Et3B and O2 in PhMe is a reaction of great synthetic worth for the highly stereocontrolled construction of (Z)-configured trisubstituted alkenes of high structural complexity.1,2 Given the superb performance of this reaction, in many extremely demanding settings,3 it is not at all surprising to find that there has been substantial interest in understanding the mechanistic origins of the high stereo- and regiocontrol that is typically observed.1-6

Our picture of these reactions1-3 (Scheme 1, mechanism 1) has them proceeding by a totally free radical mechanism in which an O-coordinated triphenyloxanoyl radical 3,3 preferentially adds to the α-carbon of the acetylene to give an inverting pair of bent stannylvinyl radicals 4, where lower hyperconjugative stabilisation in (E)-4, high internal A1.5-strain, and magnified steric repulsions collectively disfavour its H-atom abstraction from Ph3SnH. As a result, the more hyperconjugatively stabilised (Z)-inversiont (Z)-4 tends to preferentially react, since this does not experience such severe A1.5-strain, and it offers the least sterically hindered transition state for H-atom abstraction, which favours formation of the α-vinylstannane products (Z)-5. Although the initial O-directed adduct can guide the O-coordinated tin radical to the β-acetylenic carbon of 3 to give (Z)-6, because this addition step is reversible, and the O-Sn complexation persists within the β-stannylvinyl radical adducts (Z)-6, this lengthens and weakens their C-Sn bonds, to inevitably promote their rapid dissociation back into 3. In contrast, the analogous elimination from the α-stannylvinyl radicals (Z)-4 is far less facile, due to the internal O-Sn coordination not persisting within such systems,1,3 with the result that H-atom abstraction is far more favourable, and the α-vinylstannanes of structure (Z)-5 typically predominate.

The above mechanistic analysis is one that has now been very strongly supported by X-ray crystallography,1,3 by Abagin’s computer-assisted DFT calculations,5 and by our own stannylvinyl radical trapping experiments with 8 (Scheme 2),4 which afforded a tandem β-addition/radical cyclisation product 10 at a range of stannane concentrations. Moreover, because the α:β addition step is reversible, and the regiochemistry changes significantly in favour of the O-directed α-addition product 9, as the stannane concentration starts to increase (due to this promoting O-Sn complexation),

this indicates that alkyne ground state polarity and electronic control cannot be the primary or exclusive determinants of regiochemistry in these systems, for if these were solely governing outcome, then the regiochemistry of 9:10 would never change as the stannane concentration altered; it would always remain constant. So, the O-directed free radical hydrostannation mechanism of Scheme 1 (mechanism 1) must be gaining the ascendancy over the non-directed, entirely free radical, addition/H-abstraction pathway (mechanism 2) as the Ph3SnH concentration rises.

Scheme 1. The totally free radical O-directed mechanism for hydrostannation (mechanism 1), which operates at high Ph3SnH concentrations, and is experimentally supported.1,4

Scheme 2. Changing regiochemistry at increased Ph3SnH concentrations, alongside the formation of 10 from 8, collectively demonstrate that an entirely free radical, O-directed, mechanism (mechanism 1) must be operating at higher Ph3SnH concentrations, and that alkyne polarity/electronic control and a non-O-directed free radical mechanism (mechanism 2) only start to gain significant influence at much lower Ph3SnH concentrations.3

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Scheme 3. The non-directed stannyldvinyl cation mechanism,\textsuperscript{a,b} for hydrostannation, which is not experimentally supported by the DFT calculations\textsuperscript{a} nor the recorded\textsuperscript{c} polar solvent rate accelerations of the team who first proposed it (mechanism 3).

Now despite the solidity of this work, a new mechanism was proffered in 2013-14\textsuperscript{5} (Scheme 3, mechanism 3); one where the \(\alpha\)-vinylstannane products (2-15) were suggested to arise, not through a coordinately-controlled regioselective tin radical addition, but rather, through a non-O-directed, non-regioselective tin radical addition at either alkene carbon of 11.

In this respect, it was proposed that it would be of little real consequence if a mixture of \(\alpha\)- and \(\beta\)-stannylvinyl radicals 13\textsuperscript{a} and 13\textsuperscript{b} ever arose, for these would both simultaneously undergo rapid single electron transfer (SET) to \(\text{O}_2\) present in the reaction medium, and this would lead to a pair of superoxide ion/\(\alpha\)- and \(\beta\)-stannylvinyl cation ion pairs 14\textsuperscript{a} and 14\textsuperscript{b}, where the \(\beta\)-stannylvinyl cation would spontaneously undergo a 1,2-stannylnyl shift, to afford the more inductively stabilised \(\alpha\)-stannylvinyl cation pair 14\textsuperscript{a} exclusively. It was further suggested that the \(\alpha\)-stannylvinyl cation in 14\textsuperscript{a} would thereafter enjoy extra stabilisation from a dynamic partial bridging interaction with the tin substituent. It was also postulated that this \(\alpha\)-stannylvinyl cation would subsequently engage in an ion reduction with the excess stannane that was present, and that this would then afford the observed \(\alpha\)-vinylstannane product (2-15), along with a tin cation 16, which itself would get involved in a second SET with the liberated superoxide ion, to return the \(\text{O}_2\) and a new \(\text{R}_3\text{Sn}\) radical 17, which would further propagate the reaction chain.

A major problem with mechanism 3\textsuperscript{5} lies in its inability to satisfactorily explain why the \(\alpha\)-\(\beta\)-product regiochemistry (9:10) changes as the stannane concentration increases, when the alkene 8 is hydrostannated (Scheme 2).\textsuperscript{3} This is because the tenets of mechanism 3 require the \(\beta\)-stannylvinyl cation to spontaneously rearrange to its \(\alpha\)-isomer,\textsuperscript{5} due to this being more stable, and the reaction being exclusively electronically controlled. Naturally, this would give 9 as the sole product. Yet, this is not what is observed, as evidenced by Scheme 2. Mechanism 3 is also incompatible with the observation of a \(\beta\)-stannylvinyl radical cyclisation product 10 in that very same

Scheme 2 study. The DFT calculations\textsuperscript{5a} that accompany mechanism 3 also rule it out on simple thermodynamic grounds. In this regard, the postulated \(\text{O}_2\)-mediated SET conversions of 13\textsuperscript{a} to 14\textsuperscript{a} and 13\textsuperscript{b} to 14\textsuperscript{b} (where \(\text{R} = \text{R}_1 = \text{R}_2 = \text{R}_3 = \text{Me}\)) are respectively associated with \(\Delta E\) values of \(+47.27\) kcal mol\(^{-1}\) and \(+45.2\) kcal mol\(^{-1}\) for these two transitions in \(\text{C}_6\text{H}_6\) at 25 \(\degree\)C (see Scheme 3). Such barriers are far too high to allow these conversions to proceed, as proposed, except through quantum mechanical tunnelling, but none of the traditional evidence needed to support such a mechanism has been provided by the proposers of mechanism 3. The fact also that the transition of 13\textsuperscript{a} into 14\textsuperscript{a} is higher in energy than the one for the transition of 13\textsuperscript{b} into the more inductively destabilised 14\textsuperscript{b} also seems discrepant. The conversion of 14\textsuperscript{b} to 14\textsuperscript{a} is again uphill to the tune of \(+2.1\) kcal mol\(^{-1}\). Moreover, the rate accelerations that the mechanism 3 proposers have reported\textsuperscript{5c} for the hydrostannations of alkylene 18 in polar solvents, over 90 min (Scheme 4), are likewise far too small to be considered supportive of ionic mechanism 3.\textsuperscript{1} Instead, they are much more aligned\textsuperscript{1} with an entirely free radical, O-directed, mechanism of the type shown in Scheme 1 (mechanism 1).\textsuperscript{1}

Indeed, relative to THF, a net decrease in the reaction rate\textsuperscript{5c} is observed for the hydrostannation of 18 in more polar solvents.

Scheme 4. The polar solvent rate acceleration data of reference 5c that is claimed to be supportive of mechanism 3.

Now, despite the electronically-controlled stannylvinyl cationic ion pair hypothesis\textsuperscript{5} of Scheme 3 (mechanism 3) conflicting very strongly with the 2005 radical probe work of Scheme 2,\textsuperscript{1,3} and Alabugin’s later 2015 experimental work and DFT calculations,\textsuperscript{4} which further confirmed an entirely free radical O-directed mechanism for these reactions (mechanism 1), still mechanism 3\textsuperscript{5} remains active and unworn down from the literature, despite several criticisms,\textsuperscript{1,4,6} with the consequence that its mechanistic principles are still continuing to be widely disseminated within the community. This is best illustrated by a recent 2019 hydrostannation review,\textsuperscript{7} where exclusivity of discussion and mechanistic primacy were given to mechanism 3 over mechanism 1 to explain the conversion of 11 into (2-15). However, as we have seen, mechanism 3\textsuperscript{5} is at great odds with all experimental data gathered to date.\textsuperscript{1,3,4,5} Given this continuing propagation of a mechanism\textsuperscript{5} that has been significantly criticised\textsuperscript{1,4,6} (mechanism 3\textsuperscript{5}), over one that is much more reasonable and fully experimentally supported\textsuperscript{1,4,6} (mechanism 1\textsuperscript{1,3}), we felt it necessary to publish the results of our latest investigations into whether a stannylvinyl cation is a genuine intermediate in these reactions, since some in the field clearly seem unwilling to accept the unambiguous data that has been presented in Scheme 2\textsuperscript{1,3} and elsewhere,\textsuperscript{1} which all rule against it.
Therefore, to test mechanism 3 further (Scheme 5), we purposely designed a β-cyclopropyl propargyl alcohol probe 22 that we believed would give rise to an exceptionally stable, yet still quite reactive, stannyl cation intermediate 27, if it happened that mechanism 3 did hold true. It was reasoned that if 27 was indeed an authentic intermediate in the journey of 22 into vinylstannane 26, then this super-stabilised vinyl cation 27 would almost certainly react competitively with H₂O and alcohols added to the reaction medium since it would be triply stabilized: a) by neighbouring group participation from the ester carbonyl; b) by hyperconjugation with the α-R₃Sn substituent; and c) by hyperconjugation with the adjacent cyclopropane ring. It should thus have sufficient longevity in solution to undergo nucleophilic trapping by: 1) externally added nucleophiles present in excess (e.g. H₂O or MeOH) or 2) by the internal ester carbonyl to give a six-membered enol lactone (28), after subsequent nucleophilic attack on the resulting positively charged OMe group by the external nucleophile. A trapping of 27 with H₂O would, of course, lead to ketone or stannyl enone products such as 30 and 31 via 29 (Scheme 5), or potentially bring about a competitive Stang-Muller elimination through an attack of the H₂O on the R₃Sn grouping. The latter would naturally return the starting acetylene 22 in significant quantity, and would inevitably lead to little overall reaction progression.

With regard to the feasibility of achieving an α-cyclopropyl vinyl cation trapping with H₂O, the classic work of Bergman and Hanack had previously shown that α-cyclopropyl vinyl cations benefit from significant charge stabilization from the cyclopropane ring, they still retain the ability to react rapidly with external nucleophiles such as H₂O or acetate ion, either directly, or following internal 1,2-rearrangement. Muller’s highly stable bis-silyl-vinyl cations, which have even been characterised by X-ray crystallography likewise react readily with nucleophiles, but by an eliminative nucleophilic attack on silicon to give an alkynylsilane.

Most importantly as well, however, the probe 22 would inevitably afford the α-stannylvinyl radical precursor of the postulated cation 27 viz. radical 23, and if, by due modification of the hydrostannation conditions, we could identify a set of experimental circumstances where 23 could be induced to predominantly undergo fast H-atom abstraction from the stannane to give 26 while also undergoing concurrent vinyl radical eliminative β-scission of the cyclopropane ring to give the stannylhomoallenyl radical 24, and vice versa, where eliminative β-scission could be rendered more facile than concurrent stannylvinyl radical H-atom abstraction by 23, then this would unambiguously confirm that the proposed H-atom transfer must actually be proceeding through the α-stannylvinyl radical, and that 26 was not arising from an ionic reduction of the stannylvinyl cation 27 by the tin hydride. In essence, it would provide yet more convincing evidence for the O-directed stannylvinyl radical H-atom abstraction hypothesis (mechanism 1), and further rule out mechanism 3.

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

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

The formation of only a minor quantity of the reduced allenyltin product 25 in entry 10, alongside the vinylstannane 26 is clearly only compatible with the intermediacy of a stannyldiyl radical intermediate 23 that primarily undergoes fast H-atom abstraction from the stannane at rt, alongside competitive radical induced eliminative opening of the cyclopropane ring with accompanying H-atom abstraction (see Scheme 5), a process well known for α-cyclopropylvinyl radicals. This point is perhaps much better illustrated by entry 11 where, when the hydrostannation reaction was performed at 0.1 M substrate concentration and lower Ph₃SnH concentration (2 equiv), in a mixture of THF/H₂O (4:1) at 50 °C for 7 h, the ratio of 26:25 now changed very dramatically to 1:3:1, with both products being isolated in a combined 77% overall yield. Clearly, working at higher dilutions and higher reaction temperatures with lower quantities of stannane quite profoundly affects the behaviour of the intermediary stannylvinyl radical 23, it now diverting it significantly down the pathway of competitive radical induced ring-opening, alongside stannylvinyl radical H-atom abstraction from the
**Notes and references**


