

**RADICAL REACTIONS OF ENONES WITH
ELECTROPHILIC ALLYLSTANNANES**

Eric J. Enholm,* Kelley M. Moran and Paul E. Whitley

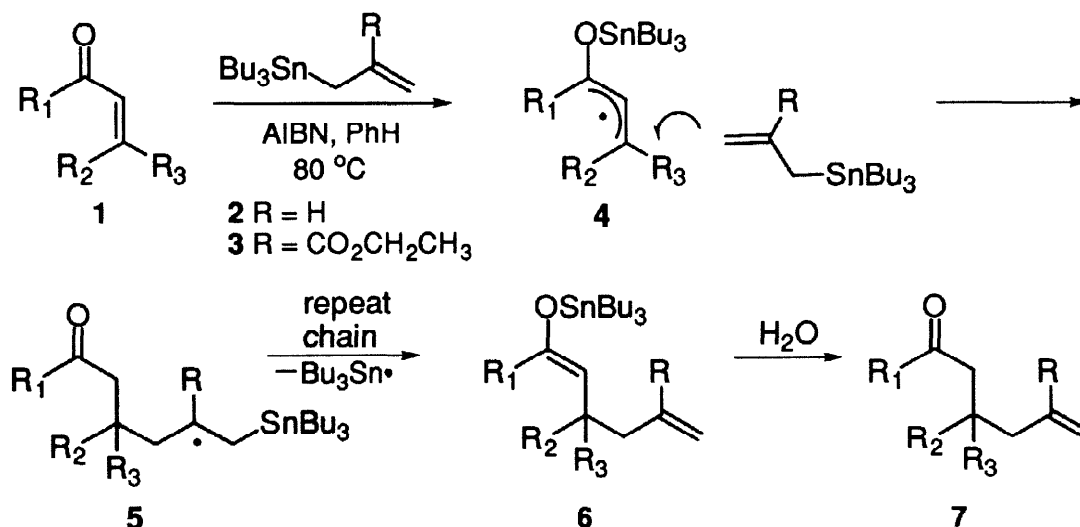
*Department of Chemistry, University of Florida
Gainesville, FL 32611, USA*

Received 7 November 1997; accepted 19 November 1997

Abstract: Reactions of allyltributylstannanes with enones were studied. Although the parent allylstannane would not react with enones, an electrophilic variation was successful. The reaction provides perhaps one of the only non-basic and non-nucleophilic alternatives to the classic conjugate additions.

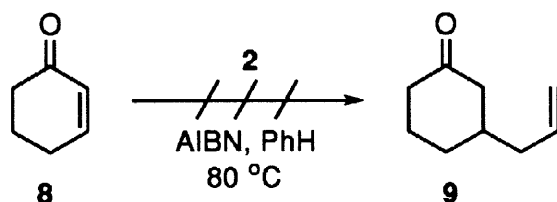
© 1998 Elsevier Science Ltd. All rights reserved.

One of the more commonly used organotin reagents in both free radical reactions and Lewis acid-mediated reactions is allyltributylstannane.¹⁻² This reagent permits the construction of new carbon-carbon bonds from free radical precursors under the standard conditions of benzene at 80 °C with AIBN initiator.³ Although alkyl halides, phenylselenides, phenylsulfides, and thiocarbonyl functions have been examined extensively in allyl tin reactions, no free radical reactions using enones as precursors have as of yet been studied.⁴

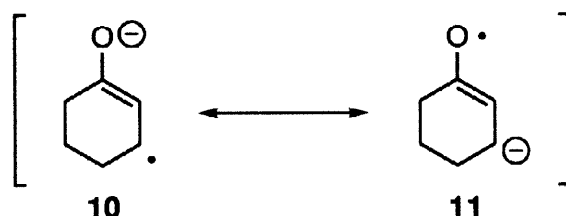


We envisioned the formation of the resonance stabilized allylic O-stannyl ketyl **4** from the reaction of enone **1** with an allyltributyltin (R = H). If delocalized radical-anion species **4** undergoes addition to a second molecule of the allylstannane, this would trigger β -scission of tin radical in **5** and produce the new allylated product **7** after water quench of tin(IV) enolate **6**.⁶ This reaction provides for the β -carbon elaboration of ketones in a manner conceptually related to a Michael addition.⁵ It differs markedly, however, from classic conjugate additions because neutral free radical conditions are utilized. The reaction sequence provides one of the only non-basic and non-nucleophilic alternatives to well-known 1,4-additions of organocuprates to enones.^{5(a)}

Thus, the successful implementation of Scheme 1 could lead to a new and synthetically very useful pathway to β -carbon-carbon bond construction from enones.



The reaction was first attempted using 2-cyclohexenone (**8**) and allyltributyltin (**2**) and AIBN in benzene. The reaction was refluxed for 24 h, but no formation of the desired allylated product **9** was realized. One explanation for this observation is that the intermediate β -radical species was nucleophilic. Although most alkyl radicals are inherently nucleophilic, radical species [**10** \leftrightarrow **11**] is particularly electron-rich due to the resonance delocalization. Resonance contributor **11** bearing anionic charge at the β -carbon enhances the nucleophilic character at that position.

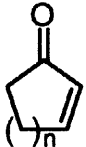
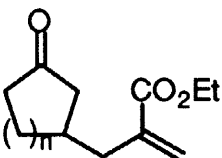
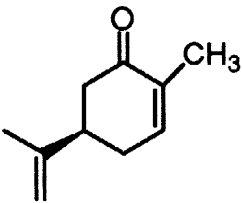
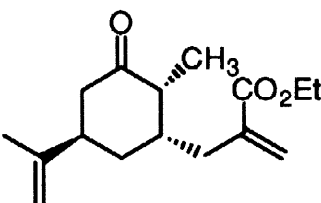
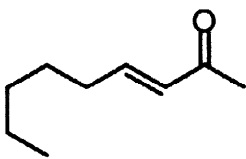
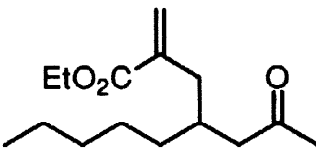
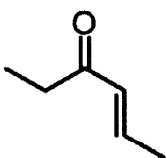
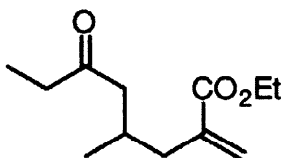


Therefore, it was determined that the radical was possibly too nucleophilic to add to the electron-rich double bond of allyltributyltin.⁶ An electron-withdrawing substituent on the alkene of the allyltributyltin should switch it to an electrophilic reagent and provide a better polarity match for the reaction with **1**. We chose the ethyl ester substituent ($R = \text{CO}_2\text{CH}_2\text{CH}_3$) since there was a literature preparation of these tin reagents from benzenesulfonyl precursors.⁷ With the desired 2-substituted allylstannane **3** synthesized, it was now possible to study its reactivity with enones.

Several enones were subjected to this new reaction and the results are shown in the Table.¹⁰ The reaction is clearly successful, constructing an ester substituted allyl substituent with each enone examined. These reactions proceed more slowly than the tin hydride transformations we have examined before. For example, complete consumption of 2-cyclohexenone (**8**) by TLC, over a 4 h period is observed with tin hydride, transferring a hydrogen atom instead of an allyl unit.⁴ In contrast, these allylation reactions require 10 h to consume **8**. Adding additional AIBN (0.2 equiv) after 5 h of reaction time had elapsed was useful and appeared to decrease the overall time required.

The two new stereocenters in (-)-carvone adduct **18** arise from attack on the nearly flat radical-anion intermediate on the face of the ring opposite the bulky 2-propene substituent. The methyl adjacent to the carbonyl in **18** is equatorial; this arises from axial protonation of the tin enolate.^{8(a),9} Related Michael reactions of (-)-carvone (**17**) produce identical stereochemical results.⁸

Radical Reactions Of Enones With Electrophilic Allyltin(IV) Reagents

Entry	Unsaturated Ketone	Product	Yield (%)
1	 12 $n = \text{CH}_2$	 13	58
2	8 $n = (\text{CH}_2)_2$	14	61
3	15 $n = (\text{CH}_2)_3$	16	67
4	 17	 18	69
5	 19	 20	63
6	 21	 22	65

In summary, a free radical method for the formation of new carbon-carbon bonds at the β -position of enones has been achieved. A 2-ester substituted allylstannane permits the formation of the β -radical and allyl addition from enone precursors. To the best of our knowledge, not only is this the first reaction of this type, but it provides perhaps one of the only non-basic and non-nucleophilic alternatives to the Michael addition reactions.

Acknowledgement. We gratefully acknowledge support by the National Science Foundation (Grant CHE-9708139) for this work.

References

- (1) Pereyre, M.; Quintard, J.P.; Rahm A. *Tin in Organic Synthesis*, Butterworths: Boston, 1987.
- (2) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergammon Press: New York, 1986; (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541; (c) Curran, D. P. *Synthesis* **1988**, 417, 489; (d) Motherwell, W.B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*, Academic Press: New York, 1992; (e) Yamamoto, Y. *Accts. Chem. Res.* **1987**, *20*, 243.
- (3) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079.
- (4) For reactions of enones with tin hydride, see: (a) Enholm, E. J.; Kinter, K. S. *J. Am. Chem. Soc.* **1991**, *113*, 7784; (b) Enholm, E. J.; Xie, Y.; Abboud, K. A. *J. Org. Chem.* **1995**, *60*, 1112; (c) Enholm, E. J.; Whitley, P. E. *Tetrahedron Lett.* **1995**, 9157; (d) Enholm, E. J.; Whitley, P. E. *Tetrahedron Lett.* **1996**, 559.
- (5) (a) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135; (b) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*, Pergamon Press: Oxford, U.K. 1992.
- (6) For reviews of ketyl radical anions, see: (a) Hirota, N. in *Radical Ions*, Kaiser, E. T.; Kevan, L. Eds., Wiley Interscience: New York, 1968, pp. 35-85; (b) Russell, G.A. in *Radical Ions*, Kaiser, E. T.; Kevan, L. Eds., Wiley Interscience, New York, 1968, pp. 87-150; (c) Forrester, A. R.; Hay, J. M.; Thompson, R. H. *Organic Chemistry of Stable Free Radicals*, Academic Press: New York, 1968, pp. 82-90.
- (7) (a) Villieras, J.; Ramband, M. *Synthesis* **1982**, 924; (b) Baldwin, J. E.; Adlington, R. M.; Lowe, C.; O'Neal, I. A.; Sanders, G. L. *J. Chem. Soc. Chem. Comm.* **1988**, 1030.
- (8) (a) Krishnamurthy, R.; Kuivila, H. G. *J. Org. Chem.* **1986**, *51*, 4947; (b) Salladie, G.; Hutt, J. *Bull. Soc. Chim. Fr.* **1986**, *4*, 643; (c) Bakuzis, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1981**, *46*, 235.
- (9) For a review of tin(IV) enolates, see: Shibata, I.; Baba, A. *Org. Prep. Proc. Int.* **1994**, *26*, 87.
- (10) Example Procedure: An enone (1 mmol), 2-ethylcarboxytributylallylstannane (804 mg, 2 mmol), and AIBN (33 mg, 0.2 mmol) were dissolved in freshly distilled benzene (0.5 mL). The resulting solution was degassed for 20 min with a stream of Ar gas and next refluxed for 10 hours. More AIBN (33 mg, 0.2 mmol) was added after 5 h reflux. The reaction was poured into water and extracted with ether (3 x 20 mL) and concentrated under reduced pressure. The crude oil was subjected to flash column chromatography to yield the product.