3788 *J. Org. Chem.* **2002,** *67,* 3788−3795

Effect of Adjacent Chiral Tertiary and Quaternary Centers on the Metal-Catalyzed Allylic Substitution Reaction

Holly L. Sebahar, Kazuhiro Yoshida, and Louis S. Hegedus*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

hegedus@lamar.colostate.edu

Received January 15, 2002

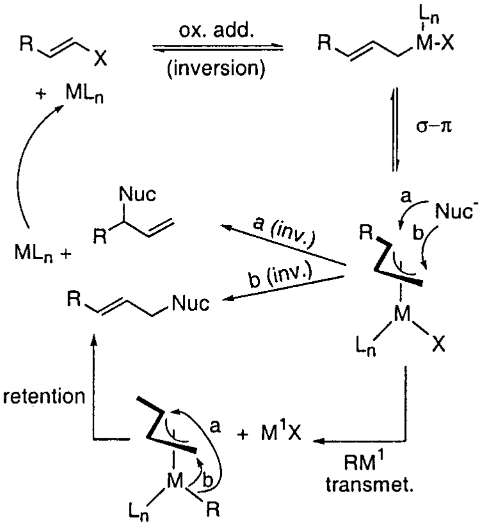
The metal-catalyzed allylic substitution reaction of **5a**,**b** and **6a** was examined. Reaction with stabilized nucleophiles led to exclusive attack at the less-hindered allylic terminus, and the stereoselectivity varied with the bidentate ligand used but favored retention. The yields and reaction times were improved with the use of microwaves. Alkylation via transmetalation was only observed with phenyl- and vinylstannatranes and gave regio- and stereoselectivity opposite those observed with the stabilized anions. The epimeric carbonates **5a** and **5b** displayed very different reactivities. Catalysts containing metals other than palladium were completely unreactive and led to recovered starting material.

Introduction

The metal-catalyzed allylic substitution reaction has been widely studied and has emerged as a powerful synthetic tool for the formation of carbon−carbon, carbon−heteroatom, and carbon−hydrogen bonds (Scheme 1).[1] The development of enantioselective versions utilizing chiral ligands further increased the synthetic utility of the process.[2]

The palladium-catalyzed reaction has been the most extensively studied and applied. It proceeds with overall retention of configuration at the reacting center, the result of inversion for the oxidative addition step, and attack of the nucleophile from the face opposite the metal. Attack of the *less*-substituted allylic terminus usually predominates, although regioselectivity can vary[3] depending on the nucleophile,[4] the ligand,[5] remote electronic effects in the substrate,[6] and through the use of tethered directing groups.[7] In contrast, main-group organometallic nucleophiles react with overall *inversion* via nucleophilic attack at the metal (transmetalation) followed by delivery of the nucleophile from the *same* face as the metal (Scheme 1).[3b,8] The regiochemistry of the alkylation depends on the main-group metal used.

Scheme 1



Although much less studied, metals other than palladium also catalyze this allylic substitution reaction, often with complementary stereo- and regioselectivity. Molybdenum catalysts favor attack at the more-substituted allylic terminus with small nucleophiles, but more sterically demanding nucleophiles attack the less-substituted end. Tungsten catalysts result in attack at the more-substituted allylic terminus regardless of the steric bulk of the nucleophile.[9] Both rhodium[10] and iridium[11] promote attack at the more-substituted allylic terminus,

---

[1] (a) Godleski, S. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, Chapter 3.3. (b) Davies, J. A. In *Comprehensive Organometallic Chemistry II*; Wilkinson, B., Stone, F. G. A., Abel, E. W., Eds.: Pergamon Press: Oxford, U.K., 1995; Vol. 9, p 291. (c) Harrington, P. J. In *Comprehensive Organometallic Chemistry II*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, U.K., 1995; Vol. 12, p 798. (d) Tsuji, J. *Palladium Reagents and Catalysts. Innovations in Organic Synthesis*; John Wiley: Chichester, 1995.

[2] (a) Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Trost, B. M. *Acc. Chem. Res.* **1996**, *29*, 355.

[3] For a detailed discussion, see: (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 4545; (b) Hoke, M. E.; Brescia, M.-R.; Bogaczyk, DeShong, P.; King, B. W.; Crimmins, M. T. *J. Org. Chem.* **2002**, *67*, 327.

[4] Keinan, E.; Sahai, M. *J. Chem. Soc., Chem. Commun.* **1984**, 648.

[5] (a) van Haaren, R. J.; Goubitz, K.; Fraanje, J.; van Strijdonck, G. P. F.; Oevering, H.; Coussens, B.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Inorg. Chem.* **2001**, *40*, 3363. (b) Blacker, A. J.; Clarke, M. L.; Loft, M. S.; Williams, J. M. J. *Org. Lett.* **1999**, *1*, 1969. (c) Amatore, C.; Jutland, A.; Barki, M. A. M.; Meyer, G.; Mottier, L. *Eur. J. Inorg. Chem.* **2001**, 873. (d) Åkermark, B.; Hansson, S.; Krakenberger, B.; Zetterberg, K.; Vitagliano, A. *Chem. Scr.* **1986**, 525.

[6] (a) Szabo, K. J. *Chem. Soc. Rev.* **2001**, *30*, 136; (b) Branchadell, V.; Moreno-Mañas, M. I.; Pajuelo, F.; Pleixats, R. *Organometallics* **1999**, *18*, 4934.

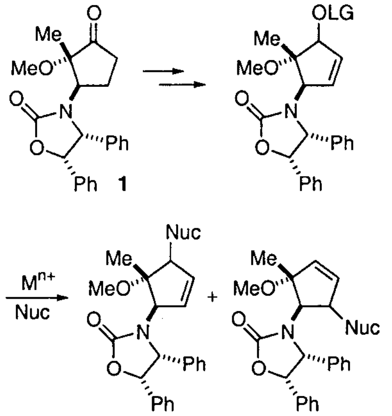
[7] (a) Itami, K.; Koike, T.; Yoshida, Yoshida, J.-I. *J. Am. Chem. Soc.* **2001**, *123*, 6957. (b) Kraft, M. E.; Fu, Z.; Procter, M. J.; Wilson, A. M.; Dasse, O. A.; Hirosawa, C. *Pure Appl. Chem.* **1998**, *70*, 1083. (c) Farthing, C. N.; Kocovský, P. *J. Am. Chem. Soc.* **1998**, *120*, 6661.

[8] (a) Takamashi, S-i.; Mori, K. *Liebigs Ann. Chem./Rec.* **1997**, 825. (b) Castaño, A. M.; Ruano, M.; Echavarren, A. M. *Tetrahedron Lett.* **1996**, *37*, 6591. (c) Farina, V.; Baker, S. R.; Benigni, D. A.; Sapino, C., Jr. *Tetrahedron Lett.* **1988**, *29*, 5739. (d) Del Valle, L.; Stille, J. K.; Hegedus, L. S. *J. Org. Chem.* **1990**, *55*, 3019. (e) Fiaud, J.-C.; Legros, J.-Y. *J. Org. Chem.* **1987**, *52*, 1907.

10.1021/jo0200318 CCC: $22.00

although only relatively simple systems have been studied to date. Even fewer examples of nickel-[12] and ruthenium-catalyzed[13] systems are known.

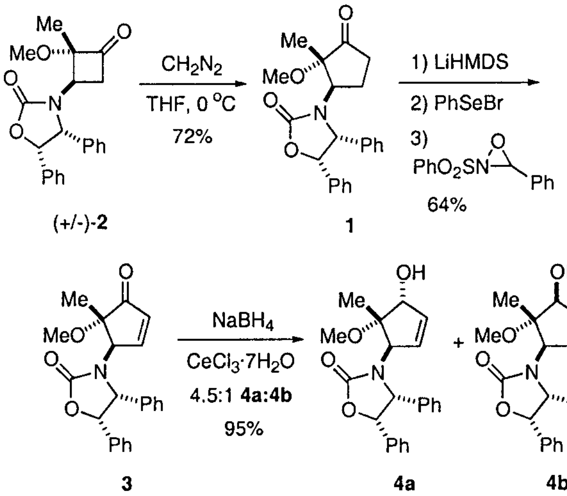
Research in these laboratories has recently focused on the utilization of chiral cyclopentanones, derived from the ring expansion[14] of photochemically produced cyclobutanones,[15] as intermediates in natural product synthesis.[16] Cyclopentanone **1**[14] could also be easily converted into substrates for the metal-catalyzed allylic substitution reaction, which would allow for the study of the effect of highly substituted *β*-positions (eq 1). Specifically, studies directed toward probing the effects of chiral tertiary and quaternary centers adjacent to the *π*-system of an allylic substrate on the regio- and stereoselectivity as well as the overall reactivity of the process were undertaken. Also, metal complexes including palladium, iridium, rhodium, tungsten, and molybdenum were compared as catalysts, and the results are presented below.



(1)

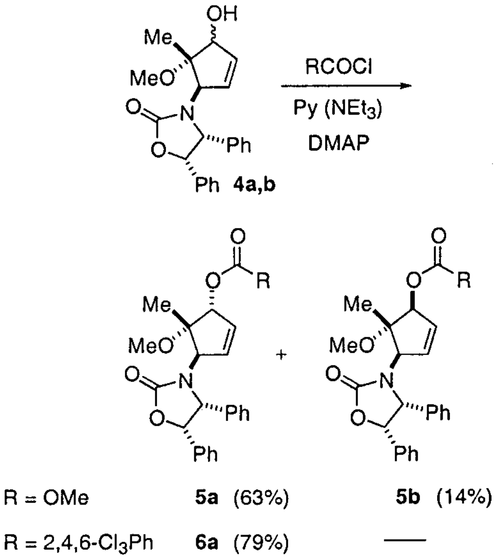
Results and Discussion

Preparation of Starting Materials. Synthesis of the substrates to be used in these studies began with known racemic cyclobutanone **2** (eq 2).[14,15] Ring expansion with diazomethane to cyclopentanone **1** proceeded in 72% yield. α-Selenation followed by oxidation and spontaneous elimination gave cyclopentenone **3** in 64% yield. Reduction with Luche conditions provided a 4.5:1 mixture of epimeric allylic alcohols.[16b]



(2)

Because the diastereoisomeric alcohols were difficult to separate, the mixture was acylated. The resulting esters were easily separated (eq 3). While both **4a** and **4b** readily underwent acylation by methyl chloroformate to form **5a** and **5b**, the considerably more sterically hindered trichlorobenzoyl chloride only underwent reaction with the less sterically hindered **4a**, forming **6a** and recoverable **4b**. The acetate and diethyl phosphate esters were also prepared. However, the acetate proved unreactive and the phosphate proved unstable, so only the carbonates **5a**,**b** and trichlorobenzoate **6a** were studied.



(3)

Palladium-Catalyzed Reactions. Substrates **5** and **6** are quite sterically hindered for both the oxidative addition step and the nucleophilic attack step. The allylic leaving group occupies a neopentyl position, and in **5a** and **6a** a large oxazolidinone group also resides on the face of attack. The resulting *π*-allylpalladium complex is similarly hindered, although the allylic terminus remote from the site of the leaving group in the complexes from **5a** and **6a** should be relatively accessible. A catalyst sufficiently nucleophilic to promote oxidative addition but electrophilic enough to allow nucleophilic attack was needed.

---

(9) (a) Malkov, A. V.; Baxendale, I. R.; Mansfield, D. J.; Kocovský, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1234. (b) Trost, B. M.; Hildrbrand, S.; Dogra, K. *J. Am. Chem. Soc.* **1999**, *121*, 10416. (c) Glorius, F.; Pfaltz, A. *Org. Lett.* **1999**, *1*, 141. (d) Trost, B. M.; Hachiya, I. *J. Am. Chem. Soc.* **1998**, *120*, 1104. (e) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590.

(10) (a) Evans, P. A.; Kennedy, L. J. *Org. Lett.* **2000**, *2*, 2213. (b) Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 6761. (c) Evans, P. A.; Nelson, J. D. *Tetrahedron Lett.* **1998**, *39*, 1729.

(11) (a) Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525. (b) Fuji, K.; Kinoshita, N.; Tanaka, K.; Kawabatu, T. *J. Chem. Soc., Chem. Commun.* **1999**, 2289. (c) Bartels, B.; Helmchen, G. *J. Chem. Soc., Chem. Commun.* **1999**, 741. (d) Takeuchi, R.; Kashio, M. *J. Am. Chem. Soc.* **1998**, *120*, 8647. (e) Takeuchi, R.; Kashio, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 263.

(12) (a) Bricout, H.; Carpentier, J. F.; Mortreux, A. *Chem. Commun.* **1997**, 1393. (b) Kobayashi, Y.; Takahisa, E.; Usmani, S. B. *Tetrahedron Lett.* **1998**, *39*, 597.

(13) (a) Kondo, T.; Ono, H.; Satake, N.; Mitsudo, T.; Watanabe, Y. *Organometallics* **1995**, *14*, 1945. (b) Morisaki, Y.; Kondo, T.; Mitsudo, T. *Organometallics* **1999**, *18*, 4742.

(14) (a) Brown, B.; Hegedus, L. S. *J. Org. Chem.* **1998**, *63*, 8012. (b) Reeder, L. M.; Hegedus, L. S. *J. Org. Chem.* **1999**, *64*, 3306.

(15) Hegedus, L. S.; Bates, R. W.; Soderberg, B. C. *J. Am. Chem. Soc.* **1991**, *113*, 923.

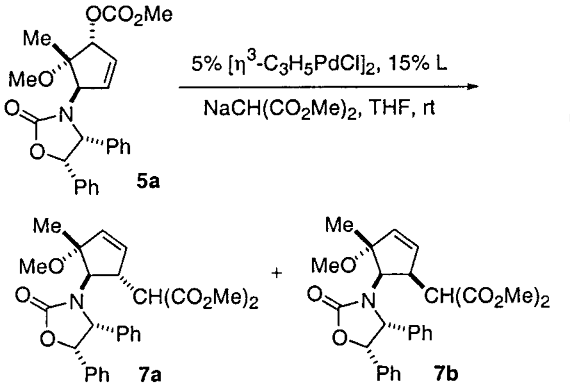
(16) (a) Brown, B.; Hegedus, L. S. *J. Org. Chem.* **2000**, *65*, 1865. (b) Wen, X.; Norling, H.; Hegedus, L. S. *J. Org. Chem.* **2000**, *65*, 2096. (c) Heileman, M. J.; Hegedus, L. S. *Synthesis* **2001**, 1356.

Table 1. Effect of Increasing Bite Angle of Bidentate Ligands

ligand	β_n (deg)	**5a** (%)	**7a** (%)	**7b** (%)
dppm[a]	72	100	0	0
dppe[b]	85	21	49	0
dppp[c]	91	4	83	5
dppf[d]	96	0	92	7
dppb[e]	98	0	82	17
dppb[f]	98	0	54	33

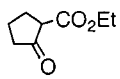
[a] Bis(diphenylphosphino)methane. [b] 1,2-Bis(diphenylphosphino)ethane. [c] 1,3-Bis(diphenylphosphino)propane. [d] 1,1′-Bis(diphenylphosphino)ferrocene. [e] 1,4-Bis(diphenylphosphino)butane. [f] 17% $[\eta^3\text{-}C_3H_5PdCl]_2$.

Ligandless catalyst precursor $Pd_2dba_3CHCl_3$, the standard catalyst $Pd(PPh_3)_4$, and the more reactive combination $PdCl_2(PPh_3)$/DIBAL proved unreactive in the test case reaction of dimethyl malonate with **5a** (eq 4), as did $[\eta^3\text{-}C_3H_5PdCl]_2/PPh_3$ or $P(OEt)_3$. Chelating diphosphines often provide more efficient catalysts than do monophosphines and the bite angle affects both the reactivity and regioselectivity.[17] Although dppm/$[\eta^3\text{-}C_3H_5PdCl]_2$ proved unreactive, ligands with larger bite angles led to reaction, with rate, conversion, and yields increasing with increasing bite angle (Table 1).[18] Attack occurred exclusively at the less-hindered allylic terminus, as anticipated, giving product **7a** with overall retention of configuration.[19] Surprisingly, as the bite angle of the catalyst increased, the product resulting from inversion of stereochemistry, **7b**, was formed.[20] This most likely resulted from Pd−Pd exchange with the π-allylpalladium intermediate.[21] If this mechanism of inversion of stereochemistry was operating, one would expect an increase in the amount of product **7b** to increase as the catalyst loading increased, and that was indeed the case (Table 1, last entry).

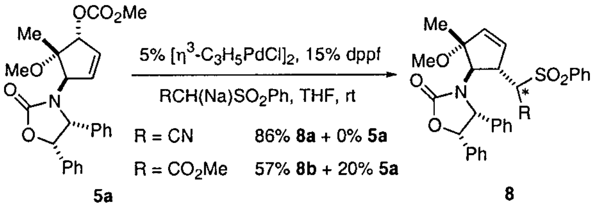


Dppf offered the best compromise between reactivity and selectivity, so its use with a broader range of nucleophiles was examined. Indeed, $PhSO_2CH_2CN$ and $PhSO_2CH_2CO_2Me$ underwent clean reaction with **5a** at room temperature to give **8** as a mixture of diastereomers in good to excellent yield (eq 5). However, most other nucleophiles proved unreactive under these mild conditions, and heating caused decomposition of the catalyst. Thus, a more robust catalyst system was sought.

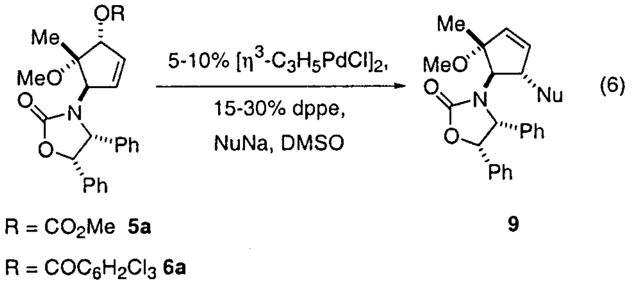
Table 2. Palladium-Catalyzed Nucleophilic Substitution Reactions of 5a or 6a

Nucleophile	Temp., °C	Time, h	%, Product[a]		Recovered **5a**%[a] or **6a**%[a]	
1. $(MeO_2C)_2CH_2$	23	1	51	**7a**	0	-
2. $(MeO_2C)_2CHCH_3$	23	0.2	55	**9a**	8	-
3. $PhSO_2CH_2CN$	50	36	0	**8a**	56	-
4. $PhSO_2CH_2CO_2Me$	70	14	27	**8b**	0	-
5. $(PhSO_2)_2CH_2$	100	12	21	**9b**	0	-
6. CH_3COPh[b]	23	5	44	**9c**	0	-
7. $(CH_3CO)_2CH_2$	60	24	33	**9d**	23	-
8. 	70	12	41	**9e**	0	-
9. $PhSO_2H$	60	0.5	64	**9f**	0	-
10. Succinimide	70-120	48	8	**9g**	-	20
11. $TsNH_2$	70	12	62	**9h**	-	0
12. Ac_2NH	70	48	3	**9i**	-	0
13. BnNHTs	40-90	36	4	**9j**	-	0
14. Phthalimide[c]	60	24	0	**9k**	-	56

[a] Yields are for isolated, purified products. [b] Li anion. [c] K anion.



The conditions shown in eq 6 proved to be the most general for the reaction of a range of nucleophiles (Table 2). The catalyst system was sufficiently reactive to undergo oxidative addition at room temperature (Table 2, entries 1, 2, and 6) and sufficiently robust to survive extended periods at higher temperatures (Table 2, entries 10 and 13). Nitrogen nucleophiles tended to attack at the carbonate carbonyl carbon in **5a**, necessitating the use of the bulkier trichlorobenzoyl ester **6a**. Despite this, the yields are only modest, at best. It is clear that the difficult step under these (and most other) conditions is the attack of the nucleophile on the sterically hindered π-allylpalladium complex. Further, the material balances for characterizable material are uniformly poor because the products (or the reactive π-allyl intermediate) are not stable to the reaction conditions when nucleophilic attack is slow. For example, with dimethyl methylmalonate as the nucleophile, after 0.2 h at 23 °C, there was 55% of the product **9a**, and 8% recovered starting material. When the reaction was allowed to proceed for 0.5 h at 23 °C, less than 10% product was isolated, along with the diene elimination product **10**.



---

(17) For a review, see: van Leeuwen, P. W. N. M.; Kramer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741.

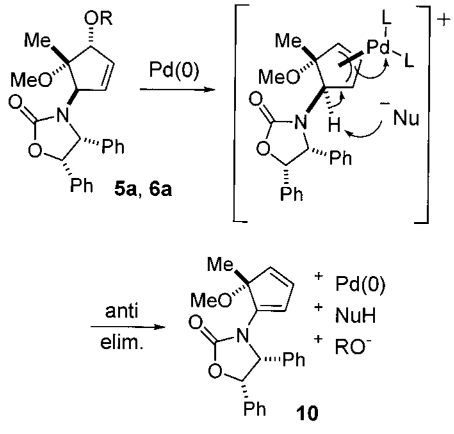
(18) Ogasawara, M.; Yoshida, K.; Hayashi, T. *Organometallics* **2000**, *19*, 1567.

(19) The stereo- and regiochemistry of **7a** was established by X-ray crystallography. See the Supporting Information for structural details.

(20) Compound **7b** was independently synthesized from the palladium-catalyzed reaction of epimeric **5b** with malonate.

(21) Granberg, K. L.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1992**, *114*, 6858.

Decomposition most likely occurs by a base-promoted (in this case, the nucleophile) anti elimination of the elements of L_nPdX-H from the π-allylpalladium intermediate (eq 7).[22] For the *product* to be decomposed by the catalyst, reverse of the nucleophilic attack is required. This has been observed in special cases.[23]



(7)

Since long reaction times were detrimental to this process, the use of microwave heating was considered. The application of microwave heating to organic reactions has attracted much attention recently due to its broad applicability and ability to dramatically improve yields and reaction times.[24] The metal-catalyzed allylic substitution reaction has exhibited impressive results with this heating method.[25]

The reason for these improvements may be that higher temperatures are attained very quickly and are sustained for only a short amount of time, therefore minimizing the amount of decomposition of the intermediate or product. Reactions were run in sealed pressure tubes using a Sharp 700 W microwave. The combinations of $[\eta^3\text{-}C_3H_5PdCl]_2$ with dppe/DMSO or dppf/THF generated the best results, and the best ligand/solvent combination varied with the nucleophile. In most cases, yields were dramatically increased and reactions were complete in 5 min, compared with 48 h required using conventional oil bath heating (Table 3). Importantly, the reaction involving phthalimide anion was observed for the first time in 63% yield.

Yields could not be optimized further because it was observed that when high powers or long reactions times were used, the reaction produced a black precipitate, possibly due to the thermal instability of the catalyst system.[26]

Allylic Alkylation of 5a via Transmetalation. Alkylation of allylic esters via transmetalation has been used much less frequently than direct nucleophilic attack for a number of reasons. Allylic esters are considerably less reactive toward oxidative addition than are halides, requiring more nucleophilic ligands, which suppress transmetalation.[8] Ester anions binds tightly to palladium, also suppressing transmetalation. Finally, reductive elimination from π-allylpalladium complexes is slow. An additional complication with substrate **5a** is the fact that the palladium in the π-allyl intermediate is flanked by two large groups that could sterically hinder transmetalation.

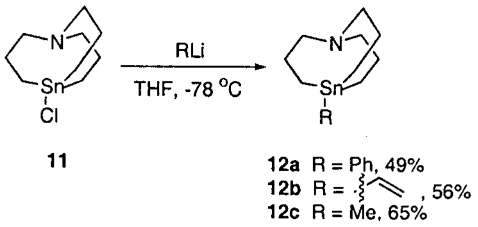
Table 3. Results of Microwave Heating

		microwave heating[a]	
substrate	nucleophile	dppe/DMSO	dppf/THF
5a	$PhSO_2CH_2CO_2Me$[b]	3 min 46% **8b**	3 × 3 min 93% **8b**
6a	succinimide[b]	5 min 29% **9g**	5 × 2 min 0% **9g**
6a	Ac_2NH[b]	2 min 46% **9i**	6 min 24% **9i**
6a	TsNHBn[b]	5 min 37% **9j**	6 min 86% **9j**
6a	phthalimide[c]	5 min 63% **9k**	

[a] Reactions were run with 20 mg **5a** or **6a**, 5% $[\eta^3\text{-}C_3H_5PdCl]_2$, 15% ligand, 1.5 equiv of nucleophilic anion in 0.4 mL of DMSO or THF at 210 W. [b] Na anion. [c] K anion.

Not surprisingly, transmetalation reactions of **5a** proved difficult. With catalysts ranging from $Pd(PPh_3)_4$, $Pd_2dba_3CHCl_3$/dppe, $[\eta^3\text{-}C_3H_5PdCl]_2$/dppf, $-P(OMe)_3$, and $-P(furyl)_3$ to $Pd(acac)_2/PPh_3$ and main group organometallics ranging from $NaBPh_4$, BnZnBr, PhZnCl, $C{=}CSnBu_3$, $PhSnMe_3$, to $(p\text{-}MeOPh)SnBu_3$, in THF, DMSO, or HMPA with or without LiCl or LiCl/CuCl either unreacted starting material or dienes resulting from either β-hydride or β-methoxide elimination were recovered.

Recently, it has been demonstrated that alkylstannatranes[27] (eq 8) are useful in promoting the Stille cross-coupling reaction.[28] Two factors are thought to cause the increased reactivity of stannatranes: the unusually long exocyclic Sn−C bond length (on average 0.1 Å longer than a typical alkylstannane)[34] and the internal tin−nitrogen coordination in the transition state. Indeed, stannatranes



(8)

---

(22) (a) Takacs, J. M.; Lawson, E. C.; Clement, F. *J. Am. Chem. Soc.* **1997**, *119*, 5956. (b) Andersson, P. G.; Schab, S. *Organometallics* **1995**, *14*, 1. (c) Schwarz, I.; Braun, M. *Chem. Eur. J.* **1999**, *5*, 2300.

(23) Dorizon, P.; Su, G.; Ludvig, G.; Nikitina, L.; Paugam, R.; Ollivier, J.; Salaün, J. *J. Org. Chem.* **1999**, *64*, 4712.

(24) For recent reviews, see: (a) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron*, **2001**, *57*, 9225, (b) Caddick, S. *Tetrahedron* **1995**, *51*, 10403; (c) Mingos, D. *Res. Chem. Intermed.* **1994**, *20*, 85.

(25) (a) Kaiser, N. K.; Brenberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3596. (b) Brenberg, U.; Lutsenko, S.; Kaiser, N.; Larhed. M.; Hallberg, A.; Moberg, C. *Synthesis* **2000**, 1004. (c) Brenberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *J. Org. Chem.* **1999**, *64*, 1082.

(26) Maleczka, R. E., Jr.; Lavis, J. M.; Clark, D. H.; Gallagher, W. P. *Org. Lett.* **2000**, *2*, 3655.

(27) (a) Jurkschat, K.; Tzschach, A. *J. Organomet. Chem.* **1986**, *315*, 45. (b) Jurkschat, K.; Tzschach, A. *J. Organomet. Chem.* **1984**, *272*, C13.

(28) (a) Jensen, M. S.; Yang, C.; Hsiao, Y.; Rivera, N.; Wells, K. M.; Chung, J. Y. L.; Yasuda, N.; Hughes, D. L.; Reider, P. J. *Org. Lett.* **2000**, *2*, 1081. (b) Vedejs, E.; Haight, A. R.; Moss, W. O. *J. Am. Chem. Soc.* **1992**, *114*, 6556.

(29) Krebs, B.; Henkel, G.; Dartmann, M. *Acta Crystallog. C.* **1989**, *45*, 1010.

(30) For X-ray structural details, see the Supporting Information.

(31) Robinson, S. D.; Shaw, B. L. *J. Chem. Soc.* **1963**, 4806.

(32) Trost, B. M.; Tometzki, G. B.; Hung, M.-H. *J. Am. Chem. Soc.* **1987**, *109*, 2176.

(33) Hevde, J. L.; Lambert, J. C.; Seroff, C. V. *Inorganic Synthesis* **1974**, *15*, 18.

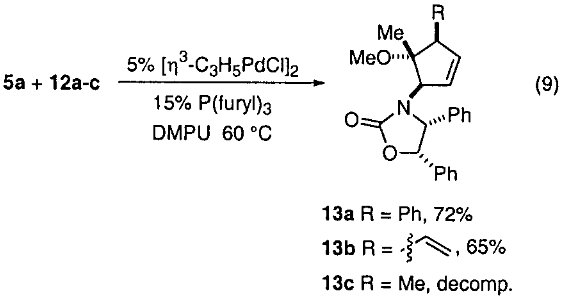
(34) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1987**, *109*, 1469.

Table 4. Comparison of Epimeric Allyl Carbonates 5a and 5b

conditions	**5a**	**5b**
$NaCH(CO_2Me)_2$ DMSO, dppe, rt	51% **7a** 30 min	22% **5b** + dec 30 min
$NaCH(CO_2Me)_2$ THF, dppf, rt	92% **7a** >5 h	88% **7b** 2 h
$N[(CH_2)_3]_3SnPh$ DMPU, $P(furyl)_3$, 60 °C	73% **13a** 12 h	dec[a]

[a] 70% free oxazolidinone recovered.

12a and **12b** proved effective with carbonate **5a**, giving good yields of alkylation products **13a** and **13b** (eq 9).



As expected, the reaction occurred with clean inversion (as shown by an X-ray crystal structure[30] of **13b**). Alkylation occurred at the allyl terminus opposite the large oxazolidinone group, in contrast to the regioselectivity of alkylation by external nucleophiles. Only decomposition was observed with methyl stannatrane **12c**, presumably due to decomposition of the π-allylpalladium intermediate due to slow transmetalation.

Reactions of Epimeric Allylic Carbonate 5b. A comparison was done of the epimeric allylic carbonates **5a** and **5b**, which revealed significant differences in reactivity (Table 4). Oxidative addition would be expected to be more facile with substrate **5b** because of the decreased steric hindrance on the bottom face of the molecule. However, now nucleophilic attack should be the slow step. Reaction with dimethyl malonate anion and dppe resulted in only decomposition. As was expected, the use of dppf, which promotes nucleophilic attack, allowed for facile product formation with dimethyl malonate anion in good yield. Reaction with phenylstannatrane resulted in decomposition, which was surprising, since both oxidative addition and transmetalation would occur on the less sterically demanding side.

It has been observed that electronic interactions between palladium and an antiperiplanar electron-withdrawing β-substituents (such as OR) of η^3-allylpalladium intermediates leads to lengthening and weakening of the C−O bond, facilitating the loss of the β-substituent.[6a,31] The isolation of free oxazolidinone is consistent with this observation.

Reaction of 5a and 5b with Other Metal Catalysts. Carbonates **5a** and **5b** proved unreactive to a range of other transition-metal systems that catalyzed allylic alkylation in simpler substrates. Thus, $NiBr_2/Zn/dppb$,[12] $(EtCN)_3W(CO)_3/bpy$,[32] $[Ir(COD)Cl]_2/P(OMe)_3$,[11d,33] (t-Bu-NC)$_4$Mo(CO)$_2$,[9e] $Mo(CO)_6$,[34] and $RhCl(PPh_3)_3/P(OR)_3$[35] all failed to catalyze reaction of **5a** or **5b** with a wide range of nucleophiles, under a wide range of conditions. In most cases, unreacted starting material was recovered in good yield, suggesting oxidative addition was the problematic step.

Conclusion

The chiral adjacent tertiary and quaternary centers had a dramatic effect on the reactivity of the metal-catalyzed allylic substitution reaction of **5a**,**b** and **6a**. Promotion of oxidative addition and nucleophilic attack required careful selection of reaction conditions. Microwave heating improved yields and reaction times with stabilized anions. The substrates were inert to standard conditions for transmetalation; however, **5a** underwent smooth reaction with vinyl- and phenylstannatranes. Stabilized nucleophiles exclusively attacked the less-hindered terminus, while transmetalation with the stannatranes occurred at the opposite end. Stereoselectivity was dependent on the bidentate ligand used, although retention of stereochemistry predominated with the stabilized nucleophiles and inversion with the stannatranes.

Experimental Section

Materials. The following compounds were prepared according to literature procedures: cyclobutanone **2**,[16a] diazomethane,[36] (±)-2-benzenesulfonyl-3-phenyloxaziridine (Davis' oxaziridine),[37] $[\eta^3\text{-}C_3H_5PdCl]_2$,[38] $Pd(PPh_3)_4$,[39] $N[(CH_2)_3]_3SnCl$ (**11**),[28b] $N[(CH_2)_3]_3SnMe$ (**12c**),[27b] phenyllithium,[40] and vinyllithium.[41]

General Procedures. THF was distilled from sodium benzophenone ketyl; DMSO, DMPU, CH_2Cl_2, HMDS, pyridine, and Et_3N were distilled from CaH_2. ^1H (300 and 400 MHz) and ^{13}C NMR (75 and 100 MHz) spectra were recorded in $CDCl_3$, and chemical shifts (δ) were given in ppm relative to $CHCl_3$. Flash column chromatography was performed with ICN 32−63 μm, 60 Å silica gel. Preparative chromatography was performed using silica gel 60 F_{254}, 250 μm. Elemental analyses were performed at M−H−W Laboratories, Phoenix, AZ. All reactions were performed under an atmosphere of Ar. Microwave reactions were carried out in a 700 W microwave oven with the glass turntable removed in pressure tubes fitted with Teflon plugs and Teflon encapsulated O-rings. ***Extreme caution*** should be taken when heating a sealed tube in a microwave oven. High pressures and temperatures are generated which have led to *explosions*. In the event of such explosions, glass shards may penetrate the walls of the oven. Thus, all reactions should be run in a fume hood with a blast shield in place. Microwave ovens specialized for synthesis that offer precise control of pressure and temperature and have built-in safety features are available from Personal Chemistry.

Cyclopentanone 1. A freshly prepared solution of diazomethane (prepared by slow addition of Diazald in 90 mL of Et_2O to 10 g of KOH in 18 mL of water and 20 mL of 95% ethanol at 65 °C and co-distillation of Et_2O/diazomethane) was poured into an Erlenmeyer flask containing cyclobutanone **2** (3.40 g, 9.76 mmol) in THF (90 mL). (*Extreme caution* is required when working with diazomethane because it can be *explosive* on heating at 100 °C or on contact with rough surfaces or solids. Scratched or ground glassware should be

---

(35) (a) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 5581. (b) Osborn, J. A.; Wilkinson, G. *Inorganic Synthesis* **1990**, *28*, 77.

(36) Black, T. H. *Aldrichim. Acta* **1983**, *16*, 3.

(37) (a) Davis, F. A.; McCauley, J. P.; Chattopadhyay, S.; Harakal, M. E.; Towson, J. C.; Watson, W. H.; Tavanaiepour, I. *J. Am. Chem. Soc.* **1987**, *109*, 3370. (b) Davis, F. A.; Chattopadhyay, S.; Towson, J. C.; Lal, S.; Reddy, T. *J. Org. Chem.* **1988**, *53*, 2087.

(38) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033.

(39) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: London, 1985.

(40) Komiya, S. *Synthesis of Organometallic Compounds. A Practical Guide*; Wiley & Sons: New York, 1997; p 324.

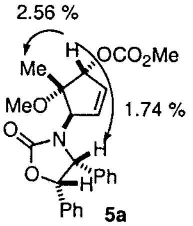
(41) Wakefield, B. J. *Organolithium Methods*; Academic Press: New York, 1988; p 46.

avoided.)[36] The reaction mixture stood for 5 h at 0 °C. Argon was bubbled through until the yellow color dissipated then the solvent was removed under reduced pressure. Flash chromatography with hexane/EtOAc (4/1 to 2/1) gave **1** as a white solid (2.57 g, 7.04 mmol, 72%): ^{1}H NMR δ 7.12 (m, 6H), 6.91 (m, 4H), 5.86 (d, $J = 7.5$ Hz, 1H), 4.98 (d, $J = 7.8$ Hz, 1H), 4.41 (t, $J = 7.5$ Hz, 1H), 3.27 (s, 3H), 2.14−2.40 (m, 2H), 1.93−2.05 (m, 1H), 1.59−1.71 (m, 1H), 1.37 (s, 3H); ^{13}C NMR δ 213.3, 158.7, 135.4, 134.0, 128.8, 128.6, 128.3, 128.1, 127.7, 126.3, 83.8, 80.6, 65.5, 56.9, 51.8, 34.8, 22.9, 14.9; IR (neat) ν 1749 cm^{-1}; mp 165−167 °C. Anal. Calcd for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34; N, 3.83. Found: C, 72.12; H, 6.25; N, 3.78.

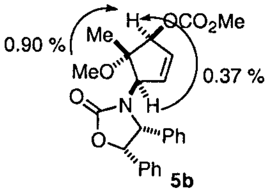
Cyclopentenone 3. Cyclopentanone **1** (2.00 g, 5.47 mmol) in THF (12 mL) was added slowly to a solution of LiHMDS [prepared from *n*-BuLi (5.52 mmol) and HMDS (2.65 mL, 12.6 mmol) in THF (10 mL) at 0 °C] at −78 °C, and this reaction mixture stirred for 2.5 h. Phenylselenyl bromide (1.42 g, 6.00 mmol) in THF (10 mL) was added via syringe pump over 20 min. After 1.5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The orange oil was passed through a plug of silica gel eluting with hexane/EtOAc (10/1 to 2/1). The selenide was dissolved in $CHCl_3$ (88 mL) and cooled to 0 °C. Pyridine (1.31 mL, 16.2 mmol) and then the Davis oxaziridine (4.38 g, 16.8 mmol) were added, and the reaction mixture was stirred vigorously for 35 min. The reaction was quenched with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. Immediate flash chromatography with hexane/EtOAc(10/1 to 2/1) gave the cyclopentenone **3** (1.27 g, 3.50 mmol, 64%) as a white solid. See ref 16c for spectral data.

Allylic Alcohols 4a,b. Cyclopentenone **3** (367 mg, 1.01 mmol) was dissolved in MeOH (30 mL) and cooled to 0 °C. $CeCl_3\cdot 7H_2O$ (535 mg, 1.44 mmol) was added, and the reaction mixture was stirred for 0.5 h before $NaBH_4$ (51 mg, 1.33 mmol) was added in portions. The reaction mixture was stirred for an additional 2.5 h, then 10% AcOH in methanol was added, and the mixture stirred vigorously for 0.5 h at 0 °C. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 30 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Column chromatography using hexane/EtOAc (3/1) gave a 4:1 mixture of diastereomeric allylic alcohols **4a**/**4b** (348 mg, 0.96 mmol, 95%), which was used without further purification. Analytical samples of the allylic alcohols were prepared by preparative thin-layer chromatography with hexane/EtOAc (3/2). **Allylic alcohol 4a:** ^{1}H NMR δ 7.09 (m, 6H), 6.98(m, 4H), 5.81 (d, $J = 7.2$ Hz, 1H), 5.72 (d, $J = 6.0$ Hz, 1H), 5.08 (m, 1H), 5.00 (m, 1H), 4.59 (d, $J = 7.2$ Hz, 1H), 4.55 (d, $J = 1.5$ Hz, 1H), 3.47 (s, 3H), 3.12 (d, $J = 9.6$ Hz, 1H), 1.54 (s, 3H); ^{13}C NMR δ 158.5, 138.6, 136.6, 133.9, 128.5, 128.4, 128.3, 128.1, 126.3, 82.6, 80.8, 64.5, 63.0, 51.4, 16.9; IR (neat) ν 3508, 1733 cm^{-1}; mp 234−235 °C. Anal. Calcd for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34; N, 3.83. Found: C, 72.45; H, 6.20; N, 3.83. **Allylic alcohol 4b:** ^{1}H NMR δ 7.11 (m, 6H), 6.94 (m, 4H), 6.00 (d, $J = 6.0$ Hz, 1H), 5.83 (d, $J = 8.1$ Hz, 1H), 5.51 (dd, $J = 2.1$, 5.4 Hz, 1H), 5.08 (d, $J = 8.4$ Hz, 1H), 4.41 (bs, 1H), 4.31 (bs, 1H), 3.16 (s, 3H), 1.42 (s, 3H); ^{13}C NMR δ 158.3, 136.6, 135.6, 134.5, 130.3, 128.7, 128.4, 128.2, 128.1, 126.2, 87.6, 80.8, 80.1, 65.8, 64.5, 51.0, 14.3; IR (neat) ν 3416, 1728 cm^{-1}; HRMS *m*/*z* (M + H) calcd for $C_{22}H_{24}NO_4$ 366.1705, found 366.1702.

Allylic Carbonates 5a,b. Pyridine (0.04 mL, 0.50 mmol) was added to a mixture of allylic alcohols **4a**,**b** (0.13 g, 0.36 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C. After 0.5 h, methyl chloroformate (0.04 mL, 1.4 mmol) then DMAP (14 mg, 0.12 mmol) were added, and the mixture was stirred at 0 °C to room temperature overnight. The reaction mixture was quenched with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (4 × 20 mL), and the combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography with hexane/EtOAc (3/1) gave allylic carbonate **5a** (82 mg, 63%) and **5b** (18 mg, 14%). **Allylic carbonate 5a:** ^{1}H NMR δ 7.09 (m, 7H), 6.99 (m, 2H), 6.82 (bs, 1H), 5.83 (d, $J = 7.6$ Hz, 1H), 5.73 (dt, $J = 1.8$, 6.0 Hz, 1H), 5.47 (dd, $J = 1.8$, 3.4 Hz, 1H), 5.34 (dt, $J = 2.0$, 6.0 Hz, 1H), 5.14 (d, $J = 2.4$ Hz, 1H), 4.67 (d, $J = 7.6$ Hz, 1H), 3.82 (s, 3H), 3.38 (s, 3H), 1.58 (s, 3H); ^{13}C NMR δ 158.2, 156.0, 136.4, 133.8, 133.0, 132.4, 128.5, 128.3, 128.1, 127.5, 126.3, 85.5, 83.4, 80.7, 64.9, 64.8, 55.2, 52.0, 18.4; IR (neat) ν 1744 cm^{-1}; mp 163−165 °C. Anal. Calcd for $C_{24}H_{25}NO_6$: C, 68.07; H, 5.95; N, 3.31. Found: C, 67.90; H, 5.88; N, 3.30. **Allylic carbonate 5b:** ^{1}H NMR δ 7.08 (m, 6H), 6.93 (m, 3H), 6.50 (bs, 1H), 5.83 (d, $J = 7.5$ H, 1H), 5.74 (dt, $J = 2.1$, 5.7 Hz, 1H), 5.35 (dd, $J = 2.7$, 6.0 Hz, 1H), 5.31 (d, $J = 2.4$ Hz, 1H), 5.01 (t, $J = 1.8$ Hz, 1H), 4.82 (d, $J = 7.5$ Hz, 1H), 3.89 (s, 3H), 3.43 (s, 3H), 1.46 (s, 3H); ^{13}C NMR δ 158.3, 155.3, 136.9, 135.7, 134.1, 131.5, 128.5, 128.4, 128.2, 128.1, 126.3, 86.9, 84.7, 80.8, 64.1, 63.6, 55.4, 51.6, 13.9; IR (neat) ν 1752 cm^{-1}; HRMS *m*/*z* (M + H) calcd for $C_{24}H_{26}NO_6$ 424.1760, found 424.1756. The stereochemistry was assigned based on the following NOE data.



5a



5b

Allylic Ester 6a. 2,4,6-Trichlorobenzoyl chloride (0.10 mL, 0.64 mmol), DMAP (53 mg, 0.43 mmol), triethylamine (0.09 mL, 0.65 mmol), and CH_2Cl_2 (3 mL) were combined in a flame-dried round-bottomed flask equipped with a reflux condenser and stir bar. This reaction mixture stirred at room temperature for 5 min, and then a solution of allylic alcohols **4a**,**b** (0.16 g, 0.43 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction mixture was heated to reflux overnight and then diluted with CH_2Cl_2 and water. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated under vacuum to give an oily yellow solid. Flash chromatography with hexane/EtOAc (10/1 to 2/1) gave allylic ester **6a** (0.15 g, 0.26 mmol, 60%) and unreacted **4b** (0.03 g, 0.08 mmol, 19%): ^{1}H NMR δ 7.35 (s, 2H), 7.11 (m, 6H), 6.99 (m, 2H), 6.86 (bs, 2H), 5.90 (dd, $J = 1.7$, 3.5 Hz, 1H), 5.87 (d, $J = 7.5$ Hz, 1H), 5.84 (dt, $J = 1.8$, 6.3 Hz, 1H), 5.40 (ddd, $J = 1.5$, 2.7, 6.3 Hz, 1H), 5.16 (m, 1H), 4.72 (d, $J = 7.2$ Hz, 1H), 3.37 (s, 3H), 1.65 (s, 3H); ^{13}C NMR δ 164.3, 158.3, 136.5, 136.4, 133.8, 133.4, 132.9, 132.1, 128.6, 128.3, 128.1, 126.3, 84.0, 83.6, 80.8, 64.9, 64.8, 51.9, 18.0; IR (neat) ν 1740 cm^{-1}; mp 110−112 °C. Anal. Calcd for $C_{29}H_{24}Cl_3NO_5$: C, 60.80; H, 4.22; N, 2.45. Found: C, 60.75; H, 4.28; N, 2.44.

General Procedure for the Allylic Substitutions. Procedure A. Allylic carbonate **5a**,**b** or ester **6a** (0.04 to 0.05 mmol), $[\eta^3\text{-}C_3H_5PdCl]_2$ (5−10%), and the bidentate ligand (15−30%) were combined in the reaction flask and purged with Ar for 10 min. DMSO or THF (0.4 mL) was added, and the reaction mixture was stirred at room temperature for 10 min before the nucleophile (1−3 equiv) was added via syringe. After the said amount of time, the reaction mixture was diluted with diethyl ether and saturated aqueous NH_4Cl. The layers were separated, and the aqueous layer was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. The products were purified with flash column chromatography on silica gel. **Procedure B,** Allylic carbonate **5a** or ester **6a** (0.04 to 0.05 mmol), $[\eta^3\text{-}C_3H_5PdCl]_2$ (5−10%), and dppe (15−30%) were combined in a pressure tube fitted with a septum and purged with Ar for 10 min. DMSO or THF (0.4 mL) was added, and the reaction mixture was shaken so that everything dissolved and then allowed to stand at room temperature for 10 min before the nucleophile (1−3 equiv) was added via syringe. The pressure tube was sealed with the Teflon plug and placed in the center of the microwave in a large beaker and irradiated for the said amount of time. The pressure tube was then immediately placed in a beaker containing cold water to stop the reaction and worked up as for procedure A.

Dimethyl Malonate Addition Product 7a. Procedure A (dppe/DMSO). A mixture of 20 mg (0.05 mmol) of allylic carbonate **5a**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (6%), dppe (16%), and sodium dimethyl malonate anion (0.14 mmol) in DMSO at room temperature for 0.2 h gave **7a** (11 mg, 0.02 mmol, 51%) after column chromatography with hexane/EtOAc (5/1 to 2/1): ^{1}H NMR δ 6.94−7.14 (m, 10H), 5.91 (d, $J = 8.1$ Hz, 1H), 5.78 (m, 2H), 5.04 (d, $J = 7.5$ Hz, 1H), 4.48 (bs, 1H), 3.71 (s, 3H), 3.58 (s, 3H), 3.50 (bs, 1H), 3.30 (bs, 1H), 3.01 (bs, 3H), 1.47 (s, 3H); ^{13}C NMR δ 168.6, 168.5, 158.2, 136.6, 135.9, 134.6, 132.3, 128.6, 128.4, 128.1, 128.0, 126.1, 89.1, 80.1, 66.2, 60.5, 52.8, 52.7, 52.6, 50.6, 43.5, 21.7; IR (neat) ν 1748 cm $^{-1}$; mp 152−154 °C; HRMS m/z (M + H) calcd for $C_{27}H_{30}NO_7$ 480.2022, found 480.2004.

Dimethyl Malonate Addition Product 7b. Procedure A. A mixture of 20 mg (0.05 mmol) of allylic carbonate **5b**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (6%), dppf (15%), and sodium dimethyl malonate anion (0.16 mmol) in THF at room temperature for 2 h gave **7b** (19 mg, 0.04 mmol, 88%) after column chromatography with hexane/EtOAc (3/1): ^{1}H NMR δ 7.10 (m, 7H), 6.99 (m, 2H), 6.89 (bs, 1H), 5.82 (d, $J = 7.2$ Hz, 1H), 5.60 (dt, $J = 2.2$, 6.0 Hz, 1H), 5.13 (d, $J = 1.6$ Hz, 1H), 5.05 (dt, $J = 2.0$, 6.2 Hz, 1H), 4.79 (d, $J = 7.2$ Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.56 (m, 1H), 3.51 (m, 1H), 3.42 (s, 3H), 1.38 (s, 3H); ^{13}C NMR δ 168.8, 168.7, 158.4, 136.7, 133.9, 133.7, 128.5, 128.4, 128.2, 128.1. 126.4, 89.6, 80.8, 64.9, 64.4, 53.2, 52.9, 52.5, 50.8, 49.7, 16.0; IR (neat) ν 1751 cm^{-1}; mp 158−160 °C; HRMS m/z (M + H) calcd for $C_{27}H_{30}NO_7$ 480.2022, found 480.2008.

(Phenylsulfonyl)acetonitrile Addition Product 8a. Procedure A. A mixture of 21 mg (0.05 mmol) of allylic carbonate **5a**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (5%), dppe (12%), and sodium (phenylsulfonyl)acetonitrile (0.150 mmol) in THF at room temperature for 5 h gave **8a** as an inseparable 2:1 mixture of diastereomers at the nitrile-bearing center (23 mg, 0.04 mmol, 86%) after column chromatography with hexane/EtOAc (2/1). The product ratio was determined by integration of the methoxy methyl resonances in the ^{1}H NMR spectrum: major isomer, 3.26 (s); minor isomer, 2.75 (s). Major isomer: ^{1}H NMR δ 7.74 (m, 3H), 7.61 (m, 2H), 7.08−7.26 (m, 6H), 6.99 (m, 4H), 6.08 (s, 2H), 5.94 (d, $J = 7.2$ Hz, 1H), 5.05 (d, $J = 7.5$ Hz, 1H), 4.78 (d, $J = 7.8$ Hz, 1H), 3.74 (d, $J = 4.5$ Hz, 1H), 3.60 (dd, $J = 3.9$, 7.5 Hz, 1H), 3.26 (s, 3H), 1.56 (s, 3H), 1.51 (s, 3H). Minor isomer: ^{1}H NMR δ 8.08 (d, $J = 7.2$ Hz, 2H), 7.75 (m, 3H), 7.01−7.27 (m, 10H), 6.08 (s, 1H), 5.93 (d, $J = 7.6$ Hz, 1H), 5.72 (d, $J = 6.0$ Hz, 1H), 5.32 (d, $J = 8.4$ Hz, 1H), 4.67 (bs, 1H), 4.19 (d, $J = 5.2$ Hz, 2H), 2.75 (s, 3H), 1.38 (s, 3H); IR (neat) ν 1747 cm^{-1}; mp 168−170 °C; HRMS m/z (M + H) calcd for $C_{30}H_{29}N_2O_5S$ 529.1797, found 529.1781.

Methyl Phenylsulfonyl Acetate Addition Product 8b. Procedure B (dppe, DMSO). A mixture of 20 mg (0.05 mmol) of allylic carbonate **5a**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (7%), dppe (15%), and sodium methyl phenylsulfonyl acetate (0.14 mmol) in DMSO and irradiation for 3 min at 210 W gave **8b** as a 1:1 mixture of diastereomers at the ester-bearing center (12 mg, 0.02 mmol, 46%). The product ratio was determined by integration of the methoxy methyl resonances in the ^{1}H NMR spectrum: 3.58 (s); 3.52 (s); ^{1}H NMR δ 7.82 (d, $J = 7.5$ Hz), 7.71 (m), 7.56 (m), 6.92−7.17 (m), 5.81−5.97 (m), 5.14 (m), 5.06 (m), 4.46 (m), 4.15 (d, $J = 7.2$ Hz), 3.97 (d, $J = 6.6$ Hz), 3.78 (m), 3.45−3.68 (m), 3.34 (m), 2.95 (m), 1.60 (bs), 1.44 (m); IR (neat) ν 1747 cm^{-1}; HRMS m/z (M + H) calcd for $C_{31}H_{32}NO_7S$ 562.1900, found 562.1881.

Dimethyl Methylmalonate Addition Product 9a. Procedure A. A mixture of 20 mg (0.05 mmol) of allylic carbonate **5a**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (5%), dppe (15%), and sodium dimethyl methylmalonate anion (0.14 mmol) in DMSO at room temperature for 0.2 h gave **9a** (13 mg, 0.03 mmol, 55%) after column chromatography with hexane/EtOAc (6/1−3/1). Several attempts to remove an unidentified impurity were unsuccessful: ^{1}H NMR δ 7.07 (m, 10H), 5.90 (d, $J = 9.3$ Hz, 1H), 5.75 (dd, $J = 1.5$, 6.3 Hz, 1H), 5.67 (dd, $J = 2.1$, 6.0 Hz, 1H), 5.02 (d, $J = 8.7$ Hz, 1H), 4.69 (dt, $J = 1.8$, 7.5 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.63 (d, $J = 8.1$ Hz, 1H), 2.40 (s, 3H), 1.37 (s, 3H).

Decomposition product, diene 10: ^{1}H NMR δ 7.11 (m, 7H), 6.98 (m, 2H), 6.80 (m, 2H), 6.62 (d, $J = 1.5$ Hz, 1H), 6.28 (m, 1H), 5.92 (d, $J = 7.5$ Hz, 1H), 5.70 (d, $J = 7.5$ Hz, 1H), 5.61 (d, $J = 5.7$ Hz, 1H), 3.26 (s, 3H), 1.02 (s, 3H); ^{13}C NMR δ 155.7, 142.7, 135.8, 134.9, 134.0, 133.7, 131.3, 130.9, 128.5, 128.23, 128.17, 126.9, 126.6, 117.7, 89.3, 81.2, 64.1, 53.1, 22.3; IR (neat) ν 1758 cm^{-1}.

Phenylstannatrane 12a. Phenyllithium (2.06 mmol) was added slowly to a suspension of stannatrane chloride **11** (0.20 g, 0.68 mmol) in THF (8 mL) at −78 °C. After the final addition, the reaction mixture was stirred at −78 °C for 2 h and then was poured into a mixture of hexanes/water (3 mL each). The layers were separated, and the organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated to give **12a** (0.11 g, 0.33 mmol, 49%) and biphenyl as a light yellow oil. The mixture was used without further purification. Distillation and chromatography on silica gel or deactivated basic alumina led to no separation in the former case and decomposition in the latter: ^{1}H NMR (for methylene protons only) (C_6D_6) δ 2.02 (t, $J = 5.8$ Hz, 6H), 1.51 (m, 6H), 0.88 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR (for methylene carbons only) ($CDCl_3$) δ 54.9, 23.5, 7.0.

Vinylstannatrane 12b. Vinyllithium (0.68 mmol) was added slowly to a suspension of stannatrane chloride **11** (0.10 g, 0.34 mmol) in THF (4 mL) at −78 °C. After the final addition, the reaction mixture stirred at −78 °C for 6 h and then was poured into a mixture of hexanes/water (3 mL each). The layers were separated, and the organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated to give **12b** (56%) and tetrabutylstannane as a light yellow oil. The mixture was used as is, and an analytical sample was obtained by distillation: ^{1}H NMR ($CDCl_3$) δ 6.90 (dd, $J = 10.5$, 15.6 Hz, 1H), 6.36 (dd, $J = 3.2$, 10.7 Hz, 1H), 5.85 (dd, $J = 3.0$, 15.6 Hz, 1H), 2.00 (t, $J = 4.2$ Hz, 6H), 1.47 (m, 6H), 0.79 (t, $J = 5.0$ Hz, 6H); ^{13}C NMR (C_6D_6) δ 151.3, 130.6, 55.0, 23.8, 7.2.

General Procedure for Allylic Substitutions with Stannatranes. Allylic carbonate **5a** (0.04 to 0.09 mmol), $[\eta^3\text{-}C_3H_5PdCl]_2$ (2−3%), and P(furyl)$_3$ (13−14%) were combined in the reaction flask and purged with Ar for 10 min. DMPU (0.2 mL) was added and the reaction mixture stirred at room temperature for 10 min before the stannatrane (1−3 equiv) was added via syringe as a solution in DMPU (0.2 mL). After 6 h, a second portion of $[\eta^3\text{-}C_3H_5PdCl]_2$ (2−3%) and P(furyl)$_3$ (13−14%) were added. After an additional 6 h, the reaction mixture was diluted with diethyl ether and water. The layers were separated, and the organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated in vacuo.

Phenyl Addition Product 13a. A mixture of 30 mg (0.07 mmol) of allylic carbonate **5a**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (5%), P(furyl)$_3$ (27%), and phenylstannatrane (0.10 mmol) in DMPU at 60 °C gave **13a** (20 mg, 0.05 mmol, 65%) and recovered **5a** (2 mg, 0.01, 7%) after preparative chromatography with hexane/EtOAc (3/2): ^{1}H NMR δ 7.38 (m, 5H), 7.14 (m, 5H), 7.07 (m, 3H), 6.91 (m, 2H), 5.79 (dt, $J = 2.1$, 6.0 Hz, 1H), 5.63 (d, $J = 7.2$ Hz, 1H), 5.28 (bs, 1H), 5.25 (dt, $J = 2.7$, 6.0 Hz, 1H), 4.61 (d, $J = 7.5$ Hz, 1H), 4.00 (bs, 1H), 3.53 (s, 3H), 0.99 (s, 3H); ^{13}C NMR δ 158.3, 140.3, 136.8, 135.3, 133.9, 129.0, 128.6, 128.4, 128.2, 128.0, 127.4, 126.4, 90.6, 80.7, 65.8, 64.2, 59.4, 51.0, 18.3; IR (neat) ν 1749 cm^{-1}; mp 178−181 °C; HRMS m/z (M + H) calcd for $C_{28}H_{28}NO_3$ 426.2069, found 426.2055.

Vinyl Addition Product 13b. A mixture of 39 mg (0.09 mmol) of allylic carbonate **5a**, $[\eta^3\text{-}C_3H_5PdCl]_2$ (6%), P(furyl)$_3$ (28%), and vinylstannatrane (0.14 mmol) in DMPU at 60 °C gave **13b** (17 mg, 0.05 mmol, 49%) and recovered **5a** (6 mg, 0.02, 16%) after preparative chromatography with hexane/EtOAc (3/2): ^{1}H NMR δ 7.10 (m, 6H), 6.96 (m, 3H), 6.60 (bs, 1H), 5.92 (ddd, $J = 6.9$, 10.2, 17.1 Hz, 1H), 5.74 (d, $J = 7.2$ Hz, 1H), 5.70 (m, 1H), 5.26 (d, $J = 10.2$ Hz, 1H), 5.07 (m, 2H), 5.01 (d, $J = 17.4$ Hz, 1H), 4.60 (d, $J = 7.8$ Hz, 1H), 3.43 (s, 3H), 3.29 (d, $J = 5.4$ Hz, 1H), 1.37 (s, 3H); ^{13}C NMR δ 158.5, 137.6, 137.0, 135.6, 134.0, 128.4, 128.3, 128.2, 128.2, 128.0, 126.4, 116.8, 88.8, 80.8, 65.5, 64.0, 57.3, 50.9, 16.9; IR (neat) ν 1747 cm^{-1}; mp 130−131 °C; HRMS m/z (M + H) calcd for $C_{24}H_{26}NO_3$ 376.1913, found 376.1912.

Acknowledgment. Support for this research under Grant No. GM26178 from the National Institutes of General Medical Sciences (Public Health Service) is gratefully acknowledged. We thank Susie Miller for acquiring the X-ray crystal structure data. Mass spectra were obtained on instruments supported by a National Institutes of Health shared instrumentation grant (Grant No. GM49631).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **1**, **4a**,**b**, **5a**,**b**, **6a, 7a**,**b**, **9b**−**d**,**f**−**k**, **10**, **12a**,**b**, **13a**,**b**, ^{1}H spectra for **8a**,**b** and **9a**,**e**, complete X-ray crystals data for compounds **7a** and **13b**, additional experimental details for compounds **7a** and **8b**, and experimental details and characterization data for compounds **9b**−**k**.

JO0200318