Tetrahedron Letters, Vol. 33, No. 43, pp. 6477-6478, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Palladium-Catalyzed Intramolecular Carbonyl Allylation via Claisen Rearrangement

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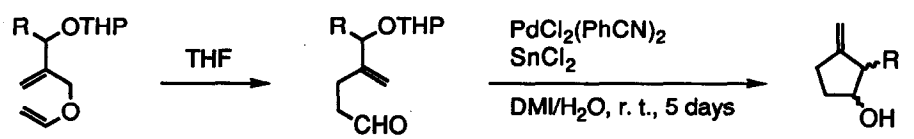
Key Words: Intramolecular Carbonyl allylation; Claisen rearrangement; palladium; tin(II) chloride.

Abstract: Palladium-catalyzed intramolecular carbonyl allylation with $SnCl_2$ by 5-substituted 4-methylene-5-(2-tetrahydropyranyloxy)pentanals, prepared by Claisen rearrangement of 2-[1-(2-tetrahydropyranyloxy)alkyl]allyl vinyl ethers, occurred regioselectively at ambient temperature in DMI/H_2O to give 2-substituted 3-methylenecyclopentanols in good yields.

Palladium-catalyzed carbonyl allylation by allylic alcohols or esters with $SnCl_2$ is one of the effective methods for regio- and diastereocontrol in acyclic systems.[1] We report here the application of this palladium-catalyzed carbonyl allylation to the formation of a 5-membered cyclic system: regioselective intramolecular carbonyl allylation by 5-substituted 4-methylene-5-(2-tetrahydropyranyloxy)pentanal **2** with $PdCl_2(PhCN)_2$-$SnCl_2$ in polar solvent.

Claisen rearrangement of 2-[1-(2-tetrahydropyranyloxy)alkyl]allyl vinyl ether **1**, which was derived from ethyl 2-(1-hydroxyalkyl)acrylate[2] via the protection of hydroxy group with DHP, the reduction of ethoxycarbonyl group with DIBAH, followed by the vinylation of allylic alcohol with ethyl vinyl ether,[3] produced 5-substituted 4-methylene-5-(2-tetrahydropyranyloxy)pentanal **2**.[4] Intramolecular carbonyl allylation (cyclization) of **2** with $PdCl_2(PhCN)_2$-$SnCl_2$ occurred in DMI-H_2O[5] at ambient temperature to give 2-substituted 3-methylenecyclopentanol **3**.[6] The results are summarized in Table 1.

Table 1. Claisen Rearrangement of **1** and Intramolecular Carbonyl Allylation (Cyclization) of **2**

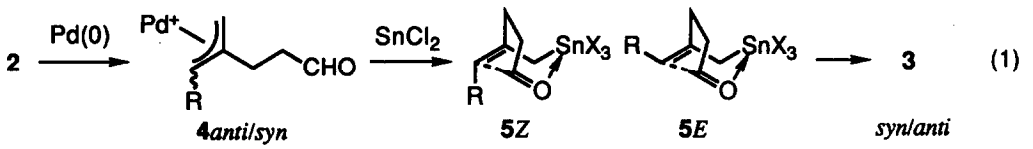


1 **2** **3**

R	Claisen Rearrangement temp (°C)	time (h)	**2**, yield (%)[a]	Intramolecular Carbonyl Allylation **3**, yield (%)	*syn:anti*[b]
Ph	160	1	47	75	32:68
4-$CH_3C_6H_4$	150	1	35	75	33:67
CH_3	150	1	57	39	44:56
n-C_5H_{11}	140	2.5	65	68	43:57
c-C_6H_{11}	140	1	64	64	36:64

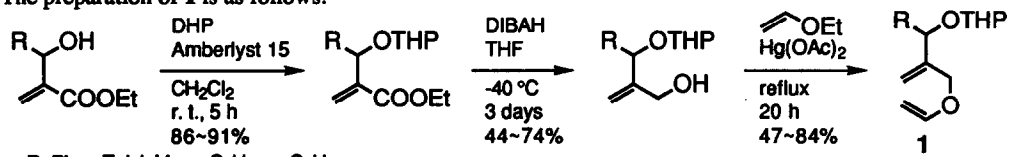
a) The yields based on the consumption of the starting materials **1** are 75~85%. b) The diastereomer ratio was determined by 270 MHz ^1H NMR (GX-270). The structure of the diastereomers (syn and anti) was confirmed by NOE measurement. See ref. 7.

The intramolecular carbonyl allylation occurred at a more substituted allylic position of π-allylpalladium complex **4**, similarly to intermolecular carbonyl allylation by allylic alcohol with $PdCl_2(PhCN)_2$-$SnCl_2$.[1a] The diastereoselectivity of the intramolecular carbonyl allylation was not so high. These results suggest that this cyclization proceeds via the formation of a *syn/anti* mixture of π-allylpalladium complex **4**, followed by a *Z/E* mixture of allylic tin intermediate **5** (eq 1).[1a]



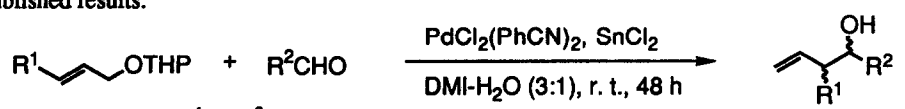
References and Notes

1. (a) Takahara, J. P.; Masuyama, Y.; Kurusu,Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577-2586. (b) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *Chem. Lett.* **1991**, 879-882. (c) Masuyama, Y.: Nimura, Y.; Kurusu, Y. *Tetrahedron Lett.* **1991**, *32*, 225-228. (d) Masuyama, Y.; Tsunoda, T.; Kurusu, Y. *Chem. Lett.* **1989**, 1647-1650. (e) Masuyama, Y.; Otake, K.; Kurusu, Y. *Tetrahedron Lett.* **1988**, *29*, 3563-3566. (f) Masuyama, Y.; Hayashi, R.; Otake, K.; Kurusu, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 44-45.
2. Hoffmann, H. M. R.; Rabe, J. *Helv. Chim. Acta* **1984**, *67*, 413-415.
3. The preparation of **1** is as follows:



R: Ph, p-Tolyl, Me, n-C_5H_{11}, c-C_6H_{11}

4. (a) Bennett, G. B. *Synthesis* **1977**, 589-606. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227-232.
5. This intramolecular carbonyl allylation of **2** did not occur in the absence of H_2O. The addition of H_2O made it possible to apply various allylic alcohols protected by DHP, namely allyl 2-tetrahydropyranyl ethers, to the palladium-catalyzed carbonyl allylation. Masuyama, Y.; Nimura, Y.; Kurusu, Y. unpublished results.



R^1: H, R^2: Ph, PhCH=CH, n-C_6H_{13}, c-C_6H_{11} 41~77%
R^1: CH_3, R^2: Ph 55% (*syn:anti*=15:85)
R^1: Ph, R^2: Ph 71% (*syn:anti*=1:99)

6. A typical procedure is as follows: To a solution of $SnCl_2$ (0.32 g, 1.7 mmol) and **2** (R: Ph, 0.18 g, 0.65 mmol) in DMI (3 ml) and H_2O (1 ml) was added $PdCl_2(PhCN)_2$ (5.0 mg, 0.013 mmol) at ambient temperature under a nitrogen atmosphere. After the mixture was stirred for 5 days, usual treatment and purification by column chromatography on silica gel (hexane:EtOAc=3:1) afforded 85 mg (0.49 mmol, 75%) of 3-methylene-2-phenylcyclopentanol **3** (R: Ph, diastereomer ratio; 68:32) as a colorless oil. ^1H NMR ($CDCl_3$) δ 1.54~1.71 (m, 0.3H), 1.76~1.93 (m, 1.4H), 1.93~2.04 (m, 0.3H), 2.28 (dt, *J*=13.6, 4.86 Hz, 0.7H), 2.34~2.44 (m, 0.3H), 2.44~2.56 (m, 0.3H), 2.60~2.75 (m, 0.7H), 3.67 (br, 0.7H), 4.04 (br, 0.3H), 4.13 (br, 0.3H), 4.21 (br, 0.7H), 4.82 (s, 0.3H), 4.84 (s, 0.7H), 4.90~4.98 (m, 0.3H), 4.92 (s, 0.3H), 5.32 (br, 0.7H), 5.48 (s, 0.7H), 7.31 (s, 5H); ^{13}C NMR ($CDCl_3$) δ major 27.5, 32.3, 74.7, 92.1, 111.2, 126.5, 127.7, 128.2, 139.2, 146.8. minor 31.0, 34.2, 80.1, 96.5, 111.9, 127.8, 128.1, 128.5, 138.8, 145.7; IR (neat) 3400, 3080, 2950, 2860, 1650, 1455, 1060, 1025, 955, 915, 760, 700; MS (relative intensity) *m/z* 174 (7.7, M^+), 173 (17), 172 (37), 167 (41), 150 (12), 149 (100), 147 (16), 130 (14), 129 (63), 115 (12), 105 (26), 91(10), 77 (12), 71 (44), 70 (11), 57 (19), 55 (12); HRMS Calcd for $C_{12}H_{14}O$: 174.1044. Found: 174.1038.
7. ^1H NMR investigation of 3-methylene-2-(4-methylphenyl)cyclopentanol **3** (R: 4-$CH_3C_6H_4$) observed NOE between CHOH and 2(6)-proton of phenyl group in a major stereoisomer. Thus the major isomer was found to be *anti*. The structure of other cyclopentanol products was analogized from the result of 3-methylene-2-(4-methylphenyl)cyclopentanol.

(Received in Japan 15 July 1992)