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Pd(0)-catalyzed addition of $Me_3SnSnMe_3$ to α,β-alkynic aldehydes and ketones. Synthesis of (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes and ketones. Preparation and synthetic uses of substituted (*Z*)-4-trimethylstannyl-1,3-butadienes

Edward Piers and Richard D. Tillyer

Abstract: Treatment (dry tetrahydrofuran, reflux) of the α,β-alkynic aldehydes **26**–**28** and ketones **29**–**36** with $Me_3SnSnMe_3$ in the presence of a catalytic amount of $(Ph_3P)_4Pd$ provides fair to excellent yields of the corresponding (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes **41**–**43** and ketones **44**–**51**. The carbonyl compounds **41**–**51**, upon reaction with methylenetriphenylphosphorane under suitable conditions, are smoothly converted into the (*Z*)-4-trimethylstannyl-1,3-butadienes **61**–**71**, respectively. Treatment of the aldehyde **41** with the anion of trimethyl phosphonoacetate and the aldehyde **42** with the anion of the phosphonoacetate **73** produces excellent yields of the 5-trimethylstannyl-2,4-heptadienoates **72** and **74**, respectively. The synthetic potential of (*Z*)-4-trimethylstannyl-1,3-butadienes is illustrated by the conversion of **62** into the functionalized, stereodefined conjugated dienes **76** and **78** and by transformation of **87** into the structurally novel diene **84**. Diels–Alder reactions of **84** with tetracyanoethylene and dimethyl acetylenedicarboxylate provide the spiro[3.5]nonane derivatives **88** and **89**, respectively.

Key words: Diels–Alder cycloaddition, organocopper(I), transmetallation, alkylidenecyclobutane, (*E*)-4-lithio-1,3-butadienes, spiro[3.5]nonane.

Résumé : Le traitement des aldéhydes **26**–**28** et des cétones **29**–**36** α,β-alcyniques avec du $Me_3SnSnMe_3$ (tétrahydrofurane sec, reflux), en présence d'une quantité catalytique de $Pd(PPh_3)_4$, conduit aux aldéhydes **41**–**43** et aux cétones **44**–**51** (*Z*)-β-triméthylstannyl-α,β-alcéniques correspondantes avec des rendements allant de corrects à excellents. Par réaction avec le méthylènetriphénylphosphorane, les composés carbonylés **41**–**51** se transforment facilement en (*Z*)-4-triméthylstannylbuta-1,3-diènes, **61**–**71**, respectivement. Le traitement de l'aldéhyde **41** avec l'anion phosphonoacétate de triméthyle et de l'aldéhyde **42** avec l'anion du phosphonoacétate **73** conduit respectivement à d'excellents rendements aux 5-triméthylstannylhepta-2,4-diénoates **72** et **74**. Le potentiel de synthèse des (*Z*)-4-triméthylstannylbuta-1,3-diènes a été illustré par la conversion du composé **62** en diènes conjugués fonctionnalisé stéréodéfinis **76** et **78** et par la transformation du composé **87** en diène **84** de structure nouvelle. Les réactions de Diels–Alder du composé **84** avec le tétracyanoéthène et l'acétylènedicarboxylate de diméthyle conduisent respectivement aux dérivés spiro[3.5]nonanes **88** et **89**.

Mots clés : cycloaddition de Diels–Alder, organocuivre(I), transmétallation, alkylidènecyclobutane, (*E*)-4-lithiobuta-1,3-diènes, spiro[3.5]nonane.

[Traduit par la rédaction]

Introduction

A recent report (1) from this laboratory disclosed, inter alia, that alkyl 2-alkynoates (general structure **1**), upon treatment with hexamethylditin in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0), are converted into the corresponding alkyl (*Z*)-2,3-bis(trimethylstannyl)-2-alkenoates **2** (eq. [1]). This process, which is generally clean and efficient, is compatible with the presence of a variety of functional groups in R^1. It was also shown (1) that the *Z* isomers **2** are thermally unstable and, when heated to 75–95°C, rearrange smoothly to the *E* isomers **3** (eq. [2]). We report in this paper that the $(Ph_3P)_4Pd$-catalyzed addition of $Me_3SnSnMe_3$ to α,β-alkynic aldehydes and ketones of general structure **4** does not lead to the formation of the corresponding α,β-bis(trimethylstannyl) α,β-alkenic carbonyl compounds, but instead provides, directly and highly stereoselectively, (*Z*)-β-

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This paper is dedicated to Professor Howard C. Clark in recognition of his contributions to Canadian chemistry.

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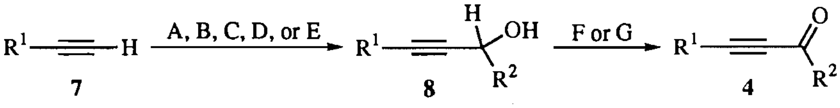
Table 1. Preparation of α,β-alkynic aldehydes and ketones.



Entry	Starting material **7**	R¹	R²	Conditions[a]	Alcohol **8**	Yield (%)[b]	Conditions[a]	Product **4**	Yield (%)[b]
1	**9**	$TBDMSO(CH_2)_2$[c]	H	A	**16**	74	F	**26**	72
2	**10**	$MOMO(CH_2)_2$[d]	H	A	**17**	80	F	**27**	57
3	**11**	$TBDMSO(CH_2)_4$[c]	H	A	**18**	81	F	**28**	74
4	**9**	$TBDMSO(CH_2)_2$[c]	Me	B	**19**	92	G	**29**	74
5	**12**	$Cl(CH_2)_3$	Me	B	**20**	85	G	**30**	74
6	**11**	$TBDMSO(CH_2)_4$[c]	Me	B	**21**	60	G	**31**	76
7	**13**	$H{-}{\equiv}{-}(CH_2)_3$	Me	C	**22**	60	G	**32**	55
8	**14**	i-Pr	Me	B	**23**	—[e]	F	**33**	56[f]
9	**9**	$TBDMSO(CH_2)_2$[c]	i-Pr	D	**24**	85	G	**34**	81
10	**15**	*t*-Bu	*n*-C_6H_{13}	E	**25**	96	G	**35**	72

[a] A: (*i*) MeLi (1 equiv.), THF, −78°C, 10 min; −20°C, 1 h; (*ii*) H_2CO (4 equiv.), warm to room temperature, then stir for 30 min. B: (*i*) as in A; (*ii*) cool to −78°C, add MeCHO (2 equiv.), −78°C, 10 min, then warm to room temperature. C: as in B except that 5 equiv. of MeCHO were used. D: as in B, except that i-PrCHO (1.5 equiv.) was used in place of MeCHO. E: as in B, except that *n*-$C_6H_{13}CHO$ (1.5 equiv.) was used in place of MeCHO. F: pyridinium chlorochromate (PCC) (1.5 equiv.), NaOAc (0.3 equiv.), CH_2Cl_2, room temperature, 2 h. G: PCC (2.5 equiv.), NaOAc (0.3 equiv.), CH_2Cl_2, room temperature, 2.5 h.

[b] Yield of purified, distilled product.

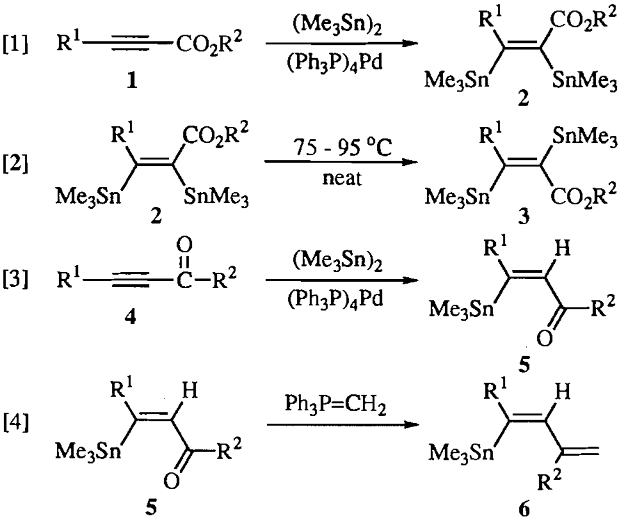
[c] TBDMS = *tert*-butyldimethylsilyl.

[d] MOM = methoxymethyl.

[e] The crude product was not purified.

[f] Overall yield from compound **14**.

trimethylstannyl α,β-alkenic aldehydes and ketones **5** in fair to excellent yields (eq. [3]) (2). Furthermore, we show that substances **5** are excellent precursors for the preparation of synthetically valuable, stereochemically homogeneous (*Z*)-4-trimethylstannyl-1,3-butadienes of general structure **6** (eq. [4]).



Results and discussion

Preparation of α,β-alkynic aldehydes and ketones

Of the 11 α,β-alkynic aldehydes and ketones employed in this study, substrates **26**–**35** were prepared as summarized in Table 1. Two straightforward synthetic steps were employed in each case. For example, sequential treatment of a solution of 4-*tert*-butyldimethylsilyloxy-1-butyne (**9**) in dry tetrahydrofuran (THF) with methyllithium (1 equiv.) and paraformaldehyde (4 equiv.) gave the primary alcohol **16**, which, upon oxidation with pyridinium chlorochromate in the presence of sodium acetate (3), provided 5-*tert*-butyldimethylsilyloxy-2-pentynal (**26**) (Table 1, entry 1). In a similar fashion, the 1-alkynes **10** and **11** were transformed, via the alcohols **17** and **18**, into the α,β-alkynic aldehydes **27** and **28**, respectively (entries 2 and 3). Analogous chemical processes, using appropriate 1-alkynes as starting materials and ethanal (entries 4–8), 2-methylpropanal (entry 9), and heptanal (entry 10) as electrophilic reagents, afforded the α,β-alkynic ketones **29**–**35**.

All the products listed in Table 1 were distilled, except for the alcohol **23** (entry 8). This substance is quite volatile and, therefore, in order to avoid excessive loss of material, crude **23** was not purified but was oxidized directly to the required ketone **33**. It should also be noted that conversion of 1,6-heptadiyne (**13**) into the secondary alcohol **22** (entry 7) was accompanied by a small amount of a polar, uncharacterized side product that was assumed to be the diol resulting from reaction at both terminal alkyne functions of the starting material.

The final ketonic substrate **36** employed in this study was prepared as shown in Scheme 1. Thus, oxidation of 4-pentyn-1-ol (**37**), followed by reaction of the resultant aldehyde **38** with vinyl magnesium bromide, provided the enynol **39**. Treatment of **39** with *tert*-butyldimethylsilyl chloride under

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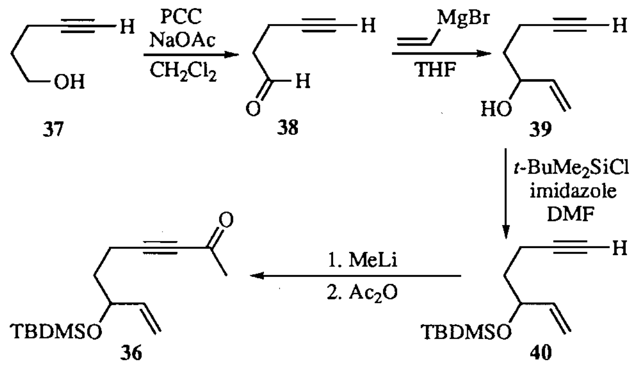
Scheme 1.



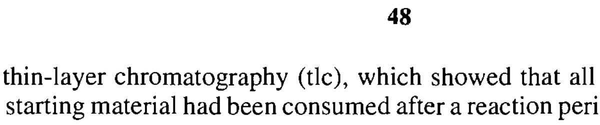
"standard" conditions (4) produced **40**, which, upon sequential treatment with methyllithium and acetic anhydride, afforded the functionalized α,β-alkynic ketone **36**.

Collectively, the substrates **26–36** contain a range of functional groups in addition to the α,β-alkynic aldehyde and ketone moieties. These include primary silyl ether, secondary allylic silyl ether, primary chloride, terminal alkyne, and terminal alkene functions. Based on the results of our earlier studies (1), it seemed highly likely that each of these functional groups would be compatible with the reaction of the substrates with hexamethylditin in the presence of a palladium(0) catalyst.

Pd(0)-catalyzed reaction of the α,β-alkynic aldehydes and ketones 26–36 with hexamethylditin

Initial experiments were carried out using the structurally simple substrate **33**. Thus, employing a procedure similar to that reported previously in connection with the Pd(0)-catalyzed reaction of hexamethylditin with α,β-alkynic esters (1), tetrakis(triphenylphosphine)palladium(0) (5 mol%) was added to a stirred solution of **33** (1 equiv.) and $Me_3SnSnMe_3$ (1 equiv.) in dry THF (argon atmosphere) and the resulting mixture was refluxed (eq. [5]). The progress of the reaction was monitored by thin-layer chromatography (tlc), which showed that all of the starting material had been consumed after a reaction period of ~5 h. Removal of most of the solvent and purification of the crude material by flash chromatography on silica gel (5) provided a single product. Inspection of the ^{1}H nuclear magnetic resonance (nmr) spectrum of this material showed clearly that the product was not the initially expected (*Z*)- (or (*E*))-α,β-bis(trimethylstannyl) α,β-alkenic ketone **52** (1), but was, in fact, (*Z*)-5-methyl-4-trimethylstannyl-3-hexen-2-one (**48**) (eq. [5]). Of particular note in the ^{1}H nmr spectrum of **48** is the presence of only one 9-proton signal (δ 0.09, $^2J_{\text{Sn–H}} = 54$ Hz) due to the Me_3Sn group and the appearance of a 1-proton doublet (δ 6.77, $J = 1.5$ Hz, $^3J_{\text{Sn–H}} = 127$ Hz[2]) derived from the alkenic proton at C-3. The magnitude of $^3J_{\text{Sn–H}}$ associated with the C-3 proton is characteristic of coupling between tin and a proton that are *trans* to one another on a carbon–carbon double bond (6). This *trans* relationship in product **48** was confirmed by a nuclear Overhauser enhancement (nOe) difference experiment in which irradiation at δ 6.77 caused an increase in the intensity of each of the signals at δ 2.75 (-C*H*Me$_2$), 1.03 (-CH*Me*$_2$), and 2.20 (C(O)Me). The enhancement of the methyl resonance of the acetyl group indicates that this substance exists largely in the conformation shown in formula **48**. Presumably, this arrangement is stabilized by coordination of the carbonyl oxygen with the tin atom (see ref. 7 and citations therein). On the other hand, the alternative (planar) conformation (see eq. [5]) would be notably destabilized by steric repulsion between the acetyl methyl group and the Me_3Sn function.

[5]



The conversion of **33** into **48** (eq. [5]) was clean and efficient (80% yield of purified product). Examination (tlc, ^{1}H nmr spectroscopy) of the crude material prior to purification showed that this dark oil did not contain the bis(trimethylstannane) **52**. Furthermore, the geometric isomer of the isolated product **48** could not be detected either. To demonstrate the generality of this process, each member of the structurally diverse set of α,β-alkynic aldehydes and ketones (**26–32**; **34–36**) (vide supra) was subjected to the Pd(0)-catalyzed reaction with hexamethylditin. The results of this study, including the transformation of **33** into **48**, are summarized in Table 2.

The conversion of α,β-alkynic aldehydes and ketones into the corresponding (*Z*)-β-trimethylstannyl α,β-alkenic carbonyl compounds does indeed turn out to be a general reaction. As shown by the data given in Table 2, the starting materials **26-36** are transformed into the products in fair to excellent yields. In each of the summarized conversions, the product was obtained as a single geometric isomer. In the ^{1}H nmr spectrum of each of the products, the resonance due to the olefinic proton exhibited a $^3J_{\text{Sn–H}}$ value consistent with that expected for the *Z* isomer (trans relationship between the trimethylstannyl group and the olefinic hydrogen) (6).

The reactions summarized in Table 2 were carried out in refluxing dry THF, with an initial substrate concentration between 0.3 and 0.6 molar. In each case, 0.05 equiv. of the palladium(0) catalyst ($(Ph_3P)_4Pd$) was employed. Under these conditions, the reactions were generally complete within reasonable reaction times. The products were conveniently purified by flash chromatography (silica gel) (5) of the crude oils derived by removal of most of the solvent (reduced pressure) from the reaction mixtures.

The reactions summarized in entries 7 and 10 of Table 2 require special mention. Reaction of the keto diyne **32** with $Me_3SnSnMe_3$ in the presence of $(Ph_3P)_4Pd$ provided in good yield (69%) (*Z*)-4-trimethylstannyl-3-nonen-8-yn-2-one (**47**) (eq. [6]). The fact that the terminal alkyne function of **32** does not interfere with the "normal" reaction of the alkynic ketone moiety is particularly noteworthy, since it is known (8) that the elements of $Me_3SnSnMe_3$ can be added to 1-alkynes

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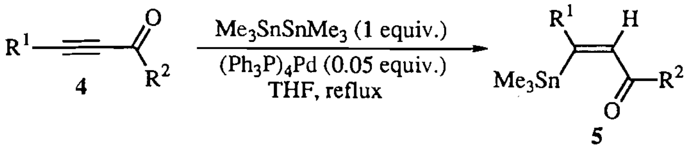
[2] This value represents the average of the (very similar) ^{117}Sn–H and ^{119}Sn–H coupling constants.

Table 2. Conversion of α,β-alkynic aldehydes and ketones **26**–**36** into (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes and ketones **41**–**51**.

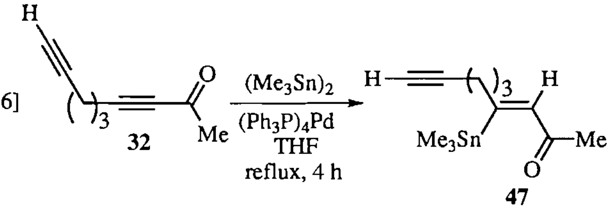


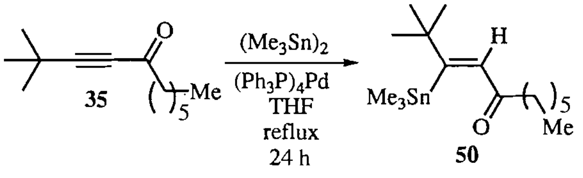
Entry	Starting material 4	R^1	R^2	Reaction time (h)	Product 5	Yield (%)[a]
1	**26**	TBDMSO(CH$_2$)$_2$[b]	H	2	**41**	87
2	**27**	MOMO(CH$_2$)$_2$[c]	H	2	**42**	76
3	**28**	TBDMSO(CH$_2$)$_4$[b]	H	2	**43**	88
4	**29**	TBDMSO(CH$_2$)$_2$[b]	Me	2	**44**	90
5	**30**	Cl(CH$_2$)$_3$	Me	3	**45**	81
6	**31**	TBDMSO(CH$_2$)$_4$[b]	Me	2	**46**	83
7	**32**	H—≡—(CH$_2$)$_3$	Me	4	**47**	69
8	**33**	i-Pr	Me	5	**48**	80
9	**34**	TBDMSO(CH$_2$)$_2$[b]	i-Pr	5	**49**	94
10	**35**	*t*-Bu	*n*-C$_6$H$_{13}$	24	**50**	48
11	**36**	H$_2$C=CH—CH(CH$_2$)$_2$[b] | OTBDMS	Me	8	**51**	95

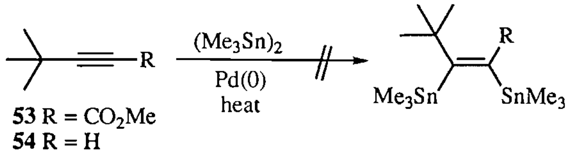
[a] Yield of purified, distilled product.
[b] TBDMS = *tert*-butyldimethylsilyl.
[c] MOM = methoxymethyl.

under conditions similar to those employed for the conversion of **32** into **47** (eq. [6]). The chemoselectivity displayed in the **32** → **47** transformation shows clearly that Pd(0)-catalyzed reactions of terminal alkynes with Me$_3$SnSnMe$_3$ are appreciably slower than those involving α,β-alkynic aldehydes and ketones.

The reaction involving substrate **35** was found to be sluggish (Table 2, entry 10, eq. [7]). Thus, even after a reaction time of 24 h, analyses (tlc, gas–liquid chromatography (glc)) of aliquots of the reaction mixture showed the presence of the starting material **35**, along with Me$_3$SnSnMe$_3$. Furthermore, monitoring of the reaction mixture by tlc indicated that, as reaction times were increased, a number of minor side products were produced. Work-up and product isolation after a reaction time of 24 h produced product **50** in 48% yield (eq. [7]). The fact that the transformation of **35** into **50** occurred at all is noteworthy, since it has been shown that neither the alkynic ester **53**[3] nor the 1-alkyne **54** (8) react with Me$_3$SnSnMe$_3$ in the presence of a Pd(0) catalyst, even after prolonged heating of the reaction mixtures (eq. [8]).

[6]


[7]


[8]


Mechanistic considerations

The Pd(0)-catalyzed addition of Me$_3$SnSnMe$_3$ to α,β-alkynic esters, as summarized in eq. [1], has been proposed to proceed via the catalytic cycle shown in Scheme 2 (1). Furthermore, the thermal rearrangement of the resultant products **2** into the corresponding geometric isomers **3** (eq. [2]) has been rationalized as shown in eq. [9] (1). Thus, according to this proposal, thermolysis of **2** results in (reversible) migration of the α-Me$_3$Sn group from carbon to the ester carbonyl oxygen to produce the trimethylstannyl allenoate intermediate **55**. A second migration of the Me$_3$Sn group back to the α carbon, but to the side of the intermediate opposite the β-Me$_3$Sn function, would provide the *E* isomer **3**. Of the three compounds shown in eq. [9], it is apparent that both **2** and **3** are more stable than the allenoate **55**. However, presumably due primarily to steric repulsion between the two Me$_3$Sn groups in the *Z* isomer **2**, the equilibrium between **2** and **3** overwhelmingly favors the latter isomer.

Presumably, the Pd(0)-catalyzed reaction of α,β-alkynic

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[3] Unpublished work carried out in these laboratories by R.T. Skerlj.

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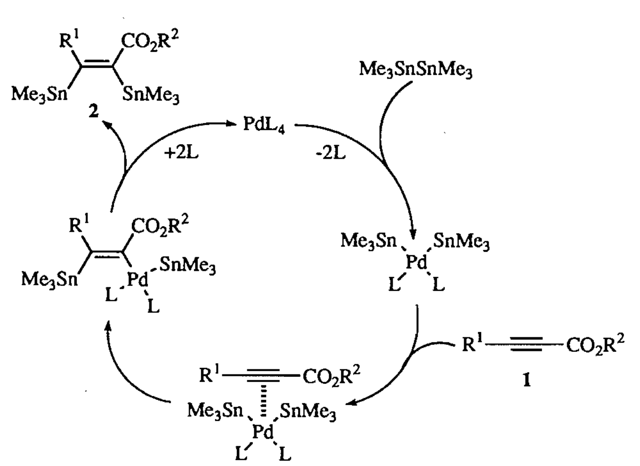
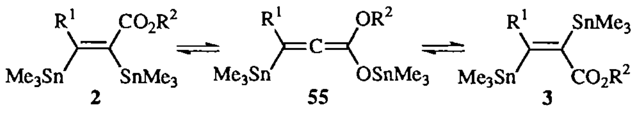
Scheme 2.

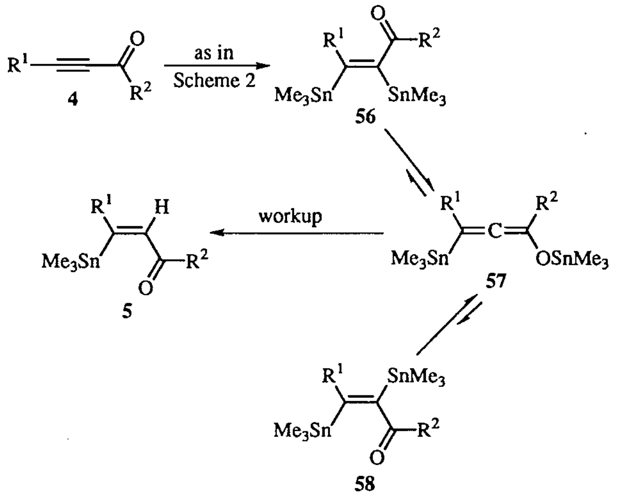


aldehydes and ketones (general formula **4**) with $Me_3SnSnMe_3$ proceeds via a catalytic cycle analogous to that shown in Scheme 2 (see eq. [10]). It seems reasonable to conclude that

[9]



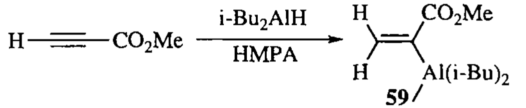
[10]



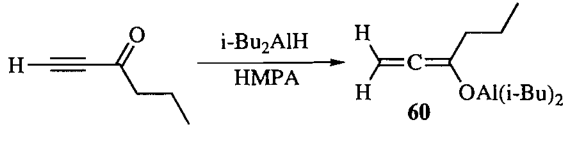
the initial products produced from these processes are the (*Z*)-2,3-bis(trimethylstannyl) α,β-alkenic carbonyl compounds of general structure **56**. To account for the fact that the isolated products are the mono(trimethylstannyl) substances **5**, we propose that **56** and the geometric isomers **58** are unstable with respect to the allenoates **57** (eq. [10]). Thus, in contrast to the ester series, it appears that the first-formed products **56** readily isomerize to the allenoates **57** and that, upon work-up, the latter species are protonated from the side opposite the β-Me_3Sn group to provide the observed products of general structure **5**.

The rationale presented above is supported to some degree by work published by Tsuda et al. (9). These workers reported that the structures of intermediates derived from the reaction of diisobutylaluminum hydride with α,β-alkynic carbonyl compounds are dependent on the nature of the carbonyl group in the substrate. Thus, for example, treatment of methyl propynoate with i-Bu_2AlH in hexamethylphosphoramide (HMPA) produces the alkenylalane **59** (eq. [11]), while an identical reaction involving 1-hexyn-3-one as the substrate affords the diisobutylalanyl allenoate **60** (eq. [12]). The similarities between these results and those derived from our studies (vide supra) are striking.

[11]



[12]



Conversion of the (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes 41–43 and ketones 44–51 into the substituted (*Z*)-4-trimethylstannyl-1,3-butadienes and related compounds

Substituted (*Z*)-4-trimethylstannyl-1,3-butadienes of general structure **6**, along with reagents and synthetic intermediates derived therefrom, are, potentially, valuable substances for organic synthesis. However, prior to the work described herein, a convenient method for preparing **6** had not been reported in the chemical literature and, consequently, the synthetic utility of these materials has not been investigated systematically. The work described above had resulted in the development of a concise, efficient, and experimentally straightforward method for preparing substituted (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes and ketones of general structure **5** (Tables 1 and 2). Obviously, these substances should serve as suitable substrates for the synthesis of the corresponding dienes **6**.

Reaction of the aldehyde **41** with methylenetriphenylphosphorane (prepared from BuLi and $[Ph_3PMe]Br$) in dry THF at room temperature provided, cleanly and efficiently, the trimethylstannyl diene **61** (Table 3, entry 1). In a similar fashion, the aldehydes **42** and **43** were transformed into the dienes **62** and **63**, respectively, in excellent yields (entries 2 and 3).

The (*Z*)-β-trimethylstannyl α,β-alkenic ketones of general structure **5** (R^2 = alkyl) could also be converted into the corresponding dienes **6** using the procedure described above, but, in these cases, complete conversion of the starting materials into products was not complete even after reaction times of several hours at room temperature. Furthermore, long reaction times created "dirty" reaction mixtures and the isolated yields of the desired trimethylstannyl dienes were generally unsatisfactory. In fact, of the ketones subjected to these conditions, only **48** was converted efficiently into the corresponding diene **68** (entry 8), although the reaction time was 10 times that required for the aldehydes **41–43**.

It seems likely that the sluggish nature of the conversion of the ketones **5** into the dienes **6** using $Ph_3P{=}CH_2$ in THF is due to a competition between the required Wittig process and an enolate-forming reaction resulting from the reagent acting as a base rather than a nucleophile. It has been reported (10) that reaction of enolizable ketones with $Ph_3P{=}CH_2$ (prepared from $[Ph_3PMe]Br$ and $NaOC(Et)Me_2$) in benzene provides the corresponding alkenes in good yields. Use of this protocol in

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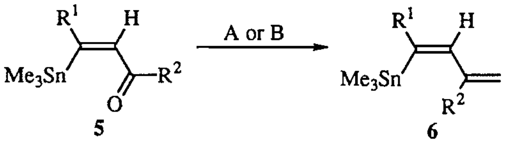
Table 3. Preparation of substituted (*Z*)-4-trimethylstannyl-1,3-butadienes **61**–**71**.

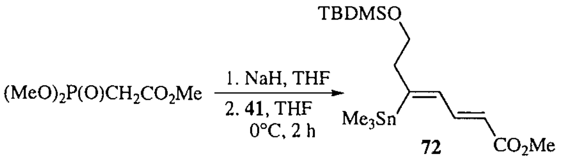


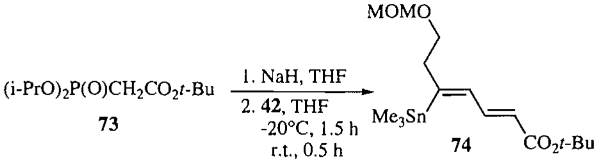
Entry	Starting material 5	R^1	R^2	Conditions[a]	Reaction time (min)	Product 6	Yield (%)[b]
1	**41**	$TBDMSO(CH_2)_2$[c]	H	A	30	**61**	87
2	**42**	$MOMO(CH_2)_2$[d]	H	A	30	**62**	82
3	**43**	$TBDMSO(CH_2)_4$[c]	H	A	30	**63**	81
4	**44**	$TBDMSO(CH_2)_2$[c]	Me	B	30	**64**	86
5	**45**	$Cl(CH_2)_3$	Me	B	30	**65**	57
6	**46**	$TBDMSO(CH_2)_4$[c]	Me	B	30	**66**	75
7	**47**	$H{-}{\equiv}{-}(CH_2)_3$	Me	B	30	**67**	83
8	**48**	i-Pr	Me	A	300	**68**	87
9	**49**	$TBDMSO(CH_2)_2$[c]	i-Pr	B	15	**69**	64
10	**50**	*t*-Bu	n-C_6H_{13}	B	30	**70**	81
11	**51**	$H_2C{=}CH{-}\underset{OTBDMS}{\underset{\vert}{CH}}(CH_2)_2$[c]	Me	B	30	**71**	85

[a] A: $Ph_3P{=}CH_2$ (prepared from $Ph_3P(Me)Br$ and *n*-BuLi in dry THF), THF, room temperature. B: $Ph_3P{=}CH_2$ (prepared from $Ph_3P(Me)Br$ and $NaOC(Et)Me_2$ in dry benzene), benzene, room temperature.
[b] Yield of purified, distilled product.
[c] TBDMS = *tert*-butyldimethylsilyl.
[d] MOM = methoxymethyl.

the present work proved to be satisfactory. As can be seen from a perusal of Table 3, subjection of the ketones **44**–**47** and **49**–**51** to these reaction conditions provided good to excellent yields of the corresponding dienes (entries 4–7, 9–11).

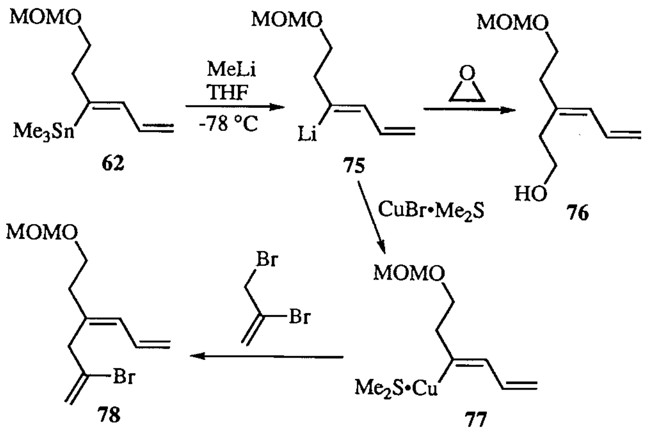
The aldehydes **41** and **42** also react smoothly with Wittig–Horner reagents. For example, treatment of **41** with the anion of trimethyl phosphonoacetate in dry THF at 0°C afforded the 5-trimethylstannyl-2,4-heptadienoate **72** in 92% yield (eq. [13]). Similarly, reaction of **42** with the reagent derived from treatment of the phosphonate **73** with NaH in dry THF gave the *tert*-butyl ester **74** (91%, eq. [14]).

[13]


[14]


All of the Wittig (**61**–**71**) and Wittig–Horner (**72**, **74**) products prepared as described above exhibited spectral properties in full accord with the assigned structures. Details are given in the experimental section.

Scheme 3.



Synthetic uses of (*Z*)-4-trimethylstannyl-1,3-butadienes

We end this discussion with a description of a brief preliminary study on the synthetic utility of the substituted (*Z*)-4-trimethylstannyl-1,3-butadienes. It is evident that these substances should be excellent precursors of organometallic reagents derived by initial transmetallation of the alkenyl Me_3Sn function. Indeed, treatment of (*Z*)-6-methoxymethoxy-4-trimethylstannyl-1,3-hexadiene (**62**) with MeLi (1.1 equiv.) in dry THF at −78°C, followed by addition of ethylene oxide to the resultant solution of the lithio diene reagent **75**, afforded the functionalized diene **76** in 71% yield (Scheme 3). On the other hand, treatment of the lithio diene **75** with 1 equiv. of copper(I) bromide – dimethyl sulfide complex (11) provided the organocopper(I) reagent **77**, which, upon reaction with 2,3-dibromopropene, gave the substituted (*Z*)-1,3,6-hep-

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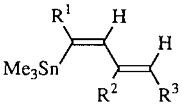
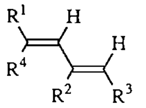
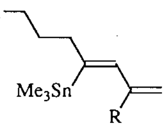
tatriene **78** (83%). Clearly, **62** and related substances of general structure **79** (Table 3 and eqs. [13] and [14]) should serve as suitable precursors for the synthesis of a wide variety of stereochemically defined dienes of general structure **80**.



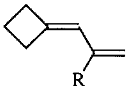
79



80



81



82

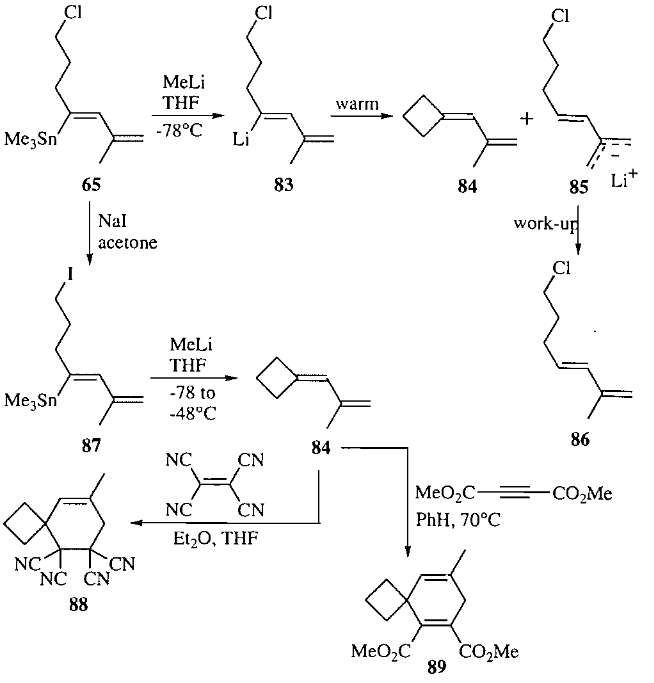
The possibility of employing functionalized (*Z*)-4-trimethylstannyl-1,3-butadienes of general structure **81** (X = leaving group) as synthetic precursors of substituted dienes possessing the novel general structure **82** was also investigated briefly (see Scheme 4). Treatment of (*Z*)-7-chloro-2-methyl-4-trimethylstannyl-1,3-heptadiene (**65**) with MeLi in dry THF at −78°C, followed by warming of the reaction mixture to −48°C, did not lead to a clean reaction. Analyses (glc) of aliquots of the reaction mixture showed the presence of two major products that, on the basis of ^{1}H nmr spectroscopy, appeared to be the desired diene **84** and the noncyclized material **86** (Scheme 4). The ratio of these two products varied somewhat, depending on the reaction conditions, but the most favorable result produced **84** and **86** in a ratio of about 6:1.

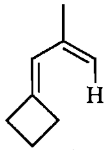
It seems reasonable to propose that the mixture of **84** and **86** is produced via a competition between two processes, one involving ring closure of the intermediate **83** (displacement of chloride ion to provide **84**) and the other involving internal proton transfer from the vinyl methyl group to the lithium-bearing carbon (five-membered cyclic transition state) to give the substituted allyllithium **85**. Protonation of the latter species during work-up would produce **86**. If this proposal is correct, increasing the rate of the ring closure reaction without appreciably affecting the rate of the proton transfer process would resolve the difficulty. To that end, treatment of the chloride **65** with NaI in acetone gave the corresponding iodide **87** (Scheme 4). Reaction of the latter compound with MeLi in dry THF (−78 to −48°C), followed by a suitable work-up procedure, gave cleanly a solution of the diene **84** in Et$_2$O–THF. No other product could be detected by gas–liquid chromatographic analyses.

Due to the volatile nature of the diene **84**, attempts to isolate it free from solvent were not carried out. Instead, the solution of **84** derived from the work-up procedure was placed under an atmosphere of argon and was treated with tetracyanoethylene, which was added in small batches. Upon complete disappearance of the starting material (analyses by glc), the mixture was concentrated and the crude product was purified by flash chromatography. Recrystallization (petroleum ether) of the acquired solid provided, in 69% yield, the functionalized spiro[3.5]nonene **88**. In a similar fashion, when a solution of the diene **84** in benzene was treated with dimethyl acetylenedicarboxylate and the resultant mixture was heated at 70°C for 36 h (argon atmosphere, sealed tube), the substituted spiro[3.5]nonadiene **89** was obtained in 70% yield (Scheme 4).

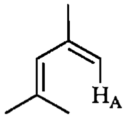
The Diels–Alder reactivity of the diene **84** is noteworthy and can probably be attributed primarily to two factors. In the conformation required for the cycloaddition reaction (see **84A**), the steric repulsion between H$_A$ and the cyclobutyl methylene group would be less severe than that present between H$_A$ and a methyl group in, for example, an acyclic diene such as **90**. Therefore, Diels–Alder reactions of **84** would be expected to be more facile than those of acyclic analogs (e.g., **90**). Furthermore, conversion of **84** into a Diels–Alder product is accompanied by a decrease in the angle strain associated with the four-membered ring, since the conversion involves translation of one of the cyclobutyl carbons from an *sp*^{2} to an *sp*^{3} center. This release of strain would be "felt" by the transition state for the cycloaddition process.

Scheme 4.





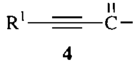
84A



90

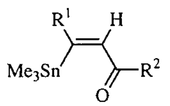
Conclusion

The research results summarized above show that readily prepared α,β-alkynic aldehydes and ketones (general structure **4**) serve as excellent synthetic precursors of the corresponding (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes and ketones (structure **5**) and that the latter substances are readily trans-



$R^1-C\equiv C-\overset{O}{\overset{\|}{C}}-R^2$

4



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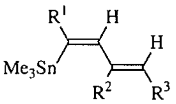
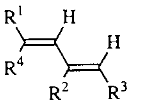


79



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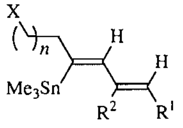
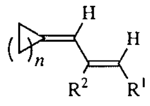
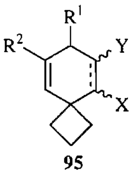


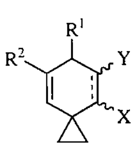
91 *n* = 2
92 *n* = 1



93 *n* = 2
94 *n* = 1



95



96

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formed into substituted, stereochemically defined dienes of general structure **79**. The possibility of using the alkenyltrimethylstannyl function in **79** as a "handle" for introducing functionalized alkyl substituents was successfully demonstrated and, thus, dienes of general structure **80** are also available via the developed methodology.

It was also shown, by the conversion of **87** into **84** (Scheme 4), that substances of general structure **91** (X = I) should serve as effective precursors for the preparation of alkyldienecyclobutanes (see **93**). Successful Diels–Alder reactions of **93** with suitable dienophiles (see the conversions of **84** into **88** and **89**, Scheme 4) would provide spiro compounds of general structure **95**. It seems likely that similar processes involving conversions of **92** (X = Cl, Br, or I) into functionalized spiro[2.5]octanes **96**, via dienes of general structure **94**, should also be possible. Studies related to these possibilities, along with investigations into further synthetic uses of (*Z*)-β-trimethylstannyl α,β-alkenic carbonyl compounds and dienes derived therefrom, are currently underway in our laboratories.

Experimental

General information

Melting points and distillation temperatures (short-path Kugelrohr distillations) are uncorrected. Infrared (ir) spectra were recorded using potassium bromide pellets or liquid films on sodium chloride discs. 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 signals for Me_4Si (δ 0) (internal standard) or $CHCl_3$ (δ 7.25), while resonances in ^{13}C nmr spectra were measured 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. Molecular mass determination (high-resolution mass spectrometry) for substances containing Me_3Sn are based on ^{120}Sn. Flash chromatography (5) and conventional column chromatography were carried out with 230–400 and 70–230 mesh silica gel (E. Merck), respectively. Thin-layer chromatography (tlc) was accomplished with commercial aluminum-backed plates (E. Merck, Type 5554). Gas–liquid chromatography (glc) was performed on instruments equipped with flame ionization detectors and 25 m × 0.21 mm fused silica columns coated with cross-linked SE-54. Commercial $(Me_3Sn)_2$ (Organometallics Inc.) was stored under an inert atmosphere (glove box) and was generally distilled (water aspirator pressure) just prior to use, while commercial $(Ph_3P)_4Pd$ was used without further purification. Aqueous NH_4Cl–NH_4OH (pH 8) was prepared by the addition of ~50 mL of aqueous ammonia (58%) to ~950 mL of saturated aqueous NH_4Cl.

Note: Unless otherwise stated, all reactions were carried out under an atmosphere of dry argon in flamed-dried glassware.

Note: All compounds for which high-resolution mass measurements are given exhibited clean ^{1}H nmr spectra and showed essentially one spot on tlc analyses.

General procedure 1. Preparation of the propargylic alcohols 16–25

To a cold (−78°C), stirred solution of the terminal alkyne (1 equiv.) in dry THF (~3–6 mL per mmol of substrate) was added a solution of MeLi (1 equiv.) in Et_2O. The mixture was stirred at −78°C for 10 min and at −20°C for 1 h. For the preparation of the primary alcohols **16–18**, solid paraformaldehyde (4 equiv.) was added and the mixture was allowed to warm to room temperature. On the other hand, for the synthesis of each of the secondary alcohols **19–25**, the solution of the lithium acetylide was recooled to −78°C prior to addition of the appropriate aldehyde and, after the mixture had been stirred at −78°C for 10 min, it was allowed to warm to room temperature. After each reaction mixture had been stirred for 30 min at room temperature, saturated aqueous $NaHCO_3$ and Et_2O were added. The phases were separated and the aqueous phase was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$) and concentrated. Each of the crude products, except substance **23** (see Table 1), was purified by flash chromatography, followed by distillation.

The following compounds were prepared via this general procedure.

*5-*tert*-Butyldimethylsilyloxy-2-pentyn-1-ol (**16**)*

Flash chromatography (130 g of silica gel, 7:3 petroleum ether – Et_2O) of the crude product derived from the terminal alkyne **9** (12) (2.8 g, 15 mmol) and paraformaldehyde (1.8 g, 4 equiv.), followed by distillation (75–80°C/0.5 Torr; 1 Torr = 133.3 Pa) of the acquired material, gave 2.4 g (74%) of the alcohol **16**, a colorless oil that displayed ir (neat): 3394, 2227, 1473, 1109 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.06 (s, 6H), 0.89 (s, 9H), 1.80–1.95 (br m, 1H), 2.43 (tt, 2H, *J* = 7, 2 Hz), 3.72 (t, 2H, *J* = 7 Hz), 4.24 (br signal, 2H); on addition of D_2O, the signal at δ 1.80–1.95 disappeared and the signal at δ 4.24 sharpened to a t (*J* = 2 Hz). Exact Mass calcd. for $C_7H_{13}O_2Si$ ($M^+ - t$-Bu): 157.0685; found: 157.0679.

*5-Methoxymethoxy-2-pentyn-1-ol (**17**)*

Purification (flash chromatography, 280 g of silica gel, 35:65 petroleum ether – Et_2O; distillation, 110–120°C/0.5 Torr) of the crude product obtained from the 1-alkyne **10** (8.5 g, 74 mmol) and paraformaldehyde (8.9 g, 4 equiv.) provided 8.6 g (80%) of the alcohol **17**, a colorless oil that exhibited ir (neat): 3424, 2227, 1151, 1111, 1029 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.75–0.90 (br m, 1H), 1.52 (tt, 2H, *J* = 6.5, 2 Hz), 3.38 (s, 3H), 3.65 (t, 2H, *J* = 6.5 Hz), 4.24 (dt, 2H, *J* = 6, 2 Hz), 4.64 (s, 2H); on addition of D_2O, the signal at δ 0.75–0.90 disappeared, and the signal at δ 4.24 collapsed to a br s. Exact Mass calcd. for $C_5H_7O_2$ ($M^+ - C_2H_5O$): 99.0446; found: 99.0446.

*7-*tert*-Butyldimethylsilyloxy-2-heptyn-1-ol (**18**)*

This compound was prepared from the terminal alkyne **11** (13) (2.0 g, 9.4 mmol) and paraformaldehyde (1.2 g, 4 equiv.). Flash chromatography of the crude product on silica gel (85 g, 7:3 petroleum ether – Et_2O) and distillation (100–110°C/0.5 Torr) of the derived oil gave 1.9 g (81%) of the alcohol **18**, a colorless oil that showed ir (neat): 3362, 2230, 1256, 1107, 838 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.04 (s, 6H), 0.86 (s, 9H), 1.57 (m, 4H), 1.78 (br s, 1H), 2.23 (m, 2H), 3.61 (t, 2H, *J* = 7 Hz), 4.24 (br t, 2H, *J* = 2 Hz); on addition of D_2O, the signal at δ 1.78 disappeared. Exact Mass calcd. for $C_9H_{27}O_2Si$ ($M^+ - t$-Bu): 185.0998; found: 185.0997.

*6-*tert*-Butyldimethylsilyloxy-3-hexyn-2-ol (**19**)*

Purification (flash chromatography, 80 g of silica gel, 7:3

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petroleum ether – Et_2O; distillation, 80–90°C/0.5 Torr) of the crude product obtained from the 1-alkyne **9** (1.5 g, 8.2 mmol) and acetaldehyde (0.7 g, 2 equiv.) provided 1.7 g (92%) of the alcohol **19**, a colorless oil that displayed ir (neat): 3368, 2250, 1256, 818 cm^{-1}; ^1H nmr (300 MHz) δ: 0.04 (s, 6H), 0.86 (s, 9H), 1.39 (d, 3H, $J = 8$ Hz), 2.25 (br s, 1H), 2.38 (dt, 2H, $J = 7$, 2 Hz), 3.68 (t, 2H, $J = 7$ Hz), 4.49 (m, 1H); on addition of D_2O, the signal at δ 2.25 disappeared, and the signal at δ 4.49 simplified to a br q ($J = 8$ Hz). Exact Mass calcd. for $C_8H_{15}O_2Si$ ($M^+ - t$-Bu): 171.0842; found: 171.0834.

*7-Chloro-3-heptyn-2-ol (**20**)*
This substance was prepared from 5-chloro-1-pentyne (**12**) (4.0 g, 39 mmol) and acetaldehyde (3.4 g, 2 equiv.). Flash chromatography of the crude product on silca gel (150 g, 7:3 petroleum ether – Et_2O) and distillation (65–70°C/0.5 Torr) of the derived oil gave 4.9 g (85%) of the alcohol **20**, a colorless oil that showed ir (neat): 3372, 1089, 1050, 881 cm^{-1}; ^1H nmr (300 MHz) δ: 1.36 (d, 3H, $J = 8$ Hz), 1.80 (quintet, 2H, $J = 8$ Hz), 2.33 (td, 2H, $J = 8$, 2 Hz), 2.75 (br s, 1H), 3.59 (t, 2H, $J = 8$ Hz), 4.46 (m, 1H); on addition of D_2O, the signal at δ 2.75 disappeared, and the signal at δ 4.46 simplified to a br q ($J = 8$ Hz). Exact Mass calcd. for $C_7H_{11}{}^{35}ClO$: 146.0499; found: 146.0504.

*8-*tert*-Butyldimethylsilyloxy-3-octyn-2-ol (**21**)*
Flash chromatography (80 g of silica gel, 7:3 petroleum ether – Et_2O) of the crude product derived from the terminal alkyne **11** (13) (2.0 g, 9.4 mmol) and acetaldehyde (0.8 g, 2 equiv.), followed by distillation (110–120°C/0.5 Torr) of the acquired material, gave 2.2 g (90%) of the alcohol **21**, a colorless oil that displayed ir (neat): 3353, 2248, 1256 cm^{-1}; ^1H nmr (300 MHz) δ: 0.33 (s, 6H), 0.87 (s, 9H), 1.40 (d, 3H, $J = 8$ Hz), 1.56 (m, 4H), 1.74–1.80 (br m, 1H), 2.22 (m, 2H), 3.60 (t, 2H, $J = 6$ Hz), 4.50 (m, 1H); on addition of D_2O the signal at δ 1.74–1.80 disappeared and the signal at δ 4.50 simplified to a br q ($J = 8$ Hz). Exact Mass calcd. for $C_{10}H_{19}O_2Si$ ($M^+ - t$-Bu): 199.1155; found: 199.1156.

*3,8-Nonadiyn-2-ol (**22**)*
This compound was derived from 1,6-heptadiyne (**13**) (1.0 g, 11 mmol) and acetaldehyde (2.4 g, 5 equiv.). Flash chromatography of the crude product on silica gel (65 g, 65:35 petroleum ether – Et_2O) and distillation (80–85°C/0.5 Torr) of the derived material afforded 0.88 g (60%) of the alcohol **22**, a colorless oil that exhibited ir (neat): 3301, 2247, 2118, 1154, 1013, 882 cm^{-1}; ^1H nmr (400 MHz) δ: 1.41 (d, 3H, $J = 6.5$ Hz), 1.65–1.75 (m, 3H), 1.95 (t, 1H, $J = 2.5$ Hz), 2.25–2.40 (m, 4H), 4.49 (m, 1H); on addition of D_2O, the signal at δ 1.65–1.75 collapsed to a quintet (2H, $J = 7$ Hz), and the signal at δ 4.49 simplified to a br q ($J = 6.5$ Hz). Exact Mass calcd. for $C_9H_{11}O$ ($M^+ - H$): 135.0810; found: 135.0815.

*5-Methyl-3-hexyn-2-ol (**23**)*
This substance was derived from 3-methyl-1-butyne (**14**) (3.0 g, 44 mmol) and acetaldehyde (3.9 g, 2 equiv.). After work-up of the reaction mixture, the solution containing the product was concentrated by distillation (atmospheric pressure) through a Vigreaux column (50 × 2 cm). Distillation (80–90°C/10 Torr) of the residual material gave a crude oil (4.6 g) that consisted mainly of the alcohol **23**. This material was used immediately for the next (oxidation) reaction (vide infra).

*7-*tert*-Butyldimethylsilyloxy-2-methyl-4-heptyn-3-ol (**24**)*
Flash chromatography (300 g of silica gel, 7:3 petroleum ether – Et_2O) of the crude product derived from the terminal alkyne **9** (12) (8.2 g, 45 mmol) and 2-methylpropanal (4.8 g, 1.5 equiv.), followed by distillation (110–120°C/0.5 Torr) of the acquired material, gave 9.7 g (85%) of the alcohol **24**, a colorless oil that displayed ir (neat): 3368, 2218, 1256, 1113, 836, 777 cm^{-1}; ^1H nmr (400 MHz) δ: 0.06 (s, 6H), 0.89 (s, 9H), 0.96, 0.98 (d, d, 3H each, $J = 6$ Hz in each case), 1.70 (br d, 1H, $J = 4$ Hz), 1.82 (m, 1H), 2.42 (td, 2H, $J = 8$, 2 Hz), 3.70 (t, 2H, $J = 8$ Hz), 4.13 (br m, 1H); on addition of D_2O, the signal at δ 1.70 disappeared, and the signal at δ 4.13 simplified to a br d ($J = 6$ Hz). Exact Mass calcd. for $C_{11}H_{21}O_2Si$ ($M^+ -$ i-Pr): 213.1311; found: 213.1318.

*2,2-Dimethyl-3-undecyn-5-ol (**25**)*
This material was synthesized from 3,3-dimethyl-1-butyne (**15**) (3.5 g, 43 mmol) and heptanal (7.3 g, 1.5 equiv.). Flash chromatography of the crude product on silica gel (250 g, 7:3 petroleum ether – Et_2O), followed by distillation (80–85°C/0.5 Torr) of the acquired liquid, gave 8.1 g (96%) of the alcohol **25**, a colorless oil that exhibited ir (neat): 3342, 2238, 1460, 1265 cm^{-1}; ^1H nmr (300 MHz) δ: 0.87 (m, 3H), 1.20 (s, 9H), 1.25–1.70 (m, 10H), 2.85 (br s, 1H), 4.33 (br t, 1H, $J = 8$ Hz); on addition of D_2O, the signal at δ 2.85 disappeared. Exact Mass calcd. for $C_{13}H_{24}O$: 196.1828; found: 196.1819.

General procedure 2. Oxidation of the alcohols 16–25 to the α,β-alkynic aldehydes 26–28 and ketones 29–35

A mixture of the alcohol (1 equiv.), NaOAc (0.3 equiv.), and pyridinium chlorochromate (1.5 equiv. for the alcohols **16–18**, 2.5 equiv. for the alcohols **19–25**) in dry CH_2Cl_2 (~5-10 mL per mmol of alcohol substrate) was stirred (2 h for the alcohols **16–18**, 2.5 h for the alcohols **19–25**) at room temperature. Dry Et_2O (the same volume as that used for the reaction mixture) was added and the mixture was filtered through a column of Florisil® (~30 g per g of propargylic alcohol), using Et_2O as eluant. The material remaining in the reaction vessel was rinsed (and sonicated) thoroughly with Et_2O, and the washings were also passed through the Florisil® column. The combined eluate was dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography and (or) distillation.

The following carbonyl compounds were prepared via this general procedure.

*5-*tert*-Butyldimethylsilyloxy-2-pentynal (**26**)*
Flash chromatography (80 g of silica gel, 5:1 petroleum ether – Et_2O) of the crude product derived from oxidation of the alcohol **16** (2.4 g, 11 mmol), followed by distillation (75–85°C/0.5 Torr) of the acquired liquid, gave 1.7 g (72%) of the aldehyde **26**, a colorless oil that exhibited ir (neat): 2740, 2207, 1673, 1275 cm^{-1}; ^1H nmr (300 MHz) δ: 0.05 (s, 6H), 0.87 (s, 9H), 2.60 (t, 2H, $J = 8$ Hz), 3.77 (t, 2H, $J = 8$ Hz), 9.15 (s, 1H). Exact Mass calcd. for $C_7H_{11}O_2Si$ ($M^+ - t$-Bu): 155.0528; found: 155.0532.

*5-Methoxymethoxy-2-pentynal (**27**)*
This compound was obtained by oxidation of the alcohol **17** (3.6 g, 25 mmol). Flash chromatography of the crude product on silica gel (120 g, 4:6 petroleum ether – Et_2O), followed by distillation (90–95°C/0.5 Torr) of the derived oil, gave 1.9 g

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(57%) of the aldehyde **27**, a colorless oil that displayed ir (neat): 2827, 2207, 1669, 1115, 1111, 963 cm^{-1}; ^{1}H nmr (400 MHz) δ: 2.72 (t, 2H, J = 7 Hz), 3.38 (s, 3H), 3.72 (t, 2H, J = 7 Hz), 4.64 (s, 2H), 9.18 (s, 1H). Exact Mass calcd. for $C_7H_9O_3$ ($M^+ - H$): 141.0551; found: 141.0546.

7-tert-*Butyldimethylsilyloxy-2-heptynal (28)*

Oxidation of the alcohol **18** (0.9 g, 3.7 mmol), followed by purification (flash chromatography, 40 g of silica gel, 5:1 petroleum ether – Et_2O; distillation, 95–100°C/0.5 Torr) of the crude product gave 0.7 g (74%) of the aldehyde **28**, a colorless oil that showed ir (neat): 2742, 2202, 1673, 838 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.65 (m, 4H), 2.46 (t, 2H, J = 8 Hz), 3.63 (t, 2H, J = 6 Hz), 9.18 (s, 1H). Exact Mass calcd. for $C_9H_{15}O_2Si$ (M^+ − t-Bu): 183.0842; found: 183.0834.

6-tert-*Butyldimethylsilyloxy-3-hexyn-2-one (29)*

This substance was derived from oxidation of the alcohol **19** (0.2 g, 0.9 mmol). Flash chromatography of the crude product on silica gel (45 g, 9:1 petroleum ether – Et_2O), followed by distillation (70–80°C/0.5 Torr) of the acquired oil furnished 0.15 g (74%) of the ketone **29**, a colorless oil that displayed ir (neat): 2214, 1680, 1113, 839 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.08 (s, 6H), 0.89 (s, 9H), 2.30 (s, 3H), 2.56 (t, 2H, J = 8 Hz), 3.76 (t, 2H, J = 8 Hz). Exact Mass calcd. for $C_8H_{13}O_2Si$ (M^+ − t-Bu): 169.0685; found: 169.0684.

7-Chloro-3-heptyn-2-one (30)

Flash chromatography (80 g of silica gel, 9:1 petroleum ether – Et_2O) of the crude product derived from the alcohol **20** (1.5 g, 10 mmol), followed by distillation (60–65°C/0.5 Torr) of the acquired liquid, gave 1.1 g (74%) of the ketone **30**, a colorless oil that showed ir (neat): 2215, 1677, 1232, 734 cm^{-1}; ^{1}H nmr (300 MHz) δ: 2.0 (quintet, 2H, J = 7 Hz), 2.30 (s, 3H), 2.54 (t, 2H, J = 7 Hz), 3.51 (t, 2H, J = 7 Hz). Exact Mass calcd. for $C_7H_9{}^{35}ClO$: 144.0343; found: 144.0343.

8-tert-*Butyldimethylsilyloxy-3-octyn-2-one (31)*

The crude product obtained from oxidation of the alcohol **21** (1.0 g, 3.9 mmol) was purified by flash chromatography (75 g of silica gel, 9:1 petroleum ether – Et_2O) and distillation (95–100°C/0.5 Torr). The resultant product **31** (0.76 g, 76%), a colorless oil, displayed ir (neat): 2212, 1680, 1360, 1104 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.04 (s, 6H), 0.88 (s, 9H), 1.62 (m, 4H), 2.30 (s, 3H), 2.38 (t, 2H, J = 7 Hz), 3.62 (t, 2H, J = 6 Hz). Exact Mass calcd. for $C_{10}H_{17}O_2Si$ (M^+ − t-Bu): 197.0998; found: 197.1006.

3,8-Nonadiyn-2-one (32)

This material was obtained by oxidation of the alcohol **22** (0.13 g, 1.0 mmol). Flash chromatography of the crude product on silica gel (35 g, 9:1 petroleum ether – Et_2O), followed by distillation (120–130°C/6.0 Torr) of the derived liquid, gave 0.07 g (55%) of the ketone **32**, a colorless oil that showed ir (neat): 2215, 1680, 1231 cm^{-1}; ^{1}H nmr (400 MHz) δ: 1.79 (quintet, 2H, J = 7 Hz), 1.98 (t, 1H, J = 2.5 Hz), 2.31 (s, 3H), 2.32 (td, 2H, J = 7, 2.5 Hz), 2.50 (t, 2H, J = 7 Hz). Exact Mass calcd. for C_9H_9O ($M^+ - H$): 133.0653; found: 133.0651.

5-Methyl-3-hexyn-2-one (33)

Oxidation of the previously prepared, crude 5-methyl-3-hexyn-2-ol (**23**) (vide supra), followed by work-up of the reaction mixture, gave a solution of the ketone **33**. Concentration of this solution by distillation (atmospheric pressure) of the solvent through a Vigreaux column (50 × 2 cm) gave an oil that, upon distillation (80–90°C/10 Torr), provided 2.7 g (57% from 3-methyl-1-butyne (**14**)) of the ketone **33**, a colorless oil that displayed ir (neat): 2208, 1679, 1228 cm^{-1}; ^{1}H nmr (300 MHz) δ: 1.20 (d, 6H, J = 8 Hz), 2.29 (s, 3H), 2.68 (septet, 1H, J = 8 Hz). Exact Mass calcd. for $C_7H_{10}O$: 110.0732; found: 110.0726.

7-tert-*Butyldimethylsilyloxy-2-methyl-4-heptyn-3-one (34)*

Flash chromatography (150 g of silica gel, 9:1 petroleum ether – Et_2O) of the crude product derived from the alcohol **24** (2.9 g, 11 mmol), followed by distillation (95–105°C/0.5 Torr) of the acquired liquid, gave 2.4 g (81%) of the ketone **34**, a colorless oil that showed ir (neat): 2214, 1676, 1118, 779 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.08 (s, 6H), 0.90 (s, 9H), 1.18 (d, 6H, J = 8 Hz), 2.58–2.68 (m, 3H), 3.80 (t, 2H, J = 6 Hz). Exact Mass calcd. for $C_{10}H_{17}O_2Si$ (M^+ − t-Bu): 197.0998; found: 197.1003.

2,2-Dimethyl-3-undecyn-5-one (35)

This compound was derived from oxidation of the alcohol **25** (4.0 g, 20 mmol). Flash chromatography of the crude product on silica gel (150 g, 9:1 petroleum ether – Et_2O) and distillation (75–80°C/0.5 Torr) of the acquired liquid provided 2.9 g (72%) of the ketone **35**, a colorless oil that exhibited ir (neat): 2213, 1675, 1263, 1142 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.87 (m, 3H), 1.28 (br s, 15H), 1.63 (m, 2H), 2.50 (t, 2H, J = 7 Hz). Exact Mass calcd. for $C_{13}H_{22}O$: 194.1672; found: 194.1680.

3-*tert*-Butyldimethylsilyloxy-1-hepten-6-yne (40)

To a stirred solution of 4-pentyn-1-ol (**37**) (3.0 g, 36 mmol) in dry CH_2Cl_2 (100 mL) was added NaOAc (0.9 g, 0.3 equiv.) and PCC (12 g, 1.5 equiv.). After the mixture had been stirred for 2 h at room temperature, dry Et_2O (~100 mL) was added and the mixture was filtered through a column of Florisil® (~100 g, elution with Et_2O). The material remaining in the reaction vessel was rinsed (and sonicated) thoroughly with Et_2O, and the washings were also passed through the Florisil® column. The combined eluate was dried ($MgSO_4$) and most of the solvent was removed by distillation (atmospheric pressure) using a Vigreaux column (50 × 2 cm). The remaining crude product **38** was dissolved in dry THF (100 mL) and the solution was cooled to −78°C. A solution of vinyl magnesium bromide (2 equiv.) in THF was added and the mixture was allowed to warm to room temperature. Saturated aqueous NH_4Cl (~50 mL) and Et_2O (50 mL) were added and the phases were separated. The aqueous phase was extracted with Et_2O and the combined organic extracts were dried ($MgSO_4$) and concentrated by distillation (atmospheric pressure) using a Vigreaux column (50 × 2 cm).

To a stirred solution of the crude oil **39** thus obtained in dry DMF (80 mL) was added imidazole (6.1 g, 2.5 equiv.) and *tert*-butyldimethylsilyl chloride (8.1 g, 1.5 equiv.). The mixture was stirred at room temperature overnight. Saturated aqueous $NaHCO_3$ (~50 mL) and Et_2O (~50 mL) were added and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. Flash chromatography of the crude product on

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silica gel (180 g, 98:2 petroleum ether – Et_2O), followed by distillation (80–90°C/0.5 Torr) of the derived oil gave 2.5 g (31%) of the alkyne **40**, a colorless oil that showed ir (neat): 3314, 3081, 2121, 1254, 838 cm^{-1}; ^1H nmr (400 MHz) δ: 0.02 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.68 (m, 2H), 1.92 (t, 1H, J = 4 Hz), 2.22 (m, 2H), 4.22 (m, 1H), 5.05 (ddd, 1H, J = 10, 2, 2 Hz), 5.17 (ddd, 1H, J = 16, 2, 2 Hz), 5.88 (ddd, 1H, J = 16, 10, 6 Hz). Exact Mass calcd. for $C_{13}H_{24}OSi$: 224.1597; found: 224.1593.

7-*tert*-Butyldimethylsilyloxy-8-nonen-3-yn-2-one (36)

To a cold (−78°C), stirred solution of the 1-alkyne **40** (0.44 g, 2.0 mmol) in dry Et_2O (10 mL) was added MeLi (1 equiv.) in Et_2O. After the reaction mixture had been stirred at −78°C for 10 min and at −20°C for 1 h, it was recooled to −78°C and then was transferred slowly (over ~10 min, via cannula) into a cold (−78°C), stirred solution of Ac_2O (2 equiv.) in dry Et_2O (8 mL). After the resultant mixture had been stirred for 10 min at −78°C and 30 min at −48°C, saturated NH_4Cl–NH_4OH (pH 8, 15 mL) was added and the vigorously stirred mixture was allowed to warm to room temperature. The phases were separated and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with saturated aqueous NH_4Cl, dried ($MgSO_4$), and concentrated. Flash chromatography of the crude product on silica gel (50 g, 9:1 petroleum ether – Et_2O), followed by distillation (90–100°C/0.5 Torr) of the acquired liquid, gave 0.33 g (63%) of the ketone **36**, a colorless oil that displayed ir (neat): 3082, 2211, 1681, 1228, 838 cm^{-1}; ^1H nmr (400 MHz) δ: 0.03 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.74 (m, 2H), 2.31 (s, 3H), 2.41 (m, 2H), 4.22 (m, 1H), 5.08 (ddd, 1H, J = 10, 2, 2 Hz), 5.19 (ddd, 1H, J = 17, 2, 2 Hz), 5.77 (ddd, 1H, J = 17, 10, 6 Hz). Exact Mass calcd. for $C_{11}H_{17}O_2Si$ (M^+ − *t*-Bu): 209.0998; found: 209.0995.

General procedure 3. Pd(0)-catalyzed reaction of α,β-alkynic aldehydes 26–28 and ketones 29–36 with hexamethylditin. Preparation of compounds 41–51

To a stirred solution of the α,β-alkynic aldehyde or ketone (1 equiv.) in dry THF (for **26**, **28**, **30**, and **33–35**, ~2 mL per mmol of substrate; for **27**, **29**, **31**, **32**, and **36**, ~3 mL per mmol of substrate) (argon atmosphere) was added $(Me_3Sn)_2$ (1 equiv.) and $Pd(Ph_3)_4$ (5 mol%). The mixture was allowed to reflux for the time indicated in Table 2. In each case, the progress of the reaction was monitored by tlc. When the reaction was complete, the solvent was removed and the viscous residual oil was purified by chromatography and distillation.

The following (*Z*)-β-trimethylstannyl α,β-alkenic aldehydes and ketones were prepared via this general procedure.

*(Z)-5-*tert*-Butyldimethylsilyloxy-3-trimethylstannyl-2-pentenal (41)*

Flash chromatography (100 g of silica gel, 95:5 petroleum ether – Et_2O) of the crude product derived from the aldehyde **26** (1.5 g, 7.1 mmol), followed by distillation (110–120°C/0.5 Torr) of the acquired oil, provided 2.4 g (87%) of the aldehyde **41**, a colorless oil that displayed ir (neat): 2743, 1685, 1563, 1099, 776 cm^{-1}; ^1H nmr (300 MHz) δ: 0.04 (s, 6H), 0.26 (s, 9H, $^2J_{Sn-H}$ = 54 Hz), 0.86 (s, 9H), 2.69 (td, 2H, J = 6.5, 1.3 Hz, $^3J_{Sn-H}$ = 46 Hz), 3.69 (t, 2H, J = 6.5 Hz), 6.68 (dt, 1H, J = 5.5, 1.3 Hz, $^3J_{Sn-H}$ = 114 Hz), 9.56 (d, 1H, J = 5.5 Hz, $^4J_{Sn-H}$ = 5.5 Hz); in nOe difference experiments, irradiation at δ 6.68 caused enhancement of the signals at δ 2.69 and 9.59, irradiation at δ 9.59 caused enhancement of the resonance at δ 6.68, and irradiation at δ 2.69 increased the intensities of the signals at δ 6.68 and 3.69; ^{13}C nmr (75.4 MHz) δ: −7.2, −5.2, 18.4, 26.0, 43.7, 62.2, 140.3, 178.2, 192.4. Exact Mass calcd. for $C_{13}H_{27}O_2SnSi$ (M^+ − Me): 363.0802; found: 363.0806.

(Z)-5-Methoxymethoxy-3-trimethylstannyl-2-pentenal (42)

Flash chromatography (120 g of silica gel, 65:35 petroleum ether – Et_2O) and distillation (100–105°C/0.5 Torr) of the crude product obtained from the aldehyde **27** (1.9 g, 13 mmol) provided 3.1 g (76%) of the product **42**, a colorless oil that showed ir (neat): 1683, 1562, 1151, 1043, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.25 (s, 9H, $^2J_{Sn-H}$ = 54 Hz), 2.77 (td, 2H, J = 6.5, 1.3 Hz, $^3J_{Sn-H}$ = 44 Hz), 3.61 (t, 2H, J = 6.5 Hz), 4.58 (s, 2H), 6.72 (dt, 1H, J = 5.5, 1.3 Hz, $^3J_{Sn-H}$ = 113 Hz), 9.59 (d, 1H, J = 5.5 Hz, $^4J_{Sn-H}$ = 5.5 Hz). Exact Mass calcd. for $C_9H_{17}O_3Sn$ (M^+ − Me): 293.0199; found: 293.0201.

*(Z)-7-*tert*-Butyldimethylsilyloxy-3-trimethylstannyl-2-heptenal (43)*

Purification (flash chromatography, 30 g of silica gel, 95:5 petroleum ether – Et_2O; distillation, 120–130°C/0.5 Torr) of the crude product acquired from 0.3 g (1.2 mmol) of the aldehyde **28** furnished 0.45 g (88%) of the product **43**, a colorless oil that exhibited ir (neat): 2742, 1685, 1562, 1256, 1106, 775 cm^{-1}; ^1H nmr (300 MHz) δ: 0.02 (s, 6H), 0.25 (s, 9H, $^2J_{Sn-H}$ = 55 Hz), 0.87 (s, 9H), 1.48 (m, 4H), 2.49 (br t, 2H, J = 6.5 Hz, $^3J_{Sn-H}$ = 47 Hz), 3.59 (t, 2H, J = 6 Hz), 6.62 (dt, 1H, J = 6, 1.3 Hz, $^3J_{Sn-H}$ = 115 Hz), 9.55 (d, 1H, J = 6 Hz, $^4J_{Sn-H}$ = 5.5 Hz); in nOe difference experiments, irradiation at δ 6.62 caused enhancement of the signals at δ 9.55 and 2.49, while irradiations at δ 9.55 and 2.49 caused, in each case, enhancement of the resonance at δ 6.62; ^{13}C nmr (300 MHz) δ: −7.3, −5.2, 18.4, 25.3, 26.0, 32.4, 41.0, 62.7, 138.6, 181.9, 192.6. Exact Mass calcd. for $C_{15}H_{31}O_2SiSn$ (M^+ − Me): 391.1115; found: 391.1112.

*(Z)-6-*tert*-Butyldimethylsilyloxy-4-trimethylstannyl-3-hexen-2-one (44)*

The crude product obtained from the starting material **29** (0.13 g, 0.58 mmol) was purified by flash chromatography (30 g of silica gel, 96:4 petroleum ether – Et_2O) and distillation (110–120°C/0.5 Torr) to produce 0.21 g (90%) of the ketone **44**, a colorless oil,that exhibited ir (neat): 1682, 1573, 1192, 1095, 776 cm^{-1}; ^1H nmr (300 MHz) δ: 0.00 (s, 6H), 0.10 (s, 9H, $^2J_{Sn-H}$ = 54 Hz), 0.84 (s, 9H), 2.19 (s, 3H), 2.63 (td, 2H, J = 6.5, 1.3 Hz, $^3J_{Sn-H}$ = 49 Hz), 3.62 (t, 2H, J = 6.5 Hz), 6.82 (br s, 1H, $^3J_{Sn-H}$ = 121 Hz); in nOe difference experiments, irradiation at δ 6.82 caused enhancement of the signals at δ 2.63 and 2.19, irradiation at δ 2.63 increased the intensity of the resonances at δ 3.62 and 6.82, and irradiation at δ 2.19 caused enhancement of the signal at δ 6.82; ^{13}C nmr (75.4 MHz) δ: −7.4, −5.3, 18.2, 25.9, 30.0, 42.5, 62.0, 136.7, 172.4, 197.3. Exact Mass calcd. for $C_{14}H_{29}O_2SiSn$ (M^+ − Me): 377.0959; found: 377.0966.

(Z)-7-Chloro-4-trimethylstannyl-3-hepten-2-one (45)

Flash chromatography (75 g of silica gel, 95:5 petroleum ether – Et_2O) of the crude product derived from 0.80 g (5.5 mmol) of

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the substrate **30**, followed by distillation (100–105°C/0.5 Torr) of the acquired oil produced 1.4 g (81%) of the ketone **45**, a colorless oil that showed ir (neat): 1682, 1572, 1202, 774 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 54 Hz), 1.85 (br quintet, 2H, J = 7 Hz), 2.23 (s, 3H), 2.59 (br t, 2H, J = 7 Hz, $^3J_{\text{Sn-H}}$ = 48 Hz), 3.50 (t, 2H, J = 7 Hz), 6.82 (br s, 1H, $^3J_{\text{Sn-H}}$ = 120 Hz); in nOe difference experiments, irradiation at δ 6.82 caused enhancement of the resonances at δ 2.59 and 2.23, while irradiation at δ 2.59 increased the intensity of the signals at δ 1.85, 3.50, and 6.82; ^{13}C nmr (75.4 MHz) δ: −7.4, 30.2, 31.6, 36.6, 44.1, 135.6, 174.6, 197.5. Exact Mass calcd. for $C_9H_{16}{}^{35}ClOSn$ (M$^+$ − Me): 294.9912; found: 294.9912.

(*Z*)-8-tert-*Butyldimethylsilyloxy-4-trimethylstannyl-3-octen-2-one* (**46**)

Purification (flash chromatography, 35 g of silica gel, 96:4 petroleum ether – Et$_2$O; distillation, 120–130°C/0.5 Torr) of the crude product obtained from 0.16 g (0.63 mmol) of the starting material **31** yielded 0.27 g (83%) of the ketone **46**, a colorless oil that displayed ir (neat): 1682, 1572, 1103, 776 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.04 (s, 6H), 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 53 Hz), 0.88 (s, 9H), 1.35–1.55 (m, 4H), 2.22 (s, 3H), 2.44 (br t, 2H, J = 6.5 Hz, $^3J_{\text{Sn-H}}$ = 49 Hz), 3.60 (t, 2H, J = 6.5 Hz), 6.79 (br s, 1H, $^3J_{\text{Sn-H}}$ = 122 Hz); in nOe difference experiments, irradiation at δ 6.79 caused enhancement of the signals at δ 2.44 and 2.22, while irradiations at δ 2.22 and 2.44 caused, in each case, enhancement of the resonance at δ 6.79; ^{13}C nmr (75.4 MHz) δ: −7.5, −5.3, 18.3, 25.6, 25.9, 30.1, 32.5, 39.7, 62.9, 134.7, 176.8, 197.6. Exact Mass calcd. for $C_{16}H_{33}O_2SiSn$ (M$^+$ − Me): 405.1272; found: 405.1266.

(*Z*)-*4-Trimethylstannyl-3-nonen-8-yn-2-one* (**47**)

Flash chromatography (35 g of silica gel, 95:5 petroleum ether – Et$_2$O) of the crude product derived from the substrate **32** (0.18 g, 1.3 mmol), followed by distillation (70–80°C/0.5 Torr) of the resultant liquid, gave 0.27 g (69%) of the ketone **47**, a colorless oil that showed ir (neat): 3308, 2119, 1681, 1571, 772 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 54 Hz), 1.63 (quintet, 2H, J = 7.5 Hz), 1.97 (t, 1H, J = 2.5 Hz), 2.19 (td, 2H, J = 7.5, 2.5 Hz), 2.22 (s, 3H), 2.54 (td, 2H, J = 7.5, 1.3 Hz, $^3J_{\text{Sn-H}}$ = 48 Hz), 6.62 (br s, 1H, $^3J_{\text{Sn-H}}$ = 120 Hz); in nOe experiments, irradiation at δ 6.62 caused signal enhancement at δ 2.54 and 2.22, irradiation at δ 2.54 caused signal enhancement at δ 6.62 and 1.63, and irradiation at δ 2.22 enhanced the signal at δ 6.62. Exact Mass calcd. for $C_{11}H_{17}OSn$ (M$^+$ − Me): 285.0302; found: 285.0302.

(*Z*)-*5-Methyl-4-trimethylstannyl-3-hexen-2-one* (**48**)

The crude product obtained from the substrate **33** (0.20 g, 1.8 mmol), upon subjection to flash chromatography (45 g of silica gel, 98:2 petroleum ether – Et$_2$O) and distillation (70–75°C/0.5 Torr), furnished 0.40 g (80%) of the ketone **48**, a colorless oil that exhibited ir (neat): 1682, 1568, 1203, 770 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.09 (s, 9H, $^2J_{\text{Sn-H}}$ = 54 Hz), 1.03 (d, 6H, J = 6.5 Hz), 2.20 (s, 3H), 2.75 (septet of d, J = 6.5, 1.5 Hz, $^3J_{\text{Sn-H}}$ = 54 Hz), 6.77 (d, 1H, J = 1.5 Hz, $^3J_{\text{Sn-H}}$ = 127 Hz); in nOe difference experiments, irradiation at δ 6.77 produced signal enhancements at δ 1.03, 2.20, and 2.75, while irradiation at δ 2.75 caused enhancement of the resonances at δ 1.03 and 6.77; ^{13}C nmr (75.4 MHz) δ: −6.9, 21.7, 30.1, 36.2, 130.7, 183.0, 197.9. Exact Mass calcd. for $C_9H_{17}OSn$ (M$^+$ − Me): 261.0301; found: 261.0297.

(*Z*)-*7*-tert-*Butyldimethylsilyloxy-2-methyl-5-trimethylstannyl-4-hepten-3-one* (**49**)

Flash chromatography (140 g of silica gel, 95:5 petroleum ether – Et$_2$O) of the crude product obtained from the substrate **34** (2.3 g, 9.2 mmol), followed by distillation (130–135°C/0.5 Torr) of the acquired liquid, afforded 3.6 g (94%) of the ketone **49**, a colorless oil that showed ir (neat): 1678, 1572, 1256, 1098, 777 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.04 (s, 6H), 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 55 Hz), 0.87 (s, 9H), 1.12 (d, 6H, J = 7 Hz), 2.66 (m, 3H), 3.66 (t, 2H, J = 6.5 Hz), 6.88 (br s, 1H, $^3J_{\text{Sn-H}}$ = 127 Hz); in nOe difference experiments, irradiations at δ 6.88 and 2.66 caused signal enhancements at δ 2.66 and 6.88, respectively. Exact Mass calcd. for $C_{16}H_{33}O_2SnSi$ (M$^+$ − Me): 405.1272; found: 405.1269.

(*Z*)-*2,2-Dimethyl-3-trimethylstannyl-3-undecen-4-one* (**50**)

Purification (flash chromatography, 75 g of silica gel, 97:3 petroleum ether – Et$_2$O; distillation, 120–130°C/0.5 Torr) of the crude product acquired from 1.0 g (5.2 mmol) of the starting material **35** furnished 0.90 g (48%) of the ketone **50**, a colorless oil that exhibited ir (neat): 1685, 1562, 779, 532 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.16 (s, 9H, $^2J_{\text{Sn-H}}$ = 53 Hz), 0.86 (m, 3H), 1.13 (s, 9H), 1.27 (br signal, 6H), 1.50–1.67 (m, 2H), 2.49 (t, 2H, J = 7.5 Hz), 6.75 (s, 1H, $^3J_{\text{Sn-H}}$ = 130 Hz); in nOe difference experiments, irradiation at δ 6.75 caused signal enhancements at δ 1.13 and 2.49, irradiation at δ 2.49 caused signal enhancements at δ 6.75 and 1.50–1.67, and irradiation at δ 1.13 increased the intensity of the resonance at δ 6.75; ^{13}C nmr (75.4 MHz) δ: −3.6, 14.1, 22.6, 24.3, 29.0, 29.7, 31.6, 40.0, 43.4, 130.3, 184.9, 201.0. Exact Mass calcd. for $C_{15}H_{29}OSn$ (M$^+$ − Me): 345.1241; found: 345.1237.

(*Z*)-*7*-tert-*Butyldimethylsilyloxy-4-trimethylstannyl-3,8-nonadien-2-one* (**51**)

Flash chromatography (75 g of silica gel, 95:5 petroleum ether – Et$_2$O) and distillation (130–135°C/0.5 Torr) of the crude product derived from the substrate **36** (0.84 g, 3.2 mmol) gave 1.3 g (95%) of the ketone **51**, a colorless oil that displayed ir (neat): 1682, 1571, 837, 776 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.02 (s, 3H), 0.05 (s, 3H), 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 54 Hz), 0.89 (s, 9H), 1.45–1.65 (m, 2H), 2.21 (s, 3H), 2.35–2.60 (m, 2H), 4.10 (m, 1H), 5.05 (ddd, 1H, J = 10, 2, 2 Hz), 5.14 (ddd, 1H, J = 18, 2, 2 Hz), 5.80 (ddd, 1H, J = 18, 10, 6 Hz), 6.80 (br s, 1H, $^3J_{\text{Sn-H}}$ = 124 Hz). Exact Mass clacd. for $C_{17}H_{33}O_2SiSn$ (M$^+$ − Me): 417.1272; found: 417.1270.

General procedure 4. Preparation of the (*Z*)-4-(trimethylstannyl)-1,3-butadienes 61–63 and 68

To a cold (0°C), stirred suspension of methyltriphenylphosphonium bromide (for **61–63**, ~1.8 mmol per mmol of substrate; for **68**, ~2.0 mmol per mmol of substrate) in dry THF (~7 mL per mmol of substrate) was added a solution of *n*-BuLi in hexane (for **61–63**, ~1.3 mmol per mmol of substrate; for **68**, ~1.5 mmol per mmol of substrate). After the resulting yellow solution/suspension had been stirred for 10 min at 0°C and for 30 min at room temperature, a solution of the aldehyde (or ketone) in dry THF (~2 mL per mmol of substrate) was added. The reaction mixture was stirred at room temperature for the time indicated in Table 3. Water (~0.5 mL per mL of reaction solu-

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tion) and Et_2O (~0.5 mL per mL of reaction solution) were added and the phases were separated. The aqueous phase was extracted with Et_2O and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The crude product was purified by chromatography and distillation.

The following (*Z*)-4-trimethylstannyl-1,3-butadienes were prepared via this general procedure.

*(Z)-6-*tert*-Butyldimethylsilyloxy-4-trimethylstannyl-1,3-hexadiene (**61**)*

Flash chromatography (120 g of silica gel, 98:2 petroleum ether – Et_2O) of the crude product obtained from the aldehyde **41** (2.7 g, 7.2 mmol), followed by distillation (105–110°C/0.5 Torr) of the acquired liquid, gave 2.4 g (87%) of the diene **61**, a colorless oil that showed ir (neat): 3087, 3049, 1621, 1574, 1100, 774 cm^{-1}; ^1H nmr (300 MHz) δ: 0.04 (s, 6H), 0.21 (s, 9H, $^2J_{Sn-H}$ = 53 Hz), 0.88 (s, 9H), 2.49 (br t, 2H J = 7 Hz, $^3J_{Sn-H}$ = 55 Hz), 3.57 (t, 2H, J = 7 Hz), 5.10 (dd, 1H, J = 11, 1.5 Hz), 5.15 (dd, 1H, J = 16, 1.5 Hz), 6.30 (m, 1H), 6.64 (br d, 1H, J = 11 Hz, $^3J_{Sn-H}$ = 131 Hz); ^{13}C nmr (75.4 MHz) δ: −8.0, −5.1, 18.4, 26.0, 43.6, 63.6, 117.1, 137.7, 142.6, 147.3. Exact Mass calcd. for $C_{14}H_{29}OSiSn$ (M^+ − Me): 361.1010; found: 361.1018. Anal. calcd. for $C_{15}H_{32}OSiSn$: C 48.02, H 8.60; found: C 48.00, H 8.70.

*(Z)-6-Methoxymethoxy-4-trimethylstannyl-1,3-hexadiene (**62**)*

Purification (flash chromatography, 230 g of silica gel, 9:1 petroleum ether – Et_2O; distillation, 95–105°C/0.5 Torr) of the crude product derived from the aldehyde **42** (5.84 g, 19.0 mmol) provided 4.76 g (82%) of the diene **62**, a colorless oil that displayed ir (neat): 3086, 1623, 1149, 1045, 771 cm^{-1}; ^1H nmr (300 MHz) δ: 0.02 (s, 9H, $^2J_{Sn-H}$ = 53 Hz), 2.55 (br t, 2H, J = 6 Hz, $^3J_{Sn-H}$ = 53 Hz), 3.24 (s, 3H), 3.50 (t, 2H, J = 6 Hz), 4.60 (s, 2H), 5.10 (br d, 1H, J = 10 Hz), 5.15 (br d, 1H, J = 17 Hz), 6.30 (m, 1H), 6.66 (br d, 1H, J = 11 Hz, $^3J_{Sn-H}$ = 125 Hz); ^{13}C nmr (75.4 MHz) δ: −8.2, 40.3, 55.0, 67.8, 96.2, 117.3, 137.6, 142.4, 147.7. Exact Mass calcd. for $C_{10}H_{19}O_2Sn$ (M^+ − Me): 291.0407; found: 291.0406.

*(Z)-8-*tert*-Butyldimethylsilyloxy-4-trimethylstannyl-1,3-octadiene (**63**)*

The crude product obtained from the aldehyde **43** (0.10 g, 0.25 mmol) was purified by flash chromatography (30 g of silica gel, 98:2 petroleum ether – Et_2O) and distillation (110–115° C/0.5 Torr) to produce 0.08 g (81%) of the diene **63**, a colorless oil that exhibited ir (neat): 3086, 1622, 1574, 1255, 1105, 775 cm^{-1}; ^1H nmr (300 MHz) δ: 0.04 (s, 6H), 0.20 (s, 9H, $^2J_{Sn-H}$ = 53 Hz), 0.88 (s, 9H), 1.30–1.55 (m, 4H), 2.28 (br t, 2H, J = 7 Hz, $^3J_{Sn-H}$ = 56 Hz), 3.59 (t, 2H, J = 6 Hz), 5.06 (dd, 1H, J = 10, 1.5 Hz), 5.13 (dd, 1H, J = 16, 1.5 Hz), 6.13 (m, 1H), 6.59 (br d, 1H, J = 11 Hz, $^3J_{Sn-H}$ = 136 Hz); ^{13}C nmr (75.4 MHz) δ: −8.1, −5.2, 18.4, 26.1, 26.5, 32.5, 40.6, 62.1, 116.5, 137.8, 140.3, 152.1. Exact Mass calcd. for $C_{16}H_{33}OSnSi$ (M^+ − Me): 389.1323; found: 389.1329.

*(Z)-2,5-Dimethyl-4-trimethylstannyl-1,3-hexadiene (**68**)*

Flash chromatography (150 g of silica gel, petroleum ether) of the crude product derived from 3.6 g (13 mmol) of the ketone **48**, followed by distillation (90–105°C/0.5 Torr) of the acquired material, gave 3.1 g (87%) of the diene **68**, a colorless oil that displayed ir (neat): 3083, 1632, 1602, 1188, 769 cm^{-1}; ^1H nmr (300 MHz) δ: 0.14 (s, 9H, $^2J_{Sn-H}$ = 52 Hz), 1.03 (d, 6H, J = 7 Hz), 1.77 (s, 3H), 2.51 (septet of d, J = 7, 1.5 Hz, $^3J_{Sn-H}$ = 60 Hz), 4.74 (br s, 1H), 4.78 (br s, 1H), 6.45 (br s, 1H, $^3J_{Sn-H}$ = 144 Hz); ^{13}C nmr (75.4 MHz) δ: −6.3, 22.7, 23.1, 36.9, 112.6, 138.5, 147.2, 152.9. Exact Mass calcd. for $C_{10}H_{19}Sn$ (M^+ − Me): 259.0509; found: 259.0512.

General procedure 5. Preparation of the (Z)-4-(trimethylstannyl)-1,3-butadienes 64–67 and 69–71

To a stirred suspension of methyltriphenylphosphonium bromide (2.5 equiv.) in dry benzene (room temperature, ~9 mL per mmol of ketone substrate used) was added a solution of sodium 2-methyl-2-butoxide (2.5 equiv.) in dry benzene (1.75 M). After the mixture had been stirred for 20 min at room temperature, a solution of the ketone (1 equiv.) in dry benzene (~4 mL per mmol of the ketone) was added and stirring was continued for the time indicated in Table 3. Water (~0.5 mL per mL of reaction solution) and Et_2O (~1 mL per mL of reaction solution) were added and the phases were separated. The aqueous phase was extracted with Et_2O and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The crude product was purified by chromatography and distillation.

The following (*Z*)-4-trimethylstannyl-1,3-butadienes were prepared via this general procedure.

*(Z)-6-*tert*-Butyldimethylsilyloxy-2-methyl-4-trimethylstannyl-1,3-hexadiene (**64**)*

Flash chromatography (35 g of silica gel, 98:2 petroleum ether – Et_2O) of the crude product derived from 0.20 g (0.51 mmol) of the ketone **44**, followed by distillation (105–110°C/0.5 Torr) of the acquired liquid, gave 0.17 mg (86%) of the diene **64**, a colorless oil that exhibited ir (neat): 3083, 1633, 1604, 1572, 1255, 774 cm^{-1}; ^1H nmr (300 MHz) δ: 0.04 (s, 6H), 0.13 (s, 9H, $^2J_{Sn-H}$ = 53 Hz), 0.88 (s, 9H), 1.76 (s, 3H), 2.45 (td, 2H, J = 7, 1.3 Hz, $^3J_{Sn-H}$ = 55 Hz), 3.56 (t, 2H, J = 7 Hz), 4.57 (br s, 1H), 4.79 (br s, 1H), 6.53 (br s, 1H, $^3J_{Sn-H}$ = 137 Hz); ^{13}C nmr (75.4 MHz) δ: −7.2, −5.2, 18.4, 22.7, 26.0, 43.6, 63.7, 112.9, 141.8, 144.9, 146.6. Exact Mass calcd. for $C_{15}H_{31}OSiSn$ (M^+ − Me): 375.1166; found: 375.1161.

*(Z)-7-Chloro-2-methyl-4-trimethylstannyl-1,3-heptadiene (**65**)*

Purification (flash chromatography, 35 g of silica gel, 98:2 petroleum ether – Et_2O; distillation, 85–90°C/0.5 Torr) of the crude product obtained from the ketone **45** (0.29 g, 0.73 mmol) gave 0.13 g (57%) of the diene **65**, a colorless oil that displayed ir (neat): 3082, 1632, 1605, 897 cm^{-1}; ^1H nmr (300 MHz) δ: 0.14 (s, 9H, $^2J_{Sn-H}$ = 53 Hz), 1.77 (s, 3H), 1.81 (quintet, 2H, J = 7 Hz), 2.38 (td, 2H, J = 7, 1.3 Hz, $^3J_{Sn-H}$ = 54 Hz), 3.50 (t, 2H, J = 7 Hz), 4.76 (br s, 1H), 4.80 (br s, 1H), 6.52 (br s, 1H, $^3J_{Sn-H}$ = 136 Hz). Exact Mass calcd. for $C_{10}H_{18}{}^{35}ClSn$ (M^+ − Me): 293.0119; found: 293.0114.

*(Z)-8-*tert*-Butyldimethylsilyloxy-2-methyl-4-trimethylstannyl-1,3-octadiene (**66**)*

The crude product obtained from the ketone **46** (0.16 g, 0.37 mmol) was purified by flash chromatography (30 g of silica gel, 97:3 petroleum ether – Et_2O) and distillation (110–115°C/0.5 Torr) to afford 0.12 g (75%) of the diene **66**, a colorless oil that showed ir (neat): 3081, 1572, 1562, 1255, 1103, 775 cm^{-1};

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^{1}H nmr (300 MHz) δ: 0.03 (s, 6H), 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 52 Hz), 0.88 (s, 9H), 1.29–1.55 (m, 4H), 1.76 (s, 3H), 2.24 (br t, 2H, J = 7 Hz, $^3J_{\text{Sn-H}}$ = 55 Hz), 3.59 (t, 2H, J = 6 Hz), 4.74 (br s, 1H), 4.79 (br s, 1H), 6.47 (br s, 1H, $^3J_{\text{Sn-H}}$ = 139 Hz); ^{13}C nmr (75.4 MHz) δ: −7.4, −5.3, 18.3, 22.7, 26.0, 26.5, 32.4, 40.4, 60.1, 112.6, 142.5, 146.2, 146.6. Exact Mass calcd. for $C_{17}H_{35}OSn$ (M$^+$ − Me): 403.1479; found: 403.1472.

*(Z)-2-Methyl-4-trimethylstannyl-1,3-nonadien-8-yne (**67**)*

The ketone **47** (1.22 g, 4.07 mmol; in 8 mL of dry benzene) was converted into the diene **67** by treatment with the Wittig reagent (2.5 equiv.; in 15 mL of dry benzene) at room temperature for 30 min. Flash chromatography (65 g of silica gel, petroleum ether) of the crude product, followed by distillation (70–80°C/0.5 Torr) of the liquid obtained, provided 1.01 g (83%) of the diene **67**, a colorless oil that exhibited ir (neat): 3212, 1632, 3082, 2120, 897, 770 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.13 (s, 9H, $^2J_{\text{Sn-H}}$ = 53 Hz), 1.57 (quintet, 2H, J = 7 Hz), 1.76 (s, 3H), 1.94 (t, 1H, J = 2.6 Hz), 2.16 (td, 2H, J = 7, 2.6 Hz), 2.34 (td, 2H, J = 7, 1.3 Hz, $^3J_{\text{Sn-H}}$ = 55 Hz), 4.75 (br s, 1H), 4.79 (br s, 1H), 6.51 (br s, 1H, $^3J_{\text{Sn-H}}$ = 139 Hz); ^{13}C nmr (75.4 MHz) δ: −7.3, 17.8, 22.7, 28.8, 39.4, 68.4, 84.4, 112.9, 143.5, 144.9, 146.6. Exact Mass calcd. for $C_{12}H_{19}Sn$ (M$^+$ − Me): 283.0509; found: 283.0510.

*(Z)-6-*tert*-Butyldimethylsilyloxy-2-isopropyl-4-trimethylstannyl-1,3-hexadiene (**69**)*

Purification (flash chromatography, 35 g of silica gel, 97:3 petroleum ether – Et$_2$O; distillation, 110–115°C/0.5 Torr) of the crude product obtained from the ketone **49** (0.17 g, 0.41 mmol), furnished 0.11 g (64%) of the diene **69**, a colorless oil that showed ir (neat): 3090, 1625, 1461, 1255, 1007, 775 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.04 (s, 6H), 0.12 (s, 9H, $^2J_{\text{Sn-H}}$ = 53 Hz), 0.87 (s, 9H), 1.02 (d, 6H, J = 7 Hz), 2.27 (br septet, 1H, J = 7 Hz), 2.48 (br t, 2H, J = 7 Hz, $^3J_{\text{Sn-H}}$ = 53 Hz), 3.56 (t, 2H, J = 7 Hz), 4.71 (br s, 1H), 4.80 (br s, 1H), 6.60 (br s, 1H, $^3J_{\text{Sn-H}}$ = 140 Hz); ^{13}C nmr (75.4 MHz) δ: −7.1, −5.2, 18.4, 21.6, 26.0, 34.0, 43.7, 63.8, 108.9, 143.4, 156.4. Exact Mass calcd. for $C_{17}H_{35}OSiSn$ (M$^+$ − Me): 403.1479; found: 403.1474.

*(Z)-5,5-Dimethyl-2-*n*-hexyl-4-trimethylstannyl-1,3-hexadiene (**70**)*

Flash chromatography (35 g of silica gel, 98:2 petroleum ether – Et$_2$O) of the crude product obtained from the ketone **50** (0.11 g, 0.31 mmol), followed by distillation (105–110°C/0.5 Torr) of the acquired material, afforded 0.09 g (81%) of the diene **70**, a colorless oil that exhibited ir (neat): 3038, 1630, 899, 770 cm^{-1}; ^{1}H nmr (300 MHz) δ: 0.15 (s, 9H, $^2J_{\text{Sn-H}}$ = 52 Hz), 0.88 (m, 3H), 1.07 (s, 9H), 1.30 (br s, 6H), 1.42 (m, 2H), 2.01 (br t, 2H, J = 8 Hz), 4.72 (br s, 1H), 4.77 (br s, 1H), 6.49 (br s, 1H, $^3J_{\text{Sn-H}}$ = 151 Hz); ^{13}C nmr (75.4 MHz) δ: −3.6, 14.2, 22.8, 22.7, 29.4, 30.7, 31.8, 37.1, 38.9, 111.2, 137.3, 151.3, 156.6. Exact Mass calcd. for $C_{16}H_{31}Sn$ (M$^+$ − Me): 343.1448; found: 343.1453.

*(Z)-7-*tert*-Butyldimethylsilyloxy-2-methyl-4-trimethylstannyl-1,3,8-nonatriene (**71**)*

The crude product acquired from the ketone **51** (0.09 g, 0.21 mmol) was purified by flash chromatography (30 g of silica gel, 97:3 petroleum ether – Et$_2$O) and distillation (125–130°C/0.5 Torr) to afford 0.08 g (85%) of the diene **71**, a colorless oil that displayed ir (neat): 3081, 1632, 1253, 1084, 775 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.04 (s, 3H), 0.06 (s, 3H), 0.14 (s, 9H, $^2J_{\text{Sn-H}}$ = 52 Hz), 0.90 (s, 9H), 1.40–1.60 (m, 2H), 1.78 (s, 3H), 2.19–2.40 (m, 2H), 4.10 (br m, 1H), 4.76 (br s, 1H), 4.80 (br s, 1H), 5.03 (ddd, 1H, J = 10, 2, 2 Hz), 5.14 (ddd, 1H, J = 17, 2, 2 Hz), 5.81 (ddd, 1H, J = 17, 10, 6 Hz), 6.50 (br s, 1H, $^3J_{\text{Sn-H}}$ = 139 Hz); ^{13}C nmr (50 MHz) δ: −7.3, −4.8, −4.3, 18.2, 22.7, 25.9, 36.4, 38.9, 73.6, 112.7, 113.7, 141.8, 142.6, 145.9, 146.7. Exact Mass calcd. for $C_{18}H_{35}OSiSn$ (M$^+$ − Me): 415.1480; found: 415.1478.

Methyl *(2E,4Z)*-7-*tert*-butyldimethylsilyloxy-5-trimethylstannyl-1,4-heptadienoate (72)

To a cold (0°C), stirred suspension of NaH (1.02 g, 21.2 mmol) in 100 mL of dry THF was added dropwise, over a period of ~5 min, trimethyl phosphonoacetate (3.87 g, 21.2 mmol) and the resultant slurry was stirred at 0°C for 5 min and at room temperature for 20 min. The mixture was then recooled to 0°C and a solution of the aldehyde **41** (5.35 g, 14.2 mmol) in 25 mL of dry THF was added. The resulting suspension was stirred at 0°C for 2 h. Water (~50 mL) and Et$_2$O (~50 mL) were added and the phases were separated. The aqueous phase was extracted with Et$_2$O (2 × 40 mL) and the combined organic extracts were washed (brine, 40 mL), dried (MgSO$_4$), and concentrated. Flash chromatography (250 g of silica gel, 94:6 petroleum ether – Et$_2$O) of the crude product and distillation (140–150°C/0.5 Torr) of the acquired liquid provided 5.65 g (92%) of the diene **72**, a colorless oil that displayed ir (neat): 1723, 1626, 1268, 1100, 776 cm^{-1}; ^{1}H nmr (400 MHz) δ: 0.03 (s, 6H), 0.27 (s, 9H, $^2J_{\text{Sn-H}}$ = 54 Hz), 0.87 (s, 9H), 2.57 (br t, 2H, J = 7 Hz, $^3J_{\text{Sn-H}}$ = 50 Hz), 3.62 (t, 2H, J = 7 Hz), 3.73 (s, 3H), 5.80 (br d, 1H, J = 15 Hz), 6.73 (br d, 1H, J = 11 Hz, $^3J_{\text{Sn-H}}$ = 122 Hz), 7.30 (dd, 1H, J = 15, 11 Hz, $^4J_{\text{Sn-H}}$ = 7 Hz); in nOe difference experiments irradiation at δ 2.57 caused signal enhancement at δ 6.73 and 3.62, irradiation at δ 5.80 caused resonance enhancement at δ 6.73, and irradiation at δ 6.73 caused enhancement of the signals at δ 5.80 and 2.57. Exact Mass calcd. for $C_{16}H_{31}O_3SnSi$ (M$^+$ − Me): 419.1065; found: 419.1070.

Preparation of the phosphonate reagent 73

A stirred mixture of triisopropyl phosphite (3.2 g, 15 mmol) and *tert*-butyl bromoacetate (3.0 g, 15 mmol) was heated at 125°C for 1.5 h. Direct distillation (fraction collected between 110 and 115°C/0.5 Torr) of the oil thus obtained gave 3.5 g (81%) of the phosphonate **73**, a colorless oil that exhibited ir (neat): 1730, 1289, 1107, 991 cm^{-1}; ^{1}H nmr (400 MHz) δ: 1.27 (d, 6H, J = 7 Hz), 1.29 (d, 6H, J = 7 Hz), 1.42 (s, 9H), 2.77 (d, 2H, $^2J_{\text{P-H}}$ = 22 Hz), 4.68 (m, 2H); ^{13}C nmr (75.4 MHz) δ: 23.8 (d, $^3J_{\text{P-C}}$ = 5 Hz), 23.95 (d, $^3J_{\text{P-C}}$ = 4 Hz), 27.8, 36.6 (d, $^1J_{\text{P-C}}$ = 134 Hz), 70.9 (d, $^2J_{\text{P-C}}$ = 6 Hz), 81.6, 164.9 (d, $^2J_{\text{P-C}}$ = 6 Hz); ^{31}P nmr (122 MHz) δ: 16.2 (tt, J = 22, 8 Hz).

***tert*-Butyl *(2E,4Z)*-7-methoxymethoxy-5-trimethylstannyl-1,4-heptadienoate (74)**

To a cold (0°C), stirred suspension of NaH (0.26 g, 6.4 mmol) in 25 mL of dry THF was added slowly, over a period of ~5 min, a solution of the phosphonate reagent **73** (1.8 g, 6.4 mmol) in 10 mL of dry THF. After the mixture had been stirred at 0°C for 5 min and at room temperature for 20 min, it

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was cooled to −20°C and a solution of the aldehyde **42** (1.17 g, 3.8 mmol) in 10 mL of dry THF was added. The mixture was stirred at −20°C for 1.5 h and was then allowed to warm to room temperature (30 min). Water (~20 mL) and Et_2O (~40 mL) were added and the phases were separated. The aqueous phase was extracted with Et_2O (2 × 20 mL) and the combined organic extracts were washed (brine, 20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the crude product on silica gel (65 g, 4:1 petroleum ether – Et_2O), followed by distillation (190–210°C/0.5 Torr) of the acquired material, gave 1.4 g (91%) of the diene **74**, a colorless oil that showed ir (neat): 1703, 1626, 1368, 1045, 770 cm^{-1}; ^1H nmr (400 MHz) δ: 0.25 (s, 9H, $^2J_{Sn-H} = 52$ Hz), 1.48 (s, 9H), 2.64 (br t, 2H, $J = 7$ Hz, $^3J_{Sn-H} = 49$ Hz), 3.33 (s, 3H), 3.54 (t, 2H, $J = 7$ Hz), 4.58 (s, 2H), 5.72 (br d, 1H, $J = 15$ Hz), 6.74 (br d, 1H, $J = 11$ Hz, $^3J_{Sn-H} = 120$ Hz), 7.21 (dd, 1H, $J = 15, 11$ Hz, $^4J_{Sn-H} = 7$ Hz); in nOe difference experiments, irradiation at δ 6.74 caused enhancement of the resonances at δ 5.72 and 2.64, irradiation at δ 2.64 caused signal enhancement at δ 3.54 and 6.74, and irradiation at δ 5.72 increased the intensity of the signal at δ 6.74; ^{13}C nmr (75.4 MHz) δ: −7.8, 28.2, 41.0, 55.3, 67.5, 80.1, 96.4, 123.2, 139.5, 144.2, 160.5, 166.5. Exact Mass calcd. for $C_{15}H_{27}O_4Sn$ (M^+ − Me): 391.0931; found: 391.0938. Anal. calcd. for $C_{16}H_{30}O_4Sn$: C 47.42, H 7.47; found: C 47.59, H 7.39.

(*E*)-3-((2-Methoxymethoxy)ethyl)-3,5-hexadien-1-ol (76)

To a cold (−78°C), stirred solution of the trimethylstannyl diene **62** (0.87 g, 2.84 mmol) in dry THF (50 mL) was added a solution of MeLi (3.1 mmol) in Et_2O. After the mixture had been stirred for 45 min at −78°C, ethylene oxide (~2.5 g, ~57 mmol) was added via a syringe (the barrel of the syringe was cooled using a piece of Dry Ice, in order to facilitate the transfer of the volatile liquid). The resulting mixture was stirred at −78°C for 5 min and at −20°C for 20 min and was then allowed to warm to room temperature (30 min). Saturated aqueous $NaHCO_3$ (10 mL) and Et_2O (30 mL) were added, the phases were separated, and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed (brine, 20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the crude product on silica gel (40 g, 2:3 petroleum ether – Et_2O) and distillation (110–120°C/0.5 Torr) of the derived liquid gave 0.38 g (71%) of the alcohol **76**, a colorless oil that exhibited ir (neat): 3401, 3085, 1647, 1150, 1109, 1039 cm^{-1}; ^1H nmr (400 MHz) δ: 1.74 (br s, 1H), 2.39 (br t, 2H, $J = 6.5$ Hz), 2.49 (t, 2H, $J = 6.5$ Hz), 3.34 (s, 3H), 3.67 (t, 2H, $J = 6.5$ Hz), 3.70 (br m, 2H), 4.61 (s, 2H), 5.05 (dd, 1H, $J = 10, 1.5$ Hz), 5.15 (dd, 1H, $J = 17, 1.5$ Hz), 6.06 (br d, 1H, $J = 11$ Hz), 6.60 (ddd, 1H, $J = 17, 11, 10$ Hz); on addition of D_2O the signal at δ 3.70 sharpened to a t ($J = 6.5$ Hz), and the signal at δ 1.74 disappeared; ^{13}C nmr (75.4 MHz) δ: 34.4, 37.1, 55.3, 61.2, 66.5, 96.4, 116.8, 129.9, 132.5, 136.3. Exact Mass calcd. for $C_{10}H_{16}O_2$ (M^+ − H_2O): 168.1151; found: 168.1152. Anal. calcd. for $C_{10}H_{18}O_3$: C 64.49, H 9.74; found: C 64.49, H 9.88.

(*Z*)-6-Bromo-4-((2-methoxymethoxy)ethyl)-1,3,6-heptatriene (78)

To a cold (−78°C), stirred solution of the trimethylstannyl diene **62** (0.35 mg, 1.13 mmol) in dry THF (5 mL) was added a solution of MeLi (1.24 mmol) in Et_2O. After the mixture had been stirred for 45 min at −78°C, $CuBr{\cdot}Me_2S$ (256 mg, 1.24 mmol) was added. The resulting bright pink solution/suspension was stirred at −78°C for 5 min and at −48°C for 15 min. To the resulting bright orange-red solution was added 2,3-dibromopropene (1.5 g, 7.6 mmol) and the resulting colorless solution was stirred at −48°C for 45 min. Aqueous NH_4Cl–NH_4OH (pH 8) (5 mL) and Et_2O (10 mL) were added and the vigorously stirred mixture was allowed to warm to room temperature. The phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed (brine, 10 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (40 g of silica gel, 9:1 petroleum ether – Et_2O), followed by distillation (100–110°C/0.5 Torr) of the acquired liquid, furnished 244 mg (83%) of the triene **78**, a colorless oil that showed ir (neat): 3086, 1626, 1150, 1072, 917 cm^{-1}; ^1H nmr (400 MHz) δ: 2.38 (br t, 2H, $J = 6$ Hz), 3.35 (br s, 5H), 3.62 (t, 2H, $J = 6$ Hz), 4.60 (s, 2H), 5.12 (dd, 1H, $J = 11, 1.5$ Hz), 5.20 (dd, 1H, $J = 17, 1.5$ Hz), 5.48 (br s, 1H), 5.62 (br s, 1H), 6.13 (br d, 1H, $J = 11$ Hz), 6.54 (ddd, 1H, $J = 17, 11, 11$ Hz); ^{13}C nmr (75.4 MHz) δ: 36.6, 42.8, 55.2, 66.1, 96.3, 117.5, 117.8, 130.4, 130.9, 132.4, 134.6. Exact Mass calcd. for $C_9H_{12}{}^{79}BrO_2$ (M^+ − C_2H_5O): 215.0072; found: 215.0064. Anal. calcd. for $C_{11}H_{17}BrO_2$: C 50.59, H 6.56; found: C 50.85, H 6.58.

(*Z*)-7-Iodo-2-methyl-4-trimethylstannyl-1,3-heptadiene (87)

A stirred solution of NaI (1.80 g, 11.8 mmol) and the trimethylstannyl diene **65** (0.36 g, 1.18 mmol) in dry acetone (10 mL) was allowed to reflux overnight. Most of the acetone was removed, Et_2O (20 mL) and water (10 mL) were added to the residue, the phases were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed (water, 10 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the crude product on silica gel (35 g, 95:5 petroleum ether – Et_2O) and distillation (100–110°C/0.5 Torr) of the derived liquid afforded 0.41 mg (86%) of the diene **87**, a colorless oil that exhibited ir (neat): 3080, 1632, 1215, 896, 769 cm^{-1}; ^1H nmr (400 MHz) δ: 0.16 (s, 9H, $^2J_{Sn-H} = 56$ Hz), 1.78 (s, 3H), 1.87 (quintet, 2H, $J = 7$ Hz), 2.34 (br t, 2H, $J = 7$ Hz, $^3J_{Sn-H} = 54$ Hz), 3.15 (t, 2H, $J = 7$ Hz), 4.76 (br s, 1H), 4.80 (br s, 1H), 6.54 (s, 1H, $^3J_{Sn-H} = 132$ Hz); ^{13}C nmr (50 MHz) δ: −7.3, 6.2, 22.7, 33.6, 40.8, 113.0, 143.8, 144.0, 146.5. Exact Mass calcd. for $C_{10}H_{18}ISn$ (M^+ − Me): 384.9477; found: 384.9476.

5,5,6,6-Tetracyano-8-methylspiro[3.5]non-8-ene (88)

To a cold (−78°C), stirred solution of the trimethylstannyl diene **87** (0.19 g, 0.47 mmol) in dry THF (2 mL) was added a solution of MeLi (0.52 mmol) in Et_2O. After the solution had been stirred for 10 min at −78°C and 20 min at −48°C, water (0.5 mL) and Et_2O (2 mL) were added and the mixture was allowed to warm to room temperature. The phases were separated and the aqueous phase was extracted with Et_2O (2 × 2 mL). The combined organic extracts were dried ($MgSO_4$). The ethereal solution of the reaction product **84** exhibited essentially one non-solvent peak by glc analyses and was used immediately in the next step. To this solution (argon atmosphere) was added (in portions of 5 mg) tetracyanoethylene (~50 mg), until the reaction was shown to be complete (glc analyses). The solvent was removed and the white solid

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obtained was dissolved in a minimum amount of Et_2O. Flash chromatography of this solution on silica gel (25 g, 1:1 petroleum ether – Et_2O) and recrystallization of the acquired solid from petroleum ether gave 0.08 mg (69%) of the spiro compound **88** as colorless crystals that displayed mp 166–167°C; ir (KBr disk): 2253, 1440, 883, 696 cm^{-1}; ^1H nmr (400 MHz) δ: 1.88 (br s, 3H), 2.08–2.10 (m, 1H), 2.17–2.24 (m, 3H), 2.73–2.75 (m, 2H), 2.95 (br s, 2H), 5.99 (br s, 1H). Exact Mass calcd. for $C_{14}H_{12}N_4$: 236.1062; found: 236.1056.

5,6-Bis(methoxycarbonyl)-8-methylspiro[3.5]nona-5,8-diene (89)

To a cold (−78°C), stirred solution of the trimethylstannyl diene **87** (0.17 g, 0.43 mmol) in dry THF (2 mL) was added a solution of MeLi (0.47 mmol) in Et_2O. After the solution had been stirred for 10 min at −78°C and 20 min at −48°C, water (0.5 mL) and benzene (2 mL) were added and the mixture was allowed to warm to room temperature. The phases were separated and the aqueous phase was extracted with benzene (3 × 1 mL). The combined organic extracts were dried ($MgSO_4$). To this solution of the crude product **84** was added dimethyl acetylenedicarboxylate (360 mg, 2.6 mmol) and the resultant solution (argon atmosphere) was heated (70°C) in a sealed tube for 36 h. The solvent was removed and the residual oil was purified by flash chromatography (30 g of silica gel, 1:1 petroleum ether – Et_2O) and distillation (100–110°C/0.5 Torr) to give 0.07 g (70%) of the spiro compound **89**, a colorless oil that crystallized on standing. Recrystallization of this material from pentane produced colorless crystals that exhibited mp 55–56°C; ir (KBr disk): 1724, 1635, 1440, 1267, 1051, 754 cm^{-1}; ^1H nmr (400 MHz) δ: 1.72 (br s, 3H), 1.72–1.80 (m, 1H), 1.92–1.96 (m, 3H), 2.58–2.59 (m, 2H), 2.82 (br s, 2H), 3.73 (s, 3H), 3.88 (s, 3H), 5.73 (br s, 1H). Exact Mass calcd. for $C_{14}H_{18}O_4$: 250.1205; found: 250.1203.

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References

1. E. Piers and R.T. Skerlj. Can. J. Chem. **72**, 2468 (1994).
2. E. Piers and R.D. Tillyer. J. Chem. Soc. Perkin Trans. 1, 2124 (1989).
3. E.J. Corey and J.W. Suggs. Tetrahedron Lett. 2647 (1975).
4. E.J. Corey and A. Venkateswarlu. J. Am. Chem. Soc. **94**, 6190 (1972).
5. W.C. Still, M. Kahn, and A. Mitra. J. Org. Chem. **43**, 2923 (1978).
6. A.J. Leusink, H.A. Budding, and J.W. Marsman. J. Organomet. Chem. **9**, 285 (1967).
7. E. Piers and P.D. Coish. Synthesis, 47 (1995).
8. T.N. Mitchell, A. Amamria, H. Killing, and D. Rutschow. J. Organomet. Chem. **304**, 257 (1986).
9. T. Tsuda, T. Yoshida, and T. Saegusa. J. Org. Chem. **53**, 1037 (1988).
10. F. Huet, M. Pellet, and J.M. Conia. Tetrahedron Lett. 3505 (1977).
11. P.G.M. Wuts. Synth. Commun. **11**, 139 (1981).
12. E. Piers and J.S.M. Wai. Can. J. Chem. **72**, 146 (1994).
13. K.C. Nicolaou, T. Ladduwahetty, and E.M. Elisseou. J. Chem. Soc. Chem. Commun. 1580 (1985).