# Cyclization Reactions of Allylic *O*-Stannyl Ketyls

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This is a summary of an investigation of the tributyltin hydride-induced cyclization reactions of unsaturated ketones with electronically deficient olefins. This reaction was initiated by an *O*-stannyl ketyl formed by the addition of a tributyltin radical to a carbonyl, which has both anionic and radical character. The intramolecular coupling produced functionalized cyclopentanes, bearing two synthetically useful carbon appendages. An activating or electron-withdrawing function on the alkene was essential to the cyclization. A dilution study revealed that excellent anti stereoselectivities (>50:1) could be achieved, and this was attributed to a reversible cyclization. Another goal of this study was to separate the radical reactivity from the anionic reactivity of the *O*-stannyl ketyl by the participation of labile functional groups and external electrophiles. The presence of minor products and enolate-trapping studies demonstrated that the anionic character of the ketyl could be utilized in the form of a tin enolate. This work represents the first free radical- and reagent-based approach to the study of the intramolecular hydrodimerization of activated alkenes.

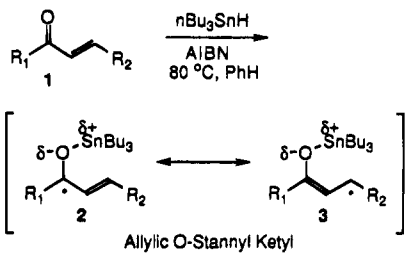
## Introduction

For more than 20 years, tributyltin hydride ($nBu_3SnH$) has been applied to a rich diversity of free radical reactions.[1] Almost all free radical reactions use $nBu_3SnH$ with halides, alkenes, thiophenyl, thiocarbonyl, and phenylselenide precursors to obtain a carbon-centered radical, which all result in a net loss of these functions in the final products.[2] If a precursor were to retain one or more heteroatoms (i.e. oxygen), the process would be more valuable and would provide functional groups for subsequent manipulations.

As a general rule, an unsaturated carbonyl species is not considered to be a good precursor to a carbon-centered radical. Quite the opposite, it generally acts as a free radical acceptor in cyclization reactions.[2] It still might function as a radical precursor under the right reaction conditions because the reaction of tributyltin radical with an $\alpha,\beta$-unsaturated carbonyl readily produces an allylic *O*-stannyl ketyl as shown in Scheme 1.[3] Several types of subsequent manipulations are possible when *O*-stannyl ketyls are used in radical cyclizations. If the radical or one-electron reactivity in **3** is used in a cyclization, then the tin enolate or two-electron reactivity can be used in reactions with suitable electrophiles ($E^+$). Even the carbonyl which is obtained after $E^+$ quenching of the tin enolate can undergo further synthetic manipulations.

We have reported on studies directed toward the use of *O*-stannyl ketyls in synthesis.[4] This interest began with simple carbonyl–alkene coupling reactions[4a] and tandem cyclizations[4c] using these potentially useful intermediates. Although there is still much to be learned,

**Scheme 1**




an allylic *O*-stannyl ketyl and its related structural variants differ markedly from standard radical reactants because they have an inherent nucleophilic/anionic component to their properties and they are more stable, due to resonance delocalization.[3-5]

Studies of ESR spectra of electrochemically derived allylic ketyls have provided some interesting details on the physical properties of the radical anion spectra of enones which do not possess acidic hydrogens. These studies show that most of the hyperfine splitting is located on the $\beta$-carbon.[6] This is supported by studies of Hückel-calculated spin densities which indicate at least 50% of the radical density is located on the $\beta$-carbon as in resonance contributer **3**, while the remaining portion is divided equally between the carbonyl carbon and the carbonyl oxygen in **2**.[6a] One might speculate, if there is an analogy between allylic *O*-stannyl ketyls and those electrochemical studies, that **3** should be the major resonance contributor. Also, electronegativity differences between the oxygen and tin atoms in an allylic *O*-stannyl ketyl leads to a nucleophilic radical which should prefer to react with an electron deficient olefin.[1]

This article summarizes an investigation of *O*-stannyl ketyls which are functionalized so that the radical can be "distanced" from the carbonyl.[4b] This distonic reactivity was accomplished by the use of unsaturated ketones.

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1995.

(1) Neumann, W. P. *Synthesis* **1987**, 665.

(2) For reviews of free radical reactions, see: (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) Hart, D. J. *Science* **1984**, *223*, 883. (e) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic Press: New York, 1992.

(3) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis;* Butterworths: Boston, 1987.

(4) (a) Enholm, E. J.; Prasad, G. *Tetrahedron Lett.* **1989**, *30*, 4939. (b) Enholm, E. J.; Kinter, K. S. *J. Am. Chem. Soc.* **1991**, *113*, 7784. (c) Enholm, E. J.; Burroff, J. A. *Tetrahedron Lett.* **1992**, *33*, 1835. (d) Enholm, E. J.; Xie, Y. *J. Org. Chem.* **1995**, *60*, 1112.

(5) (a) Sugawara, T.; Otter, B. A.; Ueda, T. *Tetrahedron Lett.* **1988**, *29*, 75. (b) Beckwith, A. L. J.; Roberts, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 5983. (c) Rawal, V.; Krishnamurthy, V.; Fabre, A. *Tetrahedron Lett.* **1993**, *34*, 2899. (d) Hart, D. J.; Krishnamurthy, R.; Pook, L. M.; Seely, F. *Tetrahedron Lett.* **1993**, *34*, 7819.

(6) (a) Russell, G. A.; Stevenson, G. R. *J. Am. Chem. Soc.* **1971**, *93*, 2432. (b) Whiffen, D. H. *Mol. Phys.* **1963**, *6*, 224. (c) Russell, G. A.; Ku, T.; Lokensgard, G. *J. Am. Chem. Soc.* **1970**, *92*, 3833.

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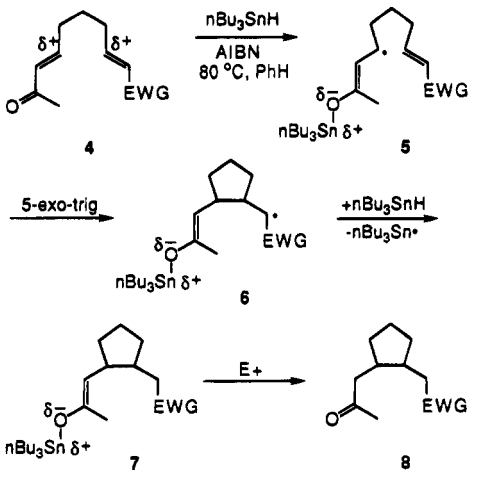
**Scheme 2**




Functionalized monocyclic and bicyclic cyclopentanes bearing synthetically useful carbon appendages were constructed. An interesting concentration effect was observed which can be attributed to the reversibility of the cyclization. This concentration effect was optimized to achieve excellent diastereoselectivities (>50:1). Both intramolecular and intermolecular reactions were examined.

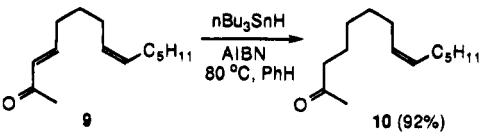
## Results and Discussion

An unsaturated appendage seemed a natural selection due to many factors, which included ease of preparation and effective delocalization of the allylic *O*-stannyl ketyl through resonance. The general transformation, shown in Scheme 2, involved the coupling of the $\beta$-carbons of dienone **4**. This is often perceived as a difficult mode of coupling because the polarities of the $\beta$-carbons of each alkene in **4** are partially positive ($\delta+$) and the atoms bear like charges. The formation of an *O*-stannyl ketyl at the $\alpha,\beta$-unsaturated ketone function readily reverses its polarity and leads to an opposite charge attraction. Prior to our studies, there were no reagent-based methods to accomplish this general transformation,[7] but because it could be viewed as a hydrodimerization coupling, there were several electrochemical methods.[8]

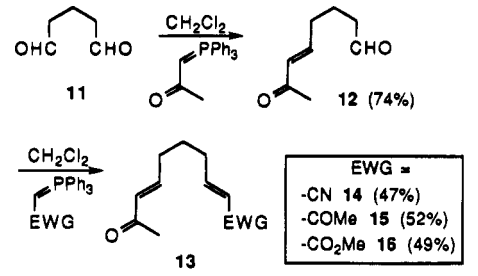
Intramolecular addition of the radical in **5** to the alkene leads to **6** by a 5-*exo-trig* ring closure. Transfer of a hydrogen atom from another molecule of tin hydride produces tin enolate **7** and gives a molecule of $nBu_3Sn^\bullet$ to carry on the chain mechanism. The tin enolate can be treated with an electrophile ($E^+$) such as water to quench the reaction and produce the formally hydrodimerized and difunctionalized cyclopentane **8**.

It was first necessary to determine whether activation of the olefin was actually essential for a successful cyclization, shown in Scheme 3.[4a] When **9** was subjected to radical cyclization conditions, only monoalkene **10** was observed which was a result of simple reduction of the conjugated olefin. Although the cyclization did not occur, these results were not surprising considering that tributyltin radical reduction of the olefin in $\alpha,\beta$-unsaturated ketones is a precedented reaction.[9] The nucleophilic character of the allylic *O*-stannyl ketyl raises the energy of the radical SOMO (singly occupied molecular orbital).[10] Higher energy SOMO's have better orbital overlap with the LUMO's of electron deficient olefins rather than those of the alkyl-substituted alkene in **9**. We had hoped that both activated and unactivated olefins could be used in this study, but this result showed that an activated alkene was an important element for success.

**Scheme 3**




**Scheme 4**




Once it was determined that an activated olefin was an important prerequisite for successful cyclizations, our attention was then focused on the synthesis of the required diene precursors. Glutaric dialdehyde (**11**) seemed ideally suited for the two-step attachment of unsaturated appendages. But, what seemed to be a trivial Wittig reaction to make aldehyde **12** became somewhat of a challenge due to the predominance of the diaddition product. When a methyl ketone-stabilized ylide (1 equiv) was added by addition funnel to a large excess (4 equiv) of dialdehyde **11**, the product ratio favored the unsaturated di-ketone over the unsaturated mono-ketone by a substantial margin of 7:1 (di:mono). Fortunately, the unsaturated diketone **15** was one of the intended starting materials. Eventually, the very slow addition of ylide (1 equiv) by addition funnel to glutaric dialdehyde (7 equiv) gave the desired monoaddition product **12** in 74% yield. The second unsaturated appendage, activated by nitrile **14** or methyl ester **16**, was next added by a Wittig reaction without problems to yield the diene starting materials (Scheme 4).

Each of the diene precursors underwent the desired radical cyclization, where the diene was dissolved in benzene (0.1 M) and $nBu_3SnH$ (3 equiv), and AIBN (0.1 equiv) was added. The mixture was degassed with argon and then heated to 85 °C, and in most reactions, the

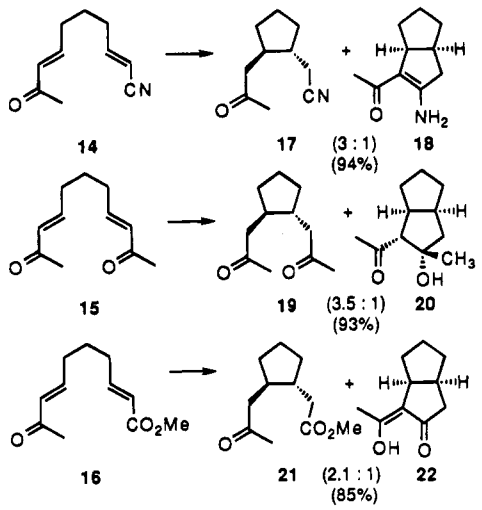
(7) There are only a few examples of a sodium-promoted intermolecular coupling of the $\beta$-carbons of activated alkenes. Most cases involve enones blocked on both ends (usually with *tert*-butyl groups): (a) Bowers, K. W.; Giese, R. W.; Grimshaw, J.; House, H. O.; Kolodny, N. H.; Kronberger, K.; Roe, D. K. *J. Am. Chem. Soc.* **1970**, *92*, 2783. (b) House, H. O.; Giese, R. W.; Kronberger, K.; Kaplan, J. P.; Simeone, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 2800.

(8) For two excellent recent reviews on (nonreagent based) electrochemical methods of $\beta$-coupling of activated olefins, see: (a) *Synthetic Organic Electrochemistry*; Fry, A. J., Ed.; John Wiley & Sons: New York, 1989; Chapter 7. (b) Little, R. D.; Baizer, M. M. In *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989. For radical cyclizations (hydrostannylation) of dienes using unactivated alkenes, see: Hanessian, S.; Leger, R. *J. Am. Chem. Soc.* **1992**, *114*, 3115 and references cited therein.

(9) (a) Pereyre, M.; Valade, J. *Bull. Chim. Fr.* **1967**, 1928. (b) Leusink, A. G.; Noltes, J. G. *Tetrahedron Lett.* **1966**, 2221. (c) Neumann, W. P.; Sommer, R.; Mueller, E. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 514. (d) Lutsinko, I. F.; Baukov, Y. I.; Belavin, I. Y. *J. Organometal. Chem.* **1970**, *24*, 359. (e) Rahm, A.; Pereyre, M. *J. Organometal. Chem.* **1975**, *88*, 79. (f) Pattenden, G. *Tetrahedron Lett.* **1987**, *28*, 1313.

(10) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976.

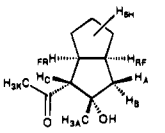
**Scheme 5**




starting material was consumed within 2 h. These reactions never seemed to suffer from the sluggish behavior previously observed[5b] with *O*-stannyl ketyls, and they were also very clean reactions. A summary of the results of these cyclizations and their products is shown in Scheme 5. The diastereomeric ratios reported for the isolated products are in good agreement with the crude GC ratios. Good yields were observed in each reaction providing the major antiproducts **17**, **19**, and **21**. These were favored by modest product diastereoselectivities which were increased markedly later, as discussed below.

The minor bicyclic syn products **18**, **20**, and **22** were formed by a second cyclization. The nitrile, ketone, and ester, respectively, which activated the olefin underwent a second intramolecular reaction with the tin enolate. In the major products **17**, **19**, and **21**, the appendages were anti to one another and too distant to close without considerable strain,[11] but when they were syn, a facile second aldol-like cyclization occurred.[4d] Overall, the sequence involved an efficient radical reaction followed by a carbonyl addition reaction.[12a] The presence of the minor products in these reactions demonstrates that the free radical ($1e^-$) and nucleophilic ($2e^-$) dual reactivity of tin ketyls is present, and these effects can be induced to react independently.[12]

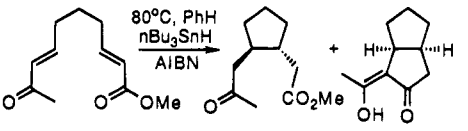
The syn product **20** from the cyclization of ketone **15** was surprisingly isolated as a single diastereomer. It is noteworthy that, in this product, four stereogenic centers were created, and of several possible diastereomeric products, only **20** was obtained. The structure was confirmed by extensive NOE difference studies summarized in Figure 1. Additionally, the hydroxyl proton's chemical shift was independent of the concentration of the sample. Therefore, it is probably intramolecularly hydrogen-bonded to the ketone.



| H(s) Irr. | Percent Effect Observed | | | | | | |
|---|---|---|---|---|---|---|---|
| | $H_A$ | $H_B$ | $H_C$ | $H_{RF}$ | $H_{SH}$ | A | K |
| $H_A$ | | 30.1 | 6.0 | | 2.7 | 2.1 | |
| $H_B$ | 26.1 | | | 6.0 | | | |
| $H_C$ | 2.8 | | | | 7.8 | 2.5 | |
| $H_{RF}$ | | 1.5 | | | 7.2 | | 0.8 |
| $H_{SH}$ | | | | | | | |
| A | | | 2.8 | | 2.2 | | |
| K | | | | 2.4 | 3.0 | | |

**Figure 1.** NOE studies of **20**.

**Scheme 6**




| Reaction Conditions | 21 : 22 (% Yield) |
|---|---|
| 1. 1.00 M in PhH, 1.1 equiv. $nBu_3SnH$ | 9 : 1 (75%) |
| 2. 0.10 M in PhH, 1.1 equiv. $nBu_3SnH$ | 25 : 1 (82%) |
| 3. 0.01 M in PhH, 1.1 equiv. $nBu_3SnH$ | >50 : 1 (82%) |

It was interesting to obtain antistereochemistry in the appendages which was in marked contrast to the general trend of cis stereochemistry in 5-hexenyl radical cyclizations.[1,2] Analogous radical cyclizations, under kinetic control, produce cis-disubstituted cyclopentanes and conform well to the classic Beckwith model.[13]

However, our cyclization involved a resonance-stabilized radical from the allylic *O*-stannyl ketyl, shown in Scheme 1. The resonance stabilization of this radical probably permitted reversibility and allowed the less stable kinetic syn product to equilibrate and form the more stable anti isomer, placing this reaction under thermodynamic control.[14] There are several examples of thermodynamic control in radical cyclizations; however, this mode of control is usually manifested in the formation of six-membered rings, rather than by the presence of the anti appendages observed here.[2,14]

If the cyclization were under thermodynamic control, then varying the concentration, and therefore the amount of $nBu_3SnH$ available for hydrogen atom transfer, might lead to improved stereoselectivities. When the reaction was examined at greater dilution, we were delighted to obtain much higher levels of stereoselectivity. Thus, **16** was cyclized at three different dilutions as shown in Scheme 6. Increasing levels of anti stereoselectivity for the ring appendages were obtained as the reaction mixture was diluted. A ratio of greater than 50:1 for the anti:syn products could be achieved at 0.01 M in benzene.

This dramatic increase in anti stereoselectivity can likely be attributed to the reversibility of the cyclization and the decreased availability of $nBu_3SnH$, shown in Scheme 7. Once the cyclized radical intermediates **23** and **24** react with a second molecule of $nBu_3SnH$ to form **25** and **26**, respectively, they are no longer able to ring open via intermediate **5** (EWG (electron-withdrawing

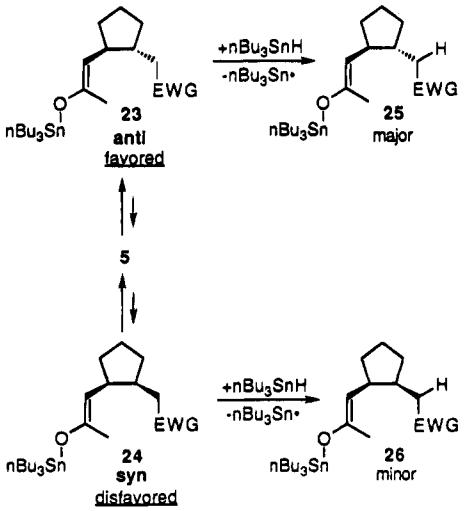
(11) (a) Kigoshi, H.; Imamura, Y.; Niwa, H.; Yamada, K. *J. Am. Chem. Soc.* **1989**, *111*, 2302. (b) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463.

(12) The sequencing of one- and two-electron reactions has only recently become possible: (a) Enholm, E. J.; Trivellas, A. *Tetrahedron Lett.* **1994**, *35*, 1627. (b) Takai, K.; Nitta, K.; Fujimura, O.; Utimoto, K. *J. Org. Chem.* **1989**, *54*, 4732. (c) Curran, D. P.; Fevig, T. L.; Totleben, M. J. *Synlett* **1990**, 733. (d) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1990**, *55*, 6171. (e) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439. (f) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943. (g) Totleben, M. J.; Curran, D. P.; Wipf, P. *J. Org. Chem.* **1992**, *57*, 1740. (h) Curran, D. P.; Totleben, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 6050. (i) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1992**, *57*, 3132.

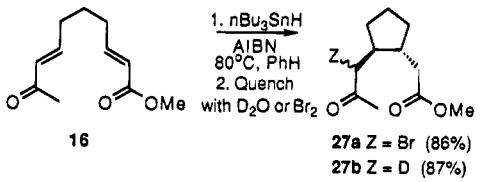
(13) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.

(14) Thermodynamic control in reversible radical cyclizations often leads to 6-*endo*-*trig* cyclizations: (a) Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386. (b) Julia, M. *Pure Appl. Chem.* **1974**, *40*, 553.

**Scheme 7**




**Scheme 8**



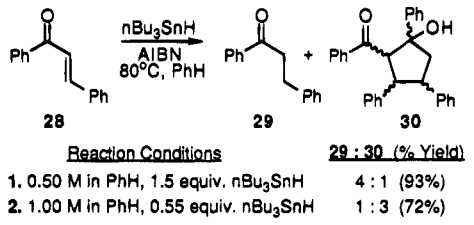

group) = $CO_2Me$). Making the reaction mixture more dilute and decreasing the availability of tin hydride allowed for more time to equilibrate before hydrogen atom transfer; thus, the equilibrium shifted from the kinetic syn isomer **24** to the thermodynamic anti isomer **23**. The dilution study clearly showed that this reaction was reversible and that excellent anti stereoselectivities could be achieved. A series of reactions using more concentrated solutions of $nBu_3SnH$ were examined to determine if the syn isomer could be obtained in useful quantities. After several attempts, including using $nBu_3SnH$ as solvent, it became doubtful that these conditions could be found.

Now that several features of the tin ketyl had been explored, we next examined two-electron chemistry on the tin enolate.[12] Although this has already been demonstrated in the structures of the minor bicyclic products, two additional experiments were performed which clearly establish the presence and potential utility of the stannyl enolate.[3,15] Since these experiments were not run in a strictly tandem sequence, we use the term "serial reactions" to refer to these reactions. In each experiment, the free radical cyclization of **16** under anti selective conditions (run no. 3, from Scheme 6) produced tin enolate intermediate **25** (see Scheme 7).

The resultant tin enolate was then immediately quenched in the same pot with either $Br_2$ or $D_2O$ to produce **27a** or **27b**, each as 2:1 mixtures of diastereomers as shown in Scheme 8. From $^1H$ NMR integration, the deuterium incorporation in **27b** was calculated to be greater than 85%.

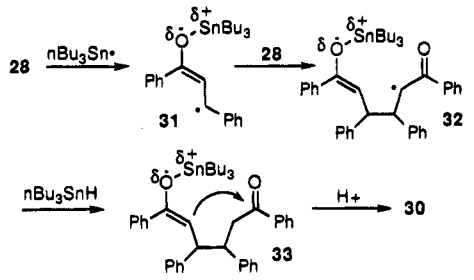
These results and those for the previously discussed bicyclic products clearly demonstrated the presence and utility of the tin enolate. Also, the monocyclic products

**Scheme 9**




| Reaction Conditions | 29 : 30 (% Yield) |
|---|---|
| 1. 0.50 M in PhH, 1.5 equiv. $nBu_3SnH$ | 4 : 1 (93%) |
| 2. 1.00 M in PhH, 0.55 equiv. $nBu_3SnH$ | 1 : 3 (72%) |

**Scheme 10**




and dilution studies showed that the radical cyclization of allylic *O*-stannyl ketyls could be both efficient and highly stereoselective. Collectively, these studies show that the one-electron reactivity in the allylic *O*-stannyl ketyl can be separated from the two-electron chemistry by sequential transformations. Thus, both types of reactivity can be achieved.[12]

Now that the effectiveness of an $\alpha,\beta$-unsaturated ketone cyclization was demonstrated on an intramolecular level, the next task was to see if it was equally effective on an intermolecular basis. Unlike the previous studies, bimolecular coupling of unsaturated ketones could occur from either the carbonyl carbon (head) or the $\beta$-olefin carbon (tail). This meant that three different coupling products were possible: head-to-head (pinacol), head-to-tail, or tail-to-tail.[8b,16] A preliminary attempt to dimerize methyl vinyl ketone under radical conditions produced a very low yield of a tail-to-tail product. The failure of this reaction to achieve useful yields was most likely due to either the volatility of the starting materials and products or the fact that the lifetime of the radical was not long enough to allow for coupling.

Both of these potential problems were circumvented in the hydrodimerization of *trans*-chalcone (**28**).[8a] The reaction conditions and product ratios are shown in Scheme 9. A careful balance existed between the concentration and the equivalents of $nBu_3SnH$. Run no. 1 showed that, if too much tin hydride was used, a simple reduction of the olefin prepared **29**.[21] In an effort to increase the amount of **30** formed, the reaction was run at higher concentration with a minimum amount of tin reagent. We were delighted to find that the previous ratio was greatly improved and that we were able to isolate **30** in 72% yield. It was isolated as an inseparable mixture of isomers whose spectra and melting point agreed with those of the published reports.[17] A proposed mechanism for the hydrodimerization of *trans*-chalcone is shown in Scheme 10.[7a] Dimer **32** was formed by the initial tail-to-tail coupling of the allylic *O*-stannyl ketyl **31** with a second molecule of *trans*-chalcone (**28**). After hydrogen atom transfer from $nBu_3SnH$, tin enolate

(15) For reactions of tin enolates, see: (a) Suzuki, M.; Yanagisawa, Y.; Noyori, R. *J. Am. Chem. Soc.* **1985**, *107*, 3348. (b) Tardella, P. A. *Tetrahedron Lett.* **1969**, 1117. (c) Nishiyama, H.; Sakuta, K.; Itoh, K. *Tetrahedron Lett.* **1984**, *25*, 2487.

(16) Tissot, P.; Surbeck, J. P.; Gulacar, F. O.; Margaretha, P. *Helv. Chim. Acta.* **1981**, *64*, 1570.

(17) Fournier, F.; Berthelot, J.; Basselier, J. J. *Tetrahedron* **1985**, *41*, 5667.

species **33** was afforded. This enolate next cyclizes by carbonyl addition and hydrolysis to construct cyclopentanol **30**.

## Conclusion

The intramolecular coupling of α,β-unsaturated ketones to activated olefins can be applied to the synthesis of substituted cyclopentanes. Excellent anti stereoselectivities can be achieved with the proper selection of reaction conditions. Additionally, the dual reactivity of the allylic *O*-stannyl ketyl can be distinguished and utilized in sequential one- and two-electron reactions.[12] Although the intermolecular coupling of unsaturated ketones was demonstrated, much additional work is needed. Collectively, this work has illustrated that α,β-unsaturated ketones are a viable radical precursor, and the degree of functionality and stereocontrol which can be achieved should allow this methodology to be applied in the synthesis of natural products.

## Experimental Section

**General.** Melting points were determined on a capillary melting point apparatus and are uncorrected. All reactions were run under an inert atmosphere of argon using flame, or heat-dried apparatus. All reactions were monitored by thin layer chromatography (TLC) and judged complete when starting material was no longer visible in the reaction mixture. All yields reported refer to isolated material judged to be homogeneous by TLC and NMR spectroscopy. Temperatures above and below ambient temperature refer to bath temperatures unless otherwise stated. Solvents and anhydrous liquid reagents were dried according to established procedures by distillation under nitrogen from an appropriate drying agent: ether, benzene, and THF from benzophenone ketyl; and $CH_2Cl_2$ from $CaH_2$. Other solvents were used "as received" from the manufacturer.

Analytical TLC was performed using precoated silica gel plates (0.25 mm) with phosphomolybdic acid in ethanol as an indicator. Column chromatography was performed using Kieselgel silica gel 60 (230–400 mesh) by standard flash[18] and suction chromatographic techniques. Product ratios were determined on a capillary gas chromatograph using a fused silica capillary column (30 m; film thickness, 0.25 μm), unless otherwise noted.

**3(*E*),8(*Z*)-Tetradecadien-2-one (9).** To a previously dried 25 mL round bottom flask (RBF) was added methyl ketone Wittig reagent (1.70 g, 5.31 mmol) along with a magnetic stirrer. 5-Undecenal[19] (0.40 g, 2.38 mmol) was weighed into a separate flask and transferred with 2.6 ml of $CHCl_3$. The reaction was quenched with water and the mixture extracted with $Et_2O$. The $Et_2O$ layer was washed with saturated brine solution, dried over $Na_2SO_4$, and concentrated in vacuo. The concentrate was purified by flash chromatography on a silica gel column to yield a clear oil (0.40 g, 81.0%): $R_f$ 0.75 (70% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 6.81 (1H, m), 6.08 (1H, d, $J$ = 16 Hz), 5.38 (2H, m), 2.26 (3H, s), 2.24 (2H, m), 2.03 (4H, m), 1.54 (2H, m), 1.30 (6H, m), 0.89 (3H, t, $J$ = 7 Hz); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 198.58, 148.23, 131.45, 131.01, 128.61, 32.58, 32.01, 31.56, 29.41, 28.18, 27.29, 26.29, 22.60, 14.08; IR (neat) 3006, 1700, 1628, 1459, 1253, 977 $cm^{-1}$; MS (CI) $m/e$ (relative intensity) 209 ($M^+$ + 1, 9), 150 (20), 137 (21), 97 (35), 95 (28), 84 (25), 81 (34), 69 (28), 67 (29), 43 (100); HRMS (CI) 209.1910 (calcd for $C_{14}H_{25}O$ 209.1905).

**7-Oxo-5-octenal (12).**[20] Glutaric dialdehyde (100 mL of a 50% aqueous solution, 552.3 mmol) was placed into a 300 mL RBF along with a magnetic stirrer. The methyl ketone Wittig reagent (25.5 g, 80.1 mmol) was dissolved in $CH_2Cl_2$ (100 mL) and the solution placed into a large addition funnel. $CH_2Cl_2$ (50 mL) was added to the dialdehyde in the reaction flask, and the ylide solution was slowly added to the reaction mixture. The addition of the ylide took about 1.5 h, and the funnel was rinsed with 10 mL of $CH_2Cl_2$. The reaction was allowed to proceed overnight, and the mixture was extracted with $H_2O$ (2 × 100 mL). The organic layer was dried with $Na_2SO_4$ and concentrated in vacuo. Column chromatography of the residue produced a colorless oil (8.28 g, 59.0 mmol, 74% yield): $R_f$ 0.40 (70% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 9.79 (1H, s), 6.77 (1H, dt, $J$ = 16.0, 6.9 Hz), 6.09 (1H, d, $J$ = 16.0 Hz), 2.52 (2H, t, $J$ = 6.9 Hz), 2.28 (5H, m), 1.84 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 201.51, 198.31, 146.65, 131.87, 42.98, 31.56, 26.95, 20.38.

**General Procedure for the Preparation of Activated Olefins.** To a previously dried flask were added the appropriate stabilized ylide (7 mmol) and a magnetic stir bar. $CHCl_3$ (3.5 mL) was then added, and the reaction mixture was stirred. Once the ylide was completely dissolved, 7-oxo-5-octenal (3.5 mmol) was added. The reaction was followed by TLC, and starting material was usually consumed in 1–2 d. The reaction mixture was concentrated in vacuo, and this residue was flash chromatographed to yield the activated olefin.

**9-Oxo-2(*E*),7(*E*)-decadienenitrile (14):** yield 47%; $R_f$ 0.55 (90% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 6.75 (2H, m), 6.09 (1H, dt, $J$ = 16.0, 1.4 Hz), 5.38 (1H, dt, $J$ = 16.0, 1.4 Hz), 2.27 (7H, m), 1.68 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 198.24, 154.81, 146.36, 131.93, 117.28, 100.55, 32.60, 31.51, 27.06, 26.08; IR (neat) 2933, 2863, 2222 (s), 1731, 1696, 1673, 1631, 1363, 1256, 976 $cm^{-1}$; MS (EI) $m/e$ (relative intensity) 164 ($M^+$ + 1, self-CI, 18), 148 (35), 55 (54), 43 (100), 41 (33), 39 (37); HRMS (EI) 163.0986 (calcd for $C_{10}H_{13}NO$ 163.0997).

**3(*E*),8(*E*)-Undecadiene-2,10-dione (15):** yield 52%; $R_f$ 0.55 (50% EtOAc/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 6.78 (2H, dt, $J$ = 16.0, 7.5 Hz), 6.04 (2H, d, $J$ = 16.0 Hz), 2.37 (10H, m), 1.67 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 198.27, 146.77, 131.78, 31.73, 27.02, 26.51; IR (neat) 2932, 1697, 1673, 1626, 1428, 1363, 1255, 1185, 977, 607 $cm^{-1}$; MS (EI) $m/e$ (relative intensity) 180 ($M^+$, 1), 137 (43), 81 (23), 43 (100); HRMS (EI) 180.1151 (calcd for $C_{11}H_{16}O_2$ 180.11503).

**Methyl 9-oxo-2(*E*),7(*E*)-decadienoate (16):** yield 49%; $R_f$ 0.40 (70% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 6.95 (1H, dt, $J$ = 16.0, 6.9 Hz), 6.78 (1H, dt, $J$ = 16.0, 6.9 Hz), 6.08 (1H, dt, $J$ = 16.0, 1.5 Hz), 5.84 (1H, dt, $J$ = 16.0, 1.5 Hz), 3.73 (3H, s), 2.24 (7H, m), 1.67 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 198.29, 166.78, 148.13, 146.90, 131.63, 121.53, 51.34, 31.57, 31.38, 26.87, 26.28; IR (neat) 1723, 1697, 1674, 1627, 1436, 1362, 1272, 1256, 1202, 977 $cm^{-1}$; MS (EI) $m/e$ (relative intensity) 197 ($M^+$ + 1, self-CI, 82), 196 ($M^+$, 2), 165 (80), 164 (31), 137 (75), 136 (55), 121 (42), 93 (61), 81 (89), 79 (28), 68 (32), 55 (51), 53 (52), 43 (100), 41 (41), 39 (56); HRMS (EI) 196.1091 (calcd for $C_{11}H_{16}O_3$ 196.1099).

**General Procedure for Radical Cyclization of Olefins.** A RBF and a condenser were flame-dried and allowed to cool under an argon atmosphere. After the flask had cooled, the activated olefin (0.5 mmol) was weighed into the flask. Then AIBN (0.05 mmol), followed by $nBu_3SnH$ (1.5 mmol) and freshly distilled benzene (5 mL), was syringed into the flask. This solution was carefully degassed for 15 min with argon. Then the reaction mixture was warmed to 85 °C until the reaction was complete by TLC. When no starting material was observed by TLC, the reaction mixture was concentrated in vacuo, and the mixture was separated by flash chromatography to give the cis- and trans-cyclized products.

**8(*Z*)-Tetradecen-2-one (10):** yield 90%; $R_f$ 0.77 (70% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 5.38 (2H, m), 2.42 (2H, t, $J$ = 8 Hz), 2.14 (3H, s), 1.97 (4H, m), 1.58 (2H, m), 1.30 (10H, m), 0.89 (3H, t, $J$ = 7 Hz); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 209.0, 130.6, 129.9, 43.7, 32.3, 31.3, 29.4, 29.3, 28.8, 27.29, 26.9, 23.6, 22.5, 14.0; IR (neat) 2926, 2855, 1719, 1462, 1358, 1286, 1161, 1075, 968, 723 $cm^{-1}$; MS (CI) $m/e$ (relative intensity) 211 ($M^+$ + 1, 92.7), 193 (32), 125 (22), 85 (41), 43 (100). Anal. Calcd for $C_{14}H_{26}O$ C, 79.94; H, 12.46. Found: C, 79.82; H, 12.40.

***trans*-2-[2-(2-Oxopropyl)cyclopentyl]ethanenitrile (17):** yield 71%; $R_f$ 0.60 (90% $Et_2O$/hexane); 300 MHz $^1H$ NMR

(18) Still, W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(19) Wilson, S. R.; Zucker, P. A.; Kim, C. W.; Villa, C. A. *Tetrahedron Lett.* **1985**, *26*, 1969.
(20) Kovalev, B. G.; Dormindontova, N. P.; Shamshurin, A. A. *Zh. Org. Khim.* **1969**, *5*, 1775.

($CDCl_3$) δ 2.7–2.3 (4H, m), 2.14 (3H, s), 1.98 (3H, m), 1.77 (1H, m), 1.55 (2H, m), 1.44 (1H, m), 1.13 (1H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 207.89, 119.15, 48.75, 41.87, 40.28, 32.66, 32.06, 30.23, 23.55, 21.96; IR (neat) 2954, 2872, 2244 (s), 1713, 1452, 1424, 1359, 1294, 1227, 1174 $cm^{-1}$; MS (EI) *m/e* (relative intensity) 166 ($M^+$ + 1, self-CI, 20), 81 (24), 58 (36), 43 (100), 34 (48); HR MS (EI) 165.11593 (calcd for $C_{10}H_{15}NO$ 165.115 36).

***cis*-2-Acetyl-3-iminobicyclo[3.3.0]octane (18):** yield 24%; $R_f$ 0.40 (90% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 3.37 (1H, m), 2.70 (2H, m), 2.23 (1H, m), 2.10 (3H, s), 1.88 (1H, m), 1.74 (1H, m), 1.53 (4H, m), 1.36 (1H, m), 1.24 (1H, br s); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 196.19, 162.76, 110.90, 48.31, 41.29, 38.22, 34.87, 34.83, 27.95, 25.81; IR (KBr) 3355, 2929, 2856, 1627, 1498, 1340, 1316, 1284, 1270, 926 $cm^{-1}$; MS (EI) *m/e* (relative intensity) 165 ($M^+$, 29), 136 (100), 43 (30), 34 (52); HRMS (EI) 165.1153 (calcd for $C_{10}H_{15}NO$ 165.1154).

***trans*-1-[2-(2-Oxopropyl)cyclopentyl]-2-propanone (19):** yield 73%; $R_f$ 0.70 (50% EtOAc/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 2.60 (2H, dd, *J* = 18, 5 Hz), 2.36 (2H, dd, *J* = 18, 9 Hz), 2.14 (6H, s), 1.89 (4H, m), 1.58 (2H, m), 1.25 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 208.68, 48.97, 40.93, 32.35, 30.26, 23.50; IR (neat) 3602, 2949, 2871, 1713, 1407, 1359, 1274, 1230, 1176, 1154 $cm^{-1}$; MS (EI) *m/e* (relative intensity) 183 ($M^+$ + 1, self-CI, 100), 125 (25), 124 (45), 81 (32), 43 (95); HRMS (EI, self-CI) 183.1387 (calcd for $C_{11}H_{19}O_2$ 183.1385).

***cis*-2(*R*)-Acetyl-3(*S*)-hydroxy-3-methylbicyclo[3.3.0]-octane (20):** $R_f$ 0.65 (50% EtOAc/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 4.09 (1H, br s), 2.86–2.67 (1H, d, *J* = 9.3 Hz), 2.23 (3H, s), 2.00 (1H, dd, *J* = 7.8, 13.2 Hz), 1.80–1.55 (6H, m), 1.31 (3H, s), 1.13 (1H, dd, *J* = 9.3, 13.2 Hz); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 214.64, 82.81, 66.34, 48.28, 47.68, 42.04, 33.26, 32.84, 32.15, 26.21, 25.63; IR (neat) 3474 (br), 2943, 2862, 1689, 1453, 1372, 1237, 1176, 1138, 934 $cm^{-1}$; MS (EI) *m/e* (relative intensity) 182 ($M^+$, 0.1), 167 (1), 124 (71), 81 (10), 66 (20), 43 (100); HRMS (CI) 183.1381 (calcd for $C_{11}H_{19}O_2$ 183.1385).

***trans*-Methyl 2-[2-(2-oxopropyl)cyclopentyl]ethanoate (21):** yield 58%; $R_f$ 0.45 (70% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 3.67 (3H, s), 2.65–2.17 (4H, m), 2.14 (3H, s), 1.89 (4H, m), 1.59 (2H, m), 1.23 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 208.66, 173.66, 51.46, 48.91, 42.01, 40.76, 39.04, 32.33, 32.10, 30.27, 23.44; IR (neat) 2952, 2872, 1738, 1716, 1436, 1359, 1258, 1194, 1176, 1155 $cm^{-1}$; MS (CI) *m/e* (relative intensity) 199 ($M^+$ + 1, 63), 167 (92), 141 (27), 81 (60), 67 (37), 43 (100); HRMS (EI) 167.1075 (calcd for $C_{11}H_{16}O_3$ – $OCH_3$ 167.1072).

***cis*-2-Acetyl-3-oxobicyclo[3.3.0]octane (22):** yield 27%; $R_f$ 0.65 (70% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 13.8 (1H, br s), 3.26 (1H, m), 2.70 (2H, m), 2.06 (3H, s), 1.92 (3H, m), 1.58 (2H, m), 1.45 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 202, 180.39, 115.27, 43.43, 42.93, 37.16, 34.80, 34.39, 26.04, 21.44; IR (neat) 2948, 2864, 1710, 1652, 1448, 1389, 1286, 1235, 937, 893 $cm^{-1}$; MS (EI) *m/e* (relative intensity) 166 ($M^+$, 76), 137 (100), 124 (30), 95 (48), 43 (98), 41 (31), 39 (32); HRMS (EI) 166.0991 (calcd for $C_{10}H_{14}O_2$ 166.0994).

**General Procedure for Enolate-Trapping Studies.** A RBF and a condenser were flame-dried and allowed to cool under an argon atmosphere. After the flask had cooled, diene precursor **16** (0.250 mmol) was weighed into the flask. Then AIBN (0.025 mmol), followed by $nBu_3SnH$ (0.265 mmol) and freshly distilled benzene (25 mL), was syringed into the flask. This solution was carefully degassed for 15 min with argon. The reaction mixture was warmed to 85 °C for 1 h, and then either $D_2O$ (excess) or $Br_2$ in $CCl_4$ (0.75 mmol) was added. When no starting material was observed on TLC, the reaction mixture was concentrated in vacuo, and the mixture was separated by flash chromatography to give trans-cyclized products.

**Methyl 2-[2-(1-bromo-2-oxopropyl)cyclopentyl]ethanoate (27a):** yield 86%; $R_f$ 0.68 (90% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 4.45 (1H, d, *J* = 7.5 Hz), 3.68 (3H, s), 2.47 (1H, dd, *J* = 7.5, 15 Hz), 2.38 (3H, s), 2.27 (1H, dd, *J* = 9, 15 Hz), 2.3–2.1 (2H, m), 1.90 (2H, m), 1.63 (2H, m), 1.45–1.2 (2H, m); 75 MHz $^{13}C$ NMR ($CDCl_3$) δ 201.96, 173.09, 60.27, 51.48, 46.41, 40.02, 38.98, 32.65, 30.16, 27.48, 23.81; IR (neat) 2953, 2871, 1736, 1436, 1358, 1257, 1198, 1166, 1086, 1014 $cm^{-1}$; MS (EI) *m/e* (relative intensity) 278 ($M^+$, $^{81}Br^-$), 276 ($M^+$, $^{79}Br^-$), 165 (11), 141 (16), 123 (15), 95 (17), 81 (18), 43 (100); HRMS (CI) 279.0417 (calcd for $C_{11}H_{18}{}^{81}BrO_3$ 279.0419).

**Methyl 2-[2-(1-deuterio-2-oxopropyl)cyclopentyl]-ethanoate (27b):** yield 87%, (85% deuterium incorporation); $R_f$ 0.60 (90% $Et_2O$/hexane); 300 MHz $^1H$ NMR ($CDCl_3$) δ 3.67 (3H, s), 2.62 (0.6H, dd, *J* = 6, 18 Hz), 2.46 (1H, dd, *J* = 6, 15 Hz), 2.35 (0.5H, dd, *J* = 9, 18 Hz), 2.21 (1H, dd, *J* = 9, 15 Hz), 2.14 (3H, s), 1.89 (4H, m), 1.59 (2H, m), 1.23 (2H, m); MS (CI) *m/e* (relative intensity) 200 ($M^+$, 25), 199 (24), 168 (100), 167 (99), 149 (3), 140 (12), 139 (9), 121 (4).

**Hydrodimerization of Chalcone (28).** Chalcone (0.206 g, 1.00 mmol) was weighed into a previously dried 5 mL RBF. Freshly distilled benzene (1 mL), a magnetic stir bar, AIBN (7.0 mg, 0.04 mmol), and $nBu_3SnH$ (0.15 mL, 0.5577 mmol) were added, and the reaction mixture was degassed for 15 min. After TLC showed that chalcone was consumed, the reaction mixture was concentrated in vacuo, and the residue was separated by column chromatography. The simple reduced product, 1,3-diphenyl-1-propanone (**29**), identical to that reported previously,[21] was obtained as a colorless solid which melted at 69–70 °C (lit. 70–72 °C). The hydrodimerized and cyclized product, **30**, identical to that reported previously,[17] was obtained as a mixture of isomers which was a colorless solid which melted at 93–101 °C (lit. 91–99 °C).

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**Supporting Information Available:** Spectral data for compounds **9**, **14**–**22**, and **27a**,**b** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(21) Hamrick, P. J., Jr.; Hauser, C. R. *J. Am. Chem. Soc.* **1959**, *81*, 493.