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Asymmetric Functionalization of Bicycloalkenes by Catalytic Enantioposition-Selective Hydrosilylation

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Abstract: Hydrosilylation of norbornene with trichlorosilane in the presence of palladium catalyst (0.01–0.1 mol %) coordinated with (*R*)-MOP ligand gave a quantitative yield of *exo*-2-trichlorosilylnorbornane, which was oxidized with hydrogen peroxide to give (1*S*,2*S*,4*R*)-*exo*-2-norbornanol in 96% ee. The similar hydrosilylation and oxidation of *endo*-5,6-dicarbomethoxy-2-norbornene, bicyclo[2.2.2]octene, and norbornadiene gave the corresponding bicyclic alcohols of 94% ee, 92% ee, and 95% ee, respectivery.

Asymmetric synthesis through a selective monofunctionalization of enantiotopic positions is one of the most attractive strategies for one-step construction of multiple chiral carbon centers.[1] In spite of the impressive development of enantioface selective asymmetric reactions catalyzed by transition metal complexes, the enantioposition selective approach still remains to be developed.[2] We have concentrated our studies on the catalytic asymmetric functionalization of meso bicyclo[2.2.1] system, because the optically active bicyclo[2.2.1]heptane derivatives represented by norbornanol are of great value as versatile chiral building blocks for the synthesis of a wide variety of important compounds.[3] Those optically active bicyclo[2.2.1]heptanes have been mainly obtained by optical resolution of racemic compounds in either chemical or enzymatic procedures,[4] or by asymmetric hydroboration[5] and Diels-Alder reactions[6] using a stoichiometric amount of chiral auxiliaries. Use of catalytic systems for the asymmetric reactions has not always been successful in terms of enantioselectivity or catalytic activity.[2,7,8] We report here that the asymmetric functionalization with >96/4 enantioposition selectivity is realized through asymmetric hydrosilylation in the presence of not more than 0.1 mol % of palladium catalyst coordinated with (*R*)-2-methoxy-2'-diphenylphosphino-1,1'-binaphthyl ((*R*)-MOP).[9,10]

Scheme 1

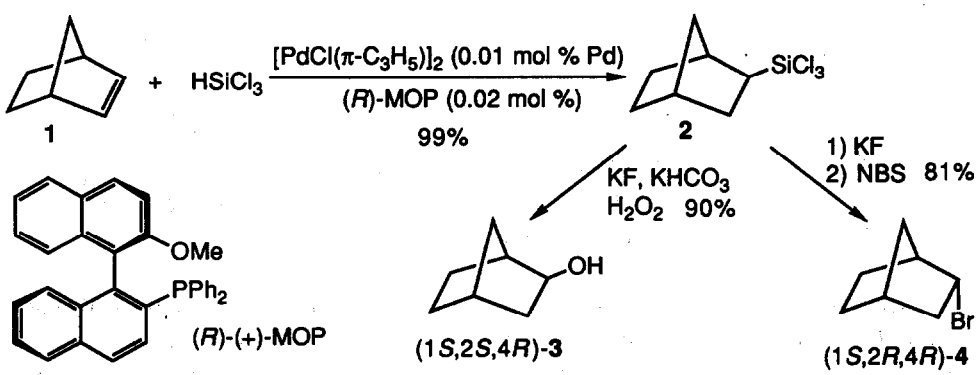


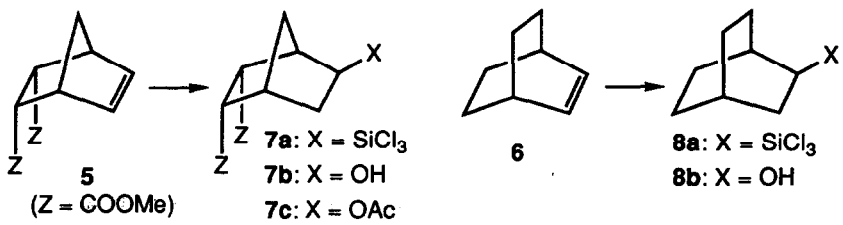
Table I. Asymmetric Hydrosilylation Catalyzed by Palladium-MOP[a]

entry	olefin	conditions	product	yield[b] % (*exo* : *endo*)[c]	yield[b] % of alcohol	% ee
1	**1**	0 °C, 24 h	**2**	100 (100 : 0)	90 (**3**)	93[d]
2	**1**	–20 °C, 3 d	**2**	99 (100 : 0)		96[d]
3	**5**	0 °C, 24 h	**7a**	100 (100 : 0)	96 (**7b**)	94[e]
4	**6**	0 °C, 24 h	**8a**	85 (—)	90 (**8b**)	92[d]
5	**9**	0 °C, 24 h	**10a**	85[f] (100 : 0)	89 (**10b**)	95[d]

[a] All reactions were run without solvent in the presence of palladium catalyst prepared in situ by mixing $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.01–0.1 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] Determined by GLC and ^1H NMR analysis. [d] Determined by HPLC analysis of (3,5-dinitrophenyl)carbamate of the alcohol with Sumichiral OA-4500 (n-hexane/dichloroethane/ethanol = 50/10/1). [e] Determined by ^1H NMR analysis of acetate **7c** using $Eu(hfc)_3$. [f] Nortricyclene **11** was also formed in 14%.

A typical procedure for the asymmetric synthesis of *exo*-2-norbornanol (**3**) from norbornene (**1**) (Scheme 1) is as follows: A mixture of norbornene (**1**, 15.0 g, 0.16 mol), trichlorosilane (20.0 mL, 0.20 mol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (2.9 mg, 0.008 mmol, 0.01 mol % Pd) and (*R*)-MOP (14.8 mg, 0.032 mmol, 2 equiv to Pd) was stirred at 0 °C for 24 h. Removal of excess silane followed by distillation (65 °C/3.5 mm Hg) gave 100% yield (36.5 g) of *exo*-2-trichlorosilylnorbornane[11,12] (**2**) as a single product. Oxidative conversion of **2** was performed with hydrogen peroxide by a modified Tamao's method[13,14] to give *exo*-2-norbornanol (**3**) in over 90% yield. Sublimation in vacuo gave 13.3 g (74% yield) of analytically pure (1*S*,2*S*,4*R*)-**3** with 93% ee. The absolute configuration was assigned on the basis of the optical rotation (**3**: $[\alpha]^{25}_D$ –2.94° (*c* 10.55, $CHCl_3$), lit.[15] $[\alpha]^{25}_D$ –3.14° (*c* 3.1, $CHCl_3$)) and the enantiomeric excess was determined by HPLC analysis[16] of the carbamate ester obtained by treatment with 3,5-dinitrophenyl isocyanate. The hydrosilylation carried out at –20 °C for 3 days (99% yield) raised the enantiomeric excess to 96% ee (entries 1 and 2 in Table I).

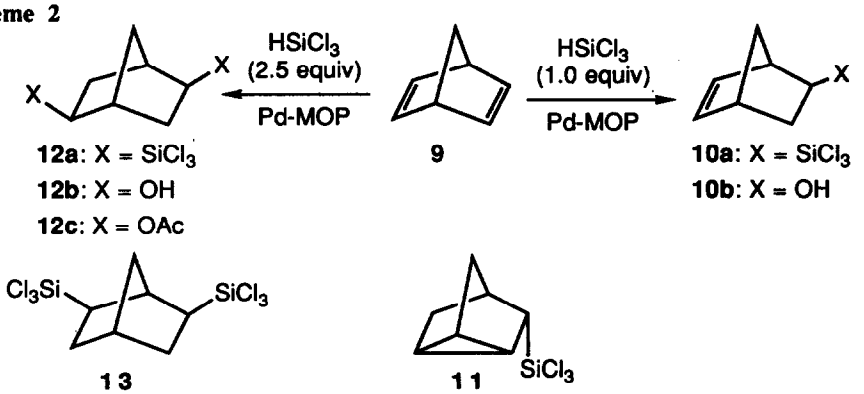
Trichlorosilane **2** can be converted into (1*S*,2*R*,4*R*)-*endo*-2-bromonorbornane (**4**)[17,18] in 81% yield by treatment with excess potassium fluoride followed by bromination of the resulting pentafluorosilicate with *N*-bromosuccinimide.[19] Dimethyl ester derivative **5** and bicyclo[2.2.2]octene **6** were also successfully subjected to the asymmetric hydrosilylation-oxidation under the similar reaction conditions to give the corresponding alcohols, (1*R*,2*S*,4*R*,5*S*,6*R*)-**7b** (94% ee)[20,21] and (2*S*)-**8b** (92% ee),[22,23] respectively (entries 3 and 4).



It is remarkable that the monofunctionalization of norbornadiene (**9**) forming *exo*-2-trichlorosilyl-5-norbornene (**10a**) is effected by the palladium-MOP catalyst with high chemo- and enantioselectivity (Scheme 2). It is in striking contrast to the reaction catalyzed by chloroplatinic acid[24] or palladium-triphenylphosphine[25]

which gives nortricyclene **11** as a major product. Thus, the reaction of **9** with 1.0 equiv of trichlorosilane and the palladium-MOP catalyst (0.1 mol %) followed by the hydrogen peroxide oxidation gave (1*R*,2*S*,4*R*)-*exo*-2-hydroxy-5-norbornene[21] (**10b**) with 95% ee (entry 5). The enantioselective hydrosilylation took place successively on the two double bonds of **9** in the reaction with 2.5 equiv of trichlorosilane, which gave 78% yield of chiral disilylnorbornane **12a** and meso isomer **13** in a ratio of 18 : 1. The oxidation of **12a** followed by acetylation of diol **12b** gave diacetate (1*R*,2*S*,4*R*,5*S*)-**12c**[26,27] with >99% ee,[28] the high purity being as expected in the double stereoselection.

Scheme 2



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20 Optical rotation of *exo*-2-trimethoxysilyl derivative which was prepared by methanolysis of **7a** is $[\alpha]^{25}_D$ +14.7° (*c* 1.3, benzene).

21 The absolute configuration was tentatively assigned by similarity in shifts using chiral shift reagent Eu(hfc)$_3$ or in elution order in the HPLC analysis.

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25 The reaction in the presence of $[PdCl(\pi\text{-}C_3H_5)]_2$ (1 mol % Pd) and PPh_3 (2 equiv to Pd) at 50 °C for 12 h gave **10** (37%) and **11** (56%).

26 $[\alpha]^{20}_D$ +7.60° (*c* 0.16, $CHCl_3$).

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28 The other enantiomer was not detected by ^1H NMR analysis using chiral shift reagent Eu(hfc)3.

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