

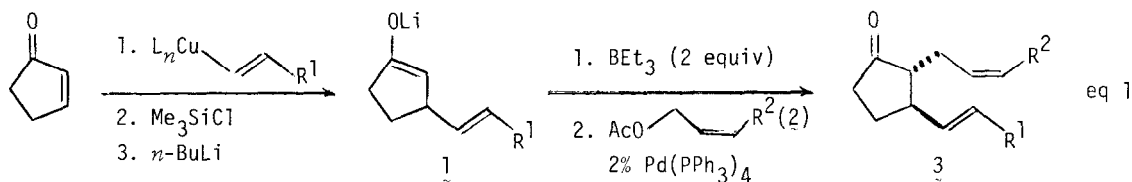
PALLADIUM-CATALYZED ALLYLATION OF LITHIUM 3-ALKENYL-1-CYCLOPENTENOLATES-TRIETHYLBORANE AND
ITS APPLICATION TO A SELECTIVE SYNTHESIS OF METHYL (Z)-JASMONATE¹

Fen-Tair Luo and Ei-ichi Negishi*

Department of Chemistry, Purdue University, W. Lafayette, Indiana 47907 U.S.A.

SUMMARY: A Pd-catalyzed allylation of 3-substituted 1-cyclopentenolates with readily obtainable and storable γ -monosubstituted (Z)-allylic acetates in a 1:1 ratio in the presence of 2 mol % of Pd(PPh₃)₄ featuring high yields and high stereo- and regioselectivities has been developed and applied to the synthesis of methyl (Z)-jasmonate.

The reaction of a 2:1 mixture of BEt₃ and a lithium 3-alkenyl-1-cyclopentenolate (1), generated by conjugate addition to cyclopentenone followed by silylation-lithiation, with one equiv of a γ -monosubstituted (Z)-allyl acetate (2) in the presence of Pd(PPh₃)₄ (2 mol %) cleanly provides 3 in high yield. The stereoselectivities with respect to the ring and allyl moieties are >98 and \geq 97%, respectively, and the corresponding regiospecificities are >98 and >90%, respectively (eq 1). Coupled with the ease of preparation and high stability of allylic acetates as well as the favorable 1/1 ratio of 1/2, the method described herein offers major advantages over the known allylation reactions of 3-alkenyl-1-cyclopentenolates.²



Conjugate addition to cyclopentenones followed by allylation of the resulting enolates (a "triple convergent" approach) has been an attractive but frustrating route to prostanoids and other cyclopentanoids.^{2,3} Although exceptions⁴ exist, it has generally been difficult to achieve allylation of regiodefined cyclopentenolates with stereo- and regiodefined allylic electrophiles, especially with their (Z)-isomers. Common difficulties include (a) loss of the allyl stereochemistry, (b) loss of the ring regiochemistry, (c) mediocre product yield (typically <50%), and (d) the requirement for a large excess of labile allylic bromides or iodides. We have recently developed the Pd-catalyzed allylation of alkenyl- and arylmetals⁵ as well as of alkali metal enoxyborates and zinc enolates.⁶ Although the reaction of alkenyl- and arylmetals with γ,γ -dialkyl-substituted allyl chlorides and acetates was highly stereo- and regioselective, the use of γ -monosubstituted (Z)-allyl derivatives (2) led to stereochemical scrambling to the extent of ca. 10%.^{5b} Neither the stereoselectivity with respect to 2 nor the regioselectivity with respect to the ring moiety in our Pd-catalyzed allylation of cyclopentenolates was known.

To rigorously determine the regio- and stereoselectivities with respect to the allyl moiety, we reacted lithium cyclopentenolate with various 2-octenyl halides and acetate in THF either in the presence or in the absence of $\text{Pd}(\text{PPh}_3)_4$ or BEt_3 . The experimental results⁷ summarized in Table I indicate the following. The reaction of (*E*)-2-octenyl acetate in the presence of both $\text{Pd}(\text{PPh}_3)_4$ (0.02 equiv) and BEt_3 (2 equiv) produces in 3 h at room temperature the desired **4a** in 77% isolated yield as a $\geq 98\%$ isomerically pure species⁸ without any attempt to separate isomers along with a trace, if any, of **5** (Entry 1). In the corresponding reaction of (*Z*)-2-octenyl acetate, the product yield and the stereoisomeric purity are 74% (91% by GLC) and 97%, respectively. However, **5** was also obtained in 5-10% (Entry 2). The use of (*Z*)-2-octenyl chloride and bromide led to an extensive stereoisomerization (Entries 3 and 4). The reaction of lithium cyclopentenolate with (*Z*)-2-octenyl acetate does not give any more than a trace of **4** in the absence of either $\text{Pd}(\text{PPh}_3)_4$ or BEt_3 , indicating that both reagents are essential⁹ (Entries 5 and 6). Under conventional conditions, the reaction of lithium cyclopentenolate with (*Z*)-2-octenyl iodide is 96% stereospecific, but the product yield is only 43% (48% by GLC) (Entry 7). The use of the corresponding bromide led to the formation of an 87/17 mixture of the (*Z*)- and (*E*)-**4** in 50% yield (Entry 8). It is important to note that, whereas the highly reactive iodide leads to the highest stereospecificity in the uncatalyzed reaction, the least reactive acetate is the most stereospecific reagent in the Pd-catalyzed reaction.

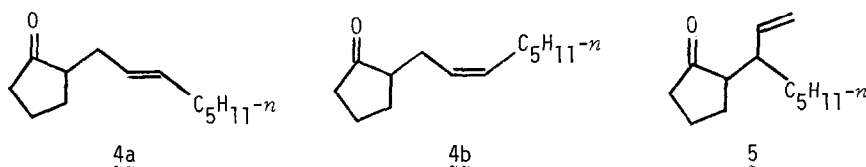
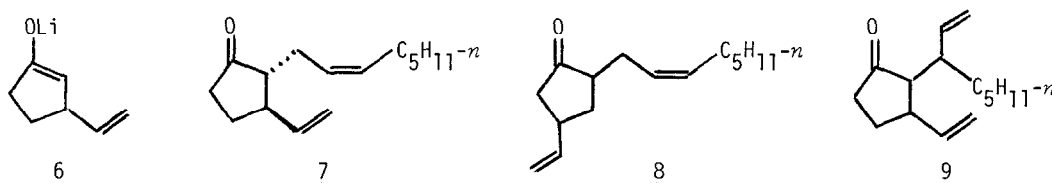


Table I. Pd-Catalyzed Reaction of Cyclopentenolates with 2-Octenyl Derivatives

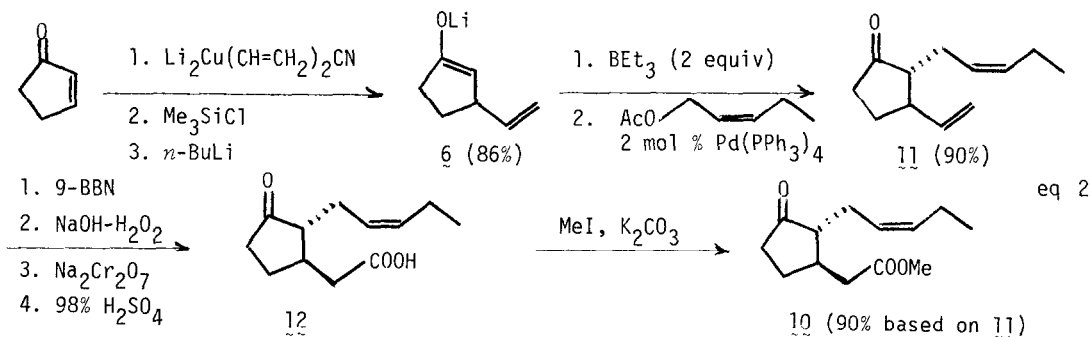
Entry	Metal in enolate	<i>n</i> -C ₅ H ₁₁ CH=CHCH ₂ X E or Z	X	Pd(PPh ₃) ₄ %	Time h	Yield ^a of 4 , %	Z/E of 4	Yield ^a of 5 , %
1	Li + 2 BEt ₃	<i>E</i>	OAc	2	3	- (77)	$\leq 2/98$	<1
2	Li + 2 BEt ₃	<i>Z</i>	OAc	2	3	91 (74)	$\geq 97/3$	5-10
3	Li + 2 BEt ₃	<i>Z</i>	Cl	2	3	81 (75)	60/40	5-10
4	Li + 2 BEt ₃	<i>Z</i>	Br	2	3	84 (75)	54/46	5
5	Li + 2 BEt ₃	<i>Z</i>	OAc	0	24	trace	-	-
6	Li	<i>Z</i>	OAc	2	24	2	-	-
7	Li	<i>Z</i>	I	0	12	48 (43)	96/4	<1
8	Li	<i>Z</i>	Br	0	12	55 (50)	87/13	6

^aBy GLC. The numbers in parentheses are isolated yields.

We then generated lithium 3-vinyl-1-cyclopentenolate (**6**) via addition of $\text{Li}_2\text{Cu}(\text{CH}=\text{CH}_2)_2\text{CN}$ ¹⁰ to cyclopentenone in ether followed by successive treatment with Me_3SiCl and *n*-BuLi in THF and carried out allylation of the enolate to determine the regioselectivity with respect to the ring moiety. The reaction of **6** with (*Z*)-2-octenyl iodide and bromide in THF (-78°C to room temperature) gave a mixture of **7** and **8** in 41% ($7/8 = 3$) and 26% ($7/8 = 1$) yields, respectively. The yields remained essentially unchanged even when a 2:1 mixture of THF and HMPA was used. Thus, the conventional method indeed suffers from low product yield and low ring-regioselectivity in the above transformation, even when allylic iodides are used. On the other hand, the reaction of **6** with (*Z*)-2-octenyl acetate in the presence of BEt_3 (2 equiv) and $\text{Pd}(\text{PPh}_3)_4$ (2 mol %) cleanly produced **7** in 64% yield (72% by GLC).¹¹ The regio- and stereoselectivities with respect to the ring moiety were ≥ 99 and $\geq 98\%$, respectively, and the corresponding figures for the allyl group were 95 and $\geq 97\%$, respectively. Fractional distillation readily separated **9** from **7**.



To demonstrate the synthetic utility of the above-developed procedure, we chose methyl (*Z*)-jasmonate⁴ (**10**) as a test system. Successive treatment of **6** with 2 equiv of BEt_3 in THF (-78 to 0°C), a solution of (*Z*)-2-penten-1-yl acetate¹² (1.1 equiv) and 2 mol % of $\text{Pd}(\text{PPh}_3)_4$ in THF (2 h at room temperature), and 3*N* HCl, followed by extraction (ether), washing with aqueous NaHCO_3 , drying over MgSO_4 , and distillation, gave ca. 97% pure **11** in 90% yield. Its hydroboration with 2 equiv of 9-borabicyclo[3.3.1]nonane (9-BBN)¹³ and oxidation with $\text{NaOH}-\text{H}_2\text{O}_2$, followed by further oxidation with $\text{Na}_2\text{Cr}_2\text{O}_7$ (4 equiv) and H_2SO_4 (98%, 16 equiv) provided crude **12**. Its treatment with $\text{MeI}-\text{K}_2\text{CO}_3$ (1.1 equiv) in dimethylformamide (8 h, room temperature) produced, after extraction (pentane), drying, and distillation, methyl (*Z*)-jasmonate¹⁴ in 90% yield from **11** (70% overall yield from cyclopentenone). The product obtained without any chromatographic separation throughout the synthesis was isomerically ca. 95% pure and essentially free from any other contaminants.



Application of the Pd-catalyzed allylation reaction to the synthesis of prostanoids will be reported elsewhere.

Acknowledgments. We thank NIH and NSF for support of this research. We also thank Hoffmann-La Roche, Inc., for additional support and Engelhard Industries for a loan of PdCl₂. Helpful discussions with Professor P. L. Fuchs of our Department are also acknowledged.

REFERENCES AND NOTES

- (1) Nickel- or Palladium-Catalyzed Cross Coupling. 27. Part 26. Chatterjee, S.; Negishi, E. submitted for publication.
- (2) (a) Patterson, J. W., Jr.; Fried, J. H. *J. Org. Chem.* 1974, 39, 2506. A 4-fold excess of an allyl bromide was used to convert a lithium 3-alkenyl-1-cyclopentenolate into 11-deoxy PGE₂ in 47% yield. However, the regio- and stereoselectivities were not described in detail. (b) Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* 1975, 97, 107. (c) Dixon, A. J.; Taylor, R. J. K.; Newton, R. F. *J. Chem. Soc. Perkin I* 1981, 1407. (d) For a successful allylation using vinyl sulfones, see Donaldson, R. E.; Fuchs, P. L. *J. Am. Chem. Soc.* 1981, 103, 2108.
- (3) Trapping enolates with other electrophiles has produced some favorable results. However, it does not permit direct allylation. (a) For trapping with formaldehyde, see Stork, G.; Isobe, M. *ibid.* 1975, 97, 6260. (b) For other more recent approaches, see Tanaka, T.; Toru, T.; Okamura, N.; Hazato, A.; Sugiura, S.; Manabe, K.; Kurozumi, S.; Suzuki, M.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett.* 1983, 24, 4103 and references therein.
- (4) For a recent paper, see Oppolzer, W.; Guo, M.; Baettig, K. *Helv. Chim. Acta* 1983, 66, 2140.
- (5) (a) Matsushita, H.; Negishi, E. *J. Am. Chem. Soc.* 1981, 103, 2882. (b) Negishi, E.; Chatterjee, S.; Matsushita, H. *Tetrahedron Lett.* 1981, 22, 3737. (c) Matsushita, H.; Negishi, E. *J. Chem. Soc. Chem. Comm.* 1982, 160. (d) See also, Hayashi, Y.; Riediker, M.; Temple, J. S.; Schwartz, J. *Tetrahedron Lett.* 1981, 22, 2629.
- (6) (a) Negishi, E.; Matsushita, H.; Chatterjee, S.; John, R. A. *J. Org. Chem.* 1982, 47, 3188. (b) Negishi, E.; Luo, F. T.; Pecora, A. J.; Silveira, A. Jr. *ibid.* 1983, 48, 2427. (c) Negishi, E.; Chatterjee, S. *Tetrahedron Lett.* 1983, 24, 1341.
- (7) All isolated compounds were identified spectroscopically. In addition, 4, 7, and 11 yielded correct elemental analytical data.
- (8) The results are in sharp contrast with nonstereospecific results obtained with tin enolates [Trost, B. M.; Keinan, E. *Tetrahedron Lett.* 1980, 21, 2591].
- (9) The reaction of lithium enolates with allylic acetates that are not stereodefined in the presence of Pd(dba)₂-dppe gives modest-to-good yields of the desired products [Fiaud, J. C.; Malleron, J. L. *J. Chem. Soc. Chem. Comm.* 1981, 1159]. However, these authors have informed us that the reaction is nonstereospecific.
- (10) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. *Tetrahedron Lett.* 1982, 23, 3755.
- (11) Our attempts to directly trap the conjugate addition product with the allylic acetate reagent have so far been unsuccessful.
- (12) This compound was prepared from 2-pentyn-1-ol via hydrogenation over Lindlar's catalyst (98% yield) [Lindlar, H.; Dubuis, R. *Org. Synth. Coll. Vol. V* 1973, 880] and acetylation (68% yield).
- (13) The use of just one equiv of 9-BBN led to competitive reduction of both vinyl and carbonyl groups.
- (14) 10: bp 113-115°C (0.2 mm); IR (neat) 1740; ¹H NMR (CDCl₃, Me₄Si) δ 0.94 (t, J = 7 Hz, 3 H), 1.1-3.0 (m, 12 H), 3.66 (s, 3 H), 5.0-5.7 (m, 2 H). ¹³C NMR (CDCl₃, Me₄Si) δ 14.08, 20.56, 25.44, 27.20, 37.58, 38.01, 38.68, 51.34, 53.84, 125.24, 133.75, 172.26, 217.96.

(Received in USA 4 February 1985)