Free radicals and Lewis acid. Chelation-controlled radical allylations of substituted α-halo- or α-phenylseleno-β-alkoxy esters. The endocyclic effect.

B. Guérin, C. Chabot, N. Mackintosh, W.W. Ogilvie, and Y. Guindon

Abstract: The radical allylation of a series of α-halo or α-phenylseleno-β-alkoxy esters in the presence of $MgBr_2 \cdot OEt_2$ is reported and compared with analogous reactions under non-chelating conditions. The addition of $MgBr_2 \cdot OEt_2$ gives excellent selectivity favoring *anti* products; in some cases ratios >100:1 are obtained. Varying the substrate substituents reveals that these reactions are quite tolerant of alkyl functionalities at the β-position. Changes to the alkoxy function indicate that a chelate is involved in the reaction. The reactions are successful with secondary iodides, bromides, and phenylselenides, as well as tertiary iodides, which all give very high ratios under chelation control. Performing less well under the same conditions are substrates with a radical exocyclic to a tetrahydrofuran ring. EDTA titration is used to determine the amount of Mg^{2+} dissolved in the allylation reaction mixture, and ^{13}C NMR is employed to better define the nature of the complex formed (chelate or monodentate) prior to the reaction. Competition experiments suggest that the chelate and monodentate pathways are in competition for the radical allylation with allyltributyltin.

Key words: allylation, radicals, Lewis acid, stereoselectivity, 1,2-induction.

Résumé : Les allylations radicalaires, pour une série d'esters α-halo or phenylseleno-β-alkoxylés, en présence de $MgBr_2 \cdot OEt_2$, sont rapportées et comparées aux réactions analogues sans acide de Lewis. L'addition de $MgBr_2 \cdot OEt_2$ conduit à une excellente sélectivité en faveur des produits *anti*, pour certains cas, des ratios >100:1 ont été obtenus. Les variations des substituants sur les substrats montrent que ces réactions tolèrent une variété de fonctions alkyles en position β. Les changements de la fonction alkoxy suggèrent qu'un chelate est impliqué lors de la réaction. Les allylations fonctionnent bien avec les iodures, les bromures ainsi qu'avec les phénylsélenures secondaires. Les iodures tertiaires donnent des ratios très élevés en présence d'acide de Lewis. Les substrats générant un radical exocyclique à un cycle tetrahydrofurane donnent de moins bons résultats sous ces conditions. Le titrage à l'EDTA a été utilisé pour déterminer la quantité de Mg^{2+} dissous dans le mélange réactionnel lors de l'allylation, et les données RMN ^{13}C ont été utilisées pour mieux définir la nature des complexes formés (chelate ou monodentate) avant la réaction. Les expériences de compétition suggèrent que les deux chemins réactionnels, chelate et monodentate, sont en compétition pour l'allylation radicalaire avec l'allyle d'étain.

Mots clés : allylation, radicaux, acide de Lewis, stéréoselectivité, induction-1,2.

1. Introduction

This decade (1) has shown that free radical based reactions could be useful synthetic approaches for making acyclic molecules with high levels of diastereoselectivity and enantioselectivity. Significant levels of stereocontrol have been achieved in strategies involving pre-existing chiral centers (2, 3) or chiral auxiliaries (4). The scope of these reactions has been expanded by using mono (5) or bidentate Lewis acids (6, 7), solvent complexation (8), and intramolecular hydrogen bonding (9). Additionally, reagent control approaches employing chiral Lewis acid or chiral tin hydride have been recently devised (10).

We have been particularly interested in studying the reactivity of radicals flanked by an ester and a stereogenic center bearing a heteroatom in reactions involving hydrogen-atom

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This article is dedicated to Professor Stephen Hanessian on the occasion of his 65th birthday. It is an accolade to my mentor, colleague, and friend, written in celebration of his many years of scientific achievement and the many more to come.

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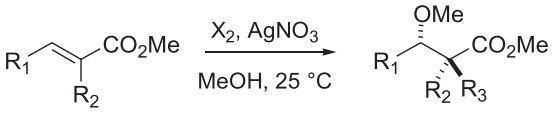
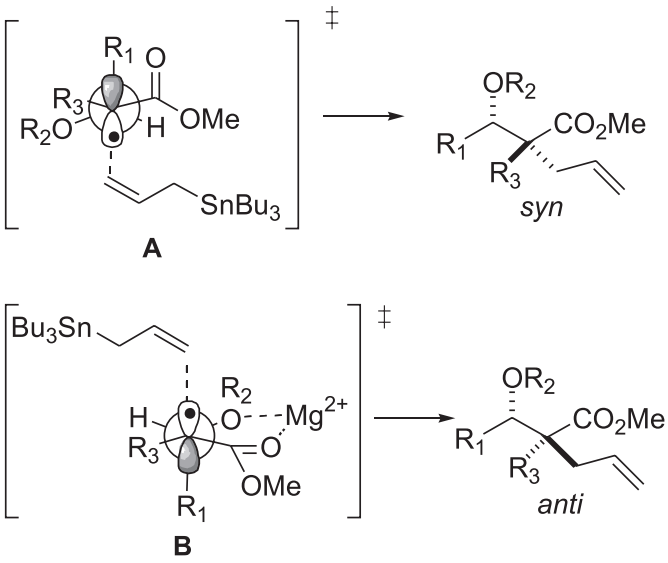
Table 1. Preparation of substrates **9**–**21** by alkoxy-etherification.



Entry	olefin	R_1	X_2	R_2	R_3	Substrate	Yield (%)
1	**1**	Me	I_2	H	I	**9**	60
2	**2**	i-Pr	I_2	H	I	**10**	38
3	**3**	c-C_6H_{11}	I_2	H	I	**11**	45
4	**4**	Ph	I_2	H	I	**12**	78
5	**4**	Ph	I_2	H	I	**13**[a]	61
6	**4**	Ph	Br_2	H	Br	**14**	70
7	**4**	Ph	PhSeBr[b]	H	PhSe	**15**	90
8	**5**[c]	Ph	I_2	I	H	**16**	77
9	**5**[c]	Ph	Br_2	Br	H	**17**	78
10	**5**[c]	Ph	PhSeBr[b]	PhSe	H	**18**	93
11	**6**	Ph	I_2	Me	I	**19**	66
12	**7**	Me	I_2	Me	I	**20**[d]	81
13	**8**	Et	I_2	Me	I	**21**[d]	42

[a]Benzylalcohol was used to give the β-benzyloxy-α-iodo-ester.
[b]PhSeBr was used with AgOTf.
[c]Methyl-*Z*-cinnamate was used to give *syn* substrate.
[d]Ethyl ester was used.

Scheme 1. (*a*) In absence of $MgBr_2 \cdot OEt_2$; (*b*) In presence of $MgBr_2 \cdot OEt_2$.



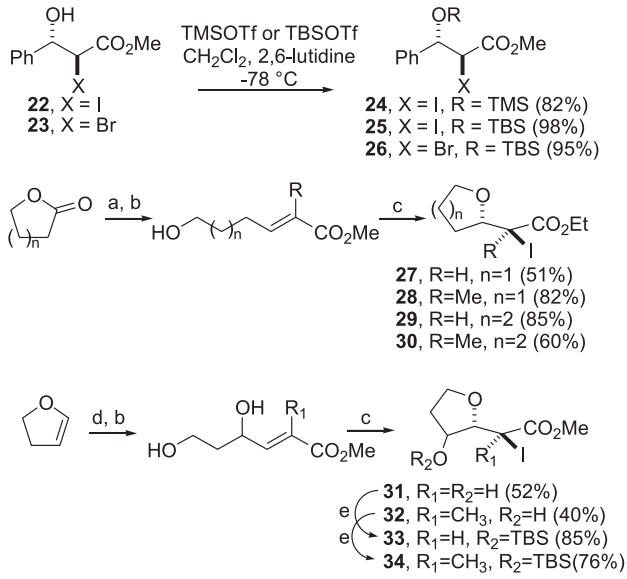
transfer (3), additions to olefins (7*e*), cyclizations (3*f*), and allylation reactions (3*b*, 3*g*, 7*b*). Our first studies dealing with the induction of new chiral centers on acyclic molecules, using free radical chemistry, spawned from unexpected experimental results. The realization that the planarity of radicals adjacent to an ester or amide group might resemble *Z*-enolates led to the hypothesis that allylic 1,3-strain (1*a*, 2*c*) could be one of the factors controlling stereoselectivity. The stereochemical outcome of the allylation reaction has been best rationalized by transition state **A** (Scheme 1*a*) (1, 2, 3, 4), which takes into account allylic 1,3-strain and electronic factors such as dipole–dipole repulsion (3) and hyperconjugative stabilization (3*e*). Thus, the *syn* isomer is the major compound obtained when such a radical intermediate, originating from the homolytic extrusion of a phenylseleno ether or a halogen, is reacted with allyltributyltin.

In response to this finding, our group hypothesized that a bidentate Lewis acid could, through complexation with the oxygen of the stereogenic center and the carbonyl of the ester, reposition the R_1 group onto the opposite face of the radical, thus allowing for a preferred attack on the top side leading to the *anti* product (Scheme 1*b*, transition state **B**). Our previous work in hydrogen-atom transfer reactions (7*a*, *e*) had shown that this approach could be feasible. Those findings inspired studies to show that the facial selectivity of a radical based allylation could be inverted (from *syn* to *anti*) through the simple expedient of adding $MgBr_2 \cdot OEt_2$ to the reaction mixture (7*b*). This strategy was further shown by both our group (7*c*) and Porter's group (11) to be successful in atom transfer reactions. Reported now are the full experimental details of chelation-controlled allylations of β-alkoxy esters, including studies on the importance of the stereochemistry of the starting material in such radical processes and on the possible formation of bidentate intermediates. Preliminary experiments that explain the need for an excess of $MgBr_2 \cdot OEt_2$ in the reaction and that elucidate further mechanistic details will also be presented.

2. Preparation of materials and standards

Secondary and tertiary iodides **9**–**13**, **16**, **19**–**21**, and bromides **14** and **17**, were prepared, by halo-etherification reaction, from the corresponding olefins **1**–**8** as shown in Table 1 (12, 13). Phenylselenides **15** and **18** were synthesized using a modification of the same method wherein AgOTf, a soluble silver salt, was used in place of $AgNO_3$. *Syn* substrates **16**–**18** were prepared from the appropriate *Z* olefin using

Scheme 2. (*a*) DIBAL-H, CH_2Cl_2, –78°C; (*b*) $Ph_3{=}C(R)CO_2Me$ (ethyl ester was used when R=Me), $PhCO_2H$, THF, reflux; (*c*) I_2, $NaHCO_3$, THF, 25°C; (*d*) *m*-CPBA, Et_2O, H_2O, 0 to 25°C; (*e*) TBSOTf, CH_2Cl_2, 2,6-lutidine, 0°C.



procedures analogous to those of the corresponding *anti* substrate (12). Silyl ethers **24**–**26** were readily derivated from the secondary alcohols (14) as described previously (Scheme 2) (15). Tetrahydrofurans **27**–**28** and tetrahydropyrans **29**–**30** were prepared in three steps as outlined in Scheme 2 (3*d*, 7*c*). DIBAL reduction of γ-butyrolatone or δ-valerolactone followed by Wittig olefination of the resultant lactols afforded the corresponding α,β-unsaturated esters. Cyclization of the olefins under kinetic conditions (I_2, $NaHCO_3$, THF, 25°C) (16) produced the expected iodoesters. Tetrahydrofurans **31** and **32** (17) were prepared by treating dihydrofuran with *m*-CPBA (H_2O–Et_2O, 82%) to give the hemiacetal that was then subjected to $Ph_3P{=}C(R)CO_2Et$ (THF, reflux). An iodocyclization reaction was done on the resulting compound. Protection of alcohols **31** and **32** (*t*-$BuMe_2SiOTf$, CH_2Cl_2, 2,6-lutidine, 0°C) gave either **33** or **34** (Scheme 2).

The relative configurations of the allylated products were established by independent synthesis and correlation of the NMR spectra (7*c*). In every case, the difference in chemical shift between the NMR resonances of the methylene protons in the allyl side chain (Δυ) for the *anti* diastereoisomers was greater than the Δυ values for the *syn* diastereoisomers. The chemical shifts of the resonances of the same hydrogens in the *anti* series were also consistently upfield to the resonances of the corresponding *syn* counterparts (18).

3. The radical-mediated allylations of α-halo- or α-phenylseleno-β-alkoxy esters

Treating a solution of 3-methyl-3-methoxy-2-iodopropionate **9** with allyltributyltin and 3 equivalents of $MgBr_2{\cdot}OEt_2$ gave a mixture of adducts in a 51:1 ratio favoring the *anti* product (Table 2, entry 1). Achieving interesting diastereoselectivity has been shown (vide infra) to require the presence of an excess of $MgBr_2{\cdot}OEt_2$. In the absence of $MgBr_2{\cdot}OEt_2$, substrate **9** showed a preference for the *syn* product, but poor selectivity was observed (entry 2). Other acyclic secondary iodides performed well under chelation-controlled conditions, affording *anti* isomers with excellent diastereofacial selectivity (entries 3, 5, 7). These substrates displayed a preference for the *syn* adduct in the absence of $MgBr_2{\cdot}OEt_2$ (entries 4, 6, 8). A greater selectivity was observed for substrate **12** when the reaction was conducted in toluene at –78°C (entry 8 versus 9).

Modifications to the β-alkoxy group (X) and their effects on the allylation reactions are shown in entries 7–15. Replacement of the methoxy group by a benzyloxy ether led to an erosion of *anti* diastereoselectivity under chelation-controlled conditions (entries 7 and 10). When the methoxy group was replaced by a silyl ether, the Lewis acid lost its influence in controlling the stereochemical outcome (entries 7, 8, 12–15). Generally, the steric congestion offered by the larger silyl groups (relative to Me) should preclude chelation of the oxygen with Lewis acid (19). As was hypothesized at the onset of this study, these results strongly suggest that the formation of cyclic intermediates, through $MgBr_2{\cdot}OEt_2$ complexation with the oxygens of the alkoxy and the carbonyl functions, is required in order to obtain *anti* adducts in this series of molecules.

In addition to *anti* iodide **12**, *anti* bromide **14** and *anti* phenylselenide **15** were also transformed into their corresponding allyl derivatives with excellent selectivity and yield when $MgBr_2{\cdot}OEt_2$ was present (entries 7, 16, and 18). For each substrate, the *anti* isomer was formed preferentially to the extent of 38:1, 19:1, and 65:1, respectively. Under the same conditions, *syn* iodide **16** led to reduced levels of diastereoselectivity and gave a 5:1 ratio in favor of the *anti* product (entry 20). By contrast, ratios greater than 20:1 were observed for *syn* bromide **17** and *syn* phenylselenide **18** (entries 22 and 24). Without Lewis acid, the allylation reactions favored the *syn* isomer (entries 8, 17, 19, 21, 23, and 25) in a consistent ratio of approximately 5:1. One should note that the presence of Lewis acid usually reverses the facial bias and is accompanied by a significant increase in diastereoselectivity (entries 7, 16, and 18 versus 8, 17, and 19, respectively).

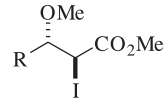
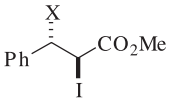
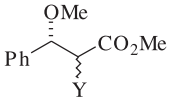
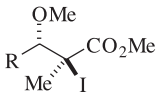
Tertiary iodides displayed excellent diastereoselectivity in chelation-controlled allylations (entries 26, 28, and 30). Since asymmetric quaternary centers are difficult to form, these reactions clearly have interesting synthetic utility (20). Compared to the secondary iodides, the tertiary iodides in the absence of $MgBr_2{\cdot}OEt_2$ showed lower reactivity[3] but slightly higher diastereoselectivity favoring the *syn* product (entries 2, 4, 6, and 8 versus 27, 29, and 31).

Assuming that the cyclic intermediate bearing a carbon-based radical was at the origin of the *anti* diastereoselectivity noted for the chelation-controlled allylation (the endocyclic effect) (Scheme 1*b*), we were anxious to evaluate the effect of a ring adjacent to the radical. Indeed, a bicyclic intermediate had to then be considered in this scenario.

Table 3 lists some preliminary results from this study. Note that entries 1 and 3 indicate a lower preference for the

[3] The lower reactivity is reflected by longer reaction times, even when conducted in hexanes at reflux.

Table 2. Radical allylation of various substrates under chelation and non-chelation control.

Entry	Substrate	Conditions[a]	Products		Ratio			Yield
			anti	*syn*	*anti*	:	*syn*	(%)
								
1	**9** : R=Me	A	**35**	**36**	51	:	1	79
2	**9** : R=Me	B	**35**	**36**	1	:	3	73
3	**10** : R=*i*Pr	A	**37**	**38**	>100	:	1	51
4	**10** : R=*i*Pr	B	**37**	**38**	1	:	3.3	82
5	**11** : R=c-C_6H_{11}	A	**39**	**40**	>100	:	1	95
6	**11** : R=c-C_6H_{11}	B	**39**	**40**	1	:	3.5	84
								
7	**12** : X=OMe	A	**41**	**42**	38	:	1	80
8	**12** : X=OMe	B[b]	**41**	**42**	1	:	5	82
9	**12** : X=OMe	B[c]	**41**	**42**	1	:	17	75
10	**13** : X=OBn	A	**43**	**44**	5	:	1	52
11	**13** : X=OBn	B[b]	**43**	**44**	1	:	10	60
12	**24** : X=OTMS	A	**45**	**46**	1	:	4	78
13	**24** : X=OTMS	B	**45**	**46**	1	:	3	84
14	**25** : X=OTBS	A	**47**	**48**	1	:	8	90
15	**25** : X=OTBS	B[b]	**47**	**48**	1	:	13	86
								
16	**14** : Y=Br (*anti*)	A	**41**	**42**	19	:	1	78
17	**14** : Y=Br (*anti*)	B[b]	**41**	**42**	1	:	5	73
18	**15** : Y=SePh (*anti*)	A	**41**	**42**	65	:	1	90
19	**15** : Y=SePh (*anti*)	B[b]	**41**	**42**	1	:	5	63
20	**16** : Y=I (*syn*)	A	**41**	**42**	5	:	1	69
21	**16** : Y=I (*syn*)	B[b]	**41**	**42**	1	:	6	84
22	**17** : Y=Br (*syn*)	A	**41**	**42**	20	:	1	80
23	**17** : Y=Br (*syn*)	B[b]	**41**	**42**	1	:	6	82
24	**18** : Y=SePh (*syn*)	A	**41**	**42**	38	:	1	76
25	**18** : Y=SePh (*syn*)	B[b]	**41**	**42**	1	:	6	86
								
26	**19** : R=Ph	A	**49**	**50**	>100	:	1	76
27	**19** : R=Ph	B	**49**	**50**	1	:	16	75
28	**20** : R=Me[d]	A	**51**	**52**	>100	:	1	65
29	**20** : R=Me[d]	B	**51**	**52**	1	:	4.5	44
30	**21** : R=Et[d]	A	**53**	**54**	90	:	1	80
31	**21** : R=Et[d]	B	**53**	**54**	1	:	4.8	45

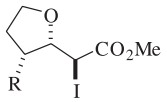
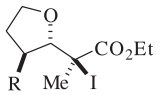
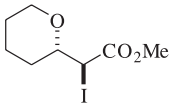
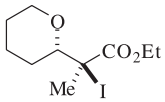
[a]A:2.0 equiv of allylSnBu$_3$, 3.0 equiv of MgBr$_2$·OEt$_2$, 0.2 equiv of Et$_3$B, CH$_2$Cl$_2$, –78°C. B:2.0 equiv of allylSnBu$_3$, 0.2 equiv of AIBN, hexanes, reflux.

[b]2.0 equiv of allylSnBu$_3$, 0.2 equiv of Et$_3$B, CH$_2$Cl$_2$, –78°C.

[c]2.0 equiv of allylSnBu$_3$, 0.2 equiv of Et$_3$B, toluene, –78°C.

[d]Ethyl ester was used.

Table 3. Radical allylation of tetrahydrofuran and tetrahydropyran derivatives under chelation and non-chelation control.

Entry	Substrate	Conditions[a]	Products *anti*	Products *syn*	Ratio *anti* : *syn*	Yield (%)
						
1	**27** : R = H	A	**55**	**56**	5 : 1	91
2	**27** : R = H	B	**55**	**56**	1 : 6	90
3	**33** : R = OTBS	A	**57**	**58**	6 : 1	80
4	**33** : R = OTBS	B	**57**	**58**	1 : 51	74
						
5	**28** : R = H	A	**59**	**60**	1 : 1	82
6	**28** : R = H	B	**59**	**60**	1 : 10	81
7	**34** : R = OTBS	A	**61**	**62**	7 : 1	70
8	**34** : R = OTBS	B	**61**	**62**	1 : 16	65
						
9	**29**	A	**63**	**64**	18 : 1	84
10	**29**	B	**63**	**64**	1 : 10	89
						
11	**30**	A	**65**	**66**	27 : 1	54
12	**30**	B	**65**	**66**	1 : 18	77

[a]A:2.0 equiv of allylSnBu$_3$, 3.0 equiv of MgBr$_2$·OEt$_2$, 0.2 equiv of Et$_3$B, CH$_2$Cl$_2$, –78°C. B:2.0 equiv of allylSnBu$_3$, 0.2 equiv of AIBN, hexanes, reflux.

anti product when the carbon bearing the radical was adjacent to a tetrahydrofuran (THF) ring and when MgBr$_2$·OEt$_2$ was present. This trend is magnified in the tertiary iodide series (entries 1 and 3 versus 5 and 7), where a 7:1 ratio favoring the *anti* isomer was the best selectivity obtained. In contrast, substrates bearing a tetrahydropyran (THP) ring α to the radical gave excellent diastereoselectivity under chelation-controlled conditions (entries 9 and 11). From the THF and THP substrates, *syn* isomers were obtained in good ratios in the absence of Lewis acid, considering that the reactions were performed in hexanes at reflux (entries 2, 4, 6, 8, 10, and 12). The bicyclic intermediate chelate with two 6-membered rings was clearly more efficient in inducing *anti* diastereoselectivity than the bicyclic intermediate with one 5- and one 6-membered ring.

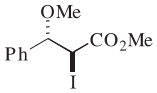
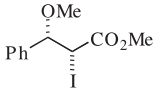
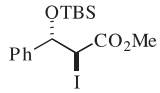
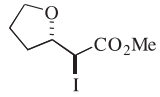
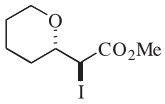
4. The role of MgBr$_2$·OEt$_2$. Determination of the amount of Mg^{2+} present in the allylation reaction by EDTA titration

With conditions for the chelation-controlled allylation optimized, we turned our attention to the problem of why an excess of MgBr$_2$·OEt$_2$ (3 equivalents) was needed to maximize diastereoselectivity. Table 4 (entries 1–3) shows that 0.25, 1, and 3 equivalents of MgBr$_2$·OEt$_2$, complexed with iodide **12,** gave ratios of 1.6:1, 7:1, and 38:1, respectively; however, no increase in ratio was noted with 5 equivalents of MgBr$_2$·OEt$_2$ (see entry 4). The results were surprising because the subequimolar amount of MgBr$_2$·OEt$_2$ was accompanied by insoluble material in the reaction medium. We had, of course, expected that one equimolar amount of Lewis acid would be sufficient for the chelation (vide infra), but our assumption had not taken into account the possibility of other competing intermediates.

To shed some light on the above results, we decided to determine the amount of Mg^{2+} actually present in the reaction mixture. The first step in doing so was to allow the Lewis acid to equilibrate at –78°C in the presence of iodide **12** (5 mL of 0.1 M solution) and allyltributyltin. After 10 min, 3 mL of the solution was filtered and analyzed for magnesium content by EDTA titration (21). Et$_3$B was added to the remaining solution to measure allylation efficacy and diastereoselectivity.

The amount of Mg^{2+} dissolved in solution increased concomitantly with the amount of MgBr$_2$·OEt$_2$ introduced at the beginning of the reaction (entries 1, 2, and 3). A maximum of 1.6 equivalents of dissolved Mg^{2+} was reached in the reaction containing 3 equivalents of MgBr$_2$·OEt$_2$ (entry 3). Concurrently, the *anti*:*syn* ratio of the allylated products steadily increased, giving a maximum selectivity of 38:1

Table 4. Determination of the amount of magnesium dissolved in allylation reaction mixtures by filtration and EDTA titration.

Entry	Substrate	Equivalents $MgBr_2 \cdot OEt_2$ added[a]	Equivalents Mg^{2+} in solution[b]	Ratio *anti* : *syn*
				
1	**12**	0.25	0.18	1.6 : 1
2	**12**	1.0	0.72	7 : 1
3	**12**	3.0	1.63	38 : 1
4	**12**	5.0	1.57	30 : 1
5	none	3.0	0.25[c]	
				
6	**16**	3.0	1.64	5 : 1
				
7	**25**	3.0	0.99	1 : 8
				
8	**27**	3.0	0.88	4.6 : 1
				
9	**29**	3.0	1.85	18 : 1

[a]Equivalents of $MgBr_2 \cdot OEt_2$ relative to the amount of substrate.

[b]Equivalents of Mg^{2+} measured relative to the amount of substrate.

[c]Experiment run under identical conditions relative to reactions with substrate present.

when the 3 equivalents of $MgBr_2 \cdot OEt_2$ were used. More than 3 equivalents of $MgBr_2 \cdot OEt_2$ did not increase further either the amount of Mg^{2+} in solution or the allylation ratio (entry 4).

In the absence of the substrate, the solubility of Mg^{2+} in CH_2Cl_2 at –78°C, relative to the amount of substrate normally used, was found to be 0.25 equivalent (entry 5). Note that the number of equivalents reported is always relative to the number of mmoles of substrate normally used. From the above results can be concluded that the intrinsic solubility of $MgBr_2 \cdot OEt_2$ in CH_2Cl_2 is low and that the substrate brings into solution an additional equivalent of Mg^{2+}, suggesting a strong interaction between the substrate and the Lewis acid. Note that there is a ca 30% excess of the added $MgBr_2 \cdot OEt_2$ that does not go into solution (entries 1 and 2), and that this amount in suspension can vary depending on the source of Lewis acid.[4] However, the ratio being the same with or without filtration strongly indicates that the insoluble materials have no effect on the outcome of the reactions.

This experimental protocol was repeated for *syn* isomer **16**, which gave the same amount of Mg^{2+} dissolved in solution but much less impressive diastereoselectivity, as already noted (entry 6).

One equivalent of Mg^{2+} was found for silyl compound derivative **25** in the presence of $MgBr_2 \cdot OEt_2$ compared to 0.25 equivalent without the substrate (entry 7 versus 1). Therefore, around 0.7 equivalent was brought in solution by the substrate. Qualitatively, this result is not so surprising. The Lewis acid can easily form a monodentate complex with substrate **25** since the latter presents a Lewis base functionality, the ester.

Similarly, THF derivative **27** (entry 8) and silyl compound **25** (entry 7), which formed a monodentate complex, extracted almost the same amount of Mg^{2+}. This contrasts the result for THP **29**, which brought into solution 1.85 equivalents of Mg^{2+} (entry 9). This is as much as methyl ether **12**, the bidentate chelate, brought. One has to remember that THF derivative **27** gave a much poorer ratio in favor of the *anti* product than THP derivative **29** afforded (entries 8 versus 9).

These measurements of Mg^{2+} dissolved in solution indicate that an equimolar complex with $MgBr_2 \cdot OEt_2$ is formed

[4]The material in suspension could be less soluble magnesium salts.

Table 5. ^1H and ^{13}C data of $MgBr_2 \cdot OEt_2$ in CD_2Cl_2 at –23 and 23°C in the presence and absence of **12**.

Entry	Mixture	Temperature (°C)	δ CH_2CH_3 (ppm)		δ CH_2CH_3 (ppm)	
			^1H	^{13}C	^1H	^{13}C
1	**12** + $MgBr_2 \cdot OEt_2$	–23	3.97	66.1	1.30	14.0
2	$MgBr_2 \cdot OEt_2$	–23	3.90	66.4	1.29	14.2
3	OEt_2	–23	3.40	65.9	1.12	15.3
4	**12** + $MgBr_2 \cdot OEt_2$	23	3.89	66.7	1.31	14.8
5	$MgBr_2 \cdot OEt_2$	23	3.80	66.7	1.29	14.8
6	OEt_2	23	3.44	66.1	1.15	15.5

with iodides **12** and **29,** which suggests a chelation. Such a condition seems to be essential for achieving good *anti* diastereoselection in this series of substrates. However, it may not be a sufficient condition, considering the modest diastereoselectivity noted for *syn* iodide **16**. This realization led us to another set of experiments, but this time using ^1H and ^{13}C NMR studies.

5. NMR studies of $MgBr_2 \cdot OEt_2$ complexes

The first consideration for this study was whether or not diethyl ether was present as a ligand on magnesium. Table 5 shows the ^1H and ^{13}C chemical shifts of diethyl ether measured alone (entries 3 and 6), in solution as part of the $MgBr_2 \cdot OEt_2$ (entries 2 and 5), or in chelate form using iodide **12** (entries 1 and 4). The latter two results being the same indicates that most if not all of the diethyl ether is still attached to the magnesium following the formation of complexes with **12**, regardless of temperature (entries 1–2, 4–5).

Previous studies done by Eliel (22), on chelates as intermediates in nucleophilic additions to α- and β-alkoxy ketones, have suggested that a strong chelation is consistent with a greater extent of change in the ^{13}C chemical shift of the carbonyl. Table 6 presents comparable NMR studies that consider various substrates in the presence of 3 equivalents of $MgBr_2 \cdot OEt_2$.

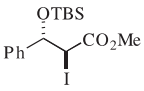
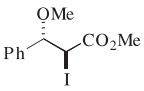
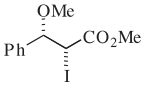
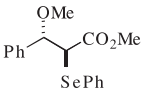
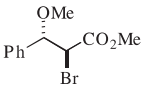
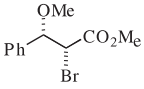
As seen in entry 1, the carbonyl signal of the ester for silyl ether **25** shifted only slightly downfield (2.7 ppm) when Lewis acid was present in the reaction, suggesting a preference for the formation of a monodentate complex with the ester. The difference in carbonyl chemical shift was significantly higher for methyl ether **12** (7.5 ppm), which is consistent with chelation (entry 2). The magnitude of these shifts concurs with Eliel's results (22).

Syn iodide **16** gave a shift of 4.8 ppm. As already shown by the solubility experiments, s*yn* iodide **16** formed a complex with $MgBr_2 \cdot OEt_2$ strong enough to bring into solution an amount of Lewis acid equivalent to that obtained from *anti* iodide **12** (Table 4, entry 6 versus 3). Yet, the ^{13}C data suggests that the *syn* iodide chelate should be qualitatively less strong than the one formed by the *anti* iodide (4.8 versus 7.5, Table 6, entries 2–3).[5] This would be consistent with the lower stereocontrol observed for **16** in chelation-controlled radical allylations.

Anti phenylselenide **15**, as well as bromides **14** and **17**, showed large displacements of the carbonyl signal upon the addition of $MgBr_2 \cdot OEt_2$ (entries 4–6) that correlate with strong chelation and high selectivity in the allylation. It would seem that the greater the carbonyl signal shift, the greater the *anti* preference; but this statement would need to be validated by additional experiments.

So far, the solubility experiments have shown that both monodentate and bidentate species bring Mg^{2+} in solution. The NMR studies have facilitated the ability to differentiate

Table 6. ^{13}C data of β-alkoxyesters in presence of saturating amount of $MgBr_2 \cdot OEt_2$ in CD_2Cl_2 at –23°C.

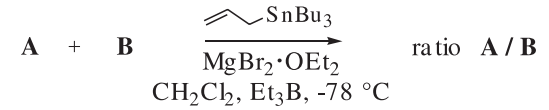
Entry	Substrate	Dd[a] C=O	Ratio[b] *anti* : *syn*
1	 **25**	2.7	1 : 8
2	 **12**	7.5	38 : 1
3	 **16**	4.8	5 : 1
4	 **15**	8.4	65 : 1
5	 **14**	6.4	19 : 1
6	 **17**	5.7	20 : 1

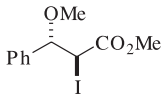
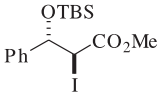
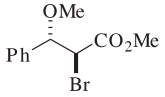
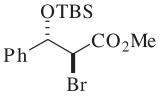
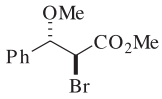
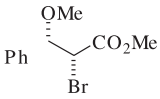
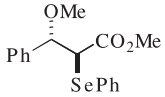
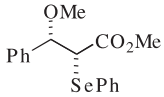
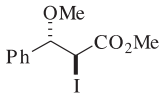
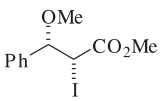
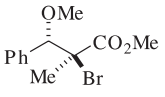
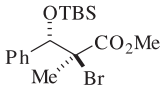
[a]Chemical shift of substrate with 3 equiv of $MgBr_2 \cdot OEt_2$ – chemical shift of substrate.

[b]See Table 1.

[5] The study of the THF derivative **27** and the THP derivative **29** under the same conditions did not give spectra of sufficient quality to be used in this study.

Table 7. Competition experiments.



Entry	Substrate **A**	Substrate **B**	Equivalents $MgBr_2 \cdot OEt_2$	Ratio[a] **A** : **B**
				
1	**12**	**25**	0	1 : 1.8
2	**12**	**25**	3	1 : 2
				
3	**14**	**26**	0	1 : 1
4	**14**	**26**	3	1 : 2
				
5	**14**	**17**	0	1 : 1
6	**14**	**17**	3	1 : 1
				
7	**15**	**18**	0	3 : 1
8	**15**	**18**	3	1 : 1
				
9	**12**	**16**	0	5 : 1
10	**12**	**16**	3	2 : 1
				
11	**67**	**68**	0[b]	1 : 1
12	**67**	**68**	5[b]	8 : 1

[a]0.5 equiv of $allylSnBu_3$, 0.5 equiv of substrates **A** and **B**.

[b]reaction was performed with Bu_3SnH, see ref 7e.

between these species prior to the reaction. Remaining to be determined is whether or not the species participate competitively in the establishment of the final product distribution resulting from the allylation reaction. Preliminary experiments involving competition reactions have been designed to shed some light in this regard. (Vide infra.)

6. Competition reactions

All of the competition experiments were performed with two substrates of equimolar amounts, which were dissolved in CH_2Cl_2 together with allyltributyltin in either the absence or presence of $MgBr_2 \cdot OEt_2$ (3 equivalents). Only half an equivalent of allyltributyltin was used to obtain 50% conversion to the allylated products. NMR spectra of the crude reaction isolates were recorded to determine the relative conversion of each reactant. The results of these experiments are summarized in Table 7.

As seen in entry 1, a 1:1.8 ratio of unreacted methyl ether **12** to unreacted silyl ether **25** was noted, indicating that the methyl ether reacted faster than the silyl ether in the absence of Lewis acid. Similar results were obtained when $MgBr_2 \cdot OEt_2$ was present in the reaction mixture (entry 2). For the analogous bromide series, the consumption of methyl ether **14** (bidentate) was found to be slightly higher than that of silyl ether **26** (monodentate) in the presence of

$MgBr_2 \cdot OEt_2$ (entry 4). In the control experiment (entry 3), performed in the absence of Lewis acid, species **14** and **26** reacted at the same rate.

Next, the relative stereochemistry of bromides, selenides, and iodides was examined. In the presence of Lewis acid, *anti* and *syn* bromides **14** and **17** reacted at the same rate, as did the corresponding selenides **15** and **18** (entries 6 and 8). *Syn* iodide **16** reacted faster than *anti* iodide **12** both in the presence and absence of Lewis acid (entries 9 and 10). Notably, both *syn* selenide **18** and *syn* iodide **16**[6] reacted faster than their *anti* counterparts in the control experiments (entries 7 and 9). This result is without explanation at this time.

Two reactions were then done in parallel with *anti* silyloxy iodide **25** under standard conditions. The sole variable was $MgBr_2 \cdot OEt_2$, which was present in only one of the reactions. Comparable yields of allylated products (80%) were repeatedly obtained; however, the time to complete the reaction was shorter when Lewis acid was present.

Apparent from these studies is that the chelate intermediate, proposed in the case of the methyl ethers, does not have a significant advantage from a reactivity standpoint over the silyl ethers, which reacted only as monodentate complexes or free substrates. As demonstrated by entries 4 and 12, under chelation-controlled conditions, the allylation reaction differs from the hydrogen-atom transfer reactions (7*e*) with the bromide substrates. In the latter case, silyl ether **68** was consumed eight times faster than methyl ether **67**, indicating that the bidentate pathway was at a strong disadvantage.

7. Discussion

The chelation of the Lewis acid to the β-alkoxy ester is envisioned as the initial step of the allylation process (Scheme 3).[7] Subsequent homolytic cleavage of the α-halide or α-phenylselenide by attack of the tin radical ($Bu_3Sn\cdot$) gives a cyclic free-radical intermediate, which may benefit from the endocyclic (chelated) effect. Note that variations in the alkoxy function, and their ultimate effect on the ratio, support strongly the involvement of an endocyclic radical (Table 2, entries 7–15). The presence of the chelate prior to the generation of the radical is also supported by our ^{13}C NMR studies. The chelate is strong enough to bring into solution an equimolar amount of magnesium.

Once formed, the chelated radical may exist in two conformers, **75** and **76**, that lead to transition states **E** and **F**, respectively. The *anti* predictive transition state **E** should be favored over the *syn* predictive **F** on both electronic and steric grounds. Electronically, the electron-poor radical should be better stabilized, through hyperconjugation, by the overlap of the C—R (R = alkyl) bond in **E** than by that of the C—H bond in **F** (3*e*). From a steric standpoint, when R_2 is a methyl group, an additional allylic 1,2-strain between R and R_2 should increase the energy of transition state **F** relative to that of **E**.

Two other transition states should also be examined. Transition state **C** considers the radical in the absence of Lewis acid, while transition state **D** reflects the radical in a monodentate complex form. Both **C** and **D** are *syn* predictive transition states.

The rate of halogen abstraction by an electropositive tin radical should be enhanced by the presence of an adjacent electron-withdrawing group, such as an ester. A more electrophilic ester, obtained via coordination with a Lewis acid, should further facilitate the abstraction rate. The rate of addition should also be improved by the reaction of a more electrophilic radical with an electron rich double bond, such as the one on the allyltributyltin. Therefore, transition state **E** should be of lower energy than **C**. Indeed, allylation was apparently faster with $MgBr_2 \cdot OEt_2$ in the parallel reactions performed for the competition experiments.

One should note that transition states **D** and **E** both benefit from activation by the Lewis acid. The fact that the methoxy and silyloxy derivatives reacted at comparable rates in competitive experiments suggests the possibility that the monodentate acyclic pathway could actually be as rapid as, and therefore an alternative to, the cyclic pathway. As depicted in Scheme 3, a potential equilibrium could exist between **74** and **75** (or **70** and **71**). After all, these species differ by only a simple folding of the substrate molecule. If such equilibrium were to exist, the difference in energy between transition states **D** and **E** would likely dictate the outcome of the reaction.

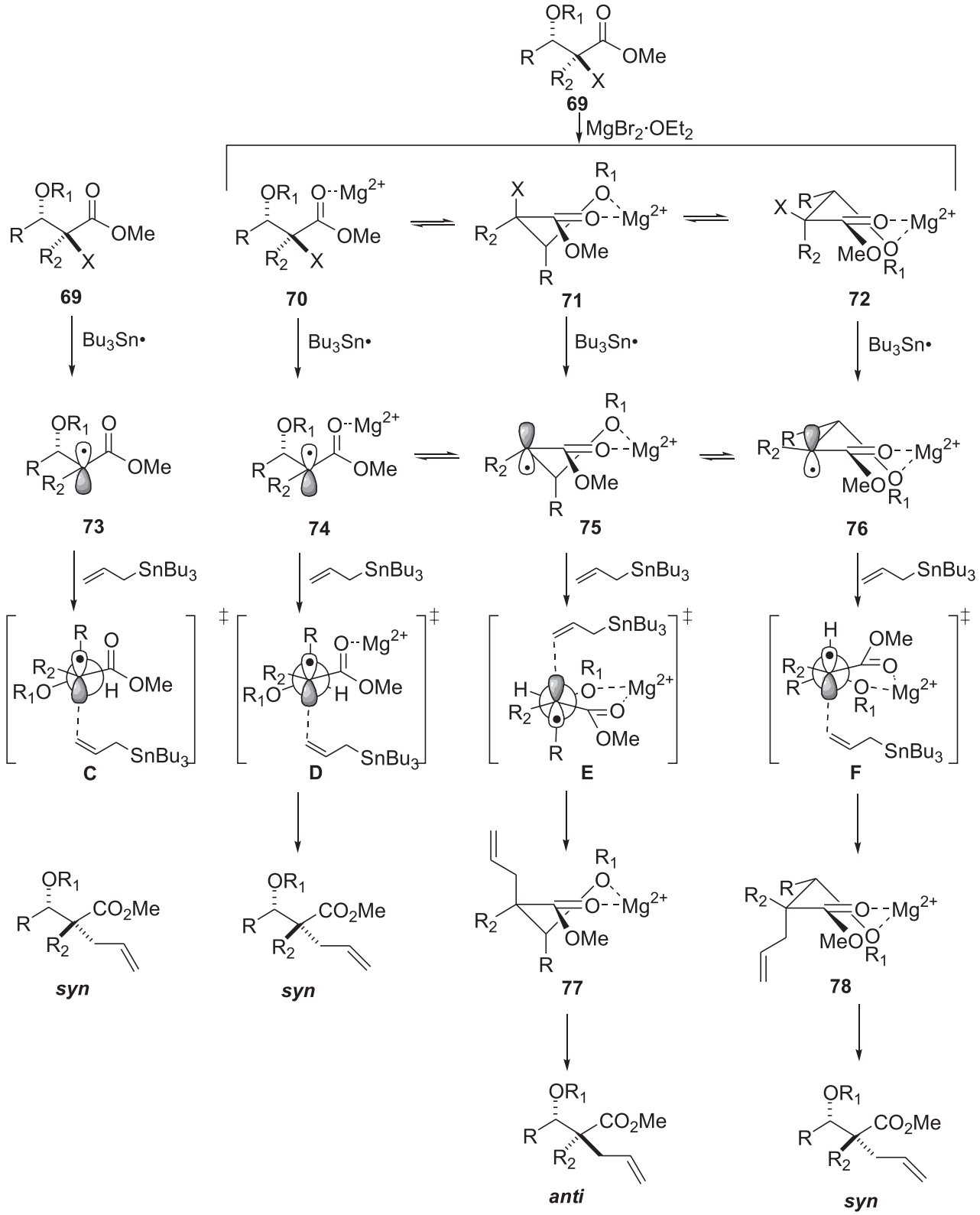
The comparable reaction rates of the silyloxy and methoxy derivatives suggest that transition states **D** and **E** are of similar energy in the allylation. This result contrasts that of competition experiments involving hydrogen-atom transfer reactions, which showed the monodentate pathway to be favored over the bidentate (7*e*), indicating that a transition state similar to **D** would be lower in energy than a transition state analogous to **E** when tributyltin hydride is involved. It should be noted that the major product obtained originated, in both cases, from the attack on the top face of the radical (transition state **E**) in the presence of $MgBr_2 \cdot OEt_2$.

It should be remembered that significant levels of selectivity and differences in ratios, depending upon the stereochemistry of the halides and selenides (precursors to the same radical), were noted for the allylation reactions (vide supra). These results, along with those obtained from competition experiments, are more consistent with the equilibrium between **74** and **75** being rather slow, which suggests that the reactions are dependent upon the pre-existing mixture of complexes **70**, **71**, and **72**.

This dependency can explain the low selectivity obtained for the THF derivatives. A potential rationale illustrated by Scheme 4 shows that, for these substrates, the formation of a bicyclic intermediate may be impaired by the development of eclipsing interactions between the C–O bond and an Mg–Br bond in the *cis* bicyclo complex. An additional eclipsing interaction could be observed between the C–I bond and the Mg–Br (or $Mg–OEt_2$) bond if the geometry of the magnesium is either square planar pyramidal or bipyramidal trigonal. Such interaction implies that the preexisting complex mixture could have contained monodentate complexes or uncomplexed substrates. The smaller amount of Mg^{2+} found in solution supports this argument. By contrast, less

[6] The ratios were also verified by ^1H NMR prior to the allylation.
[7] The ligands on Mg^{2+} have been excluded for simplicity.

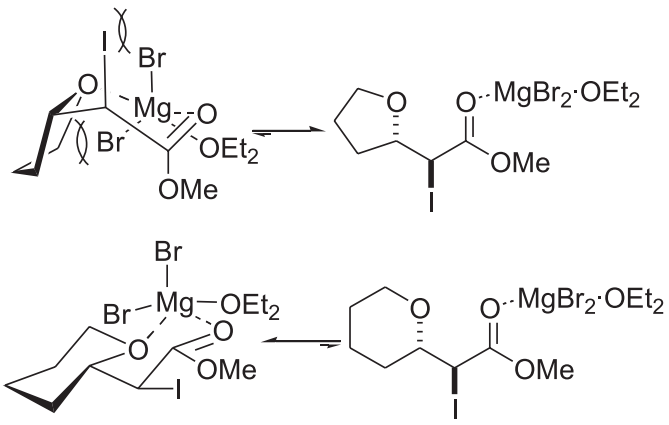
Scheme 3.



steric interaction is present for the bicyclo complex with THP. The pre-equilibrium for the THP substrates seems to favor the chelate formation. This conclusion is further supported by the high level of selectivity obtained for this series and by the amount of Mg^{2+} found in solution.

This discussion may not have sufficiently appreciated an important contributor: the $MgBr_2 \cdot OEt_2$. What is the nature of the complexes formed with the alkoxy esters and the $MgBr_2 \cdot OEt_2$? For instance, could there be two alkoxy esters serving as ligands on a magnesium (23) for the monodentate

Scheme 4.



complex (**70′**, Scheme 5)?[7] If so, an excess of $MgBr_2 \cdot OEt_2$ could then be important in the pre-equilibrium phase for assuring the formation of another species involving one alkoxy ester as a ligand, depicted as bidentate complex **71** (Scheme 3). This would explain why the equilibrium between **74** and **75** is slow. Indeed, a ligand (another substrate) might have to be displaced in order for **74′** to reach **75**; a process that may not be fast enough to allow for kinetic selection between the two pathways (Scheme 4).

Only recently has the structure of $MgBr_2 \cdot OEt_2$ been resolved (24). The structure of complexes generated by alkoxy esters and $MgBr_2 \cdot OEt_2$ remain to be better defined. This is the topic of ongoing research.

8. Conclusion

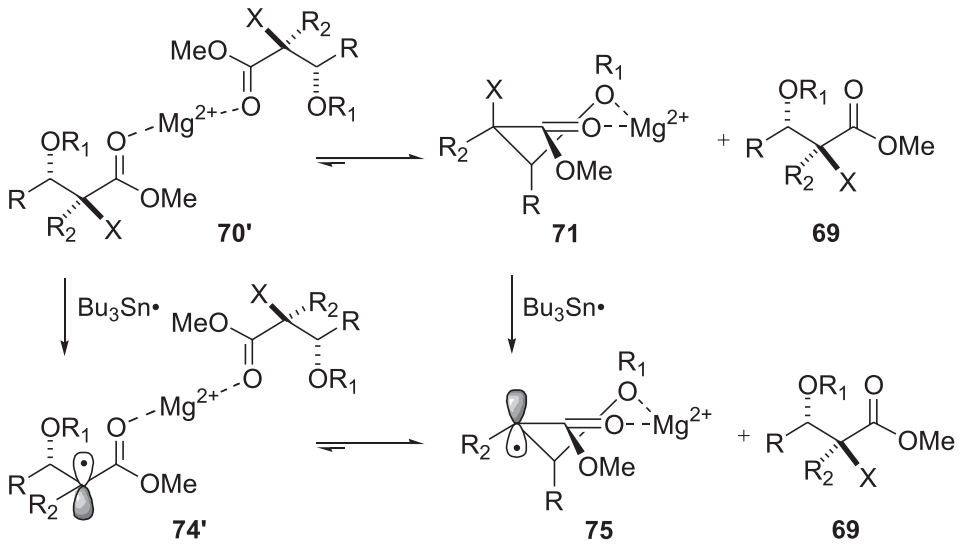
The described chemistry represents a significant advance in the field of stereocontrol in radical reactions. Our studies of substituent effects clearly establish the scope and limitations of the chelation-controlled radical allylation of α-halo or α-phenylseleno-β-alkoxy esters. This reaction tolerates a wide variety of substitutions and, except for THF and *syn* iodide substrates, gives a high level of diastereoselectivity favoring *anti* products. This is true even for secondary iodides, bromides, and phenylselenides, as well as tertiary iodides. The requirement of radical initiation and the fact that the reaction can be inhibited are indicative of a free radical process. Other types of acyclic radical-based reactions are presently being evaluated. The influence of Lewis acid on the outcome of these reactions will also be studied.

9. Experimental section

General methods

All reactions requiring anhydrous conditions were conducted under a positive nitrogen atmosphere in oven-dried glassware using standard syringe techniques. The anhydrous solvents were purchased from Aldrich and were used as received. i-Pr_2NH and Et_3N were freshly distilled from CaH_2 under N_2 atmosphere. Allyltributyltin and triethylborane (1 M solution in hexane) were also purchased from Aldrich and used as received. Flash chromatography was performed on Merck silica gel 60 (0.040–0.063 mm) using nitrogen pressure. Analytical thin-layer chromatography (TLC) was carried out on precoated (0.25 mm) Merck silica gel F-254 plates. The uncorrected melting points were determined on an electrothermal melting point apparatus. NMR spectra were recorded via Bruker AC200, AMX300, ARX400, or Varian VXR-400S spectrometers, with chemical shifts reported relative to residual chloroform at 7.26 ppm. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. CI and EI mass spectra were recorded on an MF 50 TATC instrument operating at 70 eV. FAB mass spectra were performed on a VG AutospecQ. Capillary GC analyses were performed on a Shimadzu GC-9AM instrument or a HP 6890 instrument using 0.25 mm × 30 m Supelcowax™10 and SE-30 columns.

Scheme 5.



Preparation of starting materials

The preparation and characterization data of **9**–**12** (7*d*), **14**–**21** (7*d*), **25** (7*d*), **27**–**30** (3*d*, 7*d*), and **34** (7*a*) have been reported previously.

*Methyl (±)-(2*S**,3*S**)-2-iodo-3-benzyloxy-3-phenylpropanoate (**13**)*: To a solution of methyl cinnamate (381 mg, 2.35 mmol) in benzylalcohol (3.5 mL) were added successively $AgNO_3$ (305 mg, 2.82 mmol) and iodine (710 mg, 2.82 mmol). The reaction mixture was stirred at room temperature in the dark for 24h, then filtered through celite and concentrated. The residue was taken up in EtOAc and washed with 10% $Na_2S_2O_3$, water, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated to afford a residue, which was then purified by flash chromatography (CH_2Cl_2) to afford pure iodide **13** as a white solid (568 mg, 61%); mp 50–51°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 4.31 (d, *J* = 10.6 Hz, 1H), 4.40 (d, *J* = 10.6 Hz, 1H), 4.45 (d, *J* = 11.3 Hz, 1H), 4.80 (d, *J* = 11.3 Hz, 1H), 7.18–7.41 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.80, 52.99, 71.89, 82.89, 127.85, 127.97, 128.33, 128.49, 129.08, 137.46, 137.58, 170.80; IR ($CHCl_3$) 3030, 2950, 1740, 1455 cm^{-1}; MS (FAB) 397 (MH, 8), 289 (35), 154 (49), 91 (100); HRMS calcd. for $C_{17}H_{18}O_3I$ (MH): 397.0301, found: 397.0290 (2.7 ppm). Anal. calcd. for $C_{17}H_{17}IO_3$: C 51.53, H 4.32; found: C 51.36, H 4.26.

*Methyl (±)-(2*S**,3*S**)-2-iodo-3-[(trimethylsilyl)oxy]-3-phenylpropanoate (**24**)*: To a solution of iodohydrin **22** (7*d*) (713 mg, 2.32 mmol) and 2,6-lutidine (540 μL, 4.64 mmol) in CH_2Cl_2 (25 mL) at –78°C was added slowly trimethylsilyl trifluoromethanesulfonate (670 μL, 3.48 mmol). After the reaction was judged complete by TLC, the mixture was diluted with ether and washed with water, saturated NH_4Cl, and brine. Drying over $MgSO_4$ followed by flash chromatography (4% EtOAc in hexanes) afforded silyl ether **24** as a colorless oil (720 mg, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ –0.05 (s, 9H), 3.81 (s, 3H), 4.37 (d, *J* = 10.2 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H) 7.34–7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –0.26, 27.44, 52.66, 77.21, 127.50, 128.03, 128.44, 140.32, 170.73; IR (neat) 2955, 1742, 1495, 1435, 1252, 1166, 1070, 873 cm^{-1}; MS (FAB) 379 (MH, 11), 363 (24), 289 (77), 179 (100), 121 (42); HRMS calcd. for $C_{13}H_{20}IO_3Si$ (MH) 379.0226, found: 379.0209 (4.6 ppm). Anal. calcd. for $C_{13}H_{19}IO_3Si$: C 41.28, H 5.06; found: C 41.11, H 4.80.

*Methyl (±)-(2*S**,3*S**)-2-bromo-3-[((1,1-dimethylethyl)dimethylsilyl)oxy]-3-phenylpropanoate (**26**)*: Compound **26** was prepared with bromohydrin **23** (14) (1.20 g, 4.62 mmol) and *t*-butyldimethylsilyl trifluoromethanesulfonate (1.60 mL, 6.92 mmol) following the procedure described above for **24**. Purification by flash chromatography (CH_2Cl_2) afforded silyl ether **26** as a white solid (1.64 g, 95%). Mp 38°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ –0.30 (s, 3H), 0.01 (s, 3H), 0.78 (s, 9H), 3.82 (s, 3H), 4.21 (d, *J* = 10.0 Hz, 1H), 4.98 (d, *J* = 10.0 Hz, 1H) 7.33–7.37 (m, 5H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ –5.42, –4.75, 17.95, 25.49, 49.29, 52.85, 76.61, 127.62, 128.21, 128.63, 140.02, 169.53; IR ($CDCl_3$) 2850, 1745, 1590, 1450, 1355, 1315, 1080, cm^{-1}; MS (FAB) 373 (MH, 12), 317 (17), 221 (15), 131 (13), 73 (100); HRMS calcd. for $C_{16}H_{25}{}^{79}BrO_3Si$ (MH) 372.0756, found: 372.0746 (2.7 ppm). Anal. calcd. for $C_{16}H_{25}BrO_3Si$: C 51.47, H 6.75; found: C 51.55, H 6.92.

*Ethyl (±)-(2*S**)-2-[(2*S**,3*R**)-3-((1,1-dimethylethyl)dimethylsilyl)oxytetrahydrofuran-2-yl]-2-iodopropanoate (**33**)*: Compound **33** was prepared with iodoester **31** (17) (775 mg, 2.58 mmol) and *t*-butyldimethylsilyl trifluoromethanesulfonate (0.90 mL, 3.87 mmol) following the procedure described above for **24**. Purification by flash chromatography (5% EtOAc in hexanes) afforded silyl ether **33** (908 mg, 85%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.22 (s, 3H), 0.95 (s, 9H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.91–2.09 (m, 1H), 4.04–4.12 (m, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.35–4.36 (m, 2H), 4.53–4.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.46, –4.09, 13.69, 18.01, 18.22, 25.92, 35.96, 61.79, 68.69, 72.64, 84.41, 170.54; IR (neat) 2960, 1740, 1470, 1260 cm^{-1}; MS (CI, CH_4) *m*/*z* 415 (MH^+, 95), 399 (37), 369 (100), 357 (27), 283 (39), 155 (9). Anal. calcd. for $C_{14}H_{27}IO_4Si$: C 40.58, H 6.57; found: C 40.93, H 6.43.

Allylation products

The preparation and characterization data of **35**–**42**, **47**–**56**, **63**, and **64** have been reported previously (7*d*).

General procedure for the allylation of α-iodoesters under chelation-controlled conditions (Conditions A)

To a stirred solution of α-iodoester (1 equiv) in dry CH_2Cl_2 (0.1 M) at –78°C was added $MgBr_2{\cdot}OEt_2$ (3 equiv). The mixture was stirred for 15 min at the same temperature before allyltributyltin (2 equiv) and Et_3B (0.2 equiv of a 1.0 M solution in hexanes) were added. The resulting suspension was stirred at –78°C, and 0.2 equivalent of Et_3B was added each 30 min until the reaction was judged complete by TLC. 1,3-Dinitrobenzene (0.2 equiv) was then added to the solution and the mixture was stirred an additional 15 min at –78°C. The reaction mixture was poured into a saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

*Methyl (±)-(2*S**,3*S**)-2-[propen-3-yl]-3-benzyloxy-3-phenylpropanoate (**43**)*: Compound **43** was prepared with iodoester **13** (97 mg, 0.24 mmol) following the general procedure described above. A 5:1 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (5% EtOAc in hexanes) afforded allylated products **43** and **44** (40 mg, 52%). **43**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.77–1.83 (m, 1H), 2.05–2.18 (m, 1H), 2.81–2.94 (m, 1H), 3.73 (s, 3H), 4.21 (d, *J* = 11.8 Hz, 1H), 4.39 (d, *J* = 11.8 Hz, 1H), 4.47 (d, *J* = 9.9 Hz, 1H), 4.87–4.98 (m, 2H), 5.47–5.59 (m, 1H), 7.17–7.45 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.22, 51.45, 53.07, 70.45, 82.58, 116.80, 127.43, 127.62, 127.75, 128.12, 128.40, 128.56, 134.43, 138.89, 137.97, 174.17; IR (neat) 2980, 1738, 1642, 1434, 1195 cm^{-1}; MS (FAB) 311 (MH, 100), 203 (22), 171 (25), 143 (87), 133 (83); HRMS calcd. for $C_{20}H_{23}O_3$ (MH) 311.1647, found: 311.1659 (–3.7 ppm).

*Methyl (±)-2-[propen-3-yl]-3-[(trimethylsilyl)oxy]-3-phenylpropanoate (**45** and **46**)*: Compounds **45** and **46** were prepared with iodoester **24** (63 mg, 0.17 mmol) following the general procedure described above. A 1:4 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (4% EtOAc in hexanes) afforded a mixture of allylated products **45** and **46** as a colorless oil (38 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ **45 (2*S**,3*S**)**: –0.05 (s, 9H), 1.77–1.84 (m, 1H), 2.11–2.19 (m, 1H), 3.72 (s, 3H), 4.72 (d, *J* = 9.6 Hz, 1H), 4.92–5.00 (m, 2H), 5.54–5.60 (m, 1H), 7.20–7.35 (m, 5H), **46 (2*R**,3*S**)**: 0.01 (s, 9H), 2.47–2.54 (m, 2H), 2.71–2.76 (m, 1H), 3.44 (s, 3H), 4.81 (d, *J* = 7.9 Hz, 1H), 5.01–5.08 (m, 2H), 5.68–5.82 (m, 1H), 7.20–7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ **45**: 0.04, 33.11, 51.27, 55.10, 76.76, 116.52, 126.91, 127.44, 127.83, 128.18, 134.64, 141.92, 174.82, **46**: 0.05, 32.76, 51.07, 55.19, 76.59, 116.30, 126.29, 127.44, 127.94, 135.59, 142.58, 173.31; IR (neat) 3065, 2953, 1736, 1641, 1495, 1454, 1250, 1194, 1087, 995 cm^{-1}; MS (FAB) 293.5 (MH, 58), 277.4 (30), 179 (100), 143 (55), 120 (12), 104 (20); HRMS calcd. for $C_{16}H_{25}SiO_3$ (MH) 293.1573, found: 293.1584 (–3.8 ppm).

*Ethyl (±)-(2*S*)-2-[(2S*,3R*)-3-((1,1-dimethylethyl)dimethylsilyl)oxytetrahydrofuran-2-yl]-2-[propen-3-yl]-propanoate (**57**)*: Compound **57** was prepared with iodoester **33** (30 mg, 0.08 mmol) following the general procedure described above. A 6:1 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (5% EtOAc in hexanes) afforded allylated products **57** and **58** (19 mg, 80%). **57**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.92 (s, 9H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.72–1.87 (m, 1H), 2.00–2.08 (m, 1H), 2.26–2.31 (m, 2H), 2.92–2.96 (m, 1H), 3.80–3.85 (m, 2H), 3.95–4.00 (m, 1H), 4.15–4.22 (m, 2H), 4.32–4.38 (m, 1H), 4.99–5.10 (m, 2H), 5.70–5.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.61, –4.82, 14.23, 17.79, 25.66, 33.24, 35.77, 45.62, 60.23, 66.18, 71.50, 83.63, 116.64, 134.47, 174.38; IR (neat) 2930, 2850, 1735, 1460, 1170, 1040 cm^{-1}; MS (FAB) 329 (MH, 85), 283 (85), 169 (27). Anal. calcd. for $C_{17}H_{32}O_4Si$: C 62.15, H 9.82; found: C 61.72, H 9.61.

*Ethyl (±)-(2*S*)-2-[(2S*)-tetrahydrofuran-2-yl]-2-[propen-3-yl]-2-methylpropanoate (**59**)*: Compound **59** was prepared with iodoester **28** (135 mg, 0.45 mmol) following the general procedure described above. A 1:1 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (10% EtOAc in hexanes) afforded allylated products **59** and **60** (79 mg, 82%). **59**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.69–1.92 (m, 4H), 2.08 (dd, *J* = 7.7, 13.5 Hz, 1H), 2.49 (dd, *J* = 7.1, 13.5 Hz, 1H), 3.75–3.86 (m, 2H), 4.07–4.11 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 5.03–5.10 (m, 2H), 5.65–5.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.15, 15.97, 25.92, 26.28, 40.42, 49.96, 60.04, 68.47, 83.43, 117.84, 133.64, 175.09; IR (neat) 2990, 1730, 1640, 1460, 1380, 1140, 1060 cm^{-1}; MS (FAB) m/z 213 (MH^+, 100), 167 (22), 155 (26), 137 (74), 123 (30), 109 (40); HRMS calcd. for $C_{12}H_{21}O_3$ *m*/*z* (MH^+) 213.1491, found: 213.1484 (3.1 ppm). Anal. calcd. for $C_{12}H_{20}O_3$: C 67.89, H 9.50; found: C 67.92, H 9.36.

*Ethyl (±)-(2*S*)-2-[(2S*,3R*)-3-((1,1-dimethylethyl)dimethylsilyl)oxytetrahydrofuran-2-yl]-2-[propen-3-yl]-2-methylpropanoate (**61**)*: Compound **61** was prepared with iodoester **34** (77 mg, 0.18 mmol) following the general procedure described above. A 7:1 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (5% EtOAc in hexanes) afforded allylated products **61** and **62** (43 mg, 70%). **61**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.89 (s, 9H), 1.11 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.74–1.80 (m, 1H), 1.85–1.94 (m, 1H), 2.14 (dd, *J* = 7.9, 13.5 Hz, 1H), 2.60 (dd, *J* = 6.6, 13.5 Hz, 1H), 3.82–3.95 (m, 3H), 4.11–4.19 (m, 2H); 4.29–4.32 (m, 1H), 5.04–5.10 (m, 2H), 5.67–5.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.82, –4.61, 14.13, 16.73, 17.68, 25.59, 36.40, 40.37, 48.82, 60.45, 66.91, 72.85, 91.26, 118.04, 133.53, 174.76; IR (neat) 2980, 1735, 1460, 1110, 830 cm^{-1}; MS (FAB) *m*/*z* 343 (MH^+, 13), 327 (16), 285 (100), 211 (29), 201 (18), 171 (12); HRMS calcd. for $C_{18}H_{35}O_4Si$ (MH^+) *m*/*z* 343.2305, found: 343.2290 (4.3 ppm).

*Ethyl (±)-(2*S*)-2-[(2S*)-tetrahydropyran-2-yl]-2-[propen-3-yl]-2-methylpropanoate (**65**)*: Compound **65** (59 mg, 54%) was prepared with iodoester **30** (148 mg, 0.48 mmol) following the general procedure described above. A 27:1 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (10% EtOAc in hexanes) afforded allylated product **65** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.27–1.57 (m, 5H), 1.85–1.89 (m, 1H), 2.07 (dd, *J* = 7.8, 13.5 Hz, 1H), 2.38 (dd, *J* = 7.2, 13.5 Hz, 1H), 3.33–3.41 (m, 1H), 3.48–3.52 (m, 1H), 3.93–3.97 (m, 1H), 4.07–4.22 (m, 2H), 5.01–5.07 (m, 2H), 5.63–5.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.11, 15.90, 23.58, 25.31, 25.97, 40.01, 50.29, 60.07, 68.86, 82.51, 117.76, 133.67, 176.03; IR (neat) 2930, 2870, 1725, 1640, 1435, 1080, 920 cm^{-1}; MS (FAB) *m*/*z* 227 (MH^+, 100), 199 (13), 185 (33), 151 (38), 135 (28); HRMS calcd. for $C_{13}H_{23}O_3$ (MH^+) *m*/*z* 227.1647, found: 227.1654 (–3.0 ppm).

General procedure for the allylation of α-iodoesters in the absence of Lewis acid (Conditions B)

To a solution of α-iodoester (1 equiv.) in hexanes (0.1 M) at 23°C were added allyltributyltin (2 equiv) and AIBN (0.2 equiv). After being allowed to reflux, the mixture was stirred until the reaction was judged complete by TLC.

Methyl (±)-(2R,3S*)-2-[propen-3-yl]-3-benzyloxy-3-phenylpropanoate (**44**)*: To a solution of iodoester **13** (175 mg, 0.44 mmol) in CH_2Cl_2 (4.5 mL) at –78°C were added allyltributyltin (275 μL, 0.88 mmol) and Et_3B (90 μL of a 1.0 M solution in hexanes, 0.09 mmol). The reaction mixture was stirred at –78°C with 0.2 equivalent of Et_3B added each 30 min until the reaction was judged complete by TLC. A 1:10 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (5% EtOAc in hexanes) afforded allylated products **43** and **44** (82 mg, 60%). **44**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41–2.57 (m, 1H), 2.66–2.78 (m, 1H), 2.86–2.92 (m, 1H), 3.41 (s, 3H), 4.22 (d, *J* = 11.6 Hz, 1H), 4.44 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 8.8 Hz, 2H), 4.95–5.09 (m, 2H), 5.78–5.81 (m, 1H), 7.25–7.43 (m,

10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.31, 51.12, 53.71, 70.57, 81.30, 116.64, 127.36, 127.62, 127.84, 128.08, 128.31, 128.32, 135.33, 137.94, 139.50, 172.93; IR (neat) 3030, 2949, 1736, 1641, 1454, 1356, 1166, 1067, 920 cm^{-1}; MS (FAB) *m/z* 311 (MH^+, 26), 233 (13), 143 (58), 133 (100), 121 (20), 105 (15), 91 (100). Anal. calcd. for $C_{20}H_{22}O_3$: C 77.39, H 7.14; found: C 77.19, H 7.30.

*Ethyl (±)-(2*R*)-2-[(2*S*,3*R*)-3-((1,1-dimethylethyl)dimethylsilyl)oxytetrahydrofuran-2-yl]-2-[propen-3-yl]-propanoate (**58**)*: Compound **58** was prepared with iodoester **33** (52.5 mg, 0.13 mmol) following the general procedure described above. A 1:51 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (5% EtOAc in hexanes) afforded allylated product **58** as a colorless oil (30.5 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.78–1.91 (m, 1H), 2.00–2.18 (m, 1H), 2.44–2.52 (m, 1H), 2.60–2.67 (m, 1H), 2.81–2.92 (m, 1H), 3.73–4.25 (m, 5H), 4.38–4.43 (m, 1H), 4.97–5.11 (m, 2H), 5.69–5.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.40, –4.49, 14.19, 17.87, 25.62, 34.26, 36.14, 44.33, 59.82, 65.82, 72.27, 81.66, 116.74, 134.83, 173.38; IR (neat) 2910, 1730, 1645, 1460, 1370, 1240, 1175, 1070, 820 cm^{-1}; MS (FAB) *m/z* 329 (MH^+, 12), 283 (16), 271 (82), 149 (100); HRMS calcd. for $C_{17}H_{33}O_4Si$ *m/z* (MH^+) 329.2148, found: 329.2130 (5.5 ppm).

*Ethyl (±)-(2*R*)-2-[(2*S*)-tetrahydrofuran-2-yl]-2-[propen-3-yl]-2-methylpropanoate (**60**)*: Compound **60** was prepared with iodoester **28** (163 mg, 0.55 mmol) following the general procedure described above. A 1:10 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (10% EtOAc in hexanes) afforded allylated products **59** and **60** (94 mg, 81%). **60**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.68–1.91 (m, 4H), 2.32 (dd, *J* = 7.9, 13.6 Hz, 1H), 2.54 (dd, *J* = 6.8, 13.6 Hz, 1H), 3.73–3.85 (m, 2H), 4.02–4.07 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 5.03–5.10 (m, 2H), 5.67–5.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.12, 15.86, 26.01, 26.87, 41.59, 49.83, 60.17, 68.49, 82.85, 117.62, 134.05, 174.94; IR (neat) 2990, 1730, 1645, 1465, 1380, 1140, 1065 cm^{-1}; MS (EI) *m/z* 213 (MH^+, 14), 171 (10), 142 (21), 69.5 (100); HRMS cacld for $C_{12}H_{21}O_3$ *m/z* (MH^+) 213.1491, found: 213.1499 (–3.9 ppm). Anal. calcd. for $C_{12}H_{20}O_3$: C 67.89, H 9.50; found: C 67.96, H 9.35.

*Ethyl (±)-(2*R*)-2-[(2*S*,3*R*)-3-((1,1-dimethylethyl)dimethylsilyl)oxytetrahydrofuran-2-yl]-2-[propen-3-yl]-2-methylpropanoate (**62**)*: Compound **62** was prepared with iodoester **34** (33.5 mg, 0.08 mmol) following the general procedure described above. A 1:16 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (5% EtOAc in hexanes) afforded allylated products **61** and **62** (17.5 mg, 65%). **62**: Colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.86 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.67–1.97 (m, 2H), 2.19 (dd, *J* = 7.7, 13.6 Hz, 1H), 2.57 (dd, *J* = 6.9, 13.6 Hz, 1H), 3.77–3.98 (m, 3H), 4.02–4.22 (m, 2H), 4.30–4.36 (m, 1H), 5.01–5.09 (m, 2H), 5.60–5.78 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ –4.86, –4.33, 14.19, 17.43, 17.75, 25.68, 36.59, 40.93, 48.90, 60.47, 67.03, 73.37, 91.81, 117.98, 133.93, 174.66; IR (neat) 2950, 1725, 1645, 1460, 1375, 1250, 1070, 910, 830, 770 cm^{-1}; MS (CI, CH_4) *m/z* 343 (MH^+, 25), 327 (19), 285 (9), 269 (8), 257 (12), 210 (100), 169 (10).

*Ethyl (±)-(2*R*)-2-[(2*S*)-tetrahydropyran-2-yl]-2-[propen-3-yl]-2-methylpropanoate (**66**)*: Compound **66** was prepared with iodoester **30** (187 mg, 0.60 mmol) following the general procedure described above. A 1:18 ratio of *anti*:*syn* products was determined by GC and ^{1}H NMR analyses of the crude isolate. Purification by flash chromatography (10% EtOAc in hexanes) afforded allylated product **66** as a colorless oil (105 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.36–1.53 (m, 5H), 1.82–1.86 (m, 1H), 2.30 (dd, *J* = 7.9, 13.6 Hz, 1H), 2.50 (dd, *J* = 6.9, 13.6 Hz, 1H), 3.36–3.46 (m, 2H), 3.97–4.02 (m, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 5.01–5.08 (m, 2H), 5.65–5.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.12, 15.98, 23.60, 26.01, 26.32, 40.88, 50.26, 60.12, 68.99, 81.77, 117.50, 134.33, 174.98; IR (neat) 2920, 1725, 1450, 1300, 1210, 1085, 910 cm^{-1}; MS (FAB) *m/z* 227 (MH^+, 100), 199 (13), 185 (27), 151 (31), 143 (15), 135 (25); HRMS cacld for $C_{13}H_{23}O_3$ *m/z* (MH^+) 227.1647, found: 227.1656 (–3.9 ppm). Anal. calcd. for $C_{13}H_{22}O_3$: C 68.99, H 9.80; found: C 68.58, H 10.17.

Determination of magnesium concentrations in allylation reaction mixtures by filtration and EDTA titration

Preparation of the sample: To a stirred solution of α-iodoester (0.5 mmol) in dry CH_2Cl_2 (5 mL) at –78°C was added $MgBr_2{\cdot}OEt_2$. The mixture was stirred for 15 min at this temperature before allyltributyltin (1.0 mmol) was added. A 3 mL aliquot of the solution was removed from the flask using a syringe equipped with a filter (Millex HV 0.45 mm). This 3 mL aliquot was then concentrated under reduced pressure.

Titration of magnesium by EDTA: Deionized water (5 mL) and CH_2Cl_2 (5 mL) were added to the sample. The mixture was then shaken and poured into a 125 mL erlenmeyer flask. Deionized water (10 mL), NH_3–NH_4Cl buffer solution at pH = 10 (4 mL), and six drops of Calmagite indicator were added successively to the stirred solution, which was then titrated with a standardized EDTA solution (0.099 M, Aldrich) until the color changed completely from red to blue. The amount of Mg (mmol) in the total sample = 0.099 mmol/mL × V_{EDTA} added (mL) × (5/3).

The buffer pH = 10 was prepared from concentrated NH_4OH solution (57 mL) and 7 g of NH_4Cl in sufficient deionized water to give 100 mL of solution.

The calmagite indicator solution was prepared by adding 0.05 g of calmagite to 50 mL of deionized water.

^{13}C observations of β-alkoxyesters in the presence of a saturating amount of $MgBr_2{\cdot}OEt_2$ in CD_2Cl_2 at –23°C.

To a stirred solution of α-iodoester (1 equiv) in CD_2Cl_2 (0.1 M) at –23°C was added $MgBr_2{\cdot}OEt_2$ (3 equiv). The solution was then stirred for 15 min at the same temperature. A 1.5 mL aliquot of solution was removed from the flask using a syringe equipped with a filter (Millex HV 0.45 mm). The aliquot was placed in an NMR tube and kept at –23°C

until the ^{13}C NMR spectrum was recorded on a Bruker ARX400 spectrometer at that temperature.

Competition experiments

Substrates **A** (0.5 equiv) and **B** (0.5 equiv) were dissolved in $CDCl_3$ and the mixture was analyzed by NMR ^1H integration to determine the exact **A**:**B** ratio before the allylation reaction. The solution was concentrated and redissolved in dry CH_2Cl_2 (0.1 M) at –78°C before $MgBr_2 \cdot OEt_2$ (3 equiv) was added. The mixture was then stirred for 15 min at the same temperature, and allyltributyltin (0.5 equiv) as well as Et_3B (0.2 equiv of a 1.0 M solution in hexanes) were subsequently added. The resulting suspension was stirred at –78°C, and 0.2 equivalent of Et_3B was added each 30 min until the reaction was judged complete by TLC. The reaction mixture was then poured into a saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Another ^1H NMR analysis was done on the crude mixture to determine the exact **A**:**B** ratio after the allylation reaction.

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11. Supplementary material available

^{13}C NMR spectra for compounds **23**, **43**, **45**–**46**, **58**, **61**, **62**, and **65**. Tables of NMR chemical shift correlations for allylated products (11 pages) have been deposited as supplementary material and may be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, Ontario, Canada, K1A 0S2.

References

1. For reviews see: (*a*) N.A. Porter, B. Giese, and D.P. Curran. Acc. Chem. Res. **24**, 296 (1991); (*b*) D.C. Liotta, K.A. Durkin, and J.J. Soria. Chemtracts: Org. Chem. **5**, 197 (1992); (*c*) G.S. Miracle, S.M. Cannizzaro, and N.A. Porter. Chemtracts: Org. Chem. **6**, 147 (1993); (*d*) W. Smadja. Synlett, **2**, 154 (1994); (*e*) B. Giese, W. Damm, and R. Batra. Chemtracts: Org. Chem. **7**, 355 (1994); (*f*) D.P. Curran, N.A. Porter, and B. Giese. *In* Stereochemistry of radical reactions—concepts, guidelines and synthetic applications. VCH, New York. 1996; (*g*) P. Renaud and M. Gerster. Angew. Chem. Int. Ed. Engl. **37**, 2562 (1998).
2. Selected examples: (*a*) P.A. Bartlett and J.L. Adams. J. Am. Chem. Soc. **102**, 337 (1980); (*b*) D.J. Hart and H.-C. Huang. Tetrahedron Lett. **26**, 3749 (1985); (*c*) D.J. Hart and R. Krishnamurthy. J. Org. Chem. **57**, 4457 (1992); (*d*) B. Giese, W. Damm, F. Wetterich, and H.-G. Zeitz. Tetrahedron Lett. **33**, 1863 (1992); (*e*) D.P. Curran and P.S. Ramamoorthy. Tetrahedron, **49**, 4841 (1993); (*f*) T. Morikawa, Y. Washio, S. Harada, R. Hanai, T. Kayashita, H. Nemoto, M. Shiro, and T. Taguchi. J. Chem. Soc. Perkin Trans. 1, **3**, 271 (1995); (*g*) C.J. Easton and M.C. Merrett. Tetrahedron, **53**, 1151, (1997); (*h*) H. Suzuki, S. Aoyagi, and C. Kibayashi. J. Org. Chem. **60**, 6114 (1995).
3. (*a*) Y. Guindon, C. Yoakim, R. Lemieux, L. Boisvert, D. Delorme, and J.-F. Lavallée. Tetrahedron Lett. **31**, 2845 (1990); (*b*) Y. Guindon, J.-F. Lavallée, L. Boisvert, C. Chabot, D. Delorme, C. Yoakim, D. Hall, R. Lemieux, and B. Simoneau. Tetrahedron Lett. **32**, 27 (1991); (*c*) K. Durkin, D. Liotta, J. Rancourt, J.-F. Lavallée, L. Boisvert, and Y. Guindon. J. Am. Chem. Soc. **114**, 4912 (1992); (*d*) Y. Guindon, C. Yoakim, V. Gorys, W.W. Ogilvie, D. Delorme, J. Renaud, G. Robinson, J.-F. Lavallée, A. Slassi, G. Jung, J. Rancourt, K. Durkin, and D. Liotta. J. Org. Chem. **59**, 1166 (1994); (*e*) Y. Guindon, A. Slassi, J. Rancourt, G. Bantle, M. Bencheqroun, L. Murtagh, E. Ghiro, and G. Jung. J. Org. Chem. **60**, 288 (1995); (*f*) Y. Guindon and R.C. Denis. Tetrahedron Lett. **39**, 339 (1998); (*g*) Y. Guindon, G. Jung, B. Guérin, and W.W. Ogilvie. Synlett, **3**, 213 (1998).
4. Selected examples: (*a*) D. Crich and J.W. Davies. Tetrahedron Lett. **28**, 4205 (1987); (*b*) N.A. Porter, D.M. Scott, B. Lacher, B. Giese, H.G. Zeitz, and H.J. Lindner. J. Am. Chem. Soc. **111**, 8311 (1989); (*c*) D.P. Curran, H. Qi, S.J. Geib, and N.C. DeMello. J. Am. Chem. Soc. **116**, 3131 (1994); (*d*) N.A. Porter, R.L. Carter, C.L. Mero, M.G. Roepel, and D.P. Curran. Tetrahedron, **52**, 4181 (1996), and refs. therein; (*e*) C. Andrés, J.P. Duque-Soladana, J.M. Iglesias, and R. Pedrosa. Tetrahedron Lett. **37**, 9085 (1996); (*f*) I.J. Rosenstein and T.A. Tynan. Tetrahedron Lett. **39**, 8429 (1998); (*g*) D.P. Curran, S. Geib, and N. DeMello. Tetrahedron, **55**, 5681 (1999).
5. (*a*) P. Renaud and Ribezzo. J. Am. Chem. Soc. **113**, 7803 (1991); (*b*) P. Renaud, N. Moufid, L.H. Kuo, and D.P. Curran. J. Org. Chem. **59**, 3547 (1994); (*c*) D.P. Curran and L.H. Kuo. J. Org. Chem. **59**, 3259 (1994); (*d*) M. Nishida, E. Ueyama, H. Hayashi, Y. Ohtake, Y. Yamaura, E. Yanaginuma, O. Yonemitsu, A. Nishida, and N. Kawahara. J. Am. Chem. Soc. **116**, 6455 (1994); (*e*) P. Renaud, T. Bourquard, M. Gerster, and N. Moufid. Angew. Chem. Int. Ed. Engl. **33**, 1601 (1994); (*f*) M. Nishida, H. Hayashi, Y. Yamaura, E. Yanaginuma, O. Yonemitsu, A. Nishida, and N. Kawahara. Tetrahedron Lett. **36**, 269 (1995); (*g*) M. Murakata, H. Tsutsui, and O. Hoshino. J. Chem. Soc. Chem. Commun. **4**, 481 (1995); (*h*) H. Urabe, K. Kobayashi, and F. Sato. J. Chem. Soc. Chem. Commun. **10**, 1043 (1995); (*i*) N. Moufid, P. Renaud, C. Hassler, and B. Giese. Helv. Chim. Acta. **78**, 1006 (1995).
6. (*a*) T. Toru, Y. Watanabe, M. Tsusaka, and Y. Ueno. J. Am. Chem. Soc. **115**, 10464 (1993); (*b*) K. Rück and H. Kunz. Synthesis, 1018 (1993); (*c*) H. Nagano and Y. Kuno. J. Chem. Soc. Chem. Commun. **8**, 987 (1994); (*d*) Y. Yamamoto, S. Onuki, M. Yumoto, and N. Asao. J. Am. Chem. Soc. **116**, 421 (1994); (*e*) H. Urabe, K. Yamashita, K. Suzuki, K. Kobayashi, and F. Sato. J. Org. Chem. **60**, 3576 (1995); (*f*) M. Gerster, L. Audergon, N. Moufid, and P. Renaud. Tetrahedron Lett. **37**, 6335 (1996); (*g*) M.P. Sibi, C.P. Jasperse, and J.G. Ji. J. Am. Chem. Soc. **117**, 10779 (1995); (*h*) M.P. Sibi and J.G. Ji. Angew. Chem. **2**, 190 (1996); (*i*) M.P. Sibi, J.J. Shay, and J.G. Ji. Tetrahedron Lett. **38**, 5955 (1997); (*j*) C. Ha, O.M. Musa, F.N. Martinez, and M. Newcomb. J. Org. Chem. **62**, 2704 (1997).
7. (*a*) Y. Guindon, J.-F. Lavallée, M. Linas-Brunet, G. Horner, and J. Rancourt. J. Am. Chem. Soc. **113**, 9701 (1991); (*b*) Y. Guindon, B. Guérin, C. Chabot, N. Mackintosh, and W.W. Ogilvie. Synlett, **5**, 449 (1995); (*c*) Y. Guindon, B. Guérin, C. Chabot, and W.W. Ogilvie. J. Am. Chem. Soc. **118**, 12528 (1996); (*d*) Y. Guindon, Z. Liu, and G. Jung. J. Am. Chem. Soc. **119**, 9289 (1997); (*e*) Y. Guindon and J. Rancourt. J. Org. Chem. **63**, 6554 (1998).
8. (*a*) A. Waldner, A. De Mesmaeker, P. Hoffmann, T. Mindt, and T. Winkler. Synlett, **2**, 101 (1991); (*b*) A. De Mesmaeker, A. Waldner, P. Hoffmann, and T. Mindt. Synlett, **11**, 871 (1993).

9. (*a*) D.P. Curran, A.C. Abraham, and H.-T. Liu. J. Org. Chem. **56**, 4335 (1991); (*b*) E.P. Kündig, L.-H. Xu, and P. Romanens. Tetrahedron Lett. **36**, 4047 (1995); (*c*) S. Hanessian, H. Yang, and R. Schaum. J. Am. Chem. Soc. **118**, 2507 (1996).
10. (*a*) M.P. Sibi, C.P. Jasperse, and J.G. Ji. J. Am. Chem. Soc. **117**, 10779 (1995); (*b*) J.H. Wu, R. Radinov, and N.A. Porter. J. Am. Chem. Soc. **117**, 11029 (1995); (*c*) M.P. Sibi and J.G. Ji. J. Am. Chem. Soc. **118**, 3063 (1996); (*d*) M.P. Sibi and J.G. Ji. Angew. Chem. Int. Ed. Engl. **2**, 190 (1996); (*e*) M.P. Sibi, J.G. Ji, J.H. Wu, S. Gurtler, and N.A. Porter. J. Am. Chem. Soc. **118**, 9200 (1996); (*f*) A.-R. Fhal and P. Renaud. Tetrahedron Lett. **38**, 2661 (1997); (*g*) M.P. Sibi and J.G. Ji. J. Org. Chem. **62**, 3800 (1997); (*h*) M. Blumenstein, K. Schwarzkopf, and J.O. Metzer. Angew. Chem. **3**, 235 (1994).
11. C.L. Mero and N.A. Porter. J. Am. Chem. Soc. **121**, 5155 (1999).
12. L.C. Vishwakarma and J.S. Walia. J. Indian Chem. Soc. **53**, 156 (1976).
13. The olefins were either purchased or prepared from the corresponding acids, which were commercially available. The olefin 5 was prepared by an esterification of phenylpropiolic acid (MeOH, H_2SO_4, reflux) followed by hydrogenation with modified Lindlar catalyst. See J. Rajaram, A.P.S. Narula, H.P.S. Chawla, and S. Dev. Tetrahedron, **39**, 2315 (1983).
14. For **22** see reference 7*c*, and for **23** see: J. Read and A. Andrews. J. Chem. Soc. **119**, 1774 (1921).
15. R.C. Cambie, D. Chambers, P.S. Rutledge, and P.D. Woodgate. J. Chem. Soc. Perkin Trans. 1, **20**, 2231 (1977).
16. G. Cardillo and M. Orena. Tetrahedron, **46**, 3321 (1990), and refs. therein.
17. Y. Guindon and M. Labelle. J. Am. Chem. Soc. **111**, 2204 (1989). See also reference 7*a*.
18. A similar observation has been observed in the case of reduction. See reference 4 and: F.H. Gouzoules and R.A. Whitney. J. Org. Chem. **51**, 2024 (1986).
19. Silyl ether is known to be less efficient in complexation with Lewis acid. See X. Chen, E.R. Hortelano, E.L. Eliel, and S.V. Frye. J. Am. Chem. Soc. **114**, 1778 (1992), and refs. therein.
20. K. Fuji. Chem. Rev. **93**, 2037 (1993).
21. (*a*) D.G. Christian. *In* Analytical chemistry. John Wiley & Sons Ed., New York. 1986. pp. 586–587; (*b*) D.A. Skoog, D.M. West, and F.J. Holler. *In* Fundamentals of analytical chemistry. Saunders College Publishing Ed., New York. 1988; (*c*) R.A. Day and A.L. Underwood. *In* Quantitative analysis. Prentice-Hall Ed., New York. 1986.
22. X. Chen, E.R. Hortelano, E.L. Eliel, and S.V. Frye. J. Am. Chem. Soc. **114**, 1778 (1992).
23. Under varying conditions, magnesium has been isolated with coordination numbers from two to ten, with six being the most frequent. C.E. Holloway and M. Melnik. J. Organomet. Chem. **465**, 1 (1994).
24. A. Ecker, C. Üffing, and H. Schnöckel. Chem. Eur. J. **2**, 1112 (1996).