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# Asymmetric Hydrosilylation of Dihydrofurans by Use of Palladium–MOP Catalyst

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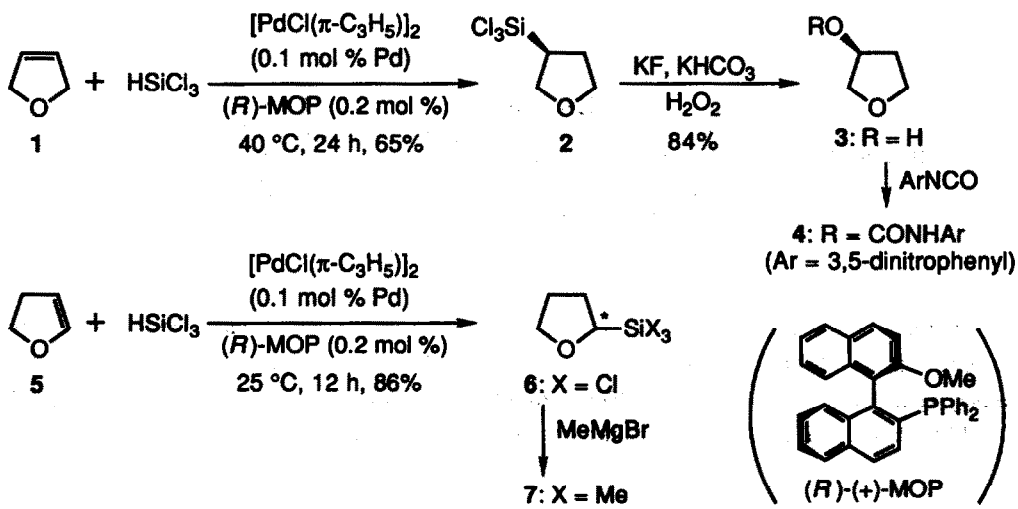
***Abstract:*** Catalytic asymmetric hydrosilylation of dihydrofuran derivatives including 7-oxabicyclo[2.2.1]heptenes with trichlorosilane proceeded in the presence of 0.1 mol % of palladium catalyst bearing (*R*)-2-methoxy-2'-diphenylphosphino-1,1'-binaphthyl ((*R*)-MOP) to give the corresponding hydrosilylation products of up to 95% ee. A regioselective opening of the bicyclic system gave a highly functionalized cyclohexane in an optically active form.

Enantioselective functionalization of olefins constitutes among the most exciting challenges in modern synthetic chemistry.[1] We have previously reported that this process is realized by catalytic asymmetric hydrosilylation of 1-alkenes[2] and bicyclic olefins[3] using palladium catalyst coordinated with a novel optically active monophosphine ligand, 2-methoxy-2'-diphenylphosphino-1,1'-binaphthyl (MOP).[4] As a part of our efforts to develop the wide utility of this catalysis, heterocyclic olefins were examined as the substrates. We describe herein the asymmetric hydrosilylation of dihydrofuran derivatives which is catalyzed by 0.1 mol % of the palladium-MOP catalyst to give optically active functionalized tetrahydrofurans of up to 95% ee.

Treatment of 2,5-dihydrofuran **1** with 1.2 equiv of trichlorosilane in the presence of $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.1 mol % of Pd) and (*R*)-MOP (2 equiv to Pd) without solvent at 40 °C for 24 h gave 3-(trichlorosilyl)tetrahydrofuran (**2**) which was isolated by bulb-to-bulb distillation in 65% yield. Oxidative cleavage of the resulting

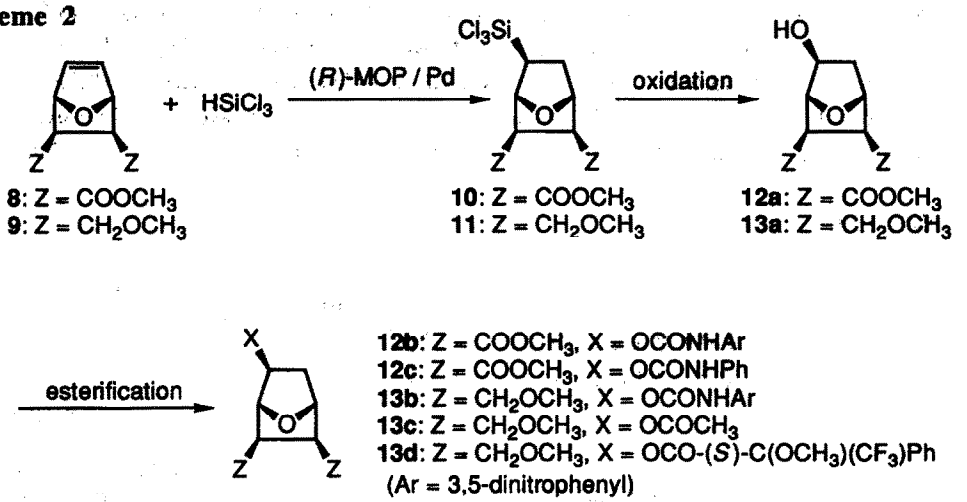
**Scheme 1**



carbon-silicon bond by modified Tamao's method[3,5] (KF, $KHCO_3$, 30% $H_2O_2$, THF-MeOH, rt, 16 h) gave alcohol **3** in 84% yield which turned out to be an *S* isomer by measurement of the optical rotation ($[\alpha]^{23}_D$ +15.0 (*c* 0.8, methanol). lit.[6] for (*S*)-**3** of 51% ee: $[\alpha]^{23}_D$ +8.92 (*c* 2.4, methanol)). The enantiomeric excess was determined to be 95% ee by HPLC analysis of 3,5-dinitrophenyl carbamate ester **4**, which was prepared by treatment of **3** with 3,5-dinitrophenyl isocyanate, using a chiral stationary phase column (Sumichiral OA-4000, n-hexane/dichloroethane/ethanol = 50/15/1) (Scheme 1). Reaction of 2,3-dihydrofuran **5** gave 2-silyltetrahydrofuran **6** in 86% yield under the similar reaction conditions and the enantiomeric excess was determined to be 82% ee by NMR experiment of methylated compound **7** ($[\alpha]^{25}_D$ +10.5 (*c* 4.20, chloroform)) in the presence of $Eu(hfc)_3$.

Monofunctionalization of the meso bicyclic olefins which contain the 2,5-dihydrofuran skeleton by the asymmetric hydrosilylation brought about simultaneous generation of multiple chiral carbon centers (Scheme 2). Thus, the asymmetric hydrosilylation of 7-oxabicyclo[2.2.1]heptenes **8** and **9** with trichlorosilane took place in the presence of Pd–(*R*)-MOP catalyst under similar conditions to give 2-silyl-7-oxabicyclo[2.2.1]heptanes **10** and **11**, respectively, in high yields. The *exo*-selectivity at the hydrosilylation was very high, no *endo*-adducts being detected. The $^1H$ NMR and HPLC analyses of the alcohols and their esters obtained by the oxidation of trichlorosilane **10** and **11** revealed that alcohols **12a** and **13a** are (1*R*,2*S*,4*R*,5*S*,6*R*) isomer of 95% ee and (1*R*,2*S*,4*R*,5*R*,6*S*) of 90% ee respectively.[7] The absolute configuration of **13** was determined by NMR studies on the MTPA ester **13d**.[8,9] The details of the hydrosilylation reactions are summarized in Table I. It is remarkable that 3-phenoxy-1-propene underwent the hydride reduction of allylic carbon-oxygen bond forming propene and phenoxysilane under the hydrosilylation conditions[10] while the reductive cleavage of carbon-oxygen bond was not observed with 2,5-dihydrofuran (**1**) or its derivatives (**8** and **9**).

**Scheme 2**




**8**: Z = $COOCH_3$
**9**: Z = $CH_2OCH_3$

**10**: Z = $COOCH_3$
**11**: Z = $CH_2OCH_3$

**12a**: Z = $COOCH_3$
**13a**: Z = $CH_2OCH_3$

**12b**: Z = $COOCH_3$, X = OCONHAr
**12c**: Z = $COOCH_3$, X = OCONHPh
**13b**: Z = $CH_2OCH_3$, X = OCONHAr
**13c**: Z = $CH_2OCH_3$, X = $OCOCH_3$
**13d**: Z = $CH_2OCH_3$, X = OCO-(*S*)-C($OCH_3$)($CF_3$)Ph
(Ar = 3,5-dinitrophenyl)

The synthetic utility of the optically active 7-oxabicyclo[2.2.1]heptanes is demonstrated by regioselective ring opening of the tetrahydrofuran forming highly functionalized cyclohexanes in optically active forms.[11] A preliminary result is shown in Scheme 3. Treatment of trimethylsilane **14** ((1*R*,2*S*,4*R*,5*R*,6*S*)-**14**: $[\alpha]^{25}_D$ +7.43 (*c* 1.75, chloroform)), which was obtained quantitatively by methylation of **11** with methylmagnesium

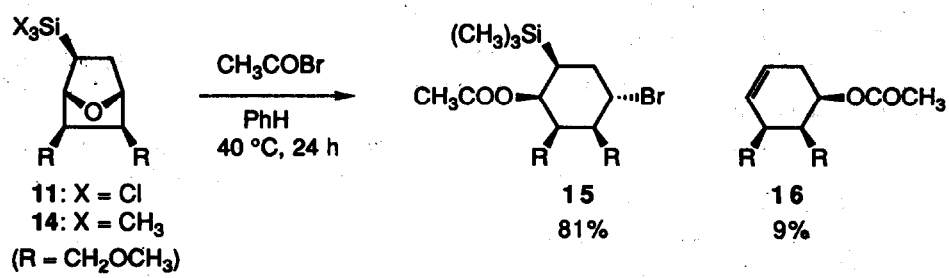
**Table I.** Asymmetric Hydrosilylation Catalyzed by Palladium-MOP[a]

| entry | olefin | conditions | product | yield[b] % (diastereoselectivity)[c] | | yield[b] % of alcohol | % ee | absolute configuration |
|---|---|---|---|---|---|---|---|---|
| 1 | **1** | 40 °C, 24 h | **2** | 65 | (—) | 83 (**3**) | 95[d] | (3*S*)[e] |
| 2 | **5** | 25 °C, 12 h | **6** | 86 | (—) | — | 82[f] | —[g] |
| 3 | **8** | 20 °C, 24 h | **10** | 91 | (100 : 0) | 87 (**12a**) | 95[d] | (1*R*,2*S*,4*R*,5*S*,6*R*)[h] |
| 4 | **9** | –20 °C, 24 h | **11** | 86 | (100 : 0) | 93 (**13a**) | 90[d] | (1*R*,2*S*,4*R*,5*R*,6*S*)[i] |

[a] All reactions were run without solvent in the presence of palladium catalyst prepared in situ by mixing $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.1 mol % Pd) and (*R*)-MOP (2 equiv to Pd). The ratio of olefin/$HSiCl_3$ is 1/1.20–1.25. [b] Isolated yield. [c] The ratio of *exo* : *endo* of silyl group. Determined by GLC and $^1H$ NMR analysis. [d] Determined by HPLC analysis of (3,5-dinitrophenyl)carbamate ester (**4** (entry 1), **12b** (entry 3), **13b** (entry 4)) with Sumichiral OA-4000 (n-hexane/dichloroethane/ethanol = 50/10/1). [e] See text. [f] Determined by $^1H$ NMR analysis of trimethylsilyl derivative **7** using Eu(hfc)$_3$. [g] Not determined. [h] Assigned by similarity of **12b** to **13b** in the order of elution in the HPLC analysis. [i] Determined by $^1H$ NMR of MTPA ester **13d** (ref 8 and 9).

bromide, with 3 equiv of acetyl bromide in benzene at 40 °C for 24 h gave 81% yield of penta-substituted cyclohexane **15**[13] along with 9% yield of cyclohexene **16**. The ring opening of the tetrahydrofuran proceeds through the activation of carbon-oxygen bond by coordination of acetyl cation on the oxygen.[12] The high selectivity forming **15** is accounted for by regioselective nucleophilic attack of bromide on one of the bridge-head carbon with inversion of configuration from sterically less hindered site. The minor product **16** may result from the attack of bromide on the sterically more hindered site followed by Peterson-like elimination of the resulting β-bromosilane.[14]

**Scheme 3**




**11**: X = Cl
**14**: X = $CH_3$
(R = $CH_2OCH_3$)

**15**
81%

**16**
9%

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7 The analytically pure samples were isolated as the corresponding ester derivatives **12c** and **13c**. **12c**: $[\alpha]^{25}_{D}$ –2.4 (*c* 0.64, acetone). **13c**: $[\alpha]^{25}_{D}$ –22.4 (*c* 1.41, chloroform).

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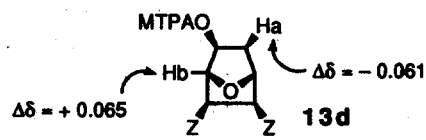
9 Selected Δδ values (ppm) on $^1$H NMR (270 MHz, $CDCl_3$) experiment of MTPA ester **13d** are shown at the right. Proton resonances of Ha and Hb in the main diastereomer of (*S*)-MTPA ester **13d** appeared at higher field by 0.061 ppm and at lower field by 0.065 ppm, respectively, than those of minor diastereomer, indicating that the absolute configuration of the main enantiomer of **13a** is 1*R*, 2*S*, 4*R*, 5*R*, 6*S* (see ref 8).

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13 (1*S*,2*R*,3*S*,4*R*,5*S*)-1-Bromo-2,3-bis(methoxymethyl)-4-acetoxy-5-(trimethylsilyl)cyclohexane (**15**): $[\alpha]^{25}_{D}$ +29.9 (*c* 1.75, chloroform). $^1$H NMR ($CDCl_3$) δ 0.11 (s, 9 H), 1.40 (ddd, *J* = 2.5, 2.9, and 13.2 Hz, 1 H), 1.71, (br d, *J* = 15.1 Hz, 1 H), 2.06 (ddd, *J* = 2.4, 2.9, and 15.1 Hz, 1 H), 2.40–2.43 (m, 1 H), 2.52 (dddd, *J* = 2.0, 2.9, 7.3, and 9.3 Hz, 1 H), 3.03–3.18 (m, 3 H), 3.19 (s, 3 H), 3.42 (s, 3 H), 3.44 (dd, *J* = 10.3 and 10.7 Hz, 1 H), 4.86 (dt, *J* = 2.4 and 2.5 Hz, 1 H), 5.28 (br s, 1 H).

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