with the coil unit through the ether oxygens, and possibly, with the mesogenic unit through the carbonyl groups. A further investigation to reveal the mechanism for the spectral changes in the mesogenic unit is currently underway by performing both the salt and temperature dependent studies.

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New Radical Allylation Reactions Using 2-Bromo-3-(phenylthio)propene and Their Application to the Synthesis of Carbocyclic Compounds[1]

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A study on the application of vinyl radical cyclization *via* free radical allylation reaction in the synthesis of various carbocyclic compounds is described. In connection with this study, a new allyl transfer reagent, 2-bromo-3-(phenylthio) propene **1** is developed and it was shown that vinyl radical cyclization through free radical allylation reaction using reagent **1** provides a valuable approach to carbocyclic systems with a reactive *exo*-alkylidene moiety, which is advantageous for further transformations.

Introduction

Over the last 10 years, many free radical methods have demonstrated their efficiency in synthetic organic chemistry and particularly free radical cyclization has emerged as one of the most important methods in the construction of a va-

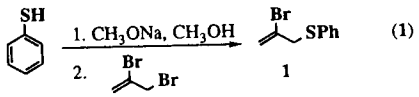
riety of cyclic compounds.[2] Ring formation by intramolecular radical addition has attracted particular interest since it can often be carried out efficiently under mild conditions and with such chemoselectivity that the use of protecting groups is minimized. Therefore, the desire to design useful radical reaction sequences has fostered the development of new methods for vinyl radical generation and cyclization. The use of vinyl radicals in the tin hydride method is very attractive because these radicals are reactive and have an advantage over alkyl radicals in the sense that the product contains a vinyl functionality which is then available for further synthetic manipulation.[3] The intramolecular addition of a vinyl radical to a multiple bond results in a product with the double bond at a predetermined position.

It has been recognized that carbon-carbon bond formation via vinyl radicals is an important synthetic operation in organic synthesis. The synthetic chemistry of vinyl radicals has been extensively developed by Stork.[4] Seychellene and Patchouli were synthesized by the method of vinyl radical cyclization.[5] Also, vinyl radical cyclization has been utilized as a useful tool in the synthesis of triquinane sesquiterpenes such as modhephene[6] and silphiperfolene.[7] There are two important methods for generating vinyl radicals.[8] The first method generates vinyl radical by the addition of tin radical to an alkyne. The second, more common method produces vinyl radical by the reaction of tin radical with vinyl bromides or vinyl iodides.

These valuable features prompted us to seek a new method for the preparation of vinyl bromide precursors which might lead to the generation of vinyl radicals. As a part of an effort to explore the synthetic utility of vinyl radical cyclization, we initiated the development of new allyl transfer reagent, 2-bromo-3-(phenylthio)propene **1**, and its reaction with various organic halides. It was our goal to provide a new method for ring formation by sequencing a radical allylation with a cyclization. We wish to report herein that the vinyl radical cyclization *via* free radical allylation reaction provides a powerful method for the construction of a wide variety of carbocyclic compounds.

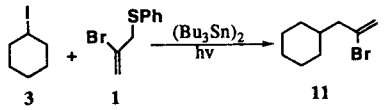
Results and Discussion

A new allyl transfer reagent, 2-bromo-3-(phenylthio)propene **1**, was prepared as shown in Eq. (1). Sodium thiophenoxide anion was generated by treatment of thiophenol with sodium methoxide in methanol. Subsequent addition of 2,3-dibromopropene afforded 2-bromo-3-(phenylthio)propene **1** in 81% yield. With a new allyl transfer reagent **1** in hand, the radical allylation using this reagent was investigated. In a typical experiment, sunlamp irradiation of the benzene solution (0.5 M) of cyclohexyliodide (1.0 equiv), 2-bromo-3-(phenylthio)propene **1** (2.0 equiv), and hexabutylditin (1.0 equiv) with a 275-W GE sunlamp at 80 ℃ for 0.5 h resulted in the formation of 2-bromo-3-cyclohexylpropene **11** in 48 % yield. The structure of allylated compound **11** was confirmed by ^{1}H NMR, ^{13}C NMR, IR, and mass spectra. The ^{1}H NMR



(1)

spectrum exhibited two new vinyl protons at δ 5.22 and 5.40, which were upfield from those of 2-bromo-3-(phenylthio)propene **1**. The ^{13}C NMR showed two vinyl carbons at δ 133.6 (singlet) and δ 117.4 (triplet). The overall allylation reaction is summarized by Eq. (2).



(2)

3 1 11

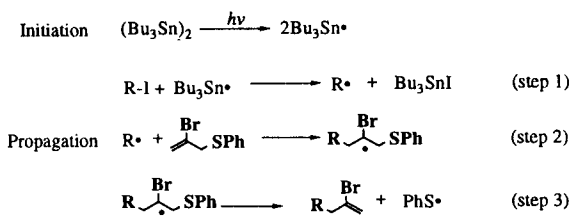
Encouraged by the above successful allylation reaction, several alkyl halides were explored as substrates for the new allylation reaction. The best results were obtained with alkyl iodides. Representative results for the reaction of 2-bromo-3-(phenylthio)propene **1** with alkyl halides are summarized in Table 1. Iodides undergo more efficient chain transfer with the tri-*n*-butyltin radical than do the corresponding bromides. As shown in Table 1, primary-iodides (entry 3-5) gave relatively modest yields while secondary- and tertiary-iodides (entry 1, 2) gave better yields. The tertiary-iodides are better atom donors than secondary- or primary-iodides, so side reactions can be minimized. The mechanism for the allylation reaction using allyl phenyl sulfide was originally rationalized by Keck.[13] By analogy the plausible mechanism for the new allyl transfer reaction is outlined in Scheme 1.

After successful allylation reactions which provide vinyl bromide compounds, the vinyl radical cyclization was next explored. The photoreaction of alkyl iodide **1a** with 2-bromo-3-(phenylthio)propene **1** in the presence of hexabutylditin was run in benzene under the standard reaction conditions

Table 1. Results of Allylation Reactions of 2-bromo-3-(phenylthio)propene **1** with Organic Halides[a]

Entry	Substrate	Product	Reaction time (h)	Yield[b] (%)
1	 2[c]	 10	0.5	84
2	 3	 11	2.0	75
3	$CH_3(CH_2)_7I$ 4	$CH_3(CH_2)_7$ Br 12	3.0	59
4	 5[d]	 13	3.0	46
5	 6[e]	 14	3.0	52
6	 7[f]	10	12.0	44
7	 8	11	12.0	41
8	$CH_3(CH_2)_7Br$ 9	12	12.0	36

[a] All the allylation reactions were performed in benzene with alkyl halides (1.0 equiv), 2-bromo-3-(phenylthio)propene **1** (2.0 equiv), hexabutylditin (1.0 equiv) with sunlamp. [b] Yields refer to isolated materials. [c] Prepared by the method of ref 9. [d] Prepared by the method of ref 10. [e] Prepared by the method of ref 11. [f] Prepared by the method of ref 12.



Scheme 1.

Scheme 2.

to afford the desired cyclization precursor **1b** in 46% yield. Subsequent vinyl radical cyclization of the vinyl bromide **1b** with tri-*n*-butyltin hydride in the presence of 1,1′-azobisisobutyronitrile (AIBN) in refluxing benzene, followed by treatment of the resulting product with I_2/DBU,[14] provided a *cis*-bicyclic product **1c** in 55% yield. The overall reaction is illustrated in Scheme 2.

The relatively low yield for the cyclization reaction is probably due to the volatility of the cyclized compound **1c** and the difficulty in removing tin by-products from the desired product **1c**. The ^{1}H NMR and mass spectra were consistent with those reported in the literature.[15]

In all of the reported work, the stereochemistry of the newly formed ring junction (5,6-membered ring) has been strictly cis. In accordance with rules for ring fusion chemistry we assign *cis*-fusion geometry to compounds **1c-4c** and **6c**.[16] The transition states for the formation of *trans*-fused bicyclic [3.4.0] products encounter significant strain to meet the stereoelectronic requirements. There is a similarly large energetic advantage for formation of *cis*-products from ring closure of the vinyl radical.

Encouraged by the above successful cyclization, the behavior of other cyclization precursors was examined. Table 2 lists our results with specific examples of the present annulation method. Subsequent cyclization of the precursor **2b** leads to the formation of *cis*-fused product **2c** in 74% yield after chromatographic separation. The ^{1}H NMR spectrum showed two vinyl protons at δ 4.98 and 4.81. The IR spectrum showed a strong absorption at 1732 cm^{-1} (C=O). Also ^{13}C NMR and mass spectra were consistent with the assigned structure. Vinyl radical cyclization with the precursor **3b** resulted in the formation of a 60/40 mixture of two diastereomers as judged by GC analysis. The structure of these two diastereomers were assigned by ^{1}H NMR, IR, ^{13}C NMR and mass spectra. The ^{1}H NMR spectrum of one product showed two vinyl protons at δ 4.99 and 4.84. The ^{1}H NMR spectrum of the other product exhibited two vinyl protons at δ 4.86 and 4.82.

The behavior of a cyclization precursor with an electron-withdrawing group at the α-position of an alkene was next examined because it has been pointed out that radical stabilizing α-substituents influence the rate of addition.[17] The vinyl bromide **4b** was subjected to the vinyl radical cyclization under standard reaction conditions. Flash chromatography of the crude product afforded **4c** as the only product in 55% yield. The ^{1}H NMR spectrum showed two characteristic vinyl protons at δ 4.89 and 4.60. The structure of cyclized product was further confirmed by ^{13}C NMR and mass spectra.

Natural products containing the spiro[4.5]decane ring system are widespread and also spirocyclic compounds (naturally occuring or from synthetic origin) serve as useful intermediates for the construction of other systems.[22] Thus we turned our attention to a spiro vinyl radical cyclization of **5b** which can provide a spiro[4.5]decane ring system. A mixture of vinyl bromide **5b** was treated with tri-*n*-butyltin hydride (1.2 equiv) and a catalytic amount of AIBN in refluxing benzene (0.1 M) for 6 h to give two inseparable isomers **5c** and **5d** in a combined yield of 67%. The ratio of the mixture could not be determined by GC and ^{1}H NMR integration. The ^{1}H NMR spectrum of the major product exhibited two alkene resonances, a terminal alkene at δ 4.82 and another at δ 4.73 ppm, which is consistent with the assigned structure. A *t*-butyl group was observed at δ 0.84 ppm and mass spectrum exhibited a parent peak at 220.

The next investigation focused on the 6-*exo* vinyl radical cyclization. Usually, the formation of six and seven-membered rings is not recommended in free radical chemistry.[1] The rate constant for radical abstraction of a hydrogen atom from alkyltin hydride is 2×10^6 M^{-1} s^{-1}. However, the rate constants for 6-*exo* and 7-*endo* ring closure of the 1-heptene radical are 5.4×10^3 s^{-1} and 7.5×10^2 s^{-1}, respectively.[23] It is believed that vinyl radicals will be more reactive towards

Table 2. Results of Vinyl Radical Cyclization *via* Radical Allylation Reaction

Entry	Organic Iodides	Vinyl Bromides[a]	Cyclized Products[a]
1	R_1= H, R_2= H (1a)[c]	R_1= H, R_2= H (46%) (1b)	R_1= H, R_2 = H (55%) (1c)
2	R_1= R_2= CO_2Et (2a)[d]	R_1= R_2= CO_2Et (36%) (2b)	R_1=R_2 = CO_2Et (74%) (2c)
3	R_1= H, R_2= CO_2Et (3a)[e]	R_1= H, R_2= CO_2Et (33%) (3b)	R_1= H, R_2=CO_2Et (61%) (3c)
4	4a[f]	4b (42%)	4c (55%)
5	5a[g]	5b (45%)	5c + 5d (67%)
6	6a[h]	6b (43%)	6c + 6d (62%)
7	7a[i]	7b (46%)	7c + 7d (60%)

[a] Yields refer to isolated materials. [b] The ratios were determined by GC analysis. [c] Prepared by the method of ref 8. [d,h,i] Prepared by the method of ref 18. [e] Prepared by the method of ref 19. [f] Prepared by the method of ref 20. [g] Prepared by the method of ref 21.

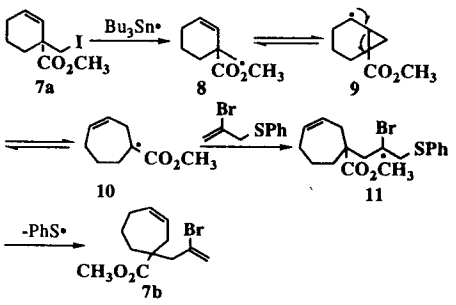
cyclization than alkyl radicals, but they also will react with tin hydride faster. Cyclization of **6b** with tributyltin hydride at 0.005 M in benzene in the presence of AIBN (0.1 equiv) afforded cyclized product **6c** (53%) along with reduced product **6d** (9%) in 62% combined yield. These two products were separated by HPLC and the cyclized product **6c** was fully characterized by ^{1}H NMR, ^{13}C NMR, IR, and mass spectral analysis. The product ratio was 85/15 as indicated by GC analysis. In the tin hydride method, a common problem is the trapping of radicals by hydrogen abstraction from the reagent before cyclization. Thus, it is believed that the modest yield of **6c** and the presence of relatively large amounts of reduced product **6d** reflect the slow cyclization of the intermediate vinyl radical.[24] The ^{1}H NMR spectrum of the cyclized product exhibited two vinyl protons at δ 4.72 and 4.65. The IR spectrum showed a strong absorption at 1720 cm^{-1} and mass spectrum showed a parent peak at 208.

The study of vinyl radical cyclization *via* free radical rearrangement was next extended to prepare a bridged bicyclic compound. Vinyl radical migrations, both planned and adventitious, are common in free radical chemistry and have been the subject of numerous studies over 30 years.[25] Interest in such rearrangements has recently been stimulated by synthetic and mechanistic studies of ring closure of suitably constituted vinyl radicals to double bonds.[26] These closures produce homoallylic radicals which may rearrange further under suitable reaction conditions to give the *endo* cyclization products.

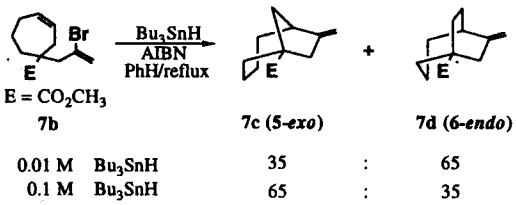
The proposed mechanism for the formation of **7b** is shown in Scheme 3. The primary alkyl radical **8**, which is generated from the abstraction of iodine atom with tributyltin radical, attacks the double bond to produce secondary radical **9**. The resulting secondary radical **9** undergoes ring cleavage to give the stabilized radical **10**. The addition of **10** to the allylating agent **1** followed by fragmentation affords the ring-expanded product **7b** as illustrated in Scheme 3.

Treatment of vinyl bromide **7b** with Bu_3SnH (1.2 equiv) in the presence of AIBN (0.2 equiv) gave 65/35 mixture of **7c** (5-*exo*) and **7d** (6-*endo*) products in 60% yield after purification by flash chromatography. This mixture was not separable by chromatography. When the cyclization reaction was conducted in a 0.01 M solution (0.1 M solution), the product ratio (5-*exo*/6-*endo*=**7c**/**7d**) was 35/65(65/35) which was determined according to GC analysis and ^{1}H NMR integration (eq. 3).

The structure assignment of a mixture of **7c** and **7d** was based on the ^{1}H NMR, IR, ^{13}C NMR and mass spectra. The



Scheme 3.



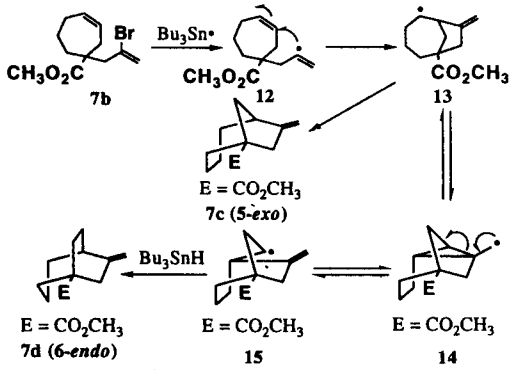
0.01 M Bu_3SnH	35	:	65
0.1 M Bu_3SnH	65	:	35

(3)

IR spectrum displayed a strong absorption at 1741 cm^{-1} (C=O) and a weak absorption 1642 cm^{-1} (C=C). Its corresponding ^{1}H NMR spectrum confirmed the presence of vinyl group in the product, as indicated by vinyl proton peaks at δ 4.74 and 4.88 respectively. Furthermore, in the ^{1}H NMR spectrum, no signals (δ 5.51-5.83) due to the vinyl group of vinyl bromide **7b** were present. The ester group was identified by the presence of methyl resonances in the ^{1}H NMR spectrum at δ 3.64 and 3.66. The structure of the product was further confirmed by ^{13}C NMR and mass spectra. Resonances in the ^{13}C NMR at δ 149.9 (two carbons overlapped), 108.8, and 105.3 supported the presence of the exocyclic vinyl group. The mass spectrum showed a parent peak at 194 (M^+) and a base peak at 135 (M^+-COOMe).

From the above reaction, we can see that the reaction conditions (tin hydride concentration) play an important role in determining the composition of products. Recently Berkowitz[27] investigated the competition between 5-*exo* and 6-*endo* modes of vinyl radical cyclization and has shown that the initially formed bicyclic radical **13** rearranges to radical **15** *via* cyclopropylcarbinyl radical **14** at low concentration of tin hydride. On the basis of his study, we proposed the likely mechanism for the vinyl radical cyclization of **7b** as depicted in Scheme 4. The stannyl radical (Bu_3Sn·) abstracts the bromine atom from vinyl bromide **7b** to generate vinyl radical **12**. The vinyl radical thus generated adds to the double bond to produce the cycloheptyl radical **13**. The alkyl radical **13** can abstract a hydrogen atom from tributyltin hydride to give the cyclized product **7c** or can attack a double bond to produce the primary radical **14**. The cyclopropylcarbinyl radical **14** undergoes fragmentation to produce the secondary radical **15** which abstracts a hydrogen atom from tributyltin hydride to give the cyclized product **7d**.

In conclusion, we have%discovered that vinyl radical cyclizations *via* radical allylation reactions provide a convenient and efficient route to various bicyclic compounds. A new allyl transfer reagent, 2-bromo-3-(phenylthio)propene **1**, was



Scheme 4.

introduced and utilized to prepare vinyl bromide precursors which led to the formation of various carbobicyclic compounds *via* vinyl radical cyclization.

Experimental

Unless otherwise noted, all reactions were run under a nitrogen atmosphere. Solvents were dried prior to use as follows: tetrahydrofuran (THF), diethyl ether, and benzene were distilled from under nitrogen from sodium-benzophenone. Methylene chloride, dimethylsulfoxide (DMSO), *N,N*-dimethyl-formamide (DMF), and acetonitrile were distilled from calcium hydride. DMF was stored over molecular sieves. Benzene was degassed by flushing with argon for 20 minutes before radical reactions. Hexamethylphosphoramide (HMPA) and all amines were distilled from CaH_2 under high vacuum, and stored over 4 Å molecular sieves under nitrogen atmosphere. All melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Boiling points under atmospheric pressure are uncorrected.

Nuclear magnetic resonance (NMR) spectra were recorded on a FT-Bruker WH-300 (300 MHz for ^1H) or a FT-Bruker AF-300 (300 MHz for ^1H NMR; 75 MHz for ^{13}C NMR). The solvent was $CDCl_3$ unless noted otherwise. Mass spectra were recorded at an ionization potential of 70 eV. Infrared spectra were obtained on a IBM IR/32 FTIR spectrometer and spectra were obtained in chloroform using a 0.2 mm path sodium chloride microcavity cells against a chloroform reference, or as a neat thin film on NaCl. Flash chromatography was performed with Keisel 60 (230-400 mesh ASTM) silica gel as a stationary phase. Analytical gas chromatography (GC) was performed on a HP-5890 instrument equipped with a fused silica capillary column (SPB-1, 30M, 0.25 μm, 0.32 mm ID) and a flame ionization detector (FID) using helium as a carrier gas. The following temperature program was used to determine the isomeric ratios and the diastereomeric ratios: initial temperature (0 min) 80 ℃; temperature ramp: 25 ℃/min; final temperature: 250 ℃; injection temperature: 250 ℃; detector temperature: 250 ℃; the carrier gas flow rate: 28 mL/min.

2-Bromo-3-(phenylthio)propene (1). To a solution of sodium methoxide (2.70 g, 50 mmol) in methanol (20 mL) was added thiophenol (5.51 g, 50 mmol) followed by 2,3-dibromopropene (11.00 g, 55 mmol). There was an immediate precipitation of sodium bromide. The reaction was allowed to stand 12 h at 25 ℃. Water was added to dissolve the sodium bromide. The upper oily layer was separated with ether (3x) and the combined organic phase was washed with brine (1x), and dried over magnesium sulfate, and the ether was removed *in vacuo*. The residue was purified by vacuum-distillation to give the product **1** (9.30 g, 81%) as a very light yellow oil: bp=89-90 ℃ (0.7 mmHg); ^1H NMR ($CDCl_3$) δ 7.51-7.20 (5H, m), 5.73 (1H, d, J=1.5 Hz), 5.47 (1H, d, J=1.5 Hz), 3.81 (2H, s); ^{13}C NMR ($CDCl_3$) δ 134.6, 130.5, 129.0, 128.7, 127.0, 119.1, 44.6; IR (thin film) 3059, 2914, 1635, 1622, 1583, 1479, 1197, 1088, 895, 738, 690 cm^{-1}.

3-(Iodomethyl)cyclohexene (5). The reaction of 3-hydroxy cyclohexene (3.0 g, 31 mmol), 30-mesh Zn-Cu couple (3.8 g, 57 mmol), and CH_2I_2 (11.0 g, 41 mmol) in ether (100 mL) was carried out under reflux for 12 h. After the reaction was complete, the reaction mixture was cooled in an ice bath and then saturated NH_4Cl (100 mL) was added slowly dropwise to the pink viscous mixture. The aqueous layer was extracted with ether (2x) and the combined ether layers were dried over anhydrous magnesium sulfate. After removal of the ether by evaporation, the remaining brownish liquid was separated by flash column chromatography (100% hexanes) to give 3-(iodomethyl)cyclohexene **5** (1.38 g, 20%) as a clear oil; ^1H NMR ($CDCl_3$) δ 5.82-5.76 (1H, m), 5.58-5.54 (1H, m), 3.20-3.09 (2H, m), 2.37-2.32 (1H, m), 1.97-1.36 (6H, a series of multiplets); ^{13}C NMR ($CDCl_3$) δ 129.7, 129.4, 37.5, 29.6, 25.3, 20.9, 14.2; IR (thin film) 3018, 2927, 2859, 1648, 1431, 1270, 1170, 887, 702 cm^{-1}; MS m/e 222 (M^+), 127, 95 (M^+-I), 67; HRMS m/e calculated for C_7H_{11} (M^+-I): 95.0860; found: 95.0861.

3-(Iodomethyl)cyclohexan-1-one (6). To a suspension of sodium hydride (400 mg, 60% in oil, 10 mmol, washed with distilled hexanes three times, nitrogen purge dried) in dry DMF (20 mL) was added trimethylsulfoxonium iodide in several portions over 10 min. The resulting mixture was allowed to stir at 25 ℃ for 30 min, after which 2-cyclohexen-1-one (961 mg, 10 mmol) in DMF (3.0 mL) was added. After 2 h, the reaction mixture was poured into ice cold aqueous HCl (2%). Extractive workup with ether (3×10 mL) followed by flash chromatography (hexanes/EtOAc=5 : 1) afforded bicyclo[4.1.0]heptan-2-one (759 mg, 69%) as a colorless oil; ^1H NMR ($CDCl_3$) δ 2.30 (1H, m), 2.24 (1H, m), 2.10-1.58 (6H, a series of multiplets), 1.25-1.18 (1H, m), 1.12-1.04 (1H, m); IR (thin film) 3017, 2934, 2863, 1690, 1350, 1244, 1069, 961, 932, 876 cm^{-1}. Aqueous HI (47%, 2.54 mmol) in HOAc (0.4 mL) was added to a solution of bicyclo[4.1.0]heptan-2-one (200 mg, 1.82 mmol) in benzene (6.0 mL) at 0 ℃. After stirring for 1 h, the reaction mixture was extracted with ether (3×10 mL). The combined organic extractions were dried over anhydrous $MgSO_4$. After removing the solvent, the desired iodide **6** (268 mg, 62%) was isolated *via* flash chromatography (hexanes/EtOAc=5 : 1) as a colorless oil; ^1H NMR ($CDCl_3$) δ 3.20 (2H, m), 2.52-1.44 (9H, a series of multiplets); IR (thin film) 2938, 2867, 1711, 1447, 1424, 1273, 1223, 1172 cm^{-1}.

2-Bromo-3-(1-methylcyclohexyl)propene (10). Compound **10** was prepared following the general procedure for **11** with 1-metyl-1-iodocyclohexane (0.34 g, 1.50 mmol), 2-bromo-3-(phenylthio)propene **1** (0.69 g, 3.00 mmol) and hexabutylditin (0.87 g, 1.50 mmol) in dry benzene (1.7 mL). Purification by MPLC (100% hexanes) gave product **10** (272 mg, 84%) as a colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 5.54 (1H, s), 5.50 (1H, s), 2.45 (2H, s), 1.56-1.35 (10H, m), 1.00 (3H, s); ^{13}C NMR ($CDCl_3$) δ 130.3 (s), 120.2 (t), 52.9 (t), 37.9 (t), 34.2 (s), 26.3 (t), 25.1 (t), 22.1 (q); IR (thin film) 2926, 2853, 1622, 1458, 1377, 1208, 1179, 1150, 885, 612 cm^{-1}; MS m/e 217 (M^+), 177, 137, 123, 109, 97, 81, 69, 55; HRMS m/e calculated for $C_{10}H_{17}$ (M^+-Br): 137.1333; found: 137.1333.

Compound **10** was also prepared following the general procedure for **11** with 1-metyl-1-bromocyclohexane (176 mg, 1.00 mmol), 2-bromo-3-(phenylthio)propene **1** (458 mg, 2.00 mmol) and hexabutylditin (580 mg, 1.00 mmol) in dry benzene (1.2 mL). Purification by MPLC (100% hexanes) gave product **10** (95 mg, 44%) as a colorless oil.

2-Bromo-3-cyclohexylpropene (11). General Procedure: A solution of cyclohexyliodide (0.32 g, 1.50 mmol), 2-

bromo-3-(phenylthio)propene **1** (0.69 g, 3.00 mmol), and hexabutylditin (0.87 g, 1.50 mmol) in dry bezene (1.7 mL) was placed in a pyrex ^{13}C NMR tube and degassed with nitrogen for 20 min. The tube was sealed with septum and irradiated with a 275-W GE sunlamp for 2 h, at which time no starting material remained by GC analysis. The crude mixture was treated with I_2/DBU and then with an excess of aqueous Oxone ($2KHSO_5$, $KHSO_4$, K_2SO_4, Aldrich) to facilitate separation, filtered through a pad of silica gel, and concentrated in vacuo. Purification of the residue by MPLC with hexanes afforded product **11** (0.23 g, 75%) as a colorless oil; ^1H NMR ($CDCl_3$) δ 5.52 (1H, s), 5.40 (1H, s), 2.27 (2H, d, J=6.8 Hz), 1.74-0.85 (11H, a series of multiplets); ^{13}C NMR ($CDCl_3$) δ 133.6 (s), 117.4 (t), 49.2 (t), 35.7 (d), 32.5 (t), 26.5 (t), 26.2 (t); IR (thin film) 2924, 2852, 1628, 1461, 1448, 1206, 1156, 883 cm^{-1}; MS, m/e 202 (M^+), 179, 149, 137, 123, 109, 97, 83, 67, 55; HRMS m/e calculated for $C_9H_{15}Br$: 202.0357; found: 202.0358.

Compound **11** was also prepared following the above general procedure with bromocyclohexane (244.6 mg, 1.50 mmol), 2-bromo-3-(phenylthio)propene **1** (687.5 mg, 3.00 mmol) and hexabutylditin (870.1 mg, 1.50 mmol) in dry benzene (1.7 mL). Purification by MPLC (100% hexanes) gave product **11** (124.0 mg, 41%) as a colorless oil.

2-Bromo-1-undecene (12). Compound **12** was prepared following the general procedure for **11** with 1-iodooctane (0.36 g, 1.50 mmol), 2-bromo-3-(phenylthio)propene **1** (0.69 g, 3.00 mmol) and hexabutylditin (0.87 g, 1.50 mmol) in dry benzene (1.5 mL). Purification by MPLC (100% hexanes) gave product **12** (206 mg, 59%); ^1H NMR ($CDCl_3$) δ 5.55 (1H, s), 5.38 (1H, s), 2.42 (2H, t, J=6.9 Hz), 1.57-0.86 (17H, a series of multiplets); ^{13}C NMR ($CDCl_3$) δ 135.1 (s), 116.2 (t), 41.5 (t), 32.0 (t), 29.7 (t), 29.6 (t), 29.4 (t), 28.5 (t), 28.0 (t), 22.8 (t), 14.2 (q); IR (thin film) 2926, 2855, 1630, 1466, 884 cm^{-1}; MS m/e 232 (M^+), 120, 111, 97, 83, 69, 55, 43; HRMS m/e calculated for $C_{11}H_{21}Br$: 232.0827; found: 232.0740.

Compound **12** was prepared following the general procedure for **11** with 1-bromooctane (193.1 mg, 1.00 mmol), 2-bromo-3-(phenylthio)propene **1** (458.3 mg, 2.00 mmol) and hexabutylditin (580.1 mg, 1.00 mmol) in dry benzene (1.0 mL). Purification by MPLC (100% hexanes) gave product **12** (83.5 mg, 36%).

3-(3-Bromo-3-butenyl)cyclohexene (13). Compound **13** was prepared following the general procedure for **11** with 3-(iodomethyl)cyclohexene (244 mg, 1.10 mmol), 2-bromo-3-(phenylthio)propene **1** (504 mg, 2.20 mmol) and hexabutylditin (638 mg, 1.10 mmol) in dry bezene (1.3 mL). Purification by flash chromatography (100% hexanes) gave product **13** (109 mg, 46%) as a colorless oil; ^1H NMR ($CDCl_3$) δ 5.70 (1H, m), 5.57 (1H, d, J=1.5 Hz), 5.39 (1H, d, J=1.5 Hz), 2.48 (2H, t, J=7.7 Hz), 2.15-1.21 (9H, a series of multiplets); ^{13}C NMR ($CDCl_3$) δ 135.0, 131.3, 127.6, 116.3, 39.0, 34.6, 34.1, 28.9, 25.4, 21.5; IR (thin film) 3017, 2928, 2858, 1619, 1452, 1330, 1162, 812 cm^{-1}; MS m/e 135 (M^+-Br), 94, 79, 67, 55; HRMS m/e calculated for $C_{10}H_{15}$ (M^+-Br): 135.1174; found: 135.1174.

3-(3-Bromo-3-butenyl)cyclohexan-1-one (14). Compound **14** was prepared following the general procedure for **11** with iodoketone **6** (161.0 mg, 0.68 mmol), 2-bromo-3-(phenylthio)propene **1** (310 mg, 1.35 mmol) and hexabutylditin (392.0 mg, 0.68 mmol) in dry benzene (0.8 mL). Purification by flash column chromatography (hexanes/EtOAc=5 : 1) gave the desired allylation product **14** (81.0 mg, 52%) as a colorless oil; ^1H NMR ($CDCl_3$) δ 5.55 (1H, s), 5.37 (1H, s), 2.44-1.22 (13H, a series of multiplets); ^{13}C NMR ($CDCl_3$) δ 211.2, 134.0, 116.8, 47.8, 41.4, 38.6, 37.8, 34.6, 31.1, 25.1; IR (thin film) 2932, 2861, 1713, 1628, 1225 cm^{-1}; MS m/e 151 (M^+-Br), 110, 97, 82, 67, 55; HRMS m/e calculated for $C_{10}H_{15}O$ (M^+-Br): 151.1123; found: 151.1123.

***cis*-1-Methylene-octahydro-1H-indene (1c).** The general procedure for vinyl radical cyclization was followed with use of vinyl bromide **13** (36.0 mg, 0.17 mmol), tributyltin hydride (54 μL, 0.20 mmol), and AIBN (5.5 mg, 0.03 mmol) in dry bezene (1.6 mL). Purification by flash chromatography (100% pentane) gave cyclized product **1c** (12.5 mg, 55%) as a colorless oil; ^1H NMR ($CDCl_3$) δ 4.87 (1H, m), 4.79 (1H, m), 2.42-2.35 (2H, m), 2.06-1.18 (12H, m); MS m/e 136 (M^+), 121, 107, 95, 79, 67, 55; HRMS m/e calculated for $C_{10}H_{16}$: 136.1252; found: 136.1253. ^{13}C NMR spectrum couldn't be obtained because of the difficulty in removing the solvent from the very volatile product. However, the ^1H NMR spectrum is identical with the literature data.

Diethyl 2-(cyclohexen-1-yl)-2-iodo-propane 1,3-dioate (2a). Diethylmalonate (6.34 g, 39.6 mmol) was added slowly from a dropping funnel to a magnetically stirred solution of sodium metal (0.91 g, 39.6 mmol) in absolute ethanol (60 mL). Stirring was continued, and after an additional 30 min, 3-bromo-cyclohexene (5.80 g, 36.0 mmol) was added slowly. The mixture was allowed to stir at 25 ℃ for 12 h, and then the solvent was removed slowly by distillation atmospheric pressure. The water was added to dissolve the sodium bromide. The upper oily layer was separated with ether (3x) and the combined organic phase was washed with brine (1x), and dried over magnesium sulfate, and the ether was removed in vacuo. The residue was purified by vacuum distillation to yield diethyl 2-(cyclohexen-1-yl)propane 1,3-dioate (5.27 g, 61%) as a clear oil; bp=90-95 ℃ (0.5 mmHg). ^1H NMR ($CDCl_3$) δ 5.79-5.73 (1H, m), 5.56-5.52 (1H, m), 4.23-4.16 (4H, q, J=6.0 Hz), 3.23 (1H, d, J=9.4 Hz), 2.90 (1H, m), 1.99 (2H, m), 1.80-1.33 (4H, m), 1.26 (6H, t, J=7.1 Hz); IR (thin film) 2982, 2936, 1732, 1448, 1096 cm^{-1}. To a suspension of sodium hydride (0.36 g, 60% in oil, 8.90 mmol, washed three times with 10 mL distilled hexanes, nitrogen purge dried) in THF (18 mL) was added diethyl 2-(cyclohexen-1-yl)propane 1,3-dioate (1.00 g, 4.00 mmol) in THF (10 mL) dropwise at 25 ℃ under nitrogen atmosphere. The reaction mixture was stirred for 1 h at 25 ℃ until the gas evolution ceased. After centrifuge, the reaction mixture was transferred to a dry flask and was cooled to −78 ℃. *N*-iodosuccimide in THF (10 mL) was then added slowly. After addition was complete and the reaction mixture was allowed to warm to 25 ℃ and was stirred for 12 h. The reaction mixture was quenched with water and extracted with ether (3×30 mL). The combined organic layers were washed with $Na_2S_2O_3$ (1x), water (3x) and dried over $MgSO_4$. The solvent was removed *in vacuo*. Purification by flash chromatography afforded **2a** as a clear oil (hexanes/EtOAc=15/1) (905 mg, 62%); ^1H NMR ($CDCl_3$) δ 5.83-5.67 (2H, m), 4.30-4.17 (4H, m), 2.69-2.67 (1H, m), 2.17-1.34 (6H, m), 1.30-1.24 (6H, m).

Diethyl 2-(2-cyclohexen-1-yl)-2-[2-bromo-1-propenyl]-1,3-dioate (2b). Compound **2b** was prepared follo-

wing the general procedure for **11** with iodoester **2a** (150 mg, 0.41 mmol), 2-bromo-3-(phenylthio)propene **1** (141 mg, 0.62 mmol) and hexabutylditin (357 mg, 0.62 mmol) in dry benzene (0.4 mL). Purification by flash column chromatography (hexanes/EtOAc=10 : 1) gave product **2b** (53.0 mg, 36%) as a clear oil; ^{1}H NMR ($CDCl_3$) δ 5.80-5.74 (2H, m), 5.68 (1H, s), 5.56 (1H, s), 4.26-4.10 (4H, m), 3.18 (2H, s), 3.04 (1H, br), 2.04-1.17 (12H, a series of multiplets); ^{13}C NMR ($CDCl_3$) δ 169.9, 169.7, 128.6 (2C), 127.9, 121.2, 61.3 (2C), 60.7, 43.1, 39.2, 25.0, 24.5, 22.4, 14.0 (2C); IR (thin film) 3055, 2984, 2938, 1726, 1625, 1446, 1368, 1266, 909, 736 cm^{-1}; MS m/e 279 (M^+-Br), 205, 193, 105, 91, 81, 77, 67, 58, 53; HRMS m/e calculated for $C_{16}H_{23}O_4$: 279.1596; found: 279.1596.

Diethyl *cis*-methylene-octahydro-1H-indene-1,1-dicarboxylate (2c). General Procedure for Vinyl Radical Cyclization; A mixture of vinyl bromide compound **2b** (70 mg, 0.20 mmol), tributyltin hydride (63 μL, 0.24 mmol), and AIBN (6.4 mg) in dry benzene (2.2 mL) was refluxed for 6 h at which time the presence of starting material was checked by GC analysis. The crude reaction mixture was treated with I_2/DBU and then filtered through a pad of silica gel. After concentration *in vacuo*, purification was accomplished by flash column chromatography (hexanes/EtOAc=8 : 1) to yield product **2c** (40.5 mg, 74%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 4.98 (1H, s), 4.81 (1H, s), 4.26-4.11 (4H, m), 3.36 (1H, d, J=18.4 Hz), 2.88-2.85 (2H, m), 2.72-2.68 (1H, m), 1.93-1.90 (1H, m), 1.65-1.58 (3H, m), 1.40-1.10 (8H, m), 0.94-0.86 (2H, m); ^{13}C NMR ($CDCl_3$) δ 172.1, 170.1, 149.0, 105.5, 62.0, 61.4, 61.3, 44.6, 42.8, 37.6, 25.2, 24.6, 24.2, 20.5, 14.2, 14.1; IR (thin film) 2982, 1732, 1447, 1069 cm^{-1}; MS m/e 280 (M^+), 234, 206, 133, 91, 55; HRMS m/e calculated for $C_{16}H_{24}O_4$: 280.1675; found: 280.1675.

Ethyl 2-(cyclohexene-1-yl)-2-iodo-propanate (3a). A mixture of 2-(cyclohexen-1-yl)propane 1,3-dioate (7.20 g, 0.03 mmol) in dimethylsulfoxide (30 mL), lithium chloride (2.50 g, 0.06 mol) and water (0.54 g, 0.03 mol) was heated at reflux (190 ℃) for 6 h. Water was then added and the mixture was extracted with ether (3x). The combined ether layers were washed with water (5x) and brine, and dried over magnesium sulfate. Concentration gave ethyl 2-(cyclohexene-1-yl)propanate (4.25 g, 84%) as a clear oil. The crude product was used in the next step without further purification; ^{1}H NMR ($CDCl_3$) δ 5.70 (1H, m), 5.53 (1H, m), 4.14 (2H, q, J=7.1 Hz), 2.58 (1H, m), 2.28 (2H, m), 1.98 (2H, m), 1.86-1.52 (3H, a series of multiplets), 1.33-1.19 (4H, m, overlapped). A mixture of diisopropylamine (0.55 mL, 3.9 mmol) and THF (18 mL) was cooled to 0 ℃. *n*-Butyllithium (1.60 M, 2.23 mL, 3.57 mmol) in hexanes was added dropwise over 2 min. The mixture was allowed to stir for 30 min at 0 ℃, then cooled down to −78 ℃. The solution of ethyl 2-(cyclohexene-1-yl)propanate (0.50 g, 2.98 mmol) in THF (9 mL) was added dropwise to the lithium diisopropylamide solution over 5 min. The mixture was allowed to stir for 1 h at −78 ℃. The resulting enolate solution was added to the solution of iodine (1.36 g, 5.36 mmol) in THF (54 mL) at −78 ℃ over 20 min through cannula. During this time, the color of the iodine solution changed from dark purple to light pink. The stirring at −78 ℃ was continued for 30 min and the reaction mixture was allowed to warm to 25 ℃. After stirring for 10 h at 25 ℃, the mixture was quenched with concentrated hydrochloric acid (0.68 mL, 8.2 mmol). Water (15 mL) was added, and the reaction mixture was extracted with ether (3×120 mL). The combined organic layers were washed with saturated sodium bicarbonate (60 mL), 5% sodium thiosulfate (60 mL), water (2×60 mL), brine (60 mL), and dried over magnesium sulfate. The solvent was then removed, leaving a brownish oil. Purification by flash column chromatography (hexanes/EtOAc=15 : 1) afforded α-iodoester **3a** (402 mg, 46%) as a light yellow oil. Because α-iodoester **3a** was unstable, it was stored in freezer and covered with aluminum foil; ^{1}H NMR ($CDCl_3$) δ 5.83 (1H, m), 5.48 (1H, m), 4.25 (2H, q, J=7.1 Hz), 4.13 (1H, m), 2.62 (1H, m), 2.04-1.19 (9H, a series of multiplets).

Ethyl 2-(2-cyclohexen-1-yl)-2-(2-bromo-2-propenyl) propane-1-carboxylate (3b). Compound **3b** was prepared following the general procedure for **11** with iodoester **3a** (82.0 mg, 0.28 mmol), 2-bromo-3-(phenylthio)propene **1** (96 mg, 0.42 mmol) and hexabutylditin (242.5 mg, 0.42 mmol) in dry benzene (0.3 mL). Purification by flash column chromatography (hexanes/EtOAc=10 : 1) gave compound **3b** (26.5 mg, 33%) as a clear oil; ^{1}H NMR ($CDCl_3$) δ 5.74 (1H,m), 5.62 (1H, s), 5.50 (1H, m), 5.42 (1H, s), 4.19-4.10 (2H, m), 2.85-2.72 (2H, m), 2.62-2.42 (2H, m), 1.98 (2H, m), 1.75-1.23 (7H, m); ^{13}C NMR ($CDCl_3$) δ 170.1, 170.0, 132.1, 130.3, 129.5, 129.3, 128.3, 128.1, 127.9, 118.5, 60.4 (2C), 60.3, 49.0, 41.0, 40.5, 37.6, 37.4, 26.6, 26.1, 25.1 (2C), 21.7, 21.6, 14.4 (2C); IR (thin film) 3023, 2980, 2935, 2862, 1731, 1630, 1432, 1373, 1175, 1034, 890 cm^{-1}; MS m/e 207 (M^+-Br), 166, 118, 81; HRMS m/e calculated for $C_{13}H_{19}O_2$ (M^+-Br): 207.1385; found: 207.1386.

Ethyl *cis*-3-metylene-octahydro-1H-indene-1-carboxylate (3c). The general procedure for vinyl radical cyclization was followed with use of vinyl bromide **3b** (100 mg, 0.35 mmol), tributyltinhydride (113 μL, 0.42 mmol), and AIBN (11.5 mg, 0.07 mmol) in dry benzene (3.3 mL). Purification by flash column chromatography (hexanes/EtOAc=25 : 1) gave cyclized product **3c** (44mg, 61%) as a colorless oil; major diastereomer (with longer retention time by GC); ^{1}H NMR ($CDCl_3$) δ 4.99 (1H, s), 4.84 (1H, s), 4.13 (2H, q, J=7.1 Hz), 2.88-2.83 (1H, m), 2.69-2.53 (2H, m), 2.33-2.25 (1H, m), 1.98-1.93 (1H, m), 1.66-1.49 (2H, m), 1.43-0.93 (9H, m); IR (thin film) 2930, 2856, 1736, 1448, 1194, 1150, 1034 cm^{-1}; MS m/e 208 (M^+), 179, 163, 135, 91, 79; HRMS m/e calculated for $C_{13}H_{20}O_2$: 208.1463; found: 208.1463. minor diastereomer (with shorter retention time by GC); ^{1}H NMR ($CDCl_3$) δ 4.86 (1H, s), 4.82 (1H, s), 4.12 (2H, q, J=7.0 Hz), 2.73-2.69 (2H, m), 2.54 (1H, m), 2.30 (1H, m), 1.96-1.23 (12H, m); ^{13}C NMR (a mixture of exo and endo, $CDCl_3$) δ 176.1, 173.7, 150.4 (2C), 105.4, 105.0, 60.4, 60.2, 46.1, 45.2, 44.5, 43.7, 43.4, 42.6, 34.3, 31.8, 27.4, 27.0, 25.2, 25.0, 23.5 (2C), 23.1, 20.6, 14.4, 14.3; MS m/e 208 (M^+), 179, 163, 135, 91, 79; HRMS m/e calculated for $C_{13}H_{20}O_2$: 208.1463; found: 208.1463; IR spectrum is similar to that of major diastereomer.

Ethyl 3-(iodomethyl-1-cyclohexene)-1-carboxylate (4a). Ethyl 2-cyclohexene-1-carboxylate (350 mg, 2.27 mmol) in benzene (3.5 mL) was added to a 1.6 M solution of Et_2Zn in toluene (4 mL, 4.5 mmol) at 0 ℃ followed by the addition of CH_2I_2 (0.45 mL, 5.62 mmol). The solution was stirred at 25 ℃ for 12 h. The reaction mixture was poured into 1 N HCl and extracted with ether (3x). The combined ether layers were washed with Na_2CO_3 (3x), brine, and dried over magnesium sulfate. Evaporation of the solvent

and then purification by flash column chromatography (hexanes/EtOAc=15 : 1) gave ethyl *cis*-bicyclo[4.1.0]heptane-2-carboxylate (239 mg, 63%) as a clear oil; ^{1}H NMR ($CDCl_3$) δ 4.15 (2H, q, J=5.8 Hz), 2.82 (1H, m), 1.97-1.02 (7H, m), 0.60 (1H, dt, J=8.9 Hz, 5.0 Hz), 0.21 (1H, q, J=5.3 Hz); IR (thin film) 3069, 2862, 2840, 1728, 1370, 1086 cm^{-1}. Compound **4a** was prepared following the procedure for **3a** with ethyl *cis*-bicyclo[4.1.0]heptane-2-carboxylate (100 mg, 0.60 mmol) in THF (2.0 mL), diisopropylamine (0.11 mL, 0.78 mmol), *n*-butyllithium (1.6 M, 0.45 mL, 0.71 mmol), and I_2 (272 mg, 1.02 mmol) in THF (10.7 mL). After purification by flash column chromatography (hexanes/EtOAc=25 : 1), ethyl 3-(iodomethyl-1-cyclohexene)-1-carboxylate, **4a** (60 mg, 34%) was obtained as a clear oil; ^{1}H NMR ($CDCl_3$) δ 6.80 (1H, s), 4.19 (2H, q, J=7.1 Hz), 3.20 (2H, m), 2.52 (1H, m), 2.29-2.36 (1H, m), 2.13-2.18 (1H, m), 1.92-1.80 (2H, m), 1.59-1.30 (5H, m); ^{13}C NMR ($CDCl_3$) δ 167.8, 140.2, 133.0, 60.6, 38.2, 28.9, 24.5, 20.8, 14.4, 11.5; IR (thin film) 2936, 1712, 1647, 1241, 1095 cm^{-1}; MS m/e 249 (M^+-OCH_3), 167, 139, 121, 93, 79, 67, 55; HRMS m/e calculated for $C_9H_{13}O_2$: 248.9776 (M^+-OCH_3); found: 208.9776 (M^+-OCH_3).

Ethyl 3-(3-bromo-3-butenyl)-1-cyclohexene-1-carboxylate (4b). Compound **4b** was prepared following the general procedure for **11** with iodoester **4a** (60 mg, 0.20 mmol), 2-bromo-3-(phenylthio)propene **1** (70 mg, 0.31 mmol), and hexabutylditin (177.5 mg, 0.31 mmol) in dry benzene (0.4 mL). Purification by flash column chromatography (hexanes/ EtOAc=8 : 1) gave compound **4b** (24.5 mg, 42%) as a clear oil; ^{1}H NMR ($CDCl_3$) δ 6.84 (1H, s), 5.60 (1H, s), 5.42 (1H, s), 4.21 (2H, q, J=7.2 Hz), 2.52 (2H, t, J=7.5 Hz), 2.34-2.15 (4H, m), 1.97-1.20 (8H, m); ^{13}C NMR ($CDCl_3$) δ 167.6, 142.5, 134.3, 133.9, 116.9, 60.4, 38.9, 34.8, 33.6, 27.9, 24.5, 21.2, 14.4; IR (thin film) 2975, 2932, 1708, 1246, 1075, 739, cm^{-1}; MS m/e 286, 166, 133, 93, 79, 67, 55; HRMS m/e calculated for $C_{13}H_{19}BrO_2$: 286.0560; found: 286.0560.

Ethyl *cis*-7-methylene-octahydro-1H-indene-1-carboxylate (4c). The general procedure for vinyl radical cyclization was followed with use of vinyl bromide **4b** (8.0 mg, 0.03 mmol), tributyltin hydride (10 μ, 0.03 mmol), and AIBN (0.92 mg, 0.01 mmol) in dry benzene (0.3 mL). Purification by flash column chromatography (hexanes/EtOAc=25 : 1) afforded cyclized product **4c** (3.2 mg, 55%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 4.89 (1H, s), 4.60 (1H, s), 4.18 (2H, m), 3.05 (1H, s), 2.63 (1H, m), 2.43-2.39 (2H, m), 2.04-1.13 (12H, m); ^{13}C NMR ($CDCl_3$) δ 175.3, 149,4, 106.6, 60.3, 45.6, 42.9, 41.2, 30.4, 28.6, 27.3, 25.5, 21.8, 14.3; IR (thin film) 2930, 1733, 1216, 639 cm^{-1}; MS m/e 208, 162, 134, 119, 93, 79, 67, 55; HRMS m/e calculated for $C_{13}H_{20}O_2$: 208.1454; found: 208.1454.

***cis*- and *trans*-1-Iodo-1-(2-propenyl)-4-*t*-butylcyclohexane (5a).** To a stirred solution of 4-(1,1-dimethylethyl)-1-(2-propenyl)cyclohexanol (0.98 g, 5.0 mmol) in dry DMF (10 mL) was added bis(trimethylsilyl)trifluoroacetamide (BSTFA, 3.57 g, 10.0 mmol) *via* syringe over 10 min at 25 ℃. The reaction mixture was stirred for 12 h at 25 ℃. The excess BSTFA was destroyed by the addition of water (10 mL). The crude product was extracted with ether (3x). and the combined organic phase was washed with water (3x) and brine (1x), and dried over anhydrous magnesium sulfate. The ether was removed *in vacuo*. Purification by flash column chromatography (100% hexanes) afforded a 6/4 mixture of axial- and equatorial-4-*t*-butyl-1-(2-propenyl)-1-(trimetylsilyloxy)cyclohexane (1.34 g, 81%) as a colorless oil; ^{1}H NMR ($CDCl_3$) equatorial: δ 5.91-5.77 (1H, m), 5.05-5.00 (2H, m), 2.26 (2H, d, J=7.2 Hz), 1.67-1.18 (9H, m), 0.85 (9H, s), 0.13 (9H, s); axial: very similar except d 2.22 (2H, d, J=9.6 Hz) and 0.11 (9H, s); IR (thin film, mixture) 3075, 2944, 2868, 1351, 1250, 1142, 1063, 838 cm^{-1}. To a stirred solution of 4-*t*-butyl-1-(2-propenyl)-1-(trimetylsilyloxy)cyclohexane (123 mg, 0.80 mmol) in dry benzene (2.5 mL) in a round bottom flask covered with aluminum foil was added iodotrimethylsilane (318 mg, 1.59 mmol) dropwise at room temperature. After stirring for 30 min at 25 ℃, the crude mixture was poured into water (20 mL). The aqueous phase was extracted with ether (3x) and the combined organic phase was washed with aqueous sodium bicarbonate (1x), aqueous sodium thiosulfate (1x), brine, and dried over $MgSO_4$. Concentration gave an unstable yellow oil **5a** (230 mg, 94%); ^{1}H NMR ($CDCl_3$) δ 6.03 (1H, m), 5.20 (2H, m), 2.70 (2H, m), 2.13-0.85 (18H, m).

***cis*- and *trans*-1-(2-bromo-2-propenyl)-1-(2-propenyl)-4-*t*-butylcyclohexane (5b).** Compound **5b** was prepared following the general procedure for **11** with **5a** (200 mg, 0.77 mmol), 2-bromo-3-(phenylthio)propene **1** (266 mg, 1.16 mmol) and hexabutylditin (673 mg, 1.16 mmol) in dry benzene. Purification by flash column chromatography (100% hexanes) afforded a 6/4 mixture of *cis*- and *trans*-diastereomers **5b** (103 mg, 45%) as indicated by ^{1}H NMR integration and GC retention time as a clear oil; ^{1}H NMR ($CDCl_3$, *cis/trans* mixture) δ 5.85 (1H, m), 5.66 (2H, m), 5.06 (2H, m), 2.55 (*cis*, 2H, s), 2.40 (*trans*, 2H, s), 2.21 (*trans*, 2H, d, J=7.3 Hz), 2.12 (*cis*, 2H, d, J=7.3 Hz), 1.79-1.54 (6H, m), 1.47-0.68 (12H, m); ^{13}C NMR ($CDCl_3$, *cis/trans* mixture) δ 134.9, 134.8, 131.1, 130.7, 120.7 (2C), 117.6 (2C), 51.9, 48.0, 47.9, 47.6, 44.1, 37.2, 37.0, 36.8, 35.6, 35.5, 32.5, 27.6 (2C), 27.3, 22.7, 22.3; IR (thin film, *cis/trans* mixture) 3076, 2941, 2868, 1622, 1454, 1366, 909, 735 cm^{-1}; MS m/e 219 (M^+-Br), 177, 137, 123, 109, 95, 67, 57; HRMS m/e calculated for $C_{16}H_{27}$-Br: 298.1296; found: 298.1297.

2-Methyl-3-methylene-8-*tert*-butyl spiro[4.5]decane (5c) and 3-Methyl-2-methylene-8-*tert*-butyl spiro[4.5]decane (5d). The reaction was conducted under tin hydride vinyl radical cyclization condition, as described for **2c** using bromide **5b** (20 mg, 0.07 mmol), Bu_3SnH (20 μL, 0.08 mmol) and AIBN (2.30 mg, 0.01 mmol) in dry benzene (0.7 mL). Evaporation of solvent *in vacuo* and purification of the residue by flash column chromatography (100% hexanes) gave an inseparable mixture of **5c** and **5d** (10 mg, 67%) as a colorless oil; ^{1}H NMR ($CDCl_3$, mixture); δ 4.82-4.52 (2H, m), 2.52-2.00 (4H, m), 1.64-0.80 (21H, m); ^{13}C NMR ($CDCl_3$, mixture) δ 158.2, 157.7, 104.2, 103.9, 50.8, 49.4, 48.3, 43.1, 42.4, 41.5, 40.4, 39.9, 39.6, 37.0, 36.8, 36.2, 35.4, 32.5, 27.7 (2C), 24.9, 24.3, 23.9, 23.8, 22.4, 22.2, 19.4, 19.3; IR (thin film, mixture) 2954, 2930, 2868, 1448, 1393, 1366 cm^{-1}; MS m/e 220 (M^+), 205, 163, 128, 107, 99, 70, 57; HRMS m/e calculated for $C_{16}H_{28}$: 220.2191; found: 220.2191.

Methyl 1-(1-iodoethyl)-2-cyclohexenyl-1-carboxylate (6a). Sodium iodide (2.19 g, 14.62 mmol) was suspended in a solution of methyl 1-(1-bromoethyl)-2-cyclohexenyl-1-carboxylate (0.90 g, 3.66 mmol) in acetone (12 mL) and the mixture was stirred at 25 ℃ for 12 h. The solvent was removed under reduced pressure and the residue was diluted

with ether (20 mL). This was then washed with water (3x), brine (1x), and dried over magnesium sulfate. The solvent was then removed *in vacuo*. Purification by flash column chromatography (hexanes/EtOAc=15 : 1) afforded iodo compound **6a** (517 mg, 48%); ^{1}H NMR ($CDCl_3$) δ 5.84 (1H, m), 5.67 (1H, m), 3.70 (3H, s), 3.09 (2H, m), 2.31-2.10 (3H, m), 1.98 (2H, m), 1.70-1.43 (3H, m); GCMS m/e 294, 235, 167, 107, 79; IR (thin film) 3025, 2936, 2870, 1729, 1649, 1432, 1207, 1162, 1005 cm^{-1}.

Methyl 1-(4-bromo-4-pentenyl)-2-cyclohexenyl-1-carboxylate (6b). Compound **6b** was prepared following the general procedure for **11** with **6a** (560 mg, 0.19 mmol), 2-bromo-3-(phenylthio)propene **1** (87.1 mg, 0.38 mmol) and hexabutylditin (165.3 mg, 0.14 mmol) in dry benzene (0.13 mL). Purification by flash column chromatography (100% hexanes) gave product **6b** (23.0 mg, 43%) as a clear oil; ^{1}H NMR ($CDCl_3$) δ 5.80 (1H, m), 5.69 (1H, m), 5.55 (1H, d, J=1.4 Hz), 5.39 (1H, d, J=1.5 Hz), 3.70 (3H, s), 2.39 (2H, m), 2.18-1.96 (4H, m), 1.70-1.43 (6H, m); ^{13}C NMR ($CDCl_3$) δ 176.4, 129.8, 129.5, 128.8, 116.9, 51.9, 46.7, 41.5, 38.7, 30.8, 24.9, 22.7, 19.7; IR (thin film) 3026, 2948, 1731, 1630, 1432, 1173, 887, 704 cm^{-1}; MS m/e 286 (M^+), 207, 147, 107, 91, 79, 67, 53; HRMS m/e calculated for $C_{13}H_{19}BrO_2$: 286.0568; found: 286.0567.

***cis*-Methyl 5-methylene bicyclo[4.4.0]decane-1-carboxylate (6c) and Methyl 1-(4-pentenyl)-2-cyclohexene-1-carboxylate (6d).** The reaction was carried out under tinhydride vinyl radical cyclization condition, as described for **2c**, using bromide **6b** (9.0 mg, 0.03 mmol), Bu_3SnH (10 μL, 0.04 mmol) and AIBN (1.0 mg) in dry benzene (6.2 mL). Evaporation of solvent *in vacuo* and purification of the residue by flash column chromatography (hexanes/EtOAc=25 : 1) gave a separable 85/15 mixture of cyclized and reduced products **6c** and **6d** (4.0 mg, 62% combined yield) as indicated by ^{1}H NMR integration and GC retention time as a clear oil: cyclic compound **6c**; ^{1}H NMR ($CDCl_3$) δ 4.72 (1H, s), 4.65 (1H, s), 3.65 (3H, s), 2.20-1.27 (17H, m); ^{13}C NMR ($CDCl_3$) δ 177.9, 150.4, 108.9, 77.3, 51.7, 49.1, 45.6, 34.8, 30.8, 27.6 (2C), 25.1, 24.8, 21.6; IR (thin film) 2939, 2866, 1720, 1647, 1466, 1382, 1217, 1097 cm^{-1}; MS m/e (mixture) 208 (M^+), 149, 107, 93, 81, 67, 55; HRMS m/e calculated for $C_{13}H_{20}O_2$: 208.1463; found: 208.1464: reduced compound **6d**; ^{1}H NMR ($CDCl_3$) δ 5.76 (1H, m), 4.96 (2H, m), 2.80 (2H, m), 2.20-1.13 (17H, a series of multiplets).

Methyl-(1-iodomethyl)-2-cyclohexenyl-1-carboxylate (7a). Compound **7a** was prepared following the procedure for **3a** with methyl 1-cyclohexene-1-carboxylate (1.0 g, 7.1 mmol), diisopropylamine (2.2 mL, 15.7 mmol), *n*-butyllithium (1.25 M, 11.4 mL, 14.3 mmol), DMPU (1.8 mL) and diiodomethane (2.9 mL, 35.7 mmol). Purification by flash column chromatography (hexanes/EtOAc=15 : 1) afforded compound **7a** (899 mg, 45%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.90 (1H, m), 5.67 (1H, m), 3.73 (3H, s), 3.42 (1H, d, J=9.6 Hz), 3.26 (1H, d, J=9.6 Hz), 2.26-1.57 (6H, m); ^{13}C NMR ($CDCl_3$) δ 173.2, 131.4, 127.5, 52.4, 47.7, 31.4, 25.1, 19.4, 14.7; IR (thin film) 3027, 2948, 1738, 1645, 1434, 1228 cm^{-1}; MS m/e 279 (M^+), 221, 153, 93, 79, 57; HRMS m/e calculated for $C_9H_{12}IO_2$: 278.9882; found: 278.9882.

Methyl 1-(2-bromo-2-propenyl)-2-cycloheptenyl-1-carboxylate (7b). Compound **7b** was prepared following the general procedure for **11** with **7a** (367.0 mg, 1.31 mmol), 2-bromo-3-(phenylthio)propene **1** (600 mg, 2.62 mmol) and hexabutylditin (760 mg, 1.31 mmol) in dry benzene (1.55 mL). Purification by flash column chromatography (hexanes/EtOAc=25 : 1) gave product **7b** (165 mg, 46%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.83 (1H, m), 5.66 (1H, m), 5.54 (1H, s), 5.51 (1H, s), 3.70 (3H, s), 2.81 (1H, d, J=14.4 Hz), 2.72 (1H, d, J=14.4 Hz), 2.52 (1H, m), 2.30-1.52 (9H, m); ^{13}C NMR ($CDCl_3$) δ 175.9, 133.8, 128.8, 127.7, 120.9, 51.7, 50.1, 47.9, 39.2, 34.8, 28.5, 22.8; IR (thin film) 3025, 2930, 2841, 1731, 1623, 1437 cm^{-1}; MS m/e 272 (M^+), 213, 193, 153, 133, 93, 77, 59; HRMS m/e calculated for $C_{12}H_{17}O_2Br$: 272.0412; found 272.0411.

Methyl 7-methylene bicyclo[4.2.1]nonane-1-carboxylate (7c) and Methyl 6-methylene bicyclo[3.2.2]nonane-1-carboxylate (7d). The reaction was conducted under tin hydride vinyl radical cyclization condition, as described for **2c**, with vinyl bromide **7b** (75 mg, 0.28 mmol), tributyltin hydride (90 μL, 0.33 mmol) and AIBN (9.1 mg) in dry benzene (27.5 mL). Evaporation of solvent *in vacuo* and purification of the residue by flash column chromatography (hexanes/EtOAc=25 : 1) afforded an inseparable 65/35 mixture of *endo*- and *exo*-products **7c** and **7d** (32 mg, 60%) as indicated by ^{1}H NMR integration and GC retention time as a colorless oil; ^{1}H NMR ($CDCl_3$, mixture): δ 4.88 (2H, m), δ 4.74 (2H, m), 3.66 (3H, s), 3.64 (3H, s), 2.89-1.48 (12H, m), 2.89-1.48 (12H, m); ^{13}C NMR ($CDCl_3$, mixture) δ 170.71 (2C), 149.9 (2C), 108.8, 105.3, 51.9 (2C), 43.6, 42.8, 41.8, 39.2, 38.8, 37.8, 37.4, 37.2, 36.1, 35.5, 29.7, 28.4, 25.6, 25.4, 23.5, 21.4; IR (mixture, thin film) 3070, 2960, 2930, 1731, 1642, 1434, 1242, 1198, 1080, 1043, 913, 878 cm^{-1}; MS m/e 194 (M^+), 179, 153, 135, 93, 79, 67, 55; HRMS m/e calculated for $C_{12}H_{18}O_2$: 194.1307; found: 194.1306.

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Potentiometric Homogeneous Enzyme-Linked Binding Assays for Riboflavin and Riboflavin Binding Protein

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Adenosine deaminase (ADA) has been utilized as the label in devising a potentiometric homogeneous assay for riboflavin and riboflavin binding protein (RBP). The proposed homogeneous assay method employs an ADA-biotin conjugate as the signal generator and an avidin-riboflavin conjugate as the signal modulator in the solution phase. The catalytic activity of the ADA-biotin conjugate is inhibited in the presence of an excess amount of the avidin-riboflavin conjugate, and the observed inhibition is reversed in an amount proportional to the concentration of RBP added. When the analyte riboflavin is added to this mixture of ADA-biotin, avidin-riboflavin and RBP, the activity of the enzyme conjugate is re-inhibited in an amount proportional to the concentration of riboflavin. Since the enzyme label used in this system is ADA, an ammonia-producing enzyme, a potentiometric rather than photometric detection scheme is used to monitor the enzymatic activity in the assay.

Introduction

Enzyme-linked binding assay methods have become important analytical methods for the selective detection of various physiological, biological and environmental substances at trace levels.[1~6] Such methods may be classified as either heterogeneous or homogeneous. The homogeneous types such as the enzyme-multiplied immunoassay technique (EMIT),[5,6] rely on the ability of analyte molecules to reverse the inhibition of enzyme-analyte conjugates induced by analyte-specific binders (*e.g.*, antibodies, binding proteins, etc.). Homogeneous assays do not require time-consuming separation of the free and bound enzyme label, and, thus, are simple, fast and easily automated.