Pergamon

Tetrahedron 56 (2000) 2753–2765

TETRAHEDRON

Cu(I)-Mediated Intramolecular Conjugate Addition of Alkenyltrimethylstannane Functions to α,β-Unsaturated Ketones: A Convenient Preparation of Functionalized *cis*-Fused Bicyclo[4.3.0]non-8-en-3-ones and Bicyclo[3.3.0]oct-6-en-3-ones

Edward Piers,* Ernest J. McEachern and Patricia A. Burns

Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, British Columbia V6T 1Z1, Canada

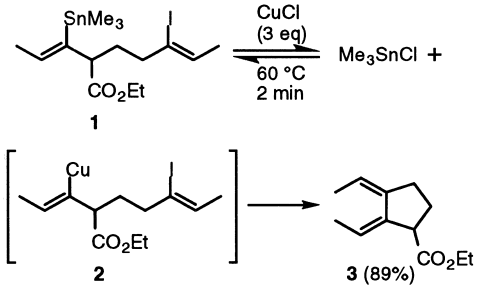
Received 23 November 1999; accepted 18 January 2000

Abstract—A new copper(I)-mediated method for effecting intramolecular conjugate addition of alkenyl functions to α,β-unsaturated ketone systems is reported. Treatment of the substrates **14**, **15**, **19**–**21**, **22** and **23** with 2.5 equiv. of CuCl in DMF at room temperature affords excellent yields of the corresponding bicyclic ketones **24**, **25**, **29**–**31**, **32** and **33**. On the other hand, treatment of substances **15**–**18** with CuCN in DMSO at 60°C provides good-to-excellent yields of the corresponding bicyclic products **25**–**28**.

Introduction

The Pd(0)-catalyzed cross-couplings of aryl- or alkenyltrialkylstannanes with aryl or alkenyl bromides, iodides, or triflates, collectively known as the Stille coupling, are well known reactions that have become very valuable in the area of organic synthesis. Indeed, the Stille coupling undoubtedly represents a powerful method for synthesizing conjugated diene systems in a stereospecific manner.[1–5] Interestingly, it was shown nearly a decade ago that the Stille reaction is co-catalyzed by Cu(I) salts.[6,7] Thus, in a set of cross-couplings reported by Liebeskind and Fengl,[6] it was found that the addition of 7–10 mol% of CuI along with the usual 5 mol% of a Pd(0) catalyst resulted in a dramatic increase of the rates of the reactions and in a notable improvement of the product yields.

In 1993, a report from our laboratory disclosed that stereospecific *intra*molecular couplings of alkenyltrimethylstannane functions with alkenyl iodides or bromides can be accomplished with 2–3 equiv. of CuCl in DMF *in the absence of a palladium(0) catalyst.*[8a] A detailed study of this novel process revealed that the reactions are rapid and efficient. An example, involving the conversion of **1** into **3**, is shown in Eq. (1). Control experiments[8b] showed that the coupling process is initiated by reaction of the Cu(I) salt with the alkenylstannane function and it seemed reasonable to conclude that the latter transformation is a transmetallation that leads to trimethylstannyl chloride and an alkenylcopper(I) species (see **2** in Eq. (1)).[8c] Strong evidence for this conclusion was subsequently provided by Farina et al.,[9] who showed that alkenyltrialkylstannanes undergo reversible transmetallation with CuI in polar solvents.



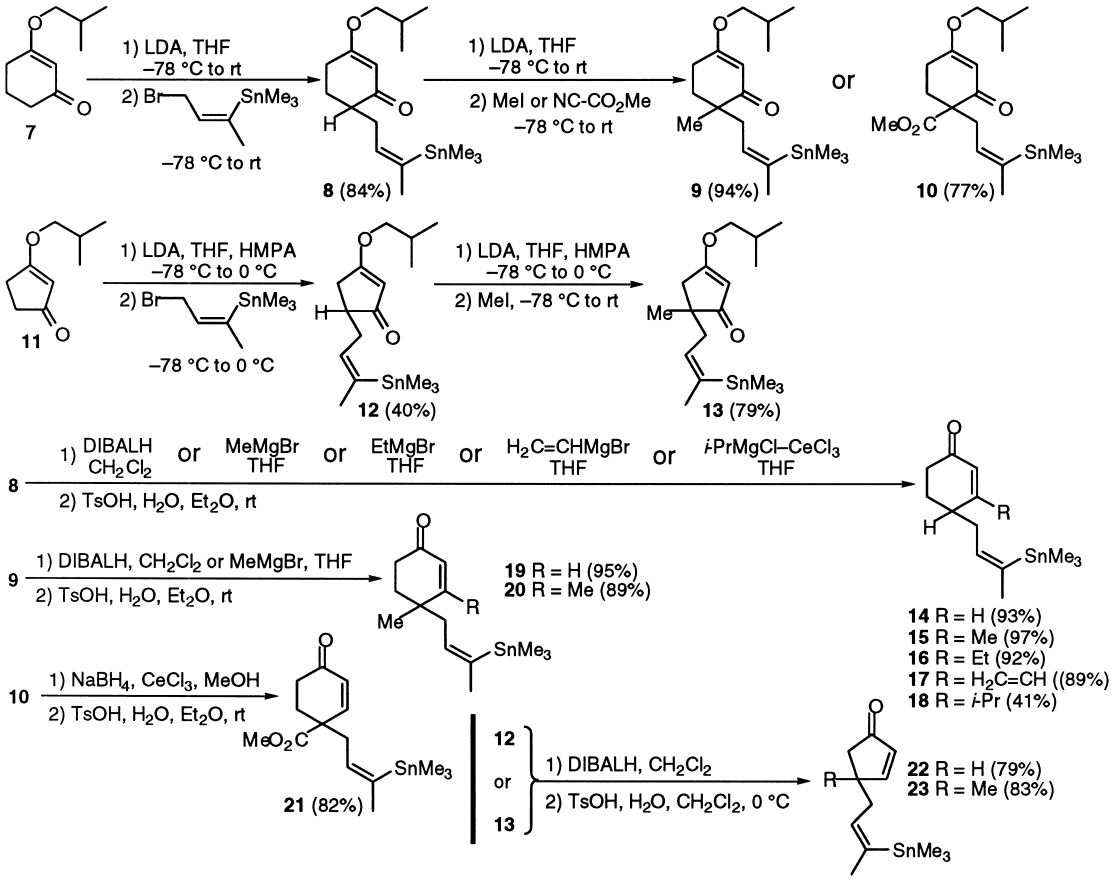
(1)

The possibility of easily generating alkenylcopper(I) intermediates as shown in Eq. (1) led to the idea of producing such species in the presence of Michael acceptor functions. More explicitly, it was decided to investigate the feasibility of carrying out synthetically useful intramolecular conjugate additions of alkenyl functions[10] to α,β-unsaturated ketones via a protocol portrayed in general terms by the conversion of **4** into **6** (Eq. (2)). Although monoalkenylcopper(I) species are generally known to be poor donor reagents in *inter*molecular conjugate additions to enones,[11] we felt that the *intra*molecular nature of the envisaged transformation (**5**→**6**, Eq. (2)) might well overcome this intrinsic difficulty. We report herein the details of

Keywords: copper(I) chloride; copper(I) cyanide; intramolecular conjugate addition; alkenyltrimethylstannanes.

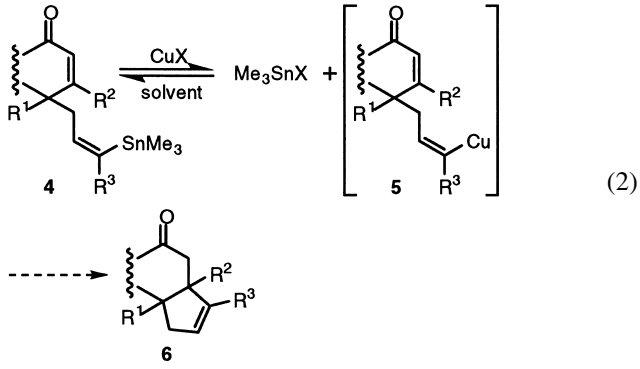
* Corresponding author. E-mail: epier@interchange.ubc.ca

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00131-9



Scheme 1.

a study that showed that this new (proposed) process can readily be put into practice.[12]



(2)

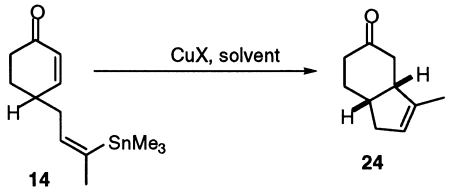
Results and Discussion

Preparation of substrates

The syntheses of the enone substrates **14**–**23** employed in this study were readily achieved by use of the effective chemistry developed by Stork and coworkers.[13] A summary is given in Scheme 1. Alkylation[13] of the functionalized enone **7**[14] with the (*Z*)-1-bromo-3-trimethylstannylbut-2-ene (prepared in two steps from ethyl (*Z*)-3-trimethystannylbut-2-enoate[15] as described in the Experimental section) afforded **8** in excellent yield. A second alkylation of **8** with MeI provided **9**, while treatment of the lithium enolate of **8** with methyl cyanoformate[16] gave the β-keto ester **10**. Transformation of the cyclopentenone derivative **11**[17] into the ketones **12** and **13** was accomplished via reactions similar to those employed for the preparation of **8** and **9** from **7**.

Reaction of **8** with each of DIBALH and a number of Grignard reagents (Scheme 1), followed, in each case, by acid hydrolysis of the resultant product under carefully defined conditions, furnished the required enones **14**–**18**. It should be noted that reaction of **8** with excess *i*-PrMgBr in THF (0°C to rt), followed by acid hydrolysis, gave **18** in poor yield (~30%). The starting material **8** was also recovered (~45%). Increasing the reaction time did not produce a higher yield of **18**. Thus, it appears that the reagent *i*-PrMgBr, in addition to adding to the carbonyl group of **8**, acted as a base to transform **8** into an enolate anion.[18] Subsequent workup and (mild) acid hydrolysis gave **18** and the starting material **8**. Use of *i*-PrMgBr in the presence of $CeCl_3$[19] in THF improved the yield of **18** to 41%, but a significant amount (29%) of **8** was still recovered. The conversions of **9** into **19** and **20** were achieved via reactions essentially identical with those employed for the **8**→**14**, **15** transformations (Scheme 1). Chemoselective reduction of **10** with $NaBH_4$–$CeCl_3$[20] in MeOH, followed by acid hydrolysis, gave the enone **21**. Finally, the conversions of **12** and **13** into the corresponding substrates **22** and **23** followed protocols similar to those used to make **14** and **19** from **8** and **9**, respectively.

Table 1. Substrate **14**: intramolecular conjugate additions



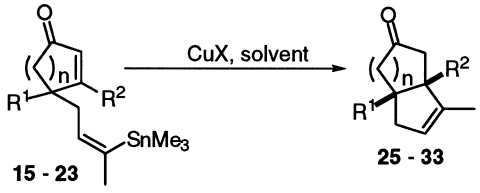
Entry	CuX (equiv.)	Solvent	Temperature (°C)	Time (h)	Yield (%)[a]
1	None	DMF	60	48	–[b]
2	CuCl (1)	DMF	rt	18[c]	88
3	CuCl (2)	DMF	rt	0.5	92
4	CuCl (2.5)	DMF	rt	0.5	96
5	CuCl (2.5)	MeCN	82	5[d]	79
6	CuCl (2.5)	DMSO	rt	1[d]	96
7	CuBr·Me_2S (2.5)	DMF	rt	18[d]	71
8	CuI (2.5)	DMF	rt	72[d]	96
9	CuSCN (2.5)	DMF	60	18	88
10	CuCN (2.5)	DMF	60	5	93
11	CuCN (2.5)	DMSO	60	5	94

[a] Isolated yield of purified product.
[b] The enone **14** was recovered in 92% yield.
[c] After 30 min, this reaction had progressed to ~50% completion.
[d] These numbers represent the time required for complete consumption of the starting material **14**; times longer than ~5 h (entries 7, 8) may be considered as approximate.

Intramolecular conjugate additions: studies with substrate 14

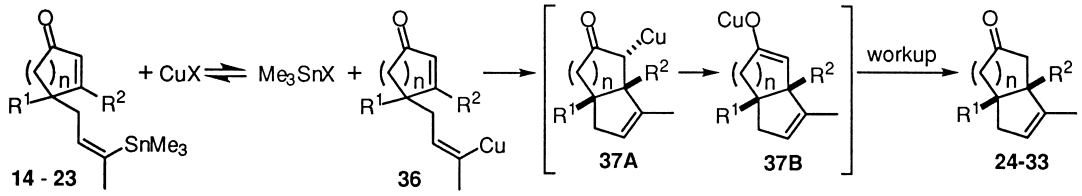
Table 1 summarizes results obtained from experiments with the structurally 'simplest' substrate **14**. When a stirred solution of this material in *N*,*N*-dimethylformamide (DMF) was warmed (60°C) for 48 h in the *absence* of a copper(I) salt, the starting material was recovered in high yield (entry 1). In sharp contrast, treatment of **14** with CuCl in DMF resulted in the formation of the bicyclic ketone **24** in excellent yields (entries 2–4). When 1 equiv. of CuCl was employed, the conversion was initially quite facile but the rate decreased

Table 2. Substrates **15**–**23**: intramolecular conjugate additions



Entry	Substrate	*n*	R^1	R^2	CuX[a]	Solvent	Temperature (°C)	Time (h)	Product	Yield (%)[b]
1	**15**	2	H	Me	CuCl	DMF	rt	1	**25**	81
2	**16**	2	H	Et	CuCl	DMF	rt	1	**26**	48[c]
3	**16**	2	H	Et	CuCl	DMF	0	1	**26**	74
4	**17**	2	H	HC=CH_2	CuCl	DMF	rt	1	**27**	6[c]
5	**18**	2	H	*i*-Pr	CuCl	DMF	rt	1	**28**	15[c]
6	**19**	2	Me	H	CuCl	DMF	rt	0.5	**29**	92
7	**20**	2	Me	Me	CuCl	DMF	rt	1	**30**	85
8	**21**	2	CO_2Me	H	CuCl	DMF	rt	0.5	**31**	90
9	**15**	2	H	Me	CuCN	DMSO[d]	60	5	**25**	92
10	**16**	2	H	Et	CuCN	DMSO[d]	60	5	**26**	91
11	**17**	2	H	HC=CH_2	CuCN	DMSO[d]	60	18	**27**	60[e]
12	**18**	2	H	*i*-Pr	CuCN	DMSO[d]	60	18	**28**	73[e]
13	**22**	1	H	H	CuCl	DMF	rt	3	**32**	76
14	**23**	1	Me	H	CuCl	DMF	rt	1.5	**33**	77

[a] All reactions were carried out with 2.5 equiv. of commercial CuX (CuCl, 99.995+%; CuCN, 99.99%). In the case of CuCl, recrystallized material (Furniss, B. S.; Hannaford, A. J.; Rogers, V.; Smith, P. W. G.; Tatchell, A. R., in *Vogel's Textbook of Practical Organic Chemistry*, 4th Ed.; Longman: London, 1978, p 287) gave essentially the same results.
[b] Isolated yield of purified product.
[c] The major by-products (entry 2) or products (entries 4, 5) of these reactions were uncyclized materials in which the Me_3Sn group of the starting material had been replaced by H or Cl.
[d] Although DMF can be used in the place of DMSO in these reactions, it was found that the reactions are somewhat cleaner in the latter solvent.
[e] The major by-product of these reactions was uncyclized material in which the Me_3Sn group of the starting material had been replaced by H.



Scheme 2.

significantly with time (entry 2). On the other hand, use of two or more equivalents of CuCl effected the efficient transformation of **14** into **24** under mild conditions in a relatively short time (entries 3, 4). For subsequent experiments, 2.5 equiv. of a copper(I) salt was routinely used. Clearly, the originally envisaged intramolecular conjugate addition process could be put into practice via an experimentally simple protocol.

Use of MeCN as the solvent in place of DMF required refluxing for 5 h to effect complete disappearance of the starting material **14** and produced the product **24** in somewhat lower yield (entry 5). On the other hand, the rate and efficiency of the conversion **14→24** in DMSO as solvent were very similar to those observed for DMF (entry 6). Consequently, for our subsequent studies, either DMF or DMSO were employed as the reaction solvents.

The use of other Cu(I) salts was also investigated. Although CuBr·Me_2S, CuI, and CuSCN effected formation of the product **24** in good-to-excellent yields (entries 7–9), the conversions were much slower than the CuCl-mediated processes. On the other hand, reactions carried out with CuCN in either DMF or DMSO (entries 10, 11) turned out to be highly efficient, although these reactions were also slower than the CuCl-mediated transformations (compare entries 4, 6 with entries 10, 11).

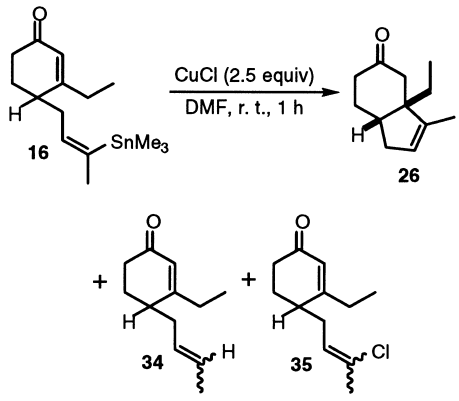
Overall, on the basis of the reactions summarized in Table 1, it is evident that the conversion **14→24** is best carried out by use of CuCl or CuCN in a polar aprotic solvent such as DMF or DMSO. These protocols were adopted for subsequent investigations.

Intramolecular conjugate additions: studies with substrates 15–23

Experiments involving the Cu(I)-mediated intramolecular conjugate additions of substrates **15**–**23** are summarized in Table 2.

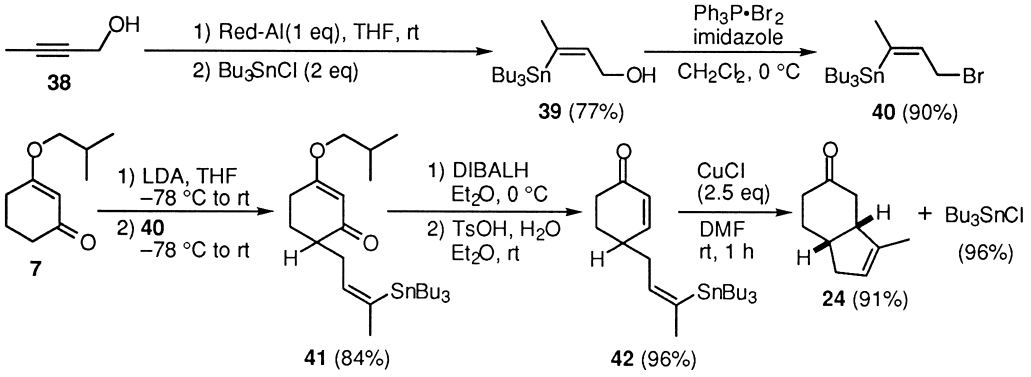
Entries 1–5 of Table 2 show that the presence of a bulky substituent at C-3 of the cyclohexenones **15**–**18** (R^1=H) has a notably negative effect on the efficiency of the cyclization process. Thus, although substrate **15**, in which the C-3 group is methyl, undergoes the conjugate addition reaction quite readily and produces the product **25** in very good yield (entry 1), subjection of the enones **16**–**18** to identical conditions provides the corresponding products in poor (entry 2) to dismal (entries 4, 5) yields. Clearly, the steric effects produced by the Et and *i*-Pr groups (entries 2, 5), as well as the combination of steric and electronic effects derived from the ethenyl group (entry 4), have a deleterious effect on the facility of the ring closures. In the case of substrate **16**, lowering the reaction temperature to 0°C improves the yield somewhat (entry 3). Apparently, the competing reactions (vide infra) become less important as the temperature is decreased.

The by-products of the reactions summarized in entries 2, 4, and 5 (Table 2) were shown to be uncyclized materials in which the Me_3Sn group is replaced by H or Cl. For example, treatment of **16** as shown in Eq. (3), followed by flash chromatography (silica gel, 4:1 pentane–Et_2O) of the crude product, provided three fractions, **26** (48%), **34** (17%), and **35** (29%). Analyses of **34** and **35** by ^{1}H NMR spectroscopy and GC-HRMS showed that, in each case, two geometric isomers were present (**34**: ~5:1; **35**: ~4:1). Similar analyses were employed to identify the constitution of the by-products derived from the reactions summarized in Table 2, entries 4 and 5. The mechanistic pathways via which these materials are produced are, at present, not clear. However, it is evident that, in the CuCl-mediated reactions of substrates in which there are sterically and/or electronically induced decreases in the rate of cyclization, competing reactions do occur.



(3)

The competing side-reactions referred to above can be ameliorated to a significant degree by use of CuCN in the place of CuCl. Thus, treatment of the substrates **15**–**18** with CuCN in DMSO at 60°C produced the corresponding products **25**–**28** with excellent (entries 9, 10) or good (entries 11, 12) efficiency. In the latter two reactions, the major by-product, in each case, was the uncyclized substance in which the Me_3Sn function was replaced by a proton. It should be explicitly noted that even though the CuCN–DMSO reactions (entries 9–12) require higher temperatures and longer reaction times than those involving CuCl–DMF (entries 1–5), the product yields derived from the former protocol are consistently higher.



Scheme 3.

The cyclizations of substrates **19**–**21** (Table 2, entries 6–8) are unexceptional, although it should be noted that a functionalized bicyclo[4.3.0]nonane system possessing methyl groups at both angular carbons is readily produced via this methodology (entry 7) and that the presence of a methoxycarbonyl group is not deleterious to the success of the process (entry 8). The experiments summarized in entries 13 and 14 show that functionalized bicyclo[3.3.0]octanes are also readily available via the CuCl-mediated cyclization protocol.

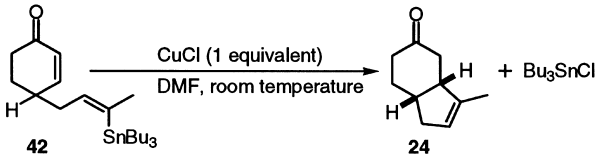
Mechanistic considerations

As already mentioned (vide supra), it has been established[8b,9] that alkenyltrialkylstannanes undergo ready (reversible) transmetallation with copper(I) salts. With this finding in mind, it seems reasonable to propose that the cyclization reactions summarized in Tables 1 and 2 (**14**–**23**→**24**–**33**, respectively) take place via a pathway summarized *in a simplified manner* in Scheme 2. Thus, transmetallation of **14**–**23** via reaction with CuX would give Me_3SnX and an 'alkenylcopper(I) intermediate' *simplistically* represented by general structure **36**. Intramolecular conjugate addition of the 'alkenylcopper(I)' function of **36** to the enone moiety (probably via a d, π^* complex between the Cu d-orbitals and the π_3^* orbital of the enone system[11,21]) would furnish initially the species **37A**, which, presumably, would isomerize to the Cu(I) enolate **37B**. Protonation of the latter intermediate would the give the observed products **24**–**33**.

Support for the first step (formation of Me_3SnCl and **36**) of the pathway given in Scheme 2, along with an indication that the reactions can also be carried out with alkenyl-*tributyl*stannane substrates, are provided by the experiments summarized in Scheme 3. Treatment of 2-butyn-1-ol (**38**) with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al®) in THF, followed by reaction of the intermediate[22] with tributylstannyl chloride, afforded the allylic alcohol **39**, which was readily converted[23] into the corresponding bromide **40**. Alkylation[13] of **7**[14] with **40** and subjection of the resultant product **41** to sequential reduction and acid hydrolysis furnished the enone **42**. When the latter substance was treated with CuCl in DMF at room temperature, the bicyclic ketone **24** and tributylstannyl chloride were isolated in yields of 91 and 96%, respectively. Clearly, in line with the proposal summarized in Scheme 2, the CuCl-mediated intramolecular conjugate addition reaction (**42**→**24**) produces 1 equiv. of Bu_3SnCl.

Some evidence in favor of the idea that the CuX-mediated ring closures (**14**–**23**→**24**–**33**, Scheme 2) are initiated by a *reversible* transmetallation step[9] is provided by the reactions summarized in Table 3. In these experiments, the substrate **42** was treated with 1 equiv. of CuCl in DMF at room temperature. The reaction carried out in the absence of added Bu_3SnCl (Table 3, entry 1) initially proceeded quite quickly (~40–50% conversion within 0.5 h), but became sluggish with time. A reaction time of approximately 18 h was required for complete conversion of **42** into **24**. When the reaction was carried in the presence of 1 equiv. of Bu_3SnCl (entry 2), the rate decreased significantly and ~48 h were required for completion of the reaction. Finally (entry 3), addition of 5 equiv. of Bu_3SnCl effectively halted the reaction. After 48 h under these conditions, analysis (GLC) of an aliquot of the reaction mixture showed the absence of the product **24** and the presence of only Bu_3SnCl and the starting material **42**. These results indicate that the addition of Bu_3SnCl shifts the equilibrium between **42** and the corresponding 'alkenylcopper(I) intermediate' (see Scheme 2) to the side of the starting material and thus essentially shuts down the intramolecular conjugate addition step.

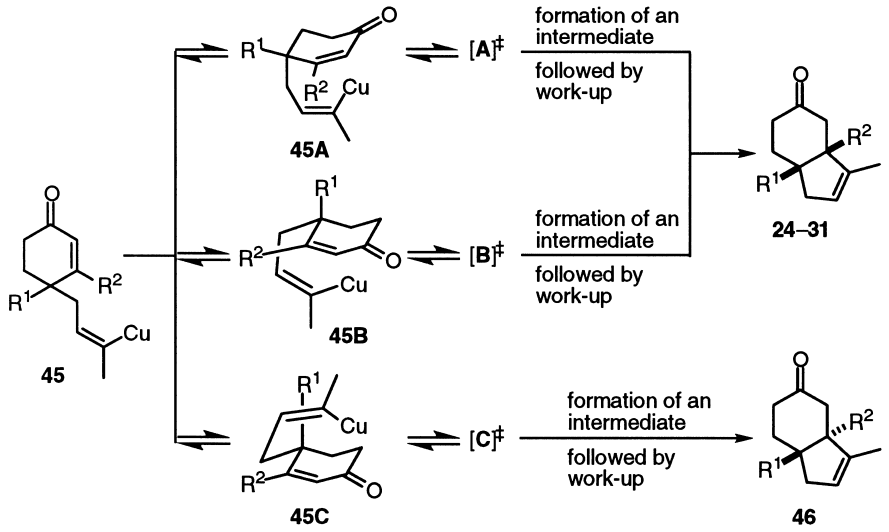
Table 3. Effect of added Bu_3SnCl on the CuCl-mediated intramolecular conjugate addition of **42**



Entry	Equivalents of Bu_3SnCl added	Time (h)
1	0	18[a]
2	1	48[a]
3	5	48[b]

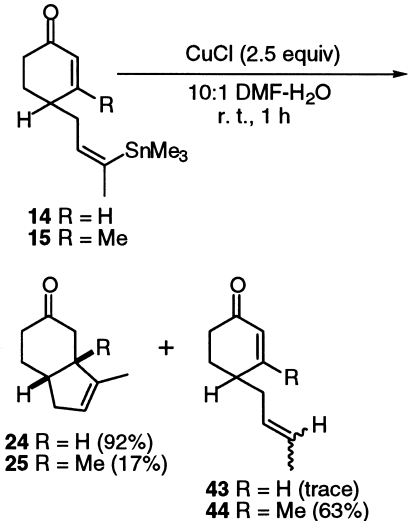
[a] This number refers to the approximate time required for complete conversion of **42** into **24**.

[b] Analysis (GLC) of the reaction mixture at this stage showed the presence of **42** and Bu_3SnCl only. None of the product **24** could be detected.



Scheme 4.

In order to assess the basicity of the (proposed) 'alkenylcopper(I) intermediate' (**36**, Scheme 2), the cyclizations of substrates **14** and **15** were carried out with 2.5 equiv. of CuCl in a 10:1 mixture of DMF and water (Eq. (4)). In the case of substrate **14**, the yield (92%) of the bicyclic ketone **24** was nearly as high as that derived from a similar reaction carried out in dry DMF (Table 1, entry 4). Only a trace amount of the protiodestannylated material **43** was produced. Clearly, for a starting material such as **14** in which the unsubstituted cyclohexenone unit is sterically and electronically a very good Michael acceptor, the presence of water does not interfere with the cyclization process. Thus, the alkenylcopper(I) intermediate, whatever its exact nature, does not appear to be highly basic.



(4)

When the enone **15** was subjected to the reaction conditions shown in Eq. (4), the cyclized product **25** was obtained in poor yield and the major product was the protiodestannylated material **44**. In this case, the methyl group on the β-carbon of the enone function inhibits, both sterically and electronically, the rate of conjugate addition and protonation of the copper(I) intermediate becomes the predominant process. These experiments show that, in the presence of a proton source such as water, the propensity of the enone system to participate in a conjugate addition process plays a crucial role in determining the course of the transformation.

In the above discussion, it was emphasized that to represent the structure of the intermediate derived from transmetallation of substrates **14**–**23** with CuX as the 'alkenylcopper(I)' species **36** (Scheme 2) is undoubtedly simplistic. In this connection, the data summarized in Table 2 (entries 3–5 and 10–12) show that for substrates (**16**–**18**) possessing a bulky substituent on the β-carbon of the enone system, the use of CuCN in DMSO or DMF provides much better yields of the cyclized products (**26**–**28**) than does the use of CuCl in DMF. These results indicate that the nature of the anion (Cl^-, CN^-) associated with the original Cu(I) source has an effect on the reactivity (and, consequently, on the structure) of the alkenylcopper(I) intermediate that participates in the conjugate addition step. At present, the actual structures of these intermediates remain obscure.

Stereochemical considerations

Assuming that the copper(I)-mediated cyclizations of cyclohexenones **14**–**21** (Tables 1 and 2) proceeds, in each case, via intermediacy of an alkenylcopper(I) species simplistically represented by **45**, it is clear from molecular modeling that the products should possess *cis*-fused ring junctions (**24**–**31**) (see Scheme 4). Thus, either (or both) of the transition states [**A**]‡ and [**B**]‡, derived from **45** via the conformations **45A** and **45B**, respectively, and leading to the *cis*-fused products **24**–**31**, can be predicted to be of lower energy than the transition state [**C**]‡ formed from **45** by way of conformation **45C** and leading to *trans*-fused products of general structure **46**. Compared with [**A**]‡ and [**B**]‡, it is evident that transition state [**C**]‡ would be destabilized by (extra) steric strain and by substantial angle strain introduced by positioning the alkenylcopper(I) carbon near to the β-carbon of the enone function. On this basis, the relative configuration of each of the bicyclic products **24**–**31** could be assigned with confidence.

In connection with the above configurational assignments, it should be noted that substances **24** and **29** have been reported previously.[24] Furthermore, the ^{1}H NMR data reported[25] for the *trans*-fused epimer of **25** differ significantly from those derived from the product obtained by CuCl-mediated cyclization of **15** (Table 2, entry 1).

With respect to the stereochemical outcome of the cyclizations of the cyclopentenones **22** and **23**, it should be clear that the transition states leading to the *cis*-fused bicyclo[3.3.0]octane systems **32** and **33**, respectively, (Table 2, entries 13, 14) would be significantly more stable than those producing the corresponding, highly strained[26] *trans*-fused isomers.

Conclusion

This study has resulted in the development of a new method to effect the intramolecular conjugate addition of alkenyl functions to α,β-unsaturated ketone systems. In particular, treatment of the cyclohexenone substrates **14**–**21** with 2.5 equiv. of CuCl or CuCN in DMF or DMSO provided good-to-excellent yields of the functionalized, *cis*-fused bicyclo[4.3.0]nonanes **24**–**31**, respectively. A similar protocol involving the cyclopentenone substrates **22** and **23** furnished the corresponding *cis*-fused bicyclo[3.3.0]-octanes **32** and **33**. It seems highly likely that this new method can be extended in a variety of ways and will find use in the complex molecule synthesis. In this regard, the results of ongoing studies[27] in our laboratory will be reported in detail in due course.

Experimental

General Information

Melting points and distillation temperatures (short-path Kugelrohr distillations) are uncorrected. Infrared (IR) spectra were recorded using liquid films (sodium chloride discs) or KBr pellets. Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded using $CDCl_3$ solutions. Signal positions in ^{1}H NMR spectra were measured relative to the signal for $CHCl_3$ (δ 7.24), while resonances in ^{13}C NMR spectra were recorded relative to the signal for $CDCl_3$ (δ 77.0). Tin–hydrogen coupling constants (J_{Sn-H}) are given as the average of the ^{117}Sn and ^{119}Sn values. Flash chromatography[28] was carried out with 230–400 mesh silica gel (E. Merck, silica gel 60). DMF and DMSO were either distilled from calcium hydride (argon atmosphere) or were dried (argon atmosphere) by three sequential treatments with activated 3 Å molecular sieves.[29] Petroleum ether refers to a mixture of alkanes with bp 35–60°C. Commercial copper(I) chloride (99.995%) and copper(I) cyanide (99.99%) were generally used without further purification. Aqueous NH_4Cl–NH_3 (pH 8) was prepared by the addition of ~50 mL of aqueous ammonia (28%) to ~950 mL of saturated aqueous NH_4Cl.

Note: Unless otherwise stated, all reactions were carried out under an inert atmosphere (dry argon) in oven- (~120°C) or flame-dried glassware.

(*Z*)-3-Trimethylstannylbut-2-en-1-ol. To a cold (0°C), stirred solution of the ethyl (*Z*)-3-trimethylstannyl-but-2-enoate[15] (100 mg, 0.36 mmol) in dry Et_2O (10 mL) was added slowly a 1.0 M solution of DIBALH in hexanes (0.9 mL, 0.9 mmol). After the mixture had been stirred for 30 min, a saturated aqueous solution of sodium potassium tartrate (11 mL) was added and the emulsion was stirred for 2 h. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (10 g of silica gel, 4:1 pentane–Et_2O) afforded 82 mg (97%) of the title alcohol, a colorless oil that exhibited IR (neat): 3343, 1627, 1436, 1069, 998, 770 cm^{-1}; ^{1}H NMR (400 MHz): δ 0.15 (s, 9H, $^2J_{Sn-H}$=53 Hz), 1.54 (t, 1H, J=6 Hz), 1.91 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 4.03 (dd, 2H, J=6, 6 Hz), 6.21 (tq, 1H, J=6, 1 Hz, $^3J_{Sn-H}$=136 Hz); ^{13}C NMR (50.3 MHz): δ −8.6, 26.2, 64.2, 138.6, 144.0. Exact mass calcd for $C_7H_{17}O^{120}Sn$ (M^++H): 237.0301; found (CI, CH_4): 237.0300. Anal. calcd for $C_7H_{16}OSn$: C 35.79, H 6.87; found: C 35.65, H 6.82.

(*Z*)-3-Tributylstannylbut-2-en-1-ol (39). To a stirred solution of but-2-yn-1-ol (107 μL, 1.43 mmol) in THF (5 mL) at rt was added a 3.4 M solution of Red-Al® in toluene (0.45 mL, 1.53 mmol). After the mixture had been stirred for 1 h, neat Bu_3SnCl (0.76 mL, 2.80 mmol) was added and the mixture was stirred overnight. A saturated aqueous solution of sodium potassium tartrate (5 mL) was added and the thick emulsion was stirred for 2 h. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (40 g of silica gel, 4:1 pentane–Et_2O) furnished 396 mg (77%) of the alcohol **39**, a colorless oil that displayed IR (neat): 3310, 1463, 1070, 1000, 874, 668, 596 cm^{-1}; ^{1}H NMR (400 MHz): δ 0.84–1.01 (m, 15H), 1.21–1.35 (m, 6H), 1.41–1.55 (m, 7H), 1.92 (br s, 3H, $^3J_{Sn-H}$=50 Hz), 4.00 (t, 2H, J=6 Hz), 6.25 (tq, 1H, J=6, 1 Hz, $^3J_{Sn-H}$=125 Hz); ^{13}C NMR (50.3 MHz): δ 10.2, 13.6, 26.9, 27.3, 29.4, 65.0, 138.8, 144.4. Exact Mass calcd for $C_{12}H_{25}O^{120}Sn$ (M^+–Bu): 305.0927; found: 305.0936. Anal. calcd for $C_{16}H_{34}OSn$: C 53.21, H 9.49; found: C 53.32, H 9.50.

(*Z*)-1-Bromo-3-trimethylstannylbut-2-ene. To a cold (0°C), stirred solution of Ph_3P Br_2.(45.0 g, 107 mmol) and imidazole (7.3 g, 107 mmol) in dry CH_2Cl_2 (300 mL) was added, dropwise, a solution of (*Z*)-3-trimethylstannylbut-2-en-1-ol (10.0 g, 42.6 mmol) in dry CH_2Cl_2 (40 mL). The cloudy white suspension was stirred for 30 min at 0°C, then about 90% of the solvent was removed under reduced pressure and pentane (100 mL) was added to the residual material. The mixture was filtered through a sintered glass funnel containing a plug of Celite® (~800 g) packed on top of a plug of silica gel (~400 g) and the collected material was washed thoroughly with pentane. The combined eluate was concentrated under reduced pressure to give 10.4 g (82%) of the title bromide, a colorless oil that exhibited IR (neat): 1437, 1200, 871, 771, 716 cm^{-1}; ^{1}H NMR (400 MHz): δ 0.23 (s, 9H, $^2J_{Sn-H}$=54 Hz), 1.94–1.96 (m, 3H, $^3J_{Sn-H}$=45 Hz), 3.92 (dq, 2H, J=8, 1 Hz), 6.26 (tq, 1H, J=8, 2 Hz, $^3J_{Sn-H}$=124 Hz); ^{13}C NMR (50.3 MHz): δ −8.5,

26.6, 34.9, 136.2, 148.8. Exact mass calcd for $C_7H_{15}{}^{79}Br^{120}Sn$: 297.9380; found: 297.9382. The instability of this compound precluded the acquisition of satisfactory elemental (C, H) analyses. However, a freshly prepared sample provided clean ^1H and ^{13}C NMR spectra.

(*Z*)-1-Bromo-3-tributylstannylbut-2-ene (40). This material was prepared from the alcohol **39** via a procedure identical with that given above. From 4.15 g (11.5 mmol) of **39** there was obtained 4.39 (90%) of **40**, a colorless oil that exhibited IR (neat): 1463, 1377, 1198, 1073, 872, 595 cm^{-1}; ^1H NMR (400 MHz): δ 0.88 (t, 9H, J=7 Hz), 0.95–1.01 (m, 6H, $^2J_{Sn-H}$=50 Hz), 1.26–1.36 (m, 6H), 1.44–1.56 (m, 6H), 1.94–1.96 (m, 3H, $^3J_{Sn-H}$=40 Hz), 3.87–3.91 (m, 2H), 6.28 (tq, 1H, J=8, 2 Hz, $^3J_{Sn-H}$=116 Hz); ^{13}C NMR (50.3 MHz): δ 10.0, 13.6, 26.9, 27.3, 29.1, 35.2, 136.0, 148.2. Exact mass calcd for $C_{12}H_{24}{}^{79}Br^{120}Sn$ (M^+–Bu): 367.0083; found: 367.0081. The instability of this compound precluded the acquisition of satisfactory elemental (C, H) analyses. However, a freshly prepared sample provided clean ^1H and ^{13}C NMR spectra.

3-Isobutoxy-6-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (8). To a cold (−78°C), stirred solution of LDA (1.02 mmol) in dry THF (10 mL) was added a solution of **7**[14] (172 mg, 1.02 mmol) in dry THF (2 mL). The mixture was warmed to rt, was stirred for 20 min, and then was recooled to −78°C. A solution of (*Z*)-1-bromo-3-trimethylstannylbut-2-ene (292 mg, 0.93 mmol) in dry THF (2 mL) was added dropwise. The mixture was stirred for 1 h at −78°C, was warmed slowly to rt and then was stirred for an additional 1 h. Aqueous NH_4Cl–NH_3 (pH ~8) (7 mL) was added and the phases were separated. The aqueous layer was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (50 g of silica gel, 4:1 pentane–Et_2O) afforded 320 mg (89%) of compound **8**, a colorless oil that exhibited IR (neat): 1660, 1610, 1384, 1193, 994, 769 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$= 53 Hz), 0.94 (d, 3H, J=7 Hz), 0.95 (d, 3H, J=7 Hz), 1.58–1.70 (m, 1H), 1.87 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.95–2.07 (m, 3H), 2.14–2.23 (m, 1H), 2.32–2.47 (m, 2H), 2.58–2.69 (m, 1H), 3.52–3.59 (m, 2H), 5.29 (br s, 1H), 5.93–5.99 (m, 1H, $^3J_{Sn-H}$=137 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 19.1, 26.2, 26.4, 27.7, 28.4, 34.3, 45.5, 74.7, 102.4, 138.3, 140.1, 177.0, 200.4. Exact mass calcd for $C_{17}H_{30}O_2{}^{120}Sn$: 386.1268; found: 386.1263. Anal. calcd for $C_{17}H_{30}O_2Sn$: C 53.02, H 7.85; found: C 53.11, H 7.78.

3-Isobutoxy-6-((*Z*)-3-tributylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (41). This substance was prepared from **7** and **40** via a procedure identical with that just described. Flash chromatography (200 g of silica gel, 4:1 pentane–Et_2O) of the crude product derived from 1.57 g (9.3 mmol) of **7** and 3.59 g (8.5 mmol) of **40** furnished 3.64 g (84%) of **41**, a colorless oil that exhibited IR (neat): 1661, 1611, 1456, 1384, 1193, 999 cm^{-1}; ^1H NMR (400 MHz): δ 0.85 (t, 9H, J=7 Hz), 0.88–0.96 (m, 12H), 1.23–1.33 (m, 6H), 1.41–1.51 (m, 6H), 1.60–1.71 (m, 1H), 1.86 (d, 3H J=1 Hz, $^3J_{Sn-H}$=42 Hz), 1.93–2.07 (m, 3H), 2.14–2.22 (m, 1H), 2.36–2.43 (m, 2H), 2.54–2.62 (m, 1H), 3.51–3.59 (m, 2H), 5.28 (br s, 1H), 5.95–6.01 (m, 1H, $^3J_{Sn-H}$=133 Hz); ^{13}C NMR (50.3 MHz): δ 9.9, 13.7, 19.0, 26.2, 27.3, 27.4, 27.7, 28.3, 29.2, 34.4, 45.6, 74.7, 102.3, 138.4, 140.1, 177.0, 200.5. Exact mass calcd for $C_{22}H_{39}O_2{}^{120}Sn$ (M^+–Bu): 455.1972; found: 455.1973. Anal. calcd for $C_{26}H_{48}O_2Sn$: C 61.07, H 9.46; found: C 61.13, H 9.61.

3-Isobutoxy-6-methyl-6-((*Z*)-3-tributylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (9). To a cold (−78°C), stirred solution of LDA (1.56 mmol) in dry THF (17 mL) was added a solution of **8** (500 mg, 1.3 mmol) in dry THF (3 mL). The solution was warmed to rt, was stirred for 30 min, and then was recooled to −78°C. Neat MeI (163 μL, 2.60 mmol) was added and the mixture was stirred at −78°C for 1 h, was warmed slowly to rt, and was stirred for an additional 1 h. Aqueous NH_4Cl–NH_3 (pH ~8) (10 mL) was added and the phases were separated. The aqueous layer was extracted with Et_2O. Flash chromatography (50 g of silica gel, 4:1 pentane–Et_2O) afforded 486 mg (94%) of **9**, a colorless oil that exhibited IR (neat): 1657, 1612, 1368, 1194, 997, 770 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$=52 Hz), 0.95 (d, 6H, J=7 Hz), 1.06 (s, 3H), 1.66 (dt, 1H, J=14, 6 Hz), 1.86 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.87–1.95 (m, 1H), 1.95–2.05 (m, 1H), 2.10 (ddd, 1H, J=14, 8, 1 Hz), 2.32–2.42 (m, 3H), 3.56 (d, 2H, J=7 Hz), 5.22 (br s, 1H), 5.89–5.95 (m, 1H, $^3J_{Sn-H}$=142 Hz); ^{13}C NMR (50.3 MHz): δ −8.7, 19.1, 22.4, 26.0, 26.4, 27.7, 32.0, 41.7, 43.4, 74.7, 101.4, 136.1, 140.8, 175.9, 203.4. Exact mass calcd for $C_{18}H_{32}O_2{}^{120}Sn$: 400.1424; found: 400.1429. Anal. calcd for $C_{18}H_{32}O_2Sn$: C 54.17, H 8.08; found: C 54.54, H 8.19.

3-Isobutoxy-6-methoxycarbonyl-6-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (10). This material was prepared from **8** (700 mg, 2.1 mmol) and NC–CO_2Me (200 μL, 2.5 mmol) via a procedure identical with that just described. Flash chromatography (50 g silica gel, 4:1 pentane–Et_2O) provided 621 mg (77%) of **10**, a colorless oil that displayed IR (neat): 1733, 1666, 1610, 1192, 993, 770 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$= 53 Hz), 0.92 (d, 3H, J=7 Hz), 0.93 (d, 3H, J=7 Hz), 1.84 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.85–1.94 (m, 1H), 1.94–2.04 (m, 1H), 2.25–2.35 (m, 2H), 2.52–2.67 (m, 3H), 3.56 (d, 2H, J=7 Hz), 3.66 (s, 3H), 5.32 (s, 1H), 5.84 (tq, 1H, J=7, 1 Hz, $^3J_{Sn-H}$=139 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 19.0, 26.41, 26.44, 27.7, 28.4, 38.8, 52.4, 55.7, 74.9, 102.2, 135.1, 142.3, 172.1, 177.1, 195.1. Exact mass calcd for $C_{19}H_{32}O_4{}^{120}Sn$: 444.1322; found: 444.1324. Anal. calcd for $C_{19}H_{32}O_4Sn$: C 51.50, H 7.28; found: C 51.17, H 7.40.

3-Isobutoxy-5-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclopent-2-en-1-one (12). To a cold (−78°C), stirred solution of LDA (12.2 mmol) in dry THF (46 mL) was added dry HMPA (2.12 mL, 12.2 mmol). The solution was warmed to 0°C, stirred for 5 min, and recooled to −78°C. A solution of **11**[17] (1.71 g, 11.1 mmol) in dry THF (12 mL) was added dropwise. The solution was stirred at −78°C for 20 min and at 0°C for 1 min and then was recooled to −78°C. A solution of (*Z*)-1-bromo-3-trimethylstannylbut-2-ene (2.20 g, 7.39 mmol) in dry THF (5 mL) was added dropwise. The reaction mixture was stirred at −78°C for 2.5 h and then was allowed to warm slowly to 0°C over a period of 1 h. The cold bath was removed and the mixture was stirred at rt for 45 min.

Water (50 mL) was added, the phases were separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (125 g of silica gel, 4:1 petroleum ether–Et_2O) and subsequent recrystallization of the solid product from pentane provided 1.11 g (40%) of **12** as colorless plates that exhibited mp 70–71°C; IR (KBr): 2962, 1697, 1596, 1351, 1174, 996, 768 cm^{-1}; ^1H NMR (400 MHz): δ (0.13 (s, 9H, $^2J_{Sn-H}$=53 Hz), 0.97 (d, 6H, J=6.7 Hz), 1.86 (s, 3H, $^3J_{Sn-H}$=47 Hz), 2.00–2.14 (m, 2H), 2.31 (dd, 1H, J=17.6, 1.5 Hz), 2.46–2.54 (m, 2H), 2.64 (dd, 1H, J=17.6, 7.0 Hz), 3.71 (d, 2H, J=6.5 Hz), 5.20 (s, 1H), 5.90 (t, 1H, J=7.0 Hz, $^3J_{Sn-H}$=139 Hz); ^{13}C NMR (75.3 MHz): δ −8.9, 18.9, 26.3, 27.8, 33.9, 36.0, 44.9, 77.9, 103.8, 137.0, 141.1, 189.1, 207.4. Exact Mass calcd for $C_{16}H_{28}O_2{}^{120}Sn$: 372.1111; found: 372.1112. Anal. calcd for $C_{16}H_{28}O_2Sn$: C 51.79, H 7.61; found: C 52.00, H 7.69.

3-Isobutoxy-5-methyl-5-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclopent-2-en-1-one (13). A cold (−78°C), stirred solution of LDA (1.74 mmol) in dry THF (11 mL) containing dry HMPA (1.90 mmol) was prepared as just described. A solution of **12** (0.588 g, 1.59 mmol) in dry THF (11 mL) was added dropwise and the mixture was stirred at −78°C for 25 min and at 0°C for 1 min and then was recooled to −78°C. Neat MeI (0.257 mL, 4.13 mmol) was added and the mixture was stirred at −78°C for 20 min and then was allowed to warm to rt and stirred for 3 h. Water (25 mL) was added, the phases were separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (70 g of silica gel, 4:1 petroleum ether–Et_2O) and subsequent distillation (125–135°C, 0.03 Torr) furnished 0.484 g (79%) of **13**, a colorless oil that displayed IR (neat): 2962, 1698, 1600, 1339, 1231, 999, 770 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$=52.5 Hz), 0.97 (d, 6H, J=6.7 Hz), 1.12 (s, 3H), 1.85 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 2.04 (m, 1H,), 2.05–2.11 (m, 1H), 2.22 (dd, 1H, J=17.4, 0.9 Hz), 2.24 (ddd, 1H, J=14.0, 6.4, 1.4 Hz), 2.57 (dd, 1H, J=17.4, 0.8 Hz), 3.70 (d, 2H, J=6.5 Hz), 5.15 (br s, 1H), 5.85 (ddd, 1H, J=8.1, 6.4, 1.6 Hz, $^3J_{Sn-H}$=139 Hz); ^{13}C NMR (75.3 MHz): δ −8.8, 19.0, 23.8, 26.41, 27.8, 40.8, 42.3, 47.0, 77.8, 102.5, 135.6, 142.0, 187.8, 210.1. Exact Mass calcd for $C_{17}H_{30}O_2{}^{120}Sn$: 386.1268; found: 386.1263. Anal. calcd for $C_{17}H_{30}O_2Sn$: C 53.02, H 7.85; found: C 52.98, H 7.86.

General procedure for the reduction (DIBALH) of substrates 8, 41, 9, 12, and 13, followed by hydrolysis–dehydration (TsOH, H_2O, Et_2O) of the resultant products

To a cold (0°C), stirred solution of the substrate (1.0 equiv.) in dry CH_2Cl_2 (~10–15 mL per mmol of substrate) was added a 1.0 M solution of DIBALH in hexanes (1.2 equiv.). After the mixture had been stirred for 30 min, a saturated aqueous solution of sodium potassium tartrate (the same volume as the total volume of the reaction mixture) was added and the thick emulsion was stirred for 2 h. The phases were separated and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. The residual material was taken up in diethyl ether or CH_2Cl_2 (~10–15 mL per mmol of substrate). Water (~0.1–0.2 mL per mmol of substrate) and $TsOH{\cdot}H_2O$ (~0.05 equiv.) were added. The resulting heterogeneous mixture was stirred at 0°C or rt for ~1 h. Saturated aqueous $NaHCO_3$ (~2 mL per mmol of substrate) was added and the phases were separated. The aqueous layer was extracted with Et_2O and the combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography.

The following compounds were prepared via this general procedure:

4-((*Z*)-3-Trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (14). Flash chromatography (200 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 3.64 g (9.5 mmol) of compound **8** afforded 2.69 g (93%) of the enone **14**, a colorless oil that exhibited IR (neat): 1684, 1450, 1388, 1249, 1210, 769 cm^{-1}; ^1H NMR (400 MHz): δ 0.14 (s, 9H, $^2J_{Sn-H}$=53 Hz), 1.61–1.72 (m, 1H), 1.89 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 2.03–2.20 (m, 3H), 2.33 (ddd, 1H, J=17, 12, 5 Hz), 2.40–2.51 (m, 2H), 5.96 (dd, 1H, J=11, 2 Hz), 6.00 (tq, 1H, J=7, 1 Hz, $^3J_{Sn-H}$=139 Hz), 6.83 (ddd, 1H, J=11, 2, 1 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 26.4, 28.8, 36.7, 37.0, 39.3, 129.2, 137.1, 141.6, 154.2, 199.6. Exact mass calcd for $C_{13}H_{22}O^{120}Sn$: 314.0693; found: 314.0699. Anal. calcd for $C_{13}H_{22}OSn$: C 49.89, H 7.08; found: C 49.98, H 7.13.

4-((*Z*)-3-Tributylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (42). Flash chromatography (100 g of silica gel, 4:1 pentane–Et_2O) of the crude material obtained from 1.52 g (3.0 mmol) of compound **41** provided 1.25 g (96%) of **42**, a colorless oil that exhibited IR (neat): 1686, 1456, 1377, 1249, 1071, 668 cm^{-1}; ^1H NMR (400 MHz): δ 0.85 (t, 9H, J=7 Hz), 0.86–0.91 (m, 6H), 1.22–1.33 (m, 6H), 1.40–1.51 (m, 6H), 1.60–1.71 (m, 1H), 1.88 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=42 Hz), 2.02–2.18 (m, 3H), 2.32 (ddd, 1H, J=18, 13, 5 Hz), 2.40–2.49 (m, 2H), 5.95 (dd, 1H, J=10, 3 Hz), 5.99–6.04 (m, 1H, $^3J_{Sn-H}$=129 Hz), 6.81–6.85 (m, 1H); ^{13}C NMR (50.3 MHz): δ 10.0, 13.6, 27.1, 27.4, 28.9, 29.2, 36.8, 37.0, 39.5, 129.1, 137.1, 141.8, 154.3, 199.7. Exact mass calcd for $C_{18}H_{31}O^{120}Sn$ (M^+–Bu): 383.1397; found: 383.1402. Anal. calcd for $C_{22}H_{40}OSn$: C 60.16, H 9.18; found: C 60.44, H 9.38.

4-Methyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (19). Flash chromatography (20 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 300 mg (0.75 mmol) of compound **9** yielded 238 mg (95%) of **19**, a colorless oil that exhibited IR (neat): 1685, 1449, 1192, 1114, 770 cm^{-1}; ^1H NMR (400 MHz): δ 0.14 (s, 9H, $^2J_{Sn-H}$=52 Hz), 1.12 (s, 3H), 1.69–1.78 (m, 1H), 1.89 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.91–2.00 (m, 1H), 2.07–2.23 (m, 2H), 2.36–2.51 (m, 2H), 5.87 (d, 1H, J=10 Hz), 5.99 (ddq, 1H, J=7, 5, 1 Hz, $^3J_{Sn-H}$=140 Hz), 6.66 (dd, 1H, J=10, 1 Hz); ^{13}C NMR (50.3 MHz): δ −8.7, 24.8, 26.6, 33.9, 34.1, 36.0, 45.7, 127.6, 135.1, 142.3, 158.6, 199.4. Exact mass calcd for $C_{14}H_{24}O^{120}Sn$: 328.0849; found: 328.0856. Anal. calcd for $C_{14}H_{24}OSn$: C 51.42, H 7.40; found: C 51.48, H 7.42.

4-((*Z*)-3-Trimethylstannylbut-2-en-1-yl)cyclopent-2-en-1-one (22). Flash chromatography (35 g of silica gel, 4:1 petroleum ether–Et_2O) of the crude oil derived from 504 mg (1.36 mmol) of compound **12** afforded 320 mg (79%) of **22**, a colorless oil that exhibited IR (neat): 1717, 1587, 1436, 1409, 1347, 1182, 771 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$=53 Hz), 1.88 (d, 3H, J=1.5 Hz, $^3J_{Sn-H}$=47 Hz), 2.01 (dd, 1H, J=19, 2 Hz), 2.19 (br t, 2H, J=7 Hz), 2.48 (dd, 1H, J=19, 6 Hz), 2.97 (m, 1H), 5.95 (td, 1H, J=7, 1.5 Hz, $^3J_{Sn-H}$=136 Hz), 6.14 (dd, 1H, J=5.5, 2 Hz), 7.60 (dd, 1H, J=5.5, 2.5 Hz); ^{13}C NMR (75.3 MHz): δ −8.9, 26.4, 39.0, 40.3, 41.6, 134.0, 136.4, 142.0, 167.8, 209.6. Exact mass calcd for $C_{12}H_{20}O^{120}Sn$: 300.0536; found: 300.0538. Anal. calcd for $C_{12}H_{20}OSn$: C 48.21, H 6.74; found: C 48.17, H 6.67.

4-Methyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclopent-2-en-1-one (23). Flash chromatography (40 g of silica gel, 4:1 petroleum ether–Et_2O) of the crude oil derived from 397 mg (1.03 mmol) of compound **13** afforded 212 mg (83%) of the enone **23**, a colorless oil that exhibited IR (neat): 1718, 1587, 1454, 1192 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$=53 Hz), 1.19 (s, 3H), 1.86 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 2.06 (d, 1H, J=18.5 Hz), 2.14 (dd, 1H, J=14, 8.5 Hz), 2.23 (ddd, 1H, J=14, 6, 1.5 Hz), 2.32 (d, 1H, J=18.5 Hz), 5.87 (ddq, 1H, J=8.5, 6, 1 Hz, $^3J_{Sn-H}$=137.5 Hz), 6.02 (d, 1H, J=5.5 Hz), 7.41 (d, 1H, J=5.5 Hz); ^{13}C NMR (75.3 MHz): δ −8.8, 26.4, 26.5, 44.8, 47.2, 132.1, 135.0, 142.9, 172.5, 209.7. Exact mass calcd for $C_{13}H_{22}O^{120}Sn$: 314.0693; found: 314.0683. Anal. calcd for $C_{13}H_{22}OSn$: C 49.89, H 7.08; found: C 49.95, H 6.95.

4-Methoxycarbonyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (21). To a cold (0°C), stirred solution of compound **10** (210 mg, 0.47 mmol) and $CeCl_3$ $7H_2O$ (840 mg, 2.4 mmol) in dry MeOH (20 mL) was added solid $NaBH_4$ (90 mg, 2.4 mmol) in several small portions. After the solution had been stirred for 1 h, water (10 mL) and Et_2O (10 mL) were added and the mixture was stirred for 15 min. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. The residual material was taken up in Et_2O (20 mL) and water (0.2 mL) and $TsOH{\cdot}H_2O$ (4 mg) were added. The resulting heterogeneous mixture was stirred at rt for 1 h. Saturated aqueous $NaHCO_3$ (5 mL) was added and the phases were separated. The aqueous layer was extracted with Et_2O and the combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (20 g of silica gel, 4:1 pentane–Et_2O) afforded 126 mg (82%) of **21**, a colorless oil that exhibited IR (neat): 1734, 1688, 1435, 1210, 771 cm^{-1}; ^1H NMR (400 MHz): δ 0.13 (s, 9H, $^2J_{Sn-H}$=53 Hz), 1.86 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=46 Hz), 1.90–2.01 (m, 2H), 2.33–2.54 (m, 4H), 3.70 (s, 3H), 5.84 (ddq, 1H, J=6, 5, 1 Hz, $^3J_{Sn-H}$=134 Hz), 5.98 (d, 1H, J=10 Hz), 6.86 (dd, 1H, J=10, 1 Hz); ^{13}C NMR (50.3 MHz): δ −8.7, 26.5, 30.7, 34.7, 43.1, 47.8, 52.5, 129.3, 133.3, 144.1, 150.5, 173.4, 198.5. Exact mass calcd for $C_{15}H_{24}O_3{}^{120}Sn$: 372.0747; found: 372.0750. Anal. calcd for $C_{15}H_{24}O_3Sn$: C 48.56, H 6.52; found: C 48.36, H 6.68.

General procedure for the reaction of ketones 8 and 9 with Grignard reagents, followed by hydrolysis–dehydration (TsOH, H_2O, Et_2O) of the resultant products

To a cold (0°C), stirred solution of the substrate (1.0 equiv.) in dry THF (~15 mL per mmol of substrate) was added, dropwise, a solution of the Grignard reagent in Et_2O or THF (2–3 equiv.). The mixture was warmed to rt and stirred for 1–18 h. Aqueous NH_4Cl–NH_3 (pH~8) (one-half the volume of the total volume of the reaction mixture) was added slowly to the solution and the mixture was stirred for 15 min. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. The residual material was taken up in Et_2O (~15 mL per mmol of substrate). Water (~0.15 mL per mmol of substrate) and $TsOH{\cdot}H_2O$ (0.05 equiv.) were added. The resulting heterogeneous mixture was stirred at rt for 1 h. Saturated aqueous $NaHCO_3$ (~2 mL per mmol substrate) was added and the phases were separated. The aqueous layer was extracted with Et_2O and the combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography.

The following compounds were prepared via this general procedure:

3-Methyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (15). The reaction time was 1 h. Flash chromatography (50 g of silica gel, 4:1 pentane–Et_2O) of the crude oil obtained from 500 mg (1.3 mmol) of **8** afforded 412 mg (97%) of **15**, a colorless oil that exhibited IR (neat): 1675, 1626, 1437, 1379, 1250, 769 cm^{-1}; ^1H NMR (400 MHz): δ 0.15 (s, 9H, $^2J_{Sn-H}$=52 Hz), 1.82–1.88 (m, 1H), 1.89 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.94 (d, 3H, J=1 Hz), 1.98–2.08 (m, 1H), 2.11–2.22 (m, 1H), 2.22–2.46 (m, 4H), 5.83 (br s, 1H), 5.97 (tq, 1H, J=7, 1 Hz, $^3J_{Sn-H}$=140 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 23.2, 26.4, 26.8, 34.2, 36.0, 39.9, 127.1, 137.8, 141.0, 165.0, 199.2. Exact mass calcd for $C_{14}H_{24}O^{120}Sn$: 328.0849; found: 328.0845. Anal. calcd for $C_{14}H_{24}OSn$: C 51.42, H 7.40; found: C 51.43, H 7.46.

3-Ethyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (16). The reaction time was 1 h. Flash chromatography (10 g of silica gel, 4:1 pentane–Et_2O) of the crude oil obtained from 120 mg (0.31 mmol) of **8** afforded 97 mg (92%) of **16**, a colorless oil that exhibited IR (neat): 1673, 1623, 1451, 1253, 873, 769 cm^{-1}; ^1H NMR (400 MHz): δ 0.14 (s, 9H, $^2J_{Sn-H}$=52 Hz), 1.07 (t, 3H, J=7 Hz), 1.88 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.87–1.96 (m, 1H), 1.96–2.07 (m, 1H), 2.11–2.47 (m, 7H), 5.83 (s, 1H), 5.97 (tq, 1H, J=7, 1 Hz, $^3J_{Sn-H}$=137 Hz); ^{13}C NMR (50.3 MHz): δ −8.9, 11.5, 26.4, 26.8, 28.8, 33.9, 36.1, 38.8, 124.6, 138.0, 140.8, 170.4, 199.5. Exact mass calcd for $C_{15}H_{26}O^{120}Sn$: 342.1006; found: 342.0998. Anal. calcd for $C_{15}H_{26}OSn$: C 52.83, H 7.68; found: C 53.15, H 7.60.

3-Ethenyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (17). The reaction time was 2 h. Flash chromatography (20 g of silica gel, 4:1 pentane–Et_2O) of

the crude oil obtained from 250 mg (0.65 mmol) of **8** afforded 196 mg (89%) of **17**, a colorless crystalline solid that displayed mp 38–39°C; IR (KBr): 1668, 1580, 1450, 1250, 1199, 990, 924, 769 cm^{-1}; ^1H NMR (400 MHz): δ 0.14 (s, 9H, $^2J_{Sn-H}$=53 Hz), 1.89 (d, 3H, J=1 Hz, $^3J_{Sn-H}$= 47 Hz), 1.96–2.12 (m, 2H), 2.13–2.25 (m, 1H), 2.26–2.39 (m, 2H), 2.47 (ddd, 1H, J=18, 14, 6 Hz), 2.67–2.75 (m, 1H), 5.47 (d, 1H, J=11 Hz), 5.67 (d, 1H, J=18 Hz), 5.90 (s, 1H), 5.97–6.04 (m, 1H, $^3J_{Sn-H}$=141 Hz), 6.37 (dd, 1H, J=18, 11 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 25.6, 26.5, 33.1, 34.0, 36.2, 120.9, 127.3, 136.9, 138.3, 140.7, 160.5, 199.9. Exact mass calcd for $C_{15}H_{24}O^{120}Sn$: 340.0849; found: 340.0842. Anal. calcd for $C_{15}H_{24}OSn$: C 53.14, H 7.14; found: C 53.37, H 7.28.

3,4-Dimethyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)-cyclohex-2-en-1-one (20). The reaction time was 5 h. Flash chromatography (20 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 300 mg (0.75 mmol) of **9** afforded 228 mg (89%) of **20**, a colorless oil that exhibited IR (neat): 1675, 1618, 1436, 860, 769, 526 cm^{-1}; ^1H NMR (400 MHz): δ 0.15 (s, 9H, $^2J_{Sn-H}$= 53 Hz), 1.12 (s, 3H), 1.66 (dt, 1H, J=14, 6 Hz), 1.87 (d, 3H, J=1 Hz, $^3J_{Sn-H}$=47 Hz), 1.89 (d, 3H, J=1 Hz), 1.96–2.12 (m, 2H), 2.28–2.42 (m, 3H), 5.80 (q, 1H, J=1 Hz), 5.88 (tq, 1H, J=7, 1 Hz, $^3J_{Sn-H}$= 139 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 20.3, 24.3, 26.5, 34.1, 34.2, 38.7, 43.3, 127.6, 135.5, 142.0, 167.9, 199.1. Exact mass calcd for $C_{15}H_{26}O^{120}Sn$: 342.1006; found: 342.1008. Anal. calcd for $C_{15}H_{26}OSn$: C 52.83, H 7.68; found: C 52.69, H 7.70.

3-Isopropyl-4-((*Z*)-3-trimethylstannylbut-2-en-1-yl)cyclohex-2-en-1-one (18). To a cold (0°C), stirred suspension of anhydrous $CeCl_3$ (400 mg, 1.6 mmol) in dry THF (15 mL) was added a 2.0 M solution of isopropylmagnesium chloride in THF (1.63 mL, 3.3 mmol). After the mixture had been stirred for 1 h, a solution of **8** (250 mg, 0.65 mmol) in dry THF (2 mL) was added dropwise. The mixture was stirred at 0°C for 1 h, was warmed to rt, and then was stirred for 1 h. Aqueous NH_4Cl–NH_3 (pH∼8) (8 mL) was added slowly to the solution and the mixture was stirred for 15 min. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. The residual material was taken up in Et_2O (20 mL). Water (0.2 mL) and $TsOH{\cdot}H_2O$ (6 mg) were added and the resulting heterogeneous mixture was stirred at rt for 1 h. Saturated aqueous $NaHCO_3$ (5 mL) was added and the phases were separated. The aqueous layer was extracted with Et_2O and the combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (10 g of silica gel, 4:1 pentane–Et_2O) of the crude oil furnished 66 mg of **8** (29% recovery) and 94 mg (41%) of **18**, a colorless oil that exhibited IR (neat): 1675, 1623, 1451, 1252, 872, 768 cm^{-1}; ^1H NMR (400 MHz): δ 0.14 (s, 9H, $^2J_{Sn-H}$= 53 Hz), 1.08 (d, 3H, J=7 Hz), 1.09 (d, 3H, J=7 Hz), 1.88 (br s, 3H, $^3J_{Sn-H}$=45 Hz), 1.93–2.01 (m, 2H), 2.12–2.22 (m, 1H), 2.23–2.34 (m, 2H), 2.36–2.48 (m, 3H), 5.84 (s, 1H), 5.94–6.00 (m, 1H, $^3J_{Sn-H}$=137 Hz); ^{13}C NMR (50.3 MHz): δ −8.8, 20.4, 22.6, 26.5, 26.6, 33.2, 33.4, 36.0, 38.3, 123.0, 138.2, 140.8, 175.4, 199.9. Exact mass calcd for $C_{16}H_{28}O^{120}Sn$: 356.1162; found: 356.1152. Anal. calcd for $C_{16}H_{28}OSn$: C 54.12, H 7.95; found: C 54.46, H 7.95.

General procedure for the CuCl-mediated intramolecular conjugate additions of substrates 14 (Table 1, entry 4), 15 (Table 2, entry 1), and 19–23 (Table 2, entries 6–8, 13, 14)

To a stirred solution of the substrate (1.0 equiv.) in dry DMF (∼17 mL per mmol of substrate) at rt was added solid CuCl (2.5 equiv.). After the mixture had been stirred for the time indicated in Tables 1 and 2, aqueous NH_4Cl–NH_3 (pH∼8) (25% of the volume of DMF) and Et_2O (25% of the volume of DMF) were added and the mixture was stirred for 15 min. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (H_2O, once; brine, once), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography.

The following compounds were prepared via this general procedure:

***cis*-9-Methylbicyclo[4.3.0]non-8-en-3-one (24)** (Table 1, entry 4). Flash chromatography (10 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 100 mg (0.32 mmol) of **14** afforded 46 mg (96%) of **24**, a colorless oil that exhibited IR (neat): 1714, 1451, 1233, 1022, 801 cm^{-1}; ^1H NMR (400 MHz): δ 1.59 (br s, 3H), 1.64–1.75 (m, 1H), 1.90–2.08 (m, 2H), 2.09–2.19 (m, 1H), 2.21–2.31, (m, 2H), 2.51 (dd, 1H, J=15, 9 Hz), 2.54–2.66 (m, 2H), 2.83–2.94 (m, 1H), 5.28 (br s, 1H); ^{13}C NMR (50.3 MHz): δ 14.4, 27.5, 34.7, 37.4, 38.7, 41.0, 46.0, 124.3, 141.1, 214.0. Exact mass calcd for $C_{10}H_{14}O$: 150.1045; found: 150.1045. Anal. calcd for $C_{10}H_{14}O$: C 79.96, H 9.39; found: C 79.98, H 9.57.

***cis*-1,9-Dimethylbicyclo[4.3.0]non-8-en-3-one (25)** (Table 2, entry 1). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 100 mg (0.31 mmol) of **15** furnished 41 mg (81%) of **25**, a colorless oil that displayed IR (neat): 1718, 1451, 1223, 1321, 812 cm^{-1}; ^1H NMR (400 MHz): δ 1.05 (s, 3H), 1.54–1.56 (m, 3H), 1.67–1.77 (m, 1H), 1.92–2.03 (m, 2H), 2.08–2.20 (m, 2H), 2.22–2.39 (m, 3H), 2.62 (ddt, 1H, J=17, 9, 2 Hz), 5.22–5.26 (m, 1H); ^{13}C NMR (50.3 MHz): δ 12.0, 27.1, 27.5, 36.4, 36.8, 43.0, 48.1, 50.2, 123.1, 145.0, 213.9. Exact mass calcd for $C_{11}H_{16}O$: 164.1201; found: 164.1195. Anal. calcd for $C_{11}H_{16}O$: C 80.44, H 9.82; found: C 80.33, H 9.99.

***cis*-6,9-Dimethylbicyclo[4.3.0]non-8-en-3-one (29)** (Table 2, entry 6). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude product acquired from 50 mg (0.15 mmol) of **19** afforded 23 mg (92%) of **29**, a colorless oil that exhibited IR (neat): 1718, 1451, 1188, 1020, 798 cm^{-1}; ^1H NMR (400 MHz): δ 1.16 (s, 3H), 1.58 (s, 3H), 1.76 (br t, 2H, J=7 Hz), 2.15–2.31 (m, 5H), 2.39–2.45 (m, 1H), 2.52 (dd, 1H, J=15, 6 Hz), 5.25 (br s, 1H); ^{13}C NMR (50.3 MHz): δ 14.7, 29.5, 34.9, 36.1, 39.4, 40.7, 46.9, 54.1, 123.9, 140.6, 213.9. Exact mass calcd for $C_{11}H_{16}O$: 164.1201; found: 164.1198. Anal. calcd for $C_{11}H_{16}O$: C 80.44, H 9.82; found: C 80.58, H 9.93.

***cis*-1,6,9-Trimethylbicyclo[4.3.0]non-8-en-3-one (30)** (Table 2, entry 7). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude material obtained from 70 mg (0.21 mmol) of **20** produced 31 mg (85%) of **30**, a crystalline solid that exhibited mp 29–30°C; IR (KBr): 1718, 1450, 1381, 1132, 1022, 799 cm^{-1}; ^1H NMR (400 MHz): δ 0.94 (s, 3H), 1.10 (s, 3H), 1.53 (dt, 3H, J=2, 1.8 Hz), 1.71 (ddd, 1H, J=14, 8, 6 Hz), 1.83 (ddd, 1H, J=14, 7, 5 Hz), 2.11–2.34 (m, 6H), 5.22–5.26 (m, 1H); ^{13}C NMR (50.3 MHz): δ 12.6, 22.2, 23.8, 36.9, 37.0, 42.6, 45.4, 48.1, 52.7, 122.9, 145.4, 213.7. Exact mass calcd for $C_{12}H_{18}O$: 178.1358; found: 178.1359. Anal. calcd for $C_{12}H_{18}O$: C 80.85, H 10.18; found: C 80.72, H 10.22.

***cis*-6-Methoxycarbonyl-9-methylbicyclo[4.3.0]non-8-en-3-one (31)** (Table 2, entry 8). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 50 mg (0.13 mmol) of **21** afforded 25 mg (90%) of **31**, a colorless oil that exhibited IR (neat): 1724 (br), 1437, 1233, 1061, 805 cm^{-1}; ^1H NMR (400 MHz): δ 1.60–1.63 (m, 3H), 1.89–1.97 (m, 1H), 2.12–2.37 (m, 4H), 2.42 (dd, 1H, J=15, 5 Hz), 2.67 (dd, 1H, J=15, 7 Hz), 2.93–3.00 (m, 1H), 3.39 (br s, 1H), 3.72 (s, 3H), 5.26–5.30 (m, 1H); ^{13}C NMR (50.3 MHz): δ 14.3, 31.2, 35.5, 40.1, 43.4, 49.7, 50.0, 52.3, 123.1, 140.2, 177.6, 211.7. Exact mass calcd for $C_{12}H_{16}O_3$: 208.1099; found: 208.1094. Anal. calcd for $C_{12}H_{16}O_3$: C 69.21, H 7.74; found: C 69.15, H 7.93.

***cis*-6-Methylbicyclo[3.3.0]oct-6-en-3-one (32)** (Table 2, entry 13). Flash chromatography (15 g of silica gel, 4:1 petroleum ether–Et_2O) of the crude material obtained from 244 mg (0.82 mmol) of **22** provided 85 mg (76%) of **32**, a colorless oil that displayed IR (neat): 1741, 1446, 1402, 1170, 1031, 796 cm^{-1}; ^1H NMR (400 MHz): δ 1.65 (m, 3H), 1.96 (ddd, 1H, J=19, 7.5, 1.5 Hz), 2.08 (dt, 1H, J=16.5, 2 Hz), 2.23 (ddd, 1H, J=19, 2, 1.5 Hz), 2.36 (ddd, 1H, J=19, 10 Hz, 1.5 Hz), 2.47 (ddd, 1H, J=19, 10, 1.5 Hz), 2.62 (m, 1H), 2.93 (m, 1H), 3.17 (br s, 1H), 5.29 (br s, 1H); ^{13}C NMR (75.3 MHz): δ 14.7, 37.6, 39.2, 40.6, 45.0, 49.1, 124.1, 141.1, 220.0. Exact Mass calcd for $C_9H_{12}O$: 136.0888; found: 136.0891. Anal. calcd for $C_9H_{12}O$: C 79.37, H 8.88; found: C 79.10, H 8.98.

***cis*-1,6-Dimethylbicyclo[3.3.0]oct-6-en-3one (33)** (Table 2, entry 14). Flash chromatography (25 g of silica gel, 9:1 petroleum ether–Et_2O) of the crude material obtained from 150 mg (0.48 mmol) of **23** afforded 55 mg (77%) of **33**, a colorless oil that displayed IR (neat): 1744, 1448, 1401, 1379, 1172, 1015, 793 cm^{-1}; ^1H NMR (400 MHz): δ 1.22 (s, 3H), 1.63 (d, 3H, J=1 Hz), 2.13 (d, 1H, J=18.5 Hz), 2.20–2.32 (m, 4H), 2.43 (ddd, 1H, J=19, 10, 1.5 Hz), 2.72 (br d, 1H, J=9 Hz), 5.52 (br s, 1H); ^{13}C NMR (75.3 MHz): δ 15.0, 26.9, 40.3, 46.1, 46.2, 52.1, 55.7, 124.0, 141.3, 219.4. Exact Mass calcd for $C_{10}H_{14}O$: 150.1045; found: 150.1046. Anal. calcd for $C_{10}H_{14}O$: C 79.96, H 9.39; found: C 79.70, H 9.39.

Conversion of 42 into 24: determination of the amount of Bu_3SnCl produced (Scheme 3)

The general procedure given above was employed. Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O, then pure Et_2O) of the crude material obtained from 100 mg (0.23 mmol) of **42** afforded 31 mg (91%) of **24** (a colorless oil that displayed spectra identical with those summarized previously (vide supra)) and 71 mg (96%) of Bu_3SnCl (^1H NMR spectrum identical with that of an authentic sample).

General procedure for the CuCN-mediated intramolecular conjugate additions of substrates 15–18 (Table 2, entries 9–12)

To a stirred solution of the substrate (1.0 equiv.) in dry DMSO (~12 mL per mmol of substrate) at rt was added solid CuCN (2.5 equiv.) and the resultant mixture was heated at 60°C for the time indicated in Table 2. Aqueous NH_4Cl–NH_3 (pH~8) (25% of the volume of DMSO) and Et_2O (25% of the volume of DMSO) were added and the mixture was stirred for 15 min. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (H_2O, once; brine, once), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography.

The following compounds were prepared via this general procedure:

***cis*-1,9-Dimethylbicyclo[4.3.0]non-8-en-3-one (25)** (Table 2, entry 9). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 50 mg (0.15 mmol) of **15** gave 23 mg (92%) of **25**, which exhibited spectra identical with those summarized previously (vide supra).

***cis*-1-Ethyl-9-methylbicyclo[4.3.0]non-8-en-3-one (26)** (Table 2, entry 10). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 50 mg (0.15 mmol) of **16** furnished 24 mg (91%) of **26**, a colorless oil that exhibited IR (neat): 1717, 1452, 1380, 1236, 794 cm^{-1}; ^1H NMR (400 MHz): δ 0.75 (t, 3H, J=7 Hz), 1.28–1.46 (m, 2H), 1.47–1.50 (m, 3H), 1.65–1.74 (m, 1H), 1.88–2.00 (m, 2H), 2.08–2.39 (m, 6H), 5.31–5.34 (m, 1H); ^{13}C NMR (50.3 MHz): δ 8.2, 12.0, 27.7, 31.9, 35.9, 37.9, 38.6, 47.5, 53.8, 124.9, 142.4, 214.3. Exact mass calcd for $C_{12}H_{18}O$: 178.1358; found: 173.1352. Anal. calcd for $C_{12}H_{18}O$: C 80.85, H 10.18; found: C 80.58, H 10.10.

***cis*-1-Ethenyl-9-methylbicyclo[4.3.0]non-8-en-3-one (27)** (Table 2, entry 11). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 68 mg (0.20 mmol) of **17** furnished 21 mg (60%) of **27**, a colorless oil that exhibited IR (neat): 1718, 1633, 1408, 1000, 917, 797 cm^{-1}; ^1H NMR (400 MHz): δ 1.48–1.52 (m, 3H), 1.68–1.77 (m, 1H), 1.95–2.08 (m, 2H), 2.17 (ddd, 1H, J=18, 8, 5 Hz), 2.26 (ddd, 1H, J=18, 8, 5 Hz), 2.34–2.42 (m, 1H), 2.38 (d, 1H, J=15 Hz), 2.60 (d, 1H, J=15 Hz), 2.67 (ddt, 1H, J=17, 9, 2 Hz), 4.90 (d, 1H, J=17 Hz), 4.98 (d, 1H, J=11 Hz), 5.36–5.41 (m, 1H), 5.70 (dd, 1H, J=17, 11 Hz); ^{13}C NMR (50.3 MHz): δ 12.4, 27.5, 36.5, 37.3, 42.4, 44.1, 56.4, 112.1, 125.1, 142.8, 144.1, 213.0. Exact mass calcd for $C_{12}H_{16}O$: 176.1201; found: 176.1200. Anal. calcd for $C_{12}H_{16}O$: C 81.77, H 9.15; found: C 81.76, H 9.14.

***cis*-1-Isopropyl-9-methylbicyclo[4.3.0]non-8-en-3-one (28)** (Table 2, entry 12). Flash chromatography (5 g of silica gel, 4:1 pentane–Et_2O) of the crude oil derived from 66 mg (0.19 mmol) of **18** furnished 26 mg (73%) of **28**, a colorless oil that exhibited IR (neat): 1718, 1677, 1466, 1379, 1236, 785 cm^{-1}; ^1H NMR (400 MHz): δ 0.73 (d, 3H, J=7 Hz), 0.89 (d, 3H, J=7 Hz), 1.48 (ddd, 3H, J=2, 2, 2 Hz), 1.62–1.71 (m, 2H), 1.83–1.98 (m, 2H), 2.12–2.18 (m, 2H), 2.18 (d, 1H, J=15 Hz), 2.36–2.42 (m, 1H), 2.53 (ddt, 1H, J=17, 9, 2 Hz), 2.60 (d, 1H, J=15 Hz), 5.32 (br s, 1H); ^{13}C NMR (50.3 MHz): δ 12.2, 17.1, 17.2, 28.1, 33.6, 33.8, 35.1, 38.6, 46.1, 57.0, 125.0, 143.0, 214.9. Exact mass calcd for $C_{13}H_{20}O$: 192.1514; found: 192.1511. Anal. calcd for $C_{13}H_{20}O$: C 81.20, H 10.48; found: C 81.50, H 10.54.

Acknowledgements

We thank NSERC of Canada and Merck Frosst Canada Inc. for financial support. A NSERC of Canada Postdoctoral Fellowship (to P. A. B.) and a NSERC of Canada Postgraduate Scholarship (to E. J. M.) are gratefully acknowledged.

References

1. Stille, J. K. *Angew. Chem. Int. Ed. Eng.* **1986**, *25*, 508.
2. Mitchell, T. N. *Synthesis* **1992**, 803.
3. Hegedus, L. S. *Organometallics in Organic Synthesis*; Schlosser, M., Ed.; Wiley: Chichester, 1994, pp 413–417.
4. Farina, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, E. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 12 (Hegedus, L. S., Ed.), pp 200–220.
5. Farina, V.; Krishnamurthy, V.; Scott, W. *J. Org. React.* **1997**, *50*, 1.
6. Liebeskind, L. S.; Fengl, R. W. *J. Org. Chem.* **1990**, *55*, 5359.
7. See also Han, X.; Stoltz, B. M.; Corey, E. J.; *J. Am. Chem. Soc.* **1999**, *121*, 7600 and citations therein.
8. (a) Piers, E.; Wong, T. *J. Org. Chem.* **1993**, *58*, 3609. (b) Piers, E.; Wong, T. Unpublished work. (c) For related work involving transmetallation of α-heteroatom-substituted alkyltributylstannanes with Cu(I) salts, see Falck, J. R.; Bhatt, R. K.; Ye, J. *J. Am. Chem. Soc.* **1995**, *117*, 5973.
9. Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905.
10. For an excellent review of the intramolecular Michael reaction, see Little, R. D.; Masjedizadeh, M. R.; Wallquist, O. (in part); McLoughlin, J. I. (in part). *Org. React.* **1995**, *47*, 315. See also Cooke, M. P.; Huang, J. J. *Synlett* **1997**, 535, and citations therein.
11. Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.
12. For a preliminary report, see Piers, E.; McEachern, E. J.; Burns, P. A. *J. Org. Chem.* **1995**, *60*, 2322.
13. Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775; Stork, G.; Danheiser, R. L.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 3414.
14. Panouse, J.; Sanié, C. *Bull. Soc. Chim. Fr.* **1956**, 1272.
15. Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron* **1989**, *45*, 363.
16. Mander, L. N.; Sethi, S. P. *Tetrahedron Lett.* **1983**, *24*, 5425.
17. Koreeda, M.; Liang, Y.; Akagi, H. *J. Chem. Soc., Chem. Commun.* **1979**, 449.
18. March, J. *Advanced Organic Chemistry*; 4th ed.; Wiley: New York, 1992, pp 926–927.
19. Crimmons, M. T.; Dedopoulou, D. *Synth. Commun.* **1992**, *22*, 1953.
20. Gemal, A. L.; Luche, J. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
21. Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015.
22. Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595. Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1984**, *25*, 2415.
23. Wiley, G. A.; Hershkowitz, R. L.; Rein, B. M.; Chung, B. C. *J. Am. Chem. Soc.* **1964**, *86*, 964; Wiley, G. A.; Rein, B. M.; Hershkowitz, R. L. *Tetrahedron Lett.* **1964**, 2509.
24. Marinovic, N. N.; Ramanathan, H. *Tetrahedron Lett.* **1983**, *24*, 1871.
25. Narula, A. S.; Sethi, S. P. *Tetrahedron Lett.* **1984**, *25*, 685.
26. Chang, S.; McNally, D.; Shary-Tehrany, S.; Hickey, M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109.
27. Piers, E.; McEachern, E. J. *Synlett* **1996**, 1087. Piers, E.; Skupinska, K. A.; Wallace, D. J. *Synlett* **1999**, 1867.
28. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
29. Burfield, D. R.; Smithers, R. S. *J. Org. Chem.* **1978**, *43*, 3966.