J. Am. Chem. Soc. 1986, 108, 3033-3040

Palladium-Catalyzed Coupling of Vinyl Triflates with Organostannanes. Synthetic and Mechanistic Studies

William J. Scott[‡] **and J. K. Stille***

Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. *Received November 25, 1985*

Abstract: The palladium-catalyzed coupling reaction of vinyl triflates with acetylenic, vinyl, allyl, and alkyl tin reagents in the presence of lithium chloride or another suitable salt takes place in high yields under mild reaction conditions; however, benzyl and phenyl tin reagents give poor yield of coupled product. The utilization of a tin or silicon hydride reagent in place of the organotin partner yields the alkene by reductive cleavage of the triflate group. The palladium-catalyzed reaction of vinyl triflates with hexamethylditin gives vinyl stannanes in high yields. Regioselectively formed vinyl triflates can be used to produce 1,3-dienes as the regioisomeric coupled products.

The coupling of organic electrophiles with organometallic reagents catalyzed by group 10[1] transition metals represents a very mild method of forming carbon–carbon bonds.[2] Until recently, the coupling of vinylic electrophiles was limited almost exclusively to vinyl halides;[2,3] accordingly, the generality of the reaction was somewhat limited.[4] The use of other electrophiles, particularly enol ether derivatives, such as methyl vinyl ethers,[5] silyl enol ethers,[6] and enol phosphates,[7] in nickel-catalyzed coupling reactions with Grignard reagents or alanes has shown that other leaving groups will undergo the necessary oxidative addition reaction. However, the necessity of using strong nucleophiles severely limits the attached functionality compatible with the coupling reaction.

The palladium-catalyzed coupling reactions of acid chlorides,[8] benzyl halides,[8n,9] aryl halides,[10] allylic halides and acetates,[8n,11] and vinyl halides[12] with organostannanes have been described.[13] These coupling reactions are extremely mild and selective, taking place in the presence of such functionality as nitriles, nitroarenes, or aldehydes.[8d] Thus, organostannanes are among the most versatile nucleophiles available for group 10 catalyzed carbon–carbon bond formation.

The palladium-catalyzed coupling of vinyl trifluoromethanesulfonates (vinyl triflates)[14] with organostannanes in the presence of lithium chloride affords the advantages of a mild coupling reaction.[15] In addition, vinyl triflates may be synthesized by using known enolate chemistry,[16] which allows the regioselective formation of the vinyl electrophile. To date, the coupling of vinyl triflates with organostannanes has been applied to the synthesis of pleraplysillin 1[15] and in an intramolecular cyclization leading to bicyclic dienes.[17] More recently, the coupling of vinyl triflates with hexamethyldistannane has been reported to yield an expeditious route to vinylstannanes and vinyllithium precursors.[18] Herein, we report on the scope and limitations of the coupling reaction of vinyl triflates with organotin reagents, as well as the effect of varying the reaction conditions. In addition, some aspects of the reaction mechanism have been tested.

Results and Discussion

Reaction Conditions. As reported earlier,[15f] 4-*tert*-butylcyclohexenyl triflate (**1**) couples in high yield with vinyltributylstannane (**2**) in the presence of 2 mol % of tetrakis(triphenylphosphine)palladium(0) [$Pd(PPh_3)_4$] and 3 equiv of lithium chloride in refluxing tetrahydrofuran (THF) to give 1-vinyl-4-*tert*-butylcyclohexene (**3**). The reaction showed first-order kinetics over the first 2 to 3 half-lives. Accordingly, this reaction was chosen as a model for a study of the effects of various conditions on the coupling reaction.

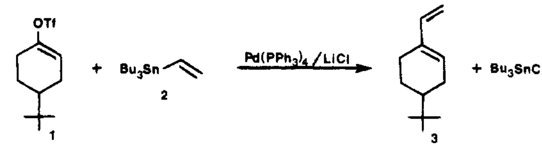


Table I. Effect of Varying Reaction Conditions on the Coupling Reaction[a]

entry	$Pd(PPh_3)_4$ (mol %)	LiCl (equiv)	$k \times 10^{-3}$ (mol **3**/mol Pd/s)[b]	t_{70} (h)[c]	% yield (GC)[d]
1	0.00	3.0			0
2	0.44	3.0	7.6[e]	11.0	>95
3	0.89	3.1	5.3	4.2	>95
4	1.98	3.0	2.7	3.6	>95
5	2.97	3.1	1.1[e]	3.0	>95
6	3.97	3.0	1.1[e]	3.2	>95
7	2.01[f]	3.0	2.5[e]	2.8	>95
8	1.98[g]	3.1	2.5	3.8	>95
9	1.99[h]	3.0	0.09	121.7	>95
10	1.97[i]	3.0	2.2	2.0	>95
11	1.99[j]	3.0	2.4	3.8	>95
12	1.97	0.0			<10
13	2.07	0.6	1.9[e]	3.0	71
14	2.04	1.1	1.7[e]	3.3	>95

[a] Reaction of 2.5 mmol of **1** with 3.0 mmol of **2** in 25 mL of THF in the presence of $Pd(PPh_3)_4$ and LiCl under Ar at 62 °C. [b] Mol Pd is the molar amount of palladium charged into the reaction. [c] Time required for a 70% GC yield of **3**. [d] Reaction quenched after 24 h. [e] Reaction did now show pseudo-first-order kinetics. Initial rate taken after ~1 h. [f] Reaction run under an atmosphere of dry air. [g] Liquid ingredients deoxygenated (freeze–pump–thaw) prior to addition. [h] Reaction run at 27 °C and quenched after 4440 h. [i] $Me_3Sn(C_2H_3)$ used in place of **2**. [j] "Aged" $Pd(PPh_3)_4$ (stored at −20 °C under air for 1 year) used.

Both palladium and lithium chloride are essential for the reaction to proceed (Table I). As the concentration of palladium

---

[‡] Department of Chemistry, University of Iowa, Iowa City, IA 52242.

(1) The group notation has been changed in accord with recent recommendations by the IUPAC and ACS nomenclature committees. Group I became groups 1 and 11, group II became groups 2 and 12, group III became groups 3 and 13, etc.

(2) For general reviews, see: (a) Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1980. (b) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis. Practical Applications of Transition Metals*; Plenum Press: New York, NY, 1984. (c) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: Berlin, 1980.

(3) For some examples of the group 10 catalyzed coupling of vinyl halides, see: (a) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151. (b) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340–345. (c) Dang, H. P.; Linstrumelle, G. *Tetrahedron Lett.* **1978**, *19*, 191–194. (d) Kosugi, M.; Hagiwara, I.; Migita, T. *Chem. Lett.* **1983**, 839–840.

(4) For example, see: Paquette, L. A.; Annis, G. D.; Schostarez, H. *J. Am. Chem. Soc.* **1982**, *104*, 6646–6653.

(5) (a) Wenkert, E.; Michelotti, E. L.; Swindell, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 2246–2247. (b) Wenkert, E.; Michelotti, E. L.; Swindell, C. S.; Tingoli, M. *J. Org. Chem.* **1984**, *49*, 4894–4899.

(6) Hayashi, T.; Katsura, Y.; Kumada, M. *Tetrahedron Lett.* **1980**, *21*, 3915–3918.

(7) (a) Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1980**, *21*, 2531–2534. (b) Takai, K.; Sato, M.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 108–115.

0002-7863/86/1508-3033$01.50/0

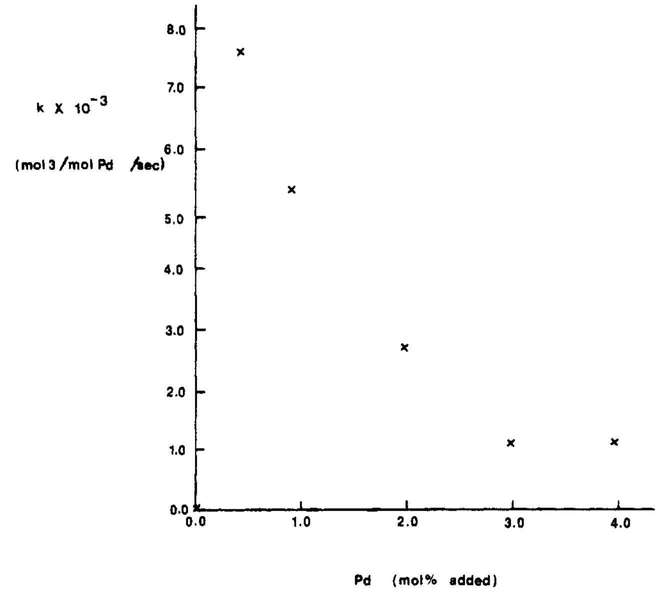


Figure 1.

Table II. Effect of Varying the Salt on the Coupling Reaction[a]

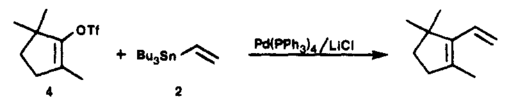
entry	salt	equiv	$k \times 10^{-3}$ (mol **3**/mol Pd_{in}/s)	t_{70} (*h*)[b]	% yield (GC)[c]
1	LiF	3.1			<10
2	LiCl	3.0	2.7	3.6	>95
3	LiBr	3.0	3.8[d]	5.9	>95
4	LiI	3.0	5.3[d]		61
5	$LiOAc \cdot 2H_2O$	3.0			<24
6	NaF	3.0			<10
7	NaCl	3.1			<10
8	KF	3.0			<10
9	KCl	3.0			<10
10	KI	3.0			<10
11	CsF	3.1	0.3	30.0	>95[e]
12	CsF (LiCl)	2.7 (0.1)	1.0	8.6	>95
13	$Bu_4NF \cdot 3H_2O$	1.3	8.2[d]	1.2	87[f]
14	Bu_4NI	3.0	18.9[d]	0.5	>95
15	$ZnCl_2$	1.9			<10
16	$ZnCl_2$ (LiCl)	2.1 (3.2)	5.5[d]		58
17	$ZnCl_2$ (LiCl)	0.2 (3.2)	5.0		>95

[a] Reaction of 2.5 mmol of **1**, 3.0 mmol of **2**, 2.0 mol % of $Pd(PPh_3)_4$, and the indicated salt in 25 mL of THF under Ar at 62 °C. [b] Time required for a 70% GC yield of **3**. [c] Reaction quenched after 24 h. [d] Reaction did not show pseudo-first-order kinetics. Initial rate taken after ~1 h. [e] Reaction quenched after 48 h. [f] Formation of 4-*tert*-butylcyclohexanone also observed.

is increased, the reaction rate, adjusted for the amount of palladium added (mol **3**/mol Pd/s) slowed (Figure 1). This may be due to increased concentrations of free phosphine in solution (vide infra), catalyst aggregation, or a change in the catalytic species in solution. The molar amount of palladium is that charged into the reaction and is not the amount of catalytically active species. Under a number of reaction conditions (Table I) the first-order kinetics were not maintained. The reaction either slowed, usually with the precipitation of palladium black (indicating a decomposition of the catalyst) or accelerated with time.

The reaction is not sensitive to the absence or presence of oxygen (entries 7 and 8). Use of vinyltrimethyltin in place of **2** initially had little effect on the rate of formation of **3**. However, as the reaction proceeded, the rate of formation of **3** accelerated, as reflected in the time required to achieve a 70% yield (t_{70}) (entry 10).

The coupling reaction is relatively insensitive to steric hindrance about the vinyl triflate. The coupling of 2,5,5-trimethylcyclopent-1-en-1-yl triflate (**4**) with **2** again displayed first-order kinetics through 3 half-lives and gave a quantitative yield of coupled product (GC). The rate of coupling of **4** with **2** ($k = 1.8 \times 10^{-3}$ mol **4**/mol Pd/s; t_{70} = 5.3 h) was somewhat slower than the coupling of **1** with **2**.



---

(8) (a) Kosugi, M.; Shimizu, Y.; Migita, T. *J. Organomet. Chem.* **1977**, *129*, C36–38. (b) Kosugi, M.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 1423–1424. (c) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638. (d) Milstein, D.; Stille, J. K. *J. Org. Chem.* **1979**, *44*, 1613–1618. (e) Kashin, A. N.; Bumagin, N. A.; Kalinovskii, I. O.; Beletskaya, I. P.; Reutov, O. A. *J. Org. Chem. USSR* **1980**, *16*, 1329–1334. (f) Guibe, F.; Four, P.; Rivere, H. *J. Chem. Soc., Chem. Commun.* **1980**, 432–433. (g) Four, P.; Guibe, F. *J. Org. Chem.* **1981**, *46*, 4439–4445. (h) Himbert, G.; Henn, L. *Tetrahedron Lett.* **1981**, *22*, 2637–2640. (i) Kashin, A. N.; Bumagina, I. G.; Bumagin, N. A.; Beletskaya, I. P. *Izu. Akad. Nauk., SSSR, Ser. Khim.* **1981**, 1433; *Chem. Abstr.* **1981**, *95*, 114976q. (j) Logue, M. W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549–2553. (k) Yamamoto, Y.; Yanai, A. *Chem. Pharm. Bull.* **1982**, *30*, 2003–2010. (l) Bumagin, N. A.; Bumagina, I. G.; Kashin, A. N.; Beletskaya, I. P. *J. Org. Chem. USSR* **1982**, *18*, 977–981. (m) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 669–670. (n) Labadie, J. W.; Stille, J. K. *J. Am. Chem Soc.* **1983**, *105*, 6129–6137. (o) Labadie, J. W.; Tueting, D.; Stille, J. K. *J. Org. Chem.* **1983**, *48*, 4634–4642. (p) Sonderquist, J. A.; Leong, W. W.-H. *Tetrahedron Lett.* **1983**, *24*, 2631–2634. (q) Labadie, J. W.; Stille, J. K. *Tetrahedron Lett.* **1983**, *24*, 4283–4286. (r) Hibino, J.; Matsuibara, S.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 2151–2154.

(9) (a) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4981–4991. (b) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992–4998. (c) Azizian, H.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1981**, *215*, 49–58.

(10) (a) Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301–302. (b) Kashin, A. N.; Bumagina, I. G.; Bumagin, N. A.; Beletskaya, I. P.; Reutov, O. A. *Izv. Akad. Nauk., SSSR, Ser. Khim.* **1980**, 479–480; *Chem. Abstr.* **1980**, *93*, 26019h. (c) Kashin, A. N.; Bumagina, I. G.; Bumagin, N. A.; Bakunin, V. N.; Beletskaya, I. P. *Izv. Akad. Nauk., SSSR, Ser. Khim.* **1980**, 2185; *Chem. Abstr.* **1981**, *94*, 30858u. (d) Kosugi, M.; Shimizu, K.; Ohtani, A.; Migita, T. *Chem. Lett.* **1981**, 829–830. (e) Kashin, A. N.; Bumagina, I. G.; Bumagin, N. A.; Beletskaya, I. P. *J. Org. Chem. USSR* **1981**, *17*, 18–24. (f) Kashin, A. N.; Bumagina, I. G.; Bumagin, N. A.; Bakunin, V. N.; Beletskaya, I. P. *J. Org. Chem. USSR* **1981**, *17*, 789–794. (g) Kosugi, M.; Kato, Y.; Kiuchi, K.; Migita, T. *Chem. Lett.* **1981**, 69–72. (h) Kosugi, M.; Suzuki, M.; Hagiwara, I.; Goto, K.; Saitoh, K.; Migita, T. *Chem. Lett.* **1982**, 939–940. (i) Kosugi, M.; Kameyama, M.; Migita, T. *Chem. Lett.* **1983**, 927–928. (j) Kosugi, M.; Sumita, T.; Ogata, T.; Sano, H.; Migita, T. *Chem. Lett.* **1984**, 1225–1226. (k) Kosugi, M.; Ishiguro, M.; Negishi, Y.; Sano, H.; Migita, T. *Chem. Lett.* **1984**, 1511–1512. (l) Bumagin, N. A.; Bumgina, I. G.; Beletskaya, I. P. *Dokl. Chem.* **1984**, *274*, 39–42. (m) Bumagin, N. A.; Bumagina, I. G.; Beletskaya, I. P. *Dokl. Chem.* **1984**, *274*, 53–55. (n) Zimmermann, E. K.; Stille, J. K. *Macromolecules* **1985**, *18*, 321–327.

(11) (a) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2591–2594. (b) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2595–2598. (c) Godschalx, J.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599–2602. (d) Beletskaya, I. P.; Kasatsin, A. N.; Lebedev, S. A.; Bumagin, N. A. *Bull. Acad. Sci. USSR* **1980**, *30*, 1994. (e) Bumagin, N. A.; Kasatsin, A. N.; Beletskaya, I. P. *Proc. Acad. Sci. USSR* **1982**, *266*, 345–348. (f) Bumagin, N. A.; Bumgina, I. G.; Kashin, A. N.; Beletskaya, I. P. *Zh. Obshch. Khim.* **1982**, *52*, 714; *Chem. Abstr.* **1982**, *97*, 39043u. (g) Keinan, E.; Greenspoon, N. *Tetrahedron Lett.* **1982**, *23*, 241–244. (h) Bumagin, N. A.; Kashin, A. N.; Beletskaya, I. P. *Dokl. Chem.* **1982**, *266*, 345–348. (i) Keinan, E.; Peretz, M. *J. Org. Chem.* **1983**, *48*, 5302–5309. (j) Godschalx, J.; Stille, J. K. *Tetrahedron Lett.* **1983**, *24*, 1905–1908. (k) Sheffy, F. K.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 7173–7175. (l) Sheffy, F. K.; Godschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833–4840. (m) Bumagin, N. A.; Kasatkin, A. N.; Beletskaya, I. P. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1984**, *33*, 588–594.

(12) Kosugi, M.; Hagiwara, I.; Migita, T. *Chem. Lett.* **1983**, 839–840.

(13) For reviews on palladium-catalyzed coupling of organostannanes, see: (a) Beletskaya, I. P. *J. Organomet. Chem.* **1983**, *250*, 551–564. (b) Kosugi, M.; Migita, T. *Yuki Gosei Kagaku Kyokaishi* **1980**, *38*, 1142–1150; *Chem. Abstr.* **1981**, *95*, 81044d. (c) Stille, J. K. *Angew. Chem., Int. Ed. Engl.*, in press.

(14) For a review on the chemistry of vinyl triflates, see: Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85–126.

(15) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630–4632.

(16) (a) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979–982. (b) Crisp, G. T.; Scott, W. J. *Synthesis* **1985**, 335–337.

(17) Piers, E.; Friesen, R. W.; Keay, B. A. *J. Chem. Soc., Chem. Commun.* **1985**, 809–810.

(18) (a) Wulff, W. D.; Peterson, G. A.; Gilbertson, S. R.; Yang, D.; Bauta, W. E.; Chan, K.-S.; Kaesler, R. W.; Faron, K. L. *Abstracts of Papers*, 190th National Meeting of the American Chemical Society, Chicago, IL; American Chemical Society: Washington, DC, 1985; ORGN 173. (b) Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K.-S.; Faron, K. L.; Gilbertson, S. R.; Kaesler, R. W.; Yang, D. C.; Murray, C. K. *J. Org. Chem.* **1986**, *51*, 277–279.

Table III. Effect of Varying the Solvent on the Coupling Reaction[a]

entry	solvent	$k \times 10^{-3}$ (mol 3/mol Pd_{in}/s)	t_{70} (h)[b]	% yield (GC)[c]
1	THF	2.7	3.6	>95
2	THF (0.56% H_2O)[d]	3.4	3.3	>95
3	THF (10% H_2O)[d]	7.5[e]		65
4	DME	0.4[e]	3.8	>95
5	dioxane	0.5[e]	3.8	>95
6	$CHCl_3$			0
7	CH_3CN	4.2[e]	3.6	77
8	$(CH_3)_2CO$[f]	0.2[e]	6.7	94
9	HMPA	≥24.7	≤0.4	>95
10	DMPU	14.8	0.7	>95
11	Sulfolane	4.0[e]		77
12	Me_2SO	7.1	1.3	>95
13	DMF	6.1[e]	1.2	>95
14	ethanol	8.5[e]		66
15	Et_3N	4.5[e]	7.5	81

[a] Reaction of 2.5 mmol of **1**, 3.0 mmol of **2**, 7.5 mmol of LiCl, 2.0 mol % $Pd(PPh_3)_4$, and 25 mL of solvent at 61-65 °C under Ar. [b] Time required for a 70% GC yield of **3**. [c] Reaction quenched after 24 h. [d] 0.56% H_2O is 3.0 molar equiv; 10% H_2O is 56 molar equiv. [e] Reaction did not obey pseudo-first-order kinetics. Initial rate taken after ~1 h. [f] Reaction run at 53 °C.

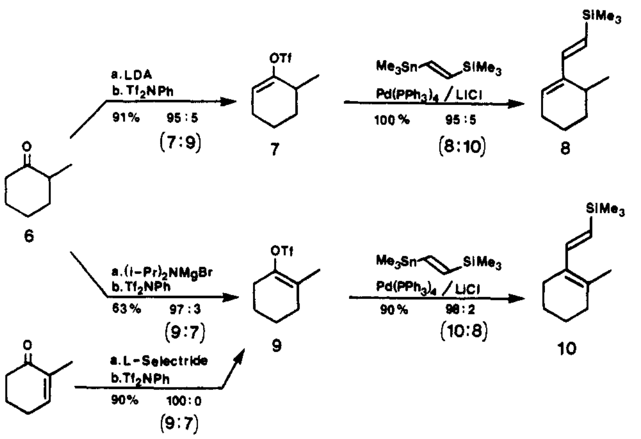
Lithium chloride was utilized in stoichiometric amounts, producing tributyltin chloride and lithium triflate. If less than an equivalent of lithium chloride was added, the reaction did not proceed to completion (entry 13). However, only 1 equiv was necessary (entry 14).

Most lithium salts may be employed in the coupling reaction (Table II). With the use of lithium bromide, the initial reaction rate increased, but the catalyst decomposed as the reaction proceeded, leading to a slightly longer reaction time (t_{70}) than with LiCl (entries 2 and 3). Lithium iodide increased the initial reaction rate even more, but the decomposition process was even faster and the coupling reaction did not proceed to completion (entry 4). Sodium and potassium salts proved unsuitable for the reaction.

The purification of reaction mixtures containing tributyltin chloride has been achieved by treatment with fluoride ion followed by filtration of the resulting insoluble tributyltin fluoride (**5**).[19] Thus it was of interest to determine whether **5** could be formed in situ. The replacement of lithium chloride with lithium, sodium, or potassium fluoride, however, gave no coupled product. Tributylammonium fluoride provided **3** and presumably **5** at greatly enhanced rates. However, 4-*tert*-butylcyclohexanone was also formed during the reaction (entry 13). Coupling **1** with **2** in the presence of cesium fluoride resulted in the decomposition of the majority of the palladium catalyst to palladium black. The reaction slowly proceeded to completion, nonetheless (entry 11). To circumvent the decomposition, a catalytic amount of lithium chloride was added along with an excess of cesium fluoride. Under these conditions, the reaction proceeded to completion at a reasonable rate. Removal of the solvent followed by trituration of the remaining oil with pentane and filtration of the resulting solids caused the removal of approximately 80% of the tin. Presumably, the remaining 20% stayed soluble as tributyltin chloride.

The addition of zinc chloride has been shown to facilitate the palladium-catalyzed coupling of organotins with electrophiles, presumably by transmetalation from the organotin to provide the corresponding organozinc chloride.[20] Addition of 2 equiv of zinc chloride and 3 equiv of lithium chloride to the reaction mixture doubled the rate of the reaction, but the catalyst decomposed during the reaction under these conditions (entry 16). Use of a catalytic amount of zinc chloride and 3 equiv of lithium chloride also increased the reaction rate, while showing first-order kinetics over 3 half-lives (entry 17). Thus, zinc chloride can be used either stoichiometrically[20] or catalytically to accelerate the rate of the coupling reaction, but it cannot replace the use of lithium chloride (entry 15).

Scheme I



The coupling reaction works well in THF, even in the presence of 3 equiv of water (Table III, entry 2). However, large amounts of water lead to catalyst decomposition (entry 3). Other ethers also were suitable solvents (entries 4 and 5).

Solvents which can both solubilize lithium chloride and act as good ligands, such as HMPA, DMPU,[21] Me_2SO, or DMF, accelerate the reaction rate. Polar solvents which do not solubilize lithium chloride well ($CHCl_3$, CH_3CN) or which do not act as good ligands (sulfolane) lead to catalyst decomposition prior to completion of the reaction. Ethanol and triethylamine caused catalyst decomposition after 30 to 40 turnovers.

Faster rates of coupling utilizing bis(triphenylphosphine)palladium(II) catalysts were observed early in the reaction, but the catalyst decomposed as the reaction proceeded (Table IV, compare entry 1 with entries 2, 4, and 8). Lowering the amount of palladium from 2.0 to 1.2 mol % accentuated the decomposition in that the reaction did not proceed to completion (entry 3). Use of an additional 2 mol % of triphenylphosphine in the reaction stabilized the catalyst and first-order kinetics were observed (entries 6 and 9), but at rates similar to those observed with $Pd(PPh_3)_4$.

Coupling in the presence of 2 mol % of bis(dibenzylideneacetonyl)palladium(0) ($Pd[dba]_2$) resulted in low yields of product (entry 10). However, addition of an additional 2 mol % of triphenylphosphine allowed the reaction to proceed to completion (entry 11). Further addition of triphenylphosphine was not helpful (entry 12). Use of 1,2-bis(diphenylphosphino)ethane in place of triphenylphosphine essentially stopped the coupling reaction (entries 13-15).

Reaction Scope. The palladium-catalyzed coupling reaction with organostannanes in the presence of lithium chloride is a very general reaction (Table V). Vinyl, alkyl, allyl, and acetylenic groups all transfer in good yield. Steric hindrance in the vinyl triflate has little effect on the reaction (entry 8). However, the coupling of two hindered partners tends to slow the reaction (entry 9). Acyclic vinyl triflates also react well (entry 10).

Neither benzyltributyltin nor benzyltrimethyltin react under these conditions. Addition of either a catalytic or a stoichiometric amount of zinc chloride did not alter this result. Triorganobenzyltins have been shown to couple with acid chlorides[8c,k,m] and benzyl halides.[9] The lack of reactivity of both the benzyl and butyl groups in benzyltributyltin (compare with entries 2 and 5) is not understood.

Reaction of **1** with either phenyltributyltin or phenyltrimethyltin led to mixtures of 1-phenyl-4-*tert*-butylcyclohexene, 4-*tert*-butylcyclohexene, and biphenyl in low conversion. Again, zinc chloride was of little help and transfer of the methyl or butyl groups was not observed.

---

[19] Leibner, J. E.; Jacobs, J. *J. Org. Chem.* **1979**, *44*, 449-450.

[20] Crisp, G. T.; Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7500-7506.

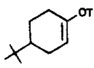
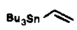
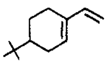
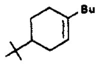
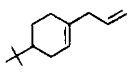
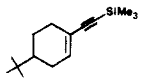
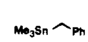
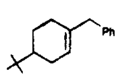
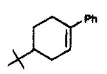
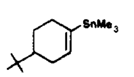
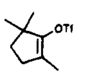
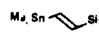
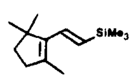
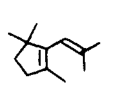
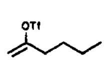
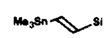
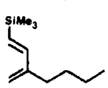
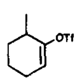
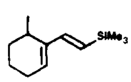
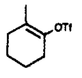
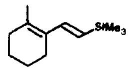
[21] For the use of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (*N*,*N'*-dimethylpropyleneurea, DMPU) as a replacement for HMPA, see: Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385-391.

Table IV. Effect of Varying the Palladium Catalyst on the Coupling Reaction[a]

entry	catalyst	added ligand	mol %	$k \times 10^{-3}$ (mol 3/mol Pd$_{in}$/s)	t_{70} (h)[b]	% yield (GC)[c]
1	$Pd(PPh_3)_4$			2.7	3.6	>95
2	$PhCH_2PdCl(PPh_3)_2$			4.7^{d}	4.8	94
3	$PhCH_2PdCl(PPh_3)_2$			4.8^{d}		53
4	$PdCl_2(PPh_3)_2$			4.4^{d}	4.4	>95
5	$PdCl_2(PPh_3)_2$[e]			0.3	33.3	>95
6	$PdCl_2(PPh_3)_2$	PPh_3	4.0	2.4	5.6	92
7	$PdCl_2[P(o\text{-}Tol)_3]_2$			2.7^{d}		35
8	$CHXPdCl(PPh_3)_2$ (**18**)[f]			4.0^{d}	4.8	>95
9	$CHXPdCl(PPh_3)_2$ (**18**)[f]	PPh_3	4.2	2.4	5.2	>95
10	$Pd(dba)_2$					23
11	$Pd(dba)_2$	PPh_3	4.2	2.6	4.0	>95
12	$Pd(dba)_2$	PPh_3	8.7	2.6	4.0	>95
13	$Pd(dba)_2$	$Ph_2PCH_2CH_2PPh_2$	2.0			$<10^{g}$
14	$Pd(dba)_2$	$Ph_2PCH_2CH_2PPh_2$	3.9	0.05		59^{g}
15	$Pd(dba)_2$	$Ph_2PCH_2CH_2PPh_2$	8.0			0^{g}

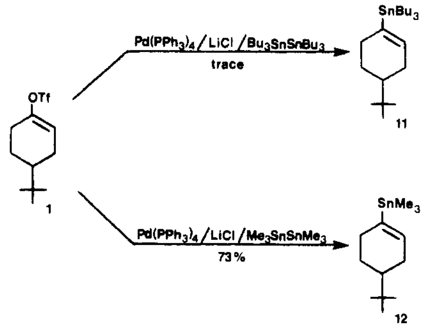
[a] Reaction of 2.5 mmol of **1**, 3.0 mmol of **2**, 7.5 mmol of LiCl, and 1.95–2.10 mol % catalyst in 25 mL of THF at 62 °C under Ar. [b] Time required for a 70% GC yield of **3**. [c] Reaction quenched after 24 h. [d] Reaction did not show first-order kinetics. Initial rate taken after ~1 h. [e] Reaction run at 27 °C and quenched after 125 h. [f] *trans*-(4-*tert*-Butylcyclohex-1-enyl)chlorobis(triphenylphosphine)palladium(II) (**18**). [g] Reaction quenched after 233 h.

Table V. Palladium-Catalyzed Coupling of Vinyl Triflates with Organotins

ENTRY	TRIFLATE	ORGANOTIN	REACTION TIME (h)[a]	PRODUCT	ISOLATED YIELD (%)[b]
1			17		91
2		Bu$_4$Sn	41		80
3			31		96
4		Me$_3$SnC≡CSiMe$_3$	41		90
5			24		trace[b]
6		Me$_3$SnPh	24		trace[b]
7		Me$_3$SnSnMe$_3$	12		73
8			36		100
9			133		80
10			17		90
11			6		100
12			100		90

[a] Reaction times are unoptimized. [b] GC analysis indicated small amounts of product formation. Reaction was not worked up.

Scheme II



The ability to regioselectively form vinyl triflates by utilizing enolate chemistry[16] and then convert the triflates into substituted olefins is illustrated in Scheme I. Treatment of 2-methylcyclohexanone (**6**) with LDA, followed by *N*-phenyltriflimide, gave 6-methylcyclohexenyl triflate (**7**) in good yield.[16a] Similarly, treatment of **6** with less than 1 equiv of bromomagnesium diisopiopylamide[22] followed by *N*-phenyltriflimide produced 2-methylcyclohexenyl triflate (**9**) in moderate yield. Alternatively, reduction of 2-methylcyclohex-2-en-1-one with L-Selectride (Aldrich) followed by treatment with N-phenyltriflimide afforded **9** as the only regioisomer observed.[16b] Either **7** or **9** could be coupled with *trans*-1-(trimethylstannyl)-2-(trimethylsilyl)ethylene to give **8** or **10**, respectively, in high yields. The 6-substituted isomer (**7**) reacted approximately ten times faster than the 2-substituted isomer (**9**). This effect on the rate of the coupling of vinyl triflates has been observed in other direct coupling reactions[18] and in the hydroformylation of vinyl triflates.[24]

The palladium-catalyzed coupling of vinyl triflates with hexamethyldistannane has been reported to give the corresponding vinyl trimethyltin in good yield.[18] While the coupling of **1** with hexabutyldistannane provided small amounts of **11**, coupling with hexamethyldistannane gave **12** in good yield (Scheme II).

This methodology was applied in a short, convergent synthesis of pleraplysillin 1 (**16**) (Scheme III). Addition of the lithium (*E*)-vinyltin cuprate **13**[26] to 3-furfuryl bromide[27] led to (*E*)-vinyltin

---

(22) Use of an excess of $(i\text{-}Pr)_2NMgBr$[23] led to a lower ratio of **9** to **7**. The same results were observed on trapping of the resulting enolate with $TMSCl/Et_3N/HMPA$. It would appear that the ratio of **9** to **7** observed in the presence of an excess of 2-methylcyclohexanone reflects the result of an equilibration prior to trapping of the enolate.

(23) Krafft, M. E.; Holton, R. E. *Tetrahedron Lett.* **1983**, *24*, 1345–1348.

(24) Baillargeon, V. B.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 452–461.

(25) For the isolation of pleraplysillin 1, see: (a) Cimino, G.; DeStefano, S.; Minale, L. *Tetrahedron* **1972**, *28*, 4761–4767. (b) Cimino, G.; DeStefano, S.; Minale, L. *Experimentia* **1974**, *30*, 864. (c) Thompson, J. E.; Walker, R. P.; Wratten, S. J.; Faulkner, D. J. *Tetrahedron Lett.* **1982**, *23*, 1865–1873.

(26) Corey, E. J.; Wollenberg, R. H. *Tetrahedron Lett.* **1975**, *16*, 2225–2226.

Scheme III

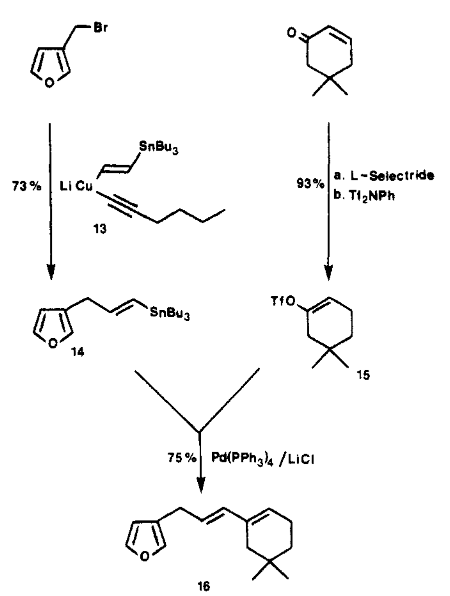


Table VI. Effect of Varying Reducing Agents on the Palldium-Catalyzed Reduction of Vinyl Triflates[a]

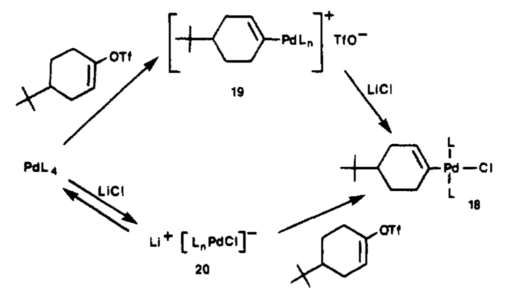
entry	reducing agent	equiv	$k \times 10^{-3}$ (mol product/mol Pd_{in}/s)	% yield (GC)[b]
1	Bu_3SnH	1.21	82.7[c]	>95 (78)
2	Et_3SiH	1.43	5.2	>95
3	$-[(CH_3)HSiO-]_n$	1.18[d]	0.5	>95 (75)
4	$LiAlH_4$[e]	1.43		14[f]
5	Li(*sec*-Bu)$_3$BH	1.20	27.3[c]	49
6	Li(*sec*-Bu)$_3$BH[e]	1.20	2.1	36
7	$NaBH_4$	1.26		<10
8	$NaBH_4$[g]	1.34		12
9	LiH	2.03		<10
10	KH	1.45		<10
11	1,4-cyclohexadiene	2.53		0
12	H_2NNH_2	2.00		0
13	H_2NNH_2[g]	2.00		<10
14	NaO_2CH	1.37		0
15	Bu_3N/HO_2CH	1.40		0
16	Bu_3N/HO_2CH[g]	1.40		26

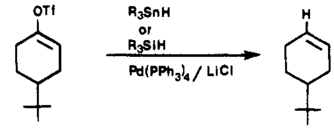
[a] Reaction of 2.5 mmol of **1**, the indicated reducing agent, 7.5 mmol of LiCl, and 2.0 mol % of $Pd(PPh_3)_4$ in 25 mL of THF under Ar at 62 °C to produce 4-*tert*-butylcyclohexene. [b] Reaction quenched after 24 h. Isolated yields in parentheses. [c] Reaction did not show pseudo-first-order kinetics. Initial rate taken after ~10 min. [d] Hydride equivalents based on 109 g/equiv. [e] Reaction run at 27 °C. [f] Formation of 4-*tert*-butylcyclohexanone also observed. [g] Reaction run without LiCl.

14 in 73% yield. Triflate **15** was prepared regiospecifically from 5,5-cyclohex-2-en-1-one[28] by conjugate reduction followed by enolate trapping with *N*-phenyltriflimide.[16b] Palladium-catalyzed coupling of **14** with **15** afforded pleraplysillin 1 in 75% yield.[29] No other isomers were detected.

Reduction of Vinyl Triflates. The ability to reduce a vinyl triflate to the corresponding alkene would provide a simple, mild, and versatile olefin synthesis from ketones. However, nucleophiles are known to react with vinyl triflates to cause either elimination or sulfur-oxygen bond cleavage.[30] Catalytic reduction with molecular hydrogen generates the saturated alkane.[31] Recently, it was shown that the palladium-catalyzed reduction of vinyl triflates to alkenes could be effected by tributyltin hydride[15] or by tributylammonium formate.[32] Silicon and tin hydrides reduced **1** readily (Table VI). More nucleophilic hydride reagents caused some competitive sulfur-oxygen bond cleavage, as well as the decomposition of the catalyst. Other metal hydride reagents gave little or no alkene (entries 7, 9, and 10).

Scheme IV



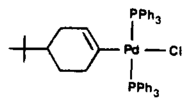


In contrast to the results obtained in reduction of vinyl triflates to olefins with tributylammonium formate in DMF,[32] use of this or other hydride transfer reagents[23] in the THF in the presence of lithium chloride gave back only starting material nearly quantitatively (entries 11, 12, 14, and 15). Reaction in the absence of lithium chloride did not give appreciably better yields (entries 8, 13, and 16).

Mechanistic Studies. A plausible, working mechanism for the palladium-catalyzed coupling of organic electrophiles with organostannanes involves the initial oxidative addition of the electrophile to the palladium(0) catalyst[2,8-13] followed by transmetalation of the organostannane to yield the corresponding bis(organo)palladium(II) complex, which rapidly undergoes reductive elimination to form the coupled product and regenerate the palladium(0) catalyst.

Reaction of $Pd(PPh_3)_4$ with 4 equiv of **1** and no lithium chloride at room temperature rapidly gave a brown solution, the $^{31}P\{H\}$ of which showed a new singlet at 22.9. This solution was stable to heat (60 °C) and to air. Removal of solvent and washing the residue with hexanes gave a dark brown powder (**17**) which could not be crystallized. Similarly, on examining the catalytic coupling of **1** with **2** in the absence of lithium chloride by $^{31}P\{H\}$ NMR, a singlet was observed at 22.9. While efforts to determine the structure of **17** are in progress, the complex has been shown not to participate as a catalyst in the coupling of **1** with **2**. Thus, in the absence of lithium chloride, the palladium is effectively removed from the reaction as **17**.

Reaction of $Pd(PPh_3)_4$ with **1** in the presence of lithium chloride immediately afforded a 1:2 mixture of a new complex (**18**) and free triphenylphosphine. The presence of a singlet in the $^{31}P\{H\}$ NMR (24.1) and a band in the IR assignable to a Pd–Cl stretch (275 cm^{-1}) as well as the absence of CF_3 in the ^{19}F NMR lead to the assignment of **18** as *trans*-(4-*tert*-butylcyclohex-1-enyl)chlorobis(triphenylphosphine)palladium(II).



18

---

(27) Parker, K. A.; Johnson, W. S. *Tetrahedron Lett.* **1969**, *10*, 1329–1332.

(28) Hiegel, G. A.; Burk, P. *J. Org. Chem.* **1973**, *38*, 3637–3639.

(29) For a prior synthesis of pleraplysillin 1, see: Masaki, Y.; Hashimoto, K.; Serizawa, Y.; Kaji, K. *Chem. Lett.* **1982**, 1879–1880.

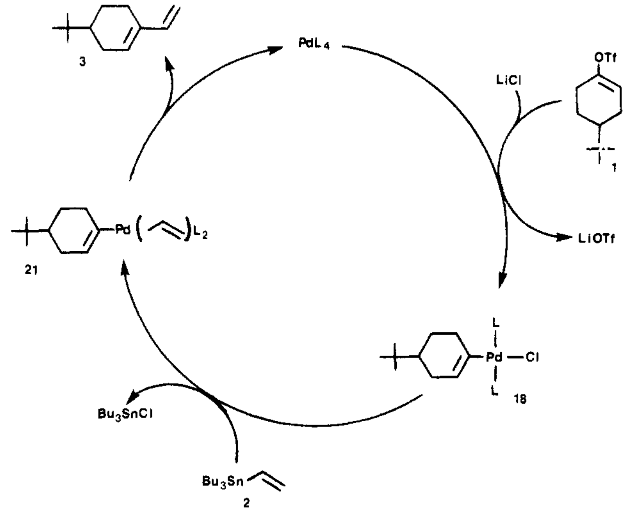
(30) (a) Summerville, R. H.; Senkler, C. A.; Schleyer P. v. R.; Dueber, T. E.; Stang, P. J. *J. Am. Chem. Soc.* **1974**, *96*, 1100–1110. (b) Stang, P. J.; Magnum, M. J.; Fox, D. P.; Haak, P. *J. Am. Chem. Soc.* **1974**, *96*, 4562–4569. (c) Garcia Martinez, A.; Espada Rios, I.; Martinez Alvarez, R.; Teso Vilar, E. *An. Quim., Ser. C* **1981**, *77*, 67–70. (d) Garcia Martinez, A.; Espada Rios, I.; Marinez Alvarez, R.; Gomez Anton, M. R.; Teso Vilar, E. *An. Quim., Ser. C* **1981**, *77*, 150–152.

(31) (a) Jigajinni, V. R.; Wightman, R. H. *Tetrahedron Lett.* **1982**, *23*, 117–120. (b) Subramanian, L. R.; Garcia Martinez, A.; Herrara Fernandez, A.; Martinez Alvarez, R. *Synthesis* **1984**, 481–485.

(32) Cacci, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1984**, *25*, 4821–4824.

(33) For a review on the use of hydride transfer reagents in palladium-catalyzed reductions, see: Johnstone, R. A. W.; Wilby, A. H.; Entwistle, I. D. *Chem. Rev.* **1985**, *85*, 129–170.

Scheme V. Proposed Mechanism for the Coupling of **1** with **2**



The reaction of $Pd(PPh_3)_4$ with lithium chloride and **1** to yield **18** can take place by either of two pathways (Scheme IV). Oxidative addition of the vinyl triflate to give the corresponding organopalladium(II) triflate complex (**19**) followed by the reaction with lithium chloride would generate **18**. Alternatively, lithium chloride could form a complex with palladium to give a salt, such as the chloropalladium(0) anion **20**. Oxidative addition of the vinyl triflate would then yield **18**. In support of this latter mechanism, treatment of a solution of $Pd(PPh_3)_4$ with LiCl afforded a new sharp singlet in the $^{31}P\{H\}$ NMR (δ 23.7). Addition of an excess of **1** to this solution immediately replaced this signal with a singlet at δ 24.1, representative of formation of **18**. Treatment of a mixture of **1** and **2** with **18** in the presence and in the absence of additional triphenylphosphine gave good yields of **3** and displayed reaction kinetics similar to those observed with other palladium(II) catalysts (Table IV, entries 8 and 9).

The stoichiometric addition of tetramethyltin to benzylchlorobis(triphenylphosphine)palladium(II) in HMPA at 60 °C for 48 h had been shown to give only a trace of ethylbenzene.[9a] However, in the presence of an excess of benzyl bromide, ethyl benzene was formed in good yield.[9a] These results were interpreted as evidence for a triorganopalladium(IV) complex in the catalytic cycle of the palladium-catalyzed coupling of organotins with benzyl halides.[9a] The reaction of **18** with 2 equiv of vinyltributyltin in THF at 62 °C for 48 h, however, gave a 60% yield of the coupled product (**3**), indicating that a palladium(IV) complex is not required for the coupling of vinyl triflates.

On the basis of these results, a catalytic cycle can be proposed in which oxidative addition of the vinyl triflate to the palladium(0) complex in the presence of lithium chloride yields **18** and lithium triflate (Scheme V). Transmetalation of **18** with vinyltributylstannane yields tributyltin chloride and the bis(organo)palladium(II) complex **21**, which rapidly undergoes reductive elimination to yield **3**, regenerating the palladium(0) catalyst.

Conclusions

Vinyl triflates have been shown to be excellent electrophiles for use in palladium-catalyzed coupling reactions. In particular, the coupling of vinyl triflates with organostannanes provides a useful two-step method for the regioselective formation of olefins from ketones.[15,17,18] This reaction requires the addition of lithium chloride or another suitable salt in order to prevent the formation of a noncatalytic palladium species and the concomitant removal of the palladium from the catalytic cycle. Attendant with this requirement is the need to employ a solvent system capable of dissolving most or all of the salt. Also, the solvent should act as a good to moderate ligand. Finally, while many palladium catalysts can be employed with varying degrees of success, tetrakis(triphenylphosphine)palladium(0) appears to be superior.

The reaction can be used for the coupling of acetylenic, vinyl, alkyl, and allylic tin reagents. However, benzyl and phenyl tin reagents work poorly for reasons which are not readily apparent. Use of hexabutylditin gives poor yields of coupled products, but hexamethylditin leads to good yields of trimethylvinylstannanes.[18]

Catalytic reduction of vinyl triflates with dihydrogen gives the corresponding alkane.[24] However, use of tributyltin hydride[15] or silyl hydride in THF or formate in DMF[32] generates olefins in good yields. Finally, reaction of vinyl triflates with olefins in the presence of a base leads to dienes *via* a Heck-olefination process.[34] Thus, vinyl triflates have been shown to be valuable intermediates for use in both synthetic organic and synthetic organometallic chemistry.

Experimental Section

^1H spectra were recorded on a Varian EM 360 (60 MHz), a JOEL FX 100 (100 MHz), or an IBM WP 270 (270 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. ^{13}C NMR were recorded on an IBM WP 270 (68 MHz) with $CDCl_3$ as solvent and internal standard. $^{31}P\{H\}$ NMR were taken on an IBM WP 200 (81 MHz) with C_6D_6 or THF-d_8 as solvent and H_3PO_4 as an external standard. Infrared spectra were taken on a Beckman 4250 spectrometer. Far-infrared spectra were taken on a Perkin-Elmer 983 spectrometer with polyethylene cells. Gas chromatographic analyses were run on a Varian 3700 gas chromatograph equipped with a $^1/_8$ in. × 6 ft 3% Se-30 column and a thermal conductivity detector. Capillary GC analyses were conducted in a Varian 3700 gas chromatograph equipped with a 0.25 mm × 50 m SE-30 column and a flame ionization detector. Low-resolution mass spectra were conducted on a V.G. Micromass 16 spectrometer. High-resolution mass spectra (HRMS) were obtained from the Midwest Center for Mass Spectroscopy at the University of Nebraska. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Tetrahydrofuran (THF) and 1,2-dimethoxyethane (DME) were distilled from potassium. Triethylamine, *p*-dioxane, acetonitrile, hexamethylphosphoramide (HMPA), *N*,*N'*-dimethylpropyleneurea (DMPU),[21] sulfolane, dimethyl sulfoxide (Me_2SO), and dimethylformamide (DMF) were distilled from calcium hydride. Chloroform was distilled from phosphorous pentoxide. The salts (LiCl, LiF, LiBr, NaF, NaCl, KF, KCl, CsF) were dried at 140 °C for 24 h prior to use.

Thin-layer chromtographic analyses (TLC) were performed on EM silica gel 60F-254 plates. Column chromatographic purifications of reaction mixtures were performed with Woelm 230-400-mesh silica gel. Bulb-to-bulb distillations were conducted with an Aldrich Kuglerohr apparatus.

Vinyl Triflates. The following vinyl triflates were prepared according to literature methods: 4-*tert*-butylcyclohexenyl triflate (**1**),[35] 2,2,5-trimethylcyclopentenyl triflate (**4**),[20] hex-1-en-2-yl triflate,[30a] 6-methylcyclohexenyl triflate (**7**),[16a] 2-methylcyclohexenyl triflate (**9**),[16b,20] and 5,5-dimethylcyclohexenyl triflate (**15**).[16b]

Organostannanes. The following organostannanes were prepared according to literature methods: vinyltributyltin,[36] vinyltrimethyltin,[37] allyltributyltin,[38] 1-(trimethylsilyl)-2-(trimethylstannyl)acetylene,[39] benzyltrimethyltin,[40] phenyltrimethyltin,[41] (*E*)-1-(trimethylsilyl)-2-(trimethylstannyl)ethylene,[42] 1-(tributylstannyl)-2-methylprop-1-ene,[43] (*E*)-1,2-bis(tributylstannyl)ethylene.[26] Tetrabutyltin, hexabutyldistannane, and hexamethyldistannane were used as received (Alfa Products).

(*E*)-1-(Tributylstannyl)-2-(3-furfuryl)ethylene (14). To a solution of 8.51 g of (*E*)-1,2-bis(tributylstannyl)ethylene (1.4 mmol) in 100 mL of THF at −78 °C was added methyllithium (10.8 mL of a 1.43 N ether solution, 1.5 mmol). The resulting solution was stirred at −78 °C for 2 h and added to a suspension of 2.45 g of hexynylcopper (1.7 mmol) in THF (40 mL) at −40 °C. After the solution was stirred for 30 min at −40 °C and cooled to −78 °C, the resulting slurry was treated with a solution of 2.26 g of 3-furfuryl bromide[27] (1.4 mmol) in THF (10 mL). The resulting mixture was allowed to warm to room temperature, filtered through a pad of Florisil, and concentrated to give a brown oil. Bulb-to-bulb distillation of this oil gave low boiling constituents (80 °C (0.2

---

[34] (a) Cacci, S.; Morena, E.; Ortar, G. *Tetrahedron Lett.* **1984**, *25*, 4821–4824. (b) Harnisch, W.; Morera, E.; Ortar, G. *J. Org. Chem.* **1985**, *50*, 1990–1992. (c) Scott, W. J.; Pena, M. R.; Sward, K.; Stoessel, S. J.; Stille, J. K. *J. Org. Chem.* **1985**, *50*, 2302–2308.

[35] Scott, W. J. Ph.D. Dissertation, Cornell University, Ithaca, NY, 1983.

[36] Seyferth, D.; Stone, F. G. A. *J. Am. Chem. Soc.* **1957**, *79*, 515–517.

[37] Seyferth, D.; Vaughn, L. G. *J. Organomet. Chem.* **1963**, *1*, 138–152.

[38] Jones, W. J.; Davies, W. C.; Bowden, S. T.; Edwards, C.; Davis, V. E.; Thomas, L. H. *J. Chem. Soc.* **1974**, 1446–1450.

[39] Menz, G.; Wrackmeyer, B. *Z. Naturforsch., B* **1977**, *32B*, 1400–1407.

[40] Kraus, C. A.; Bullard, R. H. *J. Am. Chem. Soc.* **1926**, *48*, 2131–2136.

[41] Eaborn, C.; Waters, J. A. *J. Chem. Soc.* **1962**, 1131–1132.

[42] Seyferth, D.; Vick, S. C. *J. Organomet. Chem.* **1978**, *144*, 1–12.

[43] Saihi, M. L.; Pereyre, M. *Bull. Soc. Chim. Fr.* **1977**, 1251–1255.

mmHg) followed by furan **14** (4.10 g, 73%): bp (bulb-to-bulb) 95 °C (0.2 mmHg); TLC (hexane) R_f 0.90; IR (neat) 1600, 1500, 1455 1375, 1150, 875 cm^{-1}: ^{1}H NMR (270 MHz) δ 0.90–1.06 (m, 6 H), 0.95 (t, J = 7.0 Hz, 9 H), 1.30–1.43 (m, 6 H), 1.50–1.63 (m, 6 H), 3.32 (d, J = 3.8 Hz, 2 H), 6.07 (br s, 1 H), 6.08 (br d, J = 4.1 Hz, 1 H), 6.31 (br s, 1 H), 7.27 (br s, 1 H), 7.42 (br s, 1 H); ^{13}C NMR (68 MHz) δ 9.6 (3 C), 13.6 (3 C), 27.2 (3 C), 29.2 (3 C), 33.3, 111.3, 123.4, 129.2, 139.2, 142.8, 146.4; LRMS m/z 341 ($C_{19}H_{34}{}^{16}O^{120}Sn\text{-}C_4H_9$, 88%), 285 ($C_{19}H_{34}{}^{16}O^{120}Sn\text{-}C_4H_9\text{-}C_4H_8$, 92%), 229 ($C_{19}H_{34}{}^{16}O^{120}Sn\text{-}C_4H_9\text{-}2[C_4H_8]$, 100%); HRMS calcd for $C_{15}H_{25}{}^{16}O^{120}Sn$ 341.0930 and found 341.0928, calcd for $C_{11}H_{25}{}^{16}O^{120}Sn$ 285.0303 and found 285.0301, calcd for $C_7H_9{}^{16}O^{120}Sn$ 228.9676 and found 228.9697.

Reaction Condition Studies. Reactions listed in Tables I–IV were run as follows: Solid ingredients were treated with 15 mL of the indicated solvent. To this mixture was added a solution of 2.5 mmol of 4-*tert*-butylcyclohexenyl triflate, 3.0 mmol of vinyltributyltin, and 2.5 mmol of an internal standard (either ethylbenzene or biphenyl) in 5 mL of the indicated solvent, followed by an additional 5 mL of solvent. This was then heated to 62–65 °C under a static argon atmosphere. Samples (0.1 to 0.2 mL) were removed periodically and immediately analyzed by GC or capillary GC. Conversion factors for the calculation of yields were developed within 12 h of use.

General Procedure (Table V). 1-Vinyl-4-*tert*-butylcyclohex-1-ene (3, Table V, entry 1): To a slurry of LiCl (0.54 g, 12.9 mmol) and $Pd(PPh_3)_4$ (0.099 g, 2.0 mol %) in 10 mL of THF was added a solution of 1.22 g (4.2 mmol) of **1** and 1.35 g (4.2 mmol) of **2**. This was heated to reflux for 17 h, cooled to room temperature, and diluted with 30 mL of pentane. The resulting solution was washed sequentially with water, a 10% ammonium hydroxide solution, water, and a concentrated sodium chloride solution. This solution was dried, filtered through a small pad of silica gel and concentrated to yield an oil. Bulb-to-bulb distillation of the resulting oil afforded the diene **3**[44] as a colorless oil (0.64 g, 91%): bp (bulb-to-bulb) 80 °C (0.7 mmHg); TLC (hexanes) R_f 0.74; IR (neat) 3080, 3030, 1645, 1605 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.86 (s, 9 H), 1.07–1.53 (m, 3 H), 1.84–2.35 (m, 4 H), 4.88 (d, J = 10.7 Hz, 1 H), 5.04 (d, J = 17.5 Hz, 1 H), 5.74–5.75 (m, 1 H), 6.35 (dd, J = 10.7, 17.5 Hz, 1 H); ^{13}C NMR (68 MHz) δ 23.8, 25.3, 27.2 (3 C), 27.4, 32.2, 44.4, 109.7, 129.8, 136.0, 139.4; LRMS m/z 168 (M^+, 19%).

The following compounds were prepared in an analogous manner:

1-Butyl-4-*tert*-butylcyclohex-1-ene (Table V, entry 2):[44b] TLC (hexanes) R_f 0.76; ^{1}H NMR (60 MHz) δ 0.84–0.87 (m, 12 H), 1.00–1.70 (m, 7 H), 1.70–2.30 (m, 6 H), 5.70 (m, 1 H). The ^{1}H NMR was identical with that of an authentic sample.

1-Allyl-4-*tert*-butylcyclohex-1-ene (Table V, entry 3): bp (bulb-to-bulb) 60 °C (0.03 mmHg); TLC (hexanes) R_f 0.65; IR (neat) 3060, 1660, 1390, 1360, 900 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.84 (s, 9 H), 1.03–1.32 (m, 3 H), 1.70–1.88 (m, 2 H), 1.95–2.10 (m, 2 H), 2.66 (d, J = 6.8 Hz, 2 H), 4.95–5.04 (m, 2 H), 5.40–5.42 (m, 1 H), 5.70–5.85 (m, 1 H); ^{13}C NMR (68 MHz) δ 24.3, 26.9, 27.3 (3 C), 29.9, 32.2, 42.0, 44.3, 115.3, 122.2, 136.1, 137.0; LRMS m/z 178 (M^+, 0.3%). Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.46; H, 12.21.

1-(2-(Trimethylsilyl)ethynyl)-4-*tert*-butylcyclohex-1-ene (Table V, entry 4): Bp (bulb-to-bulb) 105 °C (0.8 mmHg); TLC (hexanes) R_f 0.28; IR (neat) 3030, 2140, 1635, 1600, 1395, 1365, 1250 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.15 (s, 9 H), 0.83 (s, 9 H), 1.08–1.21 (m, 3 H), 1.74–1.85 (m, 2 H), 2.06–2.16 (m, 2 H), 6.15 (br s, 1 H); ^{13}C NMR (68 MHz) δ 0.1 (3 C), 23.7, 27.1 (3 C), 27.4, 30.6, 32.1, 43.3, 91.0, 107.1, 120.7, 136.3; LRMS m/z 234 (M^+, 5%). Anal. Calcd for $C_{15}H_{26}Si$: C, 76.85; H, 11.18. Found: C, 77.00; H, 11.01.

1-(Trimethylstannyl)-4-*tert*-butylcyclohexene (Table V, entry 7): bp (bulb-to-bulb) 110 °C (0.55 mmHg); TLC (hexanes) R_f 0.84; IR (neat) 3050, 2900, 1610, 1390, 1360; ^{1}H NMR (270 MHz) δ 0.07 (s, 9 H), 0.84 (s, 9 H), 1.16–2.23 (m, 7 H), 5.82–5.84 (m, 1 H); ^{13}C NMR (68 MHz) δ −10.5 (3 C), 25.1, 27.2 (3 C), 29.3, 32.2, 32.7, 44.3, 137.0, 139.8. Anal. Calcd for $C_{13}H_{26}Sn$: C, 51.86; H, 8.71. Found: C, 51.99; H, 8.80.

1-((*E*)-2-(Trimethylsilyl)ethen-1-yl)-2,5,5-trimethylcyclopent-1-ene (Table V, entry 8): bp (bulb-to-bulb) 75 °C (0.75 mmHg); TLC (hexane) R_f 0.83; IR (neat) 3050, 1630, 1600, 1380, 1365, 1250, 990 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.08 (s, 9 H), 1.14 (s, 6 H), 1.61 (t, J = 7.2 Hz, 2 H), 1.75 (s, 3 H), 2.24 (t, J = 7.2 Hz, 2 H), 5.87 (d, J = 19.7 Hz, 1 H), 6.52 (d, J = 19.7 Hz, 1 H); ^{13}C NMR (68 MHz) δ −1.1 (3 C), 27.4 (2 C), 35.8, 40.3, 46.7, 129.3, 137.6, 142.5, 146.8; LRMS m/z 208 (M^+, 8%). Anal. Calcd for $C_{13}H_{24}Si$: C, 74.92; H, 11.61. Found: C, 74.74; H, 11.86.

1-(2-Methylprop-1-en-1-yl)-2,5,5-trimethylcyclopent-1-ene (Table V, entry 9): bp (bulb-to-bulb) 20 °C (0.80 mmHg); IR ($CDCl_3$) 3000 (sh), 1370, 1350, 1050, 1035 cm^{-1}; ^{1}H NMR (60 MHz) δ 1.02 (s, 6 H), 1.59 (br s, 6 H), 1.65–1.90 (m, 2 H), 1.88 (br s, 3 H), 2.33 (br t, J = 7 Hz, 2 H), 5.52 (br s, 1 H); ^{13}C NMR δ 15.7, 22.7, 25.4, 27.8 (2 C), 35.4, 39.4, 119.1, 131.5, 135.4, 142.1; LRMS m/z 164 ($M^+ - CH_3$, 100%).

3-Butyl-1-((*E*)-trimethylsilyl)-1,3-butadiene (Table V, entry 10): bp (bulb-to-bulb) 40 °C (0.5 mmHg); TLC (hexanes) R_f 0.45; IR (neat) 3080, 1620, 1380, 1260, 1250, 1010, 985, 850 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.08 (s, 9 H), 0.85–0.94 (m, 3 H), 1.25–1.43 (m, 4 H), 2.20 (m, 2 H), 5.01 (br s, 2 H), 5.86 (d, J = 19.1 Hz, 1 H), 6.53 (d, J = 19.2 Hz, 1 H); ^{13}C NMR (68 MHz) δ −1.2 (3 C), 14.0, 22.7, 30.5, 31.1, 111.2, 115.7, 128.4, 146.1; LRMS m/z 184 (M^+, 1%) 183 (M^+ - H, 5%), 167 (M^+ - CH_4 - H, 31%), 73 ($SiMe_3$, 100%). Anal. Calcd for $C_{11}H_{22}Si$: C, 72.44; H, 12.16. Found: C, 72.26; H, 12.44.

(*E*)-1-(Trimethylsilyl)-2-(6-methylcyclohex-1-en-1-yl)ethylene (8; Table V, entry 11): bp (bulb-to-bulb) 50 °C (0.5 mmHg); TLC (hexanes) R_f 0.64; IR (neat) 3040, 3100, 1730, 1710, 1640, 1590 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.07 (s, 9 H), 1.07 (d, J = 7.2 Hz, 3 H), 1.54–1.69 (m, 4 H), 2.11 (m, 2 H), 2.59–2.62 (m, 1 H), 5.70–5.74 (m, 1 H), 5.74 (d, J = 19.1 Hz, 1 H), 6.39 (d, J = 19.2 Hz, 1 H); ^{13}C NMR (68 MHz) δ −1.1 (3 C), 17.9, 19.9, 26.0, 27.4, 30.0, 124.7, 129.9, 142.5, 146.5; LRMS m/z 194 (M^+, 13%). Anal. Calcd for $C_{12}H_{22}Si$: C, 74.15; H, 11.41. Found: C, 74.10; H, 11.61.

(*E*)-1-(Trimethylsilyl)-2-(2-methylcyclohex-1-en-1-yl)ethylene (10; Table V, entry 12): bp (bulb-to-bulb) 90 °C (0.8 mmHg); IR (neat) 3050, 1630, 1575, 1375, 1240, 1205, 975, 865, 825 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.09 (s, 9 H), 1.56–1.64 (m, 4 H), 1.82 (s, 3 H), 2.07–2.16 (m, 4 H), 5.75 (d, J = 18.9 Hz, 1 H), 7.06 (d, J = 19.0 Hz, 1 H); ^{13}C NMR (68 MHz) δ −1.0, 19.2, 23.1, 25.2, 29.7, 33.3, 124.9, 129.5, 134.3, 142.3; LRMS m/z 194 (M^+, 8%).

Pleraplysillin 1 (16). A mixture of lithium chloride (0.20 g, 4.7 mmol), $Pd(PPh_3)_4$ (0.031 g, 1.8 mol %), triflate **15** (0.38 g, 1.5 mmol), and vinyl tin **14** (0.61 g, 1.5 mmol) in THF (20 mL) was heated at reflux for 24 h, cooled to room temperature, and diluted with 20 mL of pentane. The resulting mixture was washed with a 5% ammonium hydroxide solution (3 × 25 mL). The combined aqueous phases were back-extracted with pentane (3 × 25 mL). The combined organics were washed with brine, filtered through a small plug of silica gel, and concentrated under reduced pressure to give a green oil. Column chromatography (silica gel, hexane) afforded 0.24 g of pleraplysillin 1 as a colorless oil (75% yield): TLC (hexanes) R_f 0.23; IR (neat) 3020, 1650, 1625, 1500, 1385, 1365, 1020, 960, 870, 770 cm^{-1}; ^{1}H NMR (100 MHz) δ 0.92 (s, 6 H), 1.33 (t, J = 6.5 Hz, 2 H), 1.90 (br s, 2 H), 2.11 (m, 2 H), 3.19 (d, J = 6.5 Hz, 2 H), 5.45–5.75 (m, 2 H), 6.13 (d, J = 15.7 Hz, 1 H), 6.26 (s, 1 H), 7.20 (br s, 1 H), 7.33 (t, J = 1.5 Hz, 1 H); ^{13}C NMR (68 MHz) δ 23.6, 28.3, 28.5 (2 C), 28.9, 35.4, 38.7, 111.2, 123.9, 126.4 (2 C), 134.6, 134.8, 139.2, 142.8; LRMS m/z 216 (M^+, 29%). Both the ^{1}H and ^{13}C spectra were identical with those of authentic samples.

4-*tert*-Butylcyclohexene (Table VI). To a slurry of 7.5 mmol of lithium chloride and 0.050 mmol of $Pd(PPh_3)_4$ in 15 mL of THF was added a solution of 2.5 mmol of **1** and 2.5 mmol of an internal standard (ethylbenzene or biphenyl) in 5 mL of THF followed by an additional 5 mL of THF and then the reducing agent. This mixture was immediately heated to reflux (62 °C) under a static argon atmosphere. Samples were removed periodically and immediately analyzed by GC or capillary GC. Conversion factors for the calculation of yields were developed within 12 h of use.

In separate procedures reactions employing tributyltin hydride (Table VI, entry 1) and poly(methylhydrosiloxane) (Table VI, entry 3) were repeated without sampling. When the reactions were complete, the resulting solutions were diluted with 25 mL of pentane, washed with a 5% ammonium hydroxide solution (3 × 25 mL), followed by a concentrated sodium chloride solution (25 mL), filtered through a plug of silica gel, and concentrated by distillation to give the 4-*tert*-butylcyclohexene as a colorless oil: IR (neat) 3020, 1655, 1390, 1365 cm^{-1}; ^{1}H NMR (60 MHz) δ 0.90 (s, 9 H), 1.10–1.90 (m, 3 H), 1.90–2.30 (m, 4 H), 5.60–5.70 (m, 2 H). Both the IR and the ^{1}H NMR spectra were identical with those of an authentic sample.

Stoichiometric Reaction of $Pd(PPh_3)_4$ with 4-*tert*-Butylcyclohexenyl Triflate (1). To a solution of 0.118 g (0.102 mmol) of $Pd(PPh_3)_4$ in 15 mL of THF under Ar was added a solution of 0.062 g (0.217 mmol) of **1**. The resulting mixture was stirred at room temperature and volatiles were removed by vacuum transfer. The resulting material was washed with hexanes to give 0.125 g of an amorphous brown solid, $^{31}P\{H\}$ NMR (C_6D_6:THF 1:1, 81 MHz) δ 22.9 (s).

Stoichiometric Reaction of $Pd(PPh_3)_4$ with 4-*tert*-Butylcyclohexenyl Triflate (1) and Lithium Chloride. To a slurry of 0.359 g (0.311 mmol) of $Pd(PPh_3)_4$ and 0.165 g (3.89 mmol) of lithium chloride in 15 mL of THF was added a solution of 0.181 g (0.632 mmol) of **1** in 5 mL of THF followed by 5 mL of THF. This was stirred at room temperature for 4 h and volatile compounds were removed by vacuum transfer. The re-

---

[44] (a) Paquette, L. A.; Melega, W. P.; Kramer, J. D. *Tetrahedron Lett.* **1976**, *17*, 4033–4036. (b) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1980**, *21*, 4313–4316.

maining solids were washed with hexanes (2 × 30 mL) and treated with 30 mL of dry benzene. The resulting white solids were removed by filtration. Solvent was removed by vacuum transfer and the resulting light cream colored solids were washed with pentane (2 × 30 mL) and vacuum dried (0.235 g, 98%): mp (sealed tube under Ar) 139–141 °C dec; IR (paraffin oil) 3065, 3040, 1580, 1565, 1480, 1435, 1430, 950, 735, 695, 685 cm^{-1}; far-IR (C_6D_6, polyethylene cell) 275 cm^{-1} (Pd-Cl); ^{1}H NMR (C_6D_6, 270 MHz) δ 0.66 (s, 9 H), 0.90–2.25 (m, 7 H), 5.10 (br s, 1 H), 7.00–8.00 (m, 30 H); ^{31}P{H} NMR (C_6D_6, 81 MHz) δ 24.1 (s). Anal. Calcd for $C_{46}H_{46}ClP_2Pd$: C, 68.83; H, 5.78; Cl, 4.42; P, 7.71. Found: C, 68.63; H, 5.80; Cl, 4.55; P, 7.56.

Acknowledgment. The authors gratefully acknowledge support for this research through Grant No. CHE-8305468 from the National Science Foundation, as well as the generous loan of the palladium through the Johnson Matthey Inc. Metal Loan Program. High-resolution mass spectral determinations were performed by the Midwest Center for Mass Spectrometry, a National Science Foundation Regional Instrumentation Facility (Grant No. CHE-8211164). Also, the authors thank Professors Faulkner,[25c] Minale,[25a,b] and Masaki[29] for supplying authentic spectra of pleraplysillin 1 and Professor Wulff[18] for furnishing a manuscript of his results. Finally, the authors thank Dr. Geoffrey T. Crisp for conducting the hexamethyldistannane coupling studies.

Total Synthesis of (+)-Jatropholones A and B: Exploitation of the High-Pressure Technique

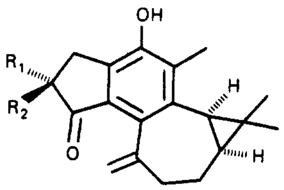
Amos B. Smith III,*[1] Nigel J. Liverton, Nicholas J. Hrib,[2] Hariharan Sivaramakrishnan, and Kevin Winzenberg

Contribution from the Department of Chemistry, The Monell Chemical Senses Center, and The Laboratory for Research on the Structure of Matter, The University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received October 16, 1985*

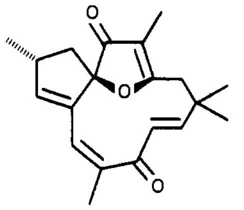
Abstract: Application of a high-pressure (5 kbar) induced Diels–Alder reaction between furan **12** and homochiral enone **6** for construction of the jatropholone skeleton is described. Subsequent aromatization, introduction of the *exo*-methylene, regioselective oxidation, and methylation afford (+)-jatropholones A and B.

Introduction and Background

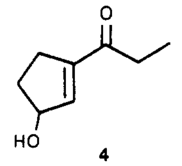
In 1979, Connolly et al. at Glasgow isolated two new diterpenes termed jatropholones A and B (**1** and **2**) from *Jatropha gossypiifolia L*,[3] the same plant that yields jatrophone (**3**).[4] Unlike jatrophone, the jatropholones were found to be biologically inactive. Their novel structure however attracted our attention in that they represent a new skeletal class of diterpenes. Furthermore, we were interested in utilizing an intermediate (i.e., **4**) developed during the course of our jatrophone work,[5] which appeared ideally suited for construction of the jatropholone skeleton (vide infra.)



1 $R_1 = H, R_2 = Me$
2 $R_1 = Me, R_2 = H$



3



4

In this, a full account,[6] we record the details of the first total synthesis of jatropholones A and B. We note in advance that the synthetic scheme, *which proved viable only through aegis of a high-pressure Diels–Alder reaction*, is short (i.e., 12 steps), reasonably efficient (6%), and establishes for the first time the absolute configuration of the jatropholones.

Prior to presentation of our synthetic analysis, it is appropriate to consider the structural features inherent in the jatropholone targets. Notable here is the close structural similarity between the jatropholones and jatrophone; note the identical peripheral array of carbons.[7] Second, jatropholones A and B are epimeric at C(2); simple base equilibration leads to their interconversion.[3] Unfortunately, as is now the norm, little chemical information concerning the jatropholones was available at the outset of this venture, aside from the usual spectral characterization and an X-ray analysis. Finally, we note with particular interest the tetracyclic array consisting of the fused 5,6,7- and 3-membered rings, a fully substituted aromatic system, and the potentially reactive C(6)-styrene functionality.

Results and Discussion

(i) A Strategy for the Construction of Jatropholones A and B. From the retrosynthetic perspective we anticipated that construction of the hexasubstituted aromatic system would be the central synthetic challenge. With this in mind, we envisioned that a Diels–Alder reaction between diene **5** and enone **6** would provide a rapid, convergent entry to the tetracyclic skeleton. Of considerable advantage here was the availability in our laboratory of enone **6**, in either racemic or homochiral form,[8] as a result of

---

(1) Camille and Henry Dreyfus Teacher–Scholar, 1978–1983. National Institutes of Health (National Cancer Institute) Career Development Award, 1980–1985. J. S. Guggenheim Fellow, 1985–1986.

(2) Recipient, American Cancer Society Postdoctoral Fellowship, 1982–1984.

(3) Purushothaman, K. K.; Chandrasekkharan, S.; Cameron, A. F.; Connolly, J. D.; Labbe, C.; Maltz, A.; Rycroft, D. S. *Tetrahedron Lett.* **1979**, 979.

(4) Kupchan, S. M.; Sigel, C. W.; Matz, M. J.; Renauld, J. A. S.; Haltiwanger, R. C.; Bryan, R. F. *J. Am. Chem. Soc.* **1970**, *92*, 4476.

(5) Smith, A. B., III; Guaciaro, M. A.; Schow, S. R.; Wovkulich, P. M.; Toder, B. H.; Hall, T. W. *J. Am. Chem. Soc.* **1981**, *103*, 219.

(6) A preliminary account of this work has already appeared: Smith, A. B., III; Liverton, N. J.; Hrib, N. J.; Sivaramakrishnan, H.; Winzenberg, K. N. *J. Org. Chem.* **1985**, *50*, 3239.

(7) For a biosynthetic postulate see: (a) Adolf, W.; Hecker, E. *Experientia* **1971**, *27*, 1393. (b) Adolf, W.; Hecker, E.; Balmain, A.; Lhomme, M. F.; Nakatani, Y.; Ourisson, G.; Ponsinet, G.; Pryce, R. J.; Santhanakrishnan, T. S.; Matyukhina, L. G.; Saltikova, I. A. *Tetrahedron Lett.* **1970**, 2241.

(8) Taylor, M. D.; Minaskanian, G.; Winzenberg, K. N.; Santone, P.; Smith, A. B., III. *J. Org. Chem.* **1982**, *47*, 3960.

0002-7863/86/1508-3040$01.50/0