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NEW CHIRAL LIGANDS, PYRIDINOOXATHIANES, FOR PALLADIUM-CATALYZED ASYMMETRIC ALLYLIC ALKYLATION

Yuko Okuyama,[a] Hiroto Nakano,*[,a] Chizuko Kabuto,[b] Erica Nozawa,[a] Kouichi Takahashi, [a] and Hiroshi Hongo [a]

[a] Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-Ku, Sendai 981-8558, Japan
[b] Instrumental Analysis Center for Chemistry, Graduate School of Science, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

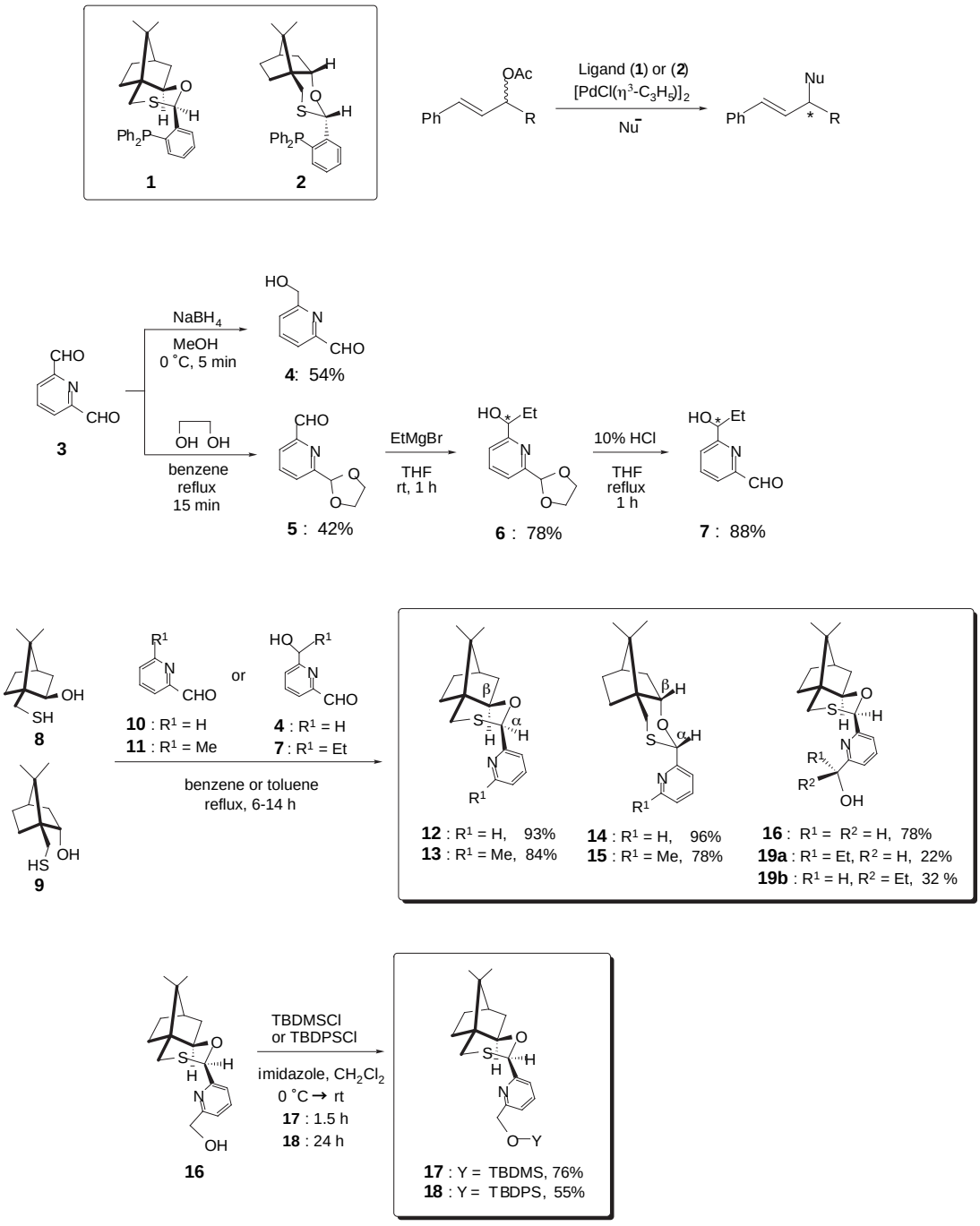
Abstract - New types of pyridinooxathiane ligands have been synthesized and their abilities as chiral catalysts examined in the palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate.

Carbon–carbon bond formation is one of the most fundamental transformations in synthetic organic chemistry. In this effect, one useful method involves the palladium-catalyzed allylation reaction, which has been studied extensively over the last decade.[1] In earlier exhaustive surveys, phosphorus containing ligands were found to be the most effective in various palladium catalyzed reactions. More recently, mixed P-N and N-S ligands have gathered increasing attention for their superior reactivity in different palladium mediated reactions and for their ease in prepartion and handling.[2] We have demonstrated that phosphinooxathianes (**1** and **2**) are effective ligands for the palladium catalyzed allylation reaction[3] and herein report the synthesis of chiral norbornane-based pyridinooxathianes as a new class of S-N ligands and their application to the allylation reaction.

Syntheses of the chiral ligands (**12-19a,b**) are described in Scheme 1. 6-Hydroxymethyl-2-pyridinecarboxaldehyde (**4**) was prepared conveniently by the selective $NaBH_4$ reduction of 2,6-pyridinedicarboxaldehyde (**3**). Monoketalization of **3**, followed by alkylation with ethylmagnesium bromide and acidic deprotection provided 6-(1-hydroxypropyl)-2-pyridinecarboxaldehyde (**7**) as a racemic mixture. Condensation of the pyridinecarboxaldehydes (**4** and **7**) with (-)-(*1S*)-10-

* Dedicated to Professor Albert I. Meyers on the occasion of his 70th birthday.

mercaptoisoborneol (**8**) or (-)-(*1S*)-10 mercaptoborneol furnished ligands (**12-16**) in good yields (**12** : 93%, **13** : 84%, **14** : 96%, **15** : 78%, **16** : 78%). Silylation of **16** with TBDMSCl or TBDPSCl gave ligands (**17** and **18**) in moderate yields (**17**: 76%, **18**: 55%).



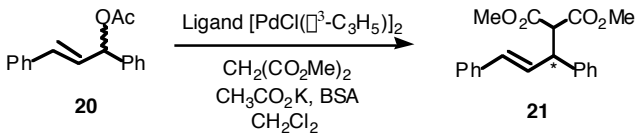
Scheme 1

The reaction of racemic pyridinecarboxaldehyde (**7**) with (-)-(*1S*)-10 mercaptoisoborneol (**8**) gave a diastereomeric mixture of pyridinooxathianes (**19a** and **19b**) which were readily separated by

preparative TLC (**19a**: 22%, **19b**: 32%). The absolute stereochemistry of the carbinol center was established by X-Ray diffraction analysis of **19b** (Figure 1). In all cases (**12-18** and **19a,b**), the assigned stereochemistry at the □-position of the 1,3-oxathiane ring was determined by analysis of their NOE difference spectra; enhancements were observed between the □- and the □-position protons when the respective □- or □-proton resonances were irradiated.

We then investigated the palladium-catalyzed allylic substitution of 1,3-diphenyl-2-propenyl acetate (**20**) with dimethyl malonate using the chiral ligands (**12-19a,b**). The reaction was carried out in the presence of □-allylpalladium chloride dimer $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and *N,O-bis*(trimethylsilyl)acetamide (BSA)[5] to give the allylation product (**21**) (Entries 1-18). The results are summarized in Table 1. When the

Table 1. Asymmetric Pd-catalyzed allylation of acetate (**20**)



Entry	Ligand	Ligand (mol%)	Temp. (°C)	Time (h)	Yield [c] (%)	Ee[d] (%)	Config.[e]
1[a]	**12**	5	rt	3	100	38	*S*
2	**12**	5	0	48	83	42	*S*
3	**13**	5	rt	6	100	53	*R*
4	**13**	5	0	48	78	62	*R*
5	**14**	5	rt	18	100	37	*R*
6	**14**	5	0	24	100	51	*R*
7	**15**	5	rt	18	100	30	*R*
8	**15**	5	0	48	92	40	*R*
9	**16**	5	rt	18	97	59	*R*
10	**16**	5	0	72	53	49	*R*
11	**17**	5	rt	24	60	65	*R*
12[b]	**17**	2.1	rt	24	80	74	*R*
13	**17**	2.1	0	72	50	83	*R*
14	**18**	2.1	rt	24	42	82	*R*
15	**18**	2.1	0	96	48	77	*R*
16	**19a**	2.1	rt	48	40	44	*R*
17	**19b**	2.1	rt	72	60	88	*R*
18	**19b**	2.1	0	72	31	85	*R*

a) Molar ratio for Entries 1-11 : $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.025 equiv.), dimethyl malonate (3 equiv.), *N,O*-bis(trimethylsilyl)acetamide (BSA) (3 equiv.), potassium acetate (0.02 equiv.), **20** (1 equiv.), ligands (**12**-**17**) (0.05 equiv.). *b)* Molar ratio for Entries 12-18 : $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.01 equiv.), dimethyl malonate (3 equiv.), BSA (3 equiv.), potassium acetate (0.02 equiv.), **20** (1 equiv.), ligands (**17**-**19a**,**b**) (0.021 equiv.). *c)* Isolated yields. *d)* Determined by chiral HPLC using a Daicel OD-H column. *e) R* or *S* configuration based on the specific rotation with literature data.[2a,b,e]

reactions were carried out at room temperature (or 0 °C) using 2.5 mol% of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and 5 mol% of ligand (**12**) linking pyridine ring, the alkylation product [(*S*)-**21**] was obtained in high yield (rt : 100%, 0 °C : 83%) but in low enantiomeric purity (rt: 38% ee, 0 °C : 42% ee)(Entries 1, 2). Employing chiral ligand (**13**) gave the antipodal alkylation product [(*R*)-**21**] in good chemical yields (rt : 100%, 0 °C : 78%) and the enantioselectivity improved marginally (rt : 53% ee, 0 °C : 62% ee) (Entries 3, 4). Ligands (**14** and **15**), the epimeric analogues of **12** and **13,** were also examined under the same reaction conditions, but this change did not give any improvements in enantioselectivity (Entries 5-8). Likewise, the hydroxymethyl ligand (**16**) did not afford any significant changes in enantioselectivity (Entries 9,10). Next, the effect of substituents on the 6-position of the pyridine ring were examined, and the chiral ligands (**17** and **18**), with bulkier TBDMS and TBDPS ethers as siloxyalkyl substituents on 6-position of pyridine ring, were therefore employed in this reaction (Entries 11-15). The results indicated that these ligands gave superior levels of enantioselectivity [**17**: 83% ee, **18**: 82% ee], albeit in poor chemical yields (Entries 13 and 14). Finally, we tested the effectiveness of the diastereomeric chiral ligands (**19a** and **19b**) (Entries 16-18). Although ligand (**19a**) was ineffective in this reaction (Entry 16), its epimer (**19b**) gave the best result (60% yield and 88% ee) by using 1 mol% of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and 2.1 mol% of ligand at room temperature for 72 h (Entry 17).

From the above results, it is clear that pyridinooxathiane (**19a**) is a good ligand for the allylation reaction as described above. Further, the bulky substituent on the 6-position of the pyridine ring would be expected to increase the stabilization of the sterically favored diastereomeric transition state to afford the enantiomerically enriched product. In this description, we assume that the palladium-catalyzed reaction proceeds *via* one of two diastereomeric palladium-allyl complexes (**22** and **23**) in the reaction involving the chiral ligand (**19b**). Considering that nucleophilic attack usually occurs predominantly at the allyl terminus from *trans* to the better π-acceptor (N in imine >S)[6] and that the (*R*) product was obtained as the major enantiomer, the reaction likely proceeds through an M-type (**22**) rather than a W-type (**23**) intermediate. Furthermore, the reason that the ligand (**19b**) is more effective than the ligand (**19a**) is considered as follows: by having a bulkier ethyl group in the intermediate (**23**) (cf. the hydroxyl group in **24**) on the same side of the coordination site, this would favor the diastereomeric transition state (**22**)

leading to (*R*)-enantiomeric product. Such a consideration is supported from the X-Ray structure of **19b**, which shows the close contact between the N-atom of pyridine and the H-atom of ethyl group.

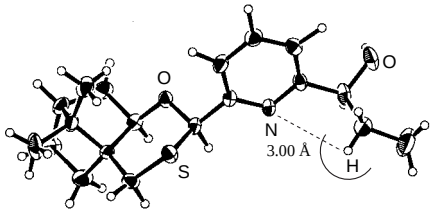
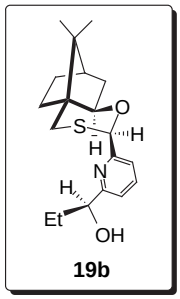


Figure 1. ORTEP drawing of **19b**



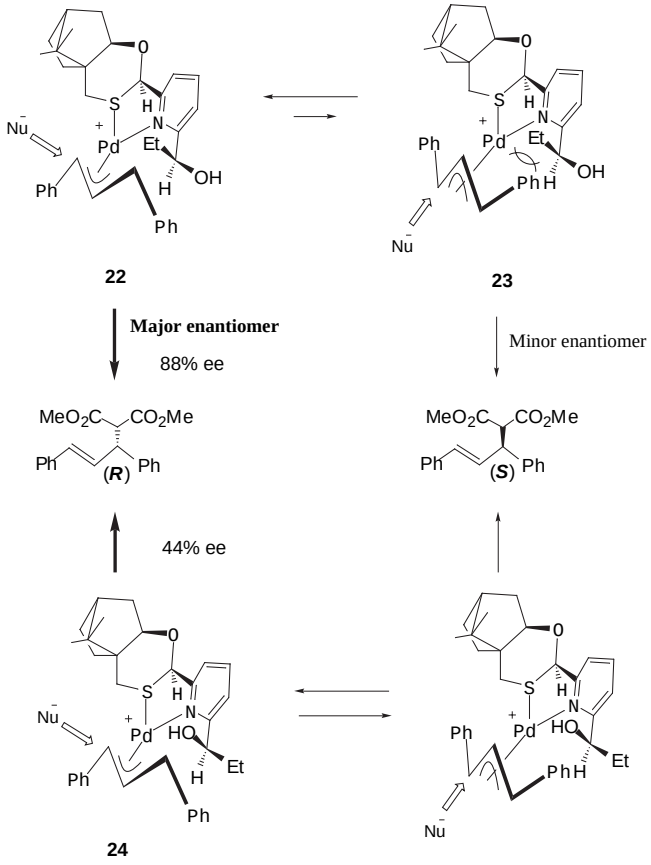


Figure 2. Assumed conformation of π-allyl palladium complexes with ligands (**19a** and **19b**)

In summary, we have prepared new pyridinooxathiane ligands (**12-19a,b**) and disclose the chiral ligand (**19b**) as a new and effective ligand in the asymmetric allylic alkylation reaction.

EXPERIMENTAL

General. IR spectra were measured with a PERKIN ELMER 1725X spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GSX 270 and a JEOL JNM-LA 600 spectrometers with TMS as

an internal standard. MS was taken on a JEOL-JNM-DX 303 spectrometers and elemental analysis was performed by a PERKIN-ELMER 2400 CHN Elemental Analyzer. Optical rotations were measured with a JASCO-DPI-370 digital polarimeter.

6-Hydroxymethyl-2-pyridinecarboxaldehyde (4).

To a solution of 2,6-pyridinedicarboxaldehyde (**3**) (100 mg, 0.74 mmol) in MeOH (7 mL) was added $NaBH_4$ (7 mg, 0.19 mmol) at 0 ˚C, and the mixture was stirred for 5 min. The reaction was quenched with H_2O (10 mL) and extracted with ether. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel with hexane/AcOEt (1 : 3) as an eluent to give a white solid (**4**) (54.8 mg) in 54% yield. mp 66-68 ˚C (hexane-$CHCl_3$). IR (film) cm^{-1}: 3156, 1713, 1601. ^{1}H-NMR ($CDCl_3$) δ: 10.08 (s, 1H), 7.87-7.91 (m, 2H), 7.56 (m, 1H), 4.89 (s, 2H), 3.76 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ : 193.07, 160.30, 151.64, 137.79, 124.90, 120.57, 64.15. Ms *m/z* : 137 (M^+). HRMS calcd for $C_7H_7NO_2$: 137.0477, found : 137.0498.

2,6-Pyridinedicarboxaldehyde monoethylene acetal (5).

2,6-Pyridinedicarboxaldehyde (**3**) (410 mg, 3 mmol), ethylene glycol (93 mg, 1.5 mmol), *p*-toluenesulfonic acid monohydrate (29 mg, 0.15 mmol) and benzene (15 mL) were placed in a flask equipped with a Dean-Stark trap. The mixture was refluxed for 15 min. The solvent was evaporated under a reduced pressure and the residue was subjected to column chromatography on silica gel with hexane/ether (3 : 1) as an eluent to give a colorless oil (**5**) (228 mg) in 42% yield. IR (film) cm^{-1}: 1713, 1593. ^{1}H-NMR ($CDCl_3$) δ: 10.11 (s, 1H), 7.94-7.96 (m, 2H), 7.79 (dd, J = 2.7 Hz, 6.5 Hz, 1H), 5.94 (s, 1H), 4.10-4.24 (m, 4H). ^{13}C-NMR ($CDCl_3$) δ : 193.00, 157.73, 152.04, 137.73, 124.68, 121.47, 102.84, 65.48, 65.48. Ms *m/z* : 178 (M^+-1). HRMS calcd for $C_9H_9NO_2$: 179.0582, found : 179.0586.

6-(1-Hydroxypropyl)-2-pyridinecarboxaldehyde monoethylene acetal (6).

To a solution of compound (**5**) (330 mg, 1.84 mmol) in THF (6 mL) was added ethylmagnesium bromide [2 mL (3 mol/L ether), 6 mmol] at rt, and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was quenched with sat. NH_4Cl and extracted with $CHCl_3$. The organic

layer was dried over $MgSO_4$. The solvent was evaporated under a reduced pressure and the residue was purified by preparative TLC (ether) to give a colorless oil (**6**) (300 mg) in 78% yield. IR (film) cm^{-1}: 1597. ^{1}H-NMR ($CDCl_3$) δ: 7.74 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 5.86 (s, 1H), 4.71 (m, 1H), 4.04-4.23 (m, 5H), 1.64-1.96 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ : 161.70, 155.67, 137.40, 120.67, 119.01, 103.69, 73.65, 65.59, 65.58, 31.24, 9.43. Ms *m/z* : 208 (M^+-1). HRMS calcd for $C_{11}H_{15}NO_3$: 209.1052, found : 209.1081.

6-(1-Hydroxypropyl)-2-pyridinecarboxaldehyde (7).

A mixture of compound (**6**) (300 mg, 1.43 mmol), 10% HCl (3 mL) and THF (6 mL) was refluxed for 1 h. The reaction mixtures were quenched with sat. $NaHCO_3$ at 0 ˚C and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated under a reduced pressure to give the crude product that was purified by preparative TLC (ether) to give a colorless oil (**7**) (208 mg) in 88% yield. IR (film) cm^{-1}: 1716. ^{1}H-NMR ($CDCl_3$) δ: 10.09 (s, 1H), 7.88-7.90 (m, 2H), 7.53 (m, 1H), 4.81 (dd, *J* = 4.7 Hz, 7.2 Hz, 1H), 3.94 (br s, 1H), 1.69-2.03 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ : 193.16, 163.09, 151.36, 137.70, 124.79, 120.28, 73.87, 31.28, 9.37. Ms *m/z* : 165 (M^+). HRMS calcd for $C_9H_{11}NO_2$: 165.0790, found : 165.0814.

General procedure for preparations of chiral ligands (12-16).

(*1S*)-(-)-10-Mercaptoisoborneol (**8**) (50 mg, 0.27 mmol) and (*1S*)-(-)-10-Mercaptoborneol (**9**) (50 mg, 0.27 mmol), 2-pyridinecarboxaldehydes (**4, 10, 11**) (32 mg, 0.30 mmol), *p*-toluenesulfonic acid monohydrate (10 mg, 0.054 mmol) and benzene (**12-15**: 10 mL) or toluene (**16**: 10 mL) respectively, were placed in a flask equipped with a Dean-Stark trap. The mixture was refluxed for 6 h (**12-15**) or 14 h (**16**). The solvent was evaporated under a reduced pressure and the residue was purified by preparative TLC (hexane : ether = 3 : 1) to give the corresponding products (**12-16**).

(1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (12).

Obtained (69 mg, 93%) as a white solid, mp 71-73 °C (hexane-ether). $[\alpha]_D^{24}$ = -58.92˚ (c 1.68, $CHCl_3$). IR (KBr) cm^{-1}: 1590, 750, 726. ^{1}H-NMR ($CDCl_3$) δ: 8.53 (d, *J* = 4.5 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H),

7.57 (d, *J* = 7.7 Hz, 1H), 7.20 (m, 1H), 5.85 (s, 1H), 3.81 (dd, *J* = 3.1 Hz, 7.9 Hz, 1H), 3.31 (d, *J* = 14.2 Hz, 1H), 2.85 (d, *J* = 14.2 Hz, 1H), 2.04 (m, 1H), 1.70-1.82 (m, 3H), 1.54 (m, 1H), 1.45 (s, 3H), 0.98-1.09 (m, 2H), 0.95 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ : 158.24, 148.51, 136.66, 122.86, 120.94, 85.60, 84.15, 46.76, 45.53, 42.21, 37.85, 34.35, 29.57, 27.24, 23.40, 20.44. *Anal.* Calcd for $C_{16}H_{21}NOS$: C, 69.78; H, 7.69; N, 5.09. Found : C, 69.49; H, 7.96; N, 5.09. Ms *m/z* : 275 (M^+).

(1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-(5-methyl)pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (13).

Obtained (65 mg, 84%) as a white solid, mp 144-146 °C (hexane-ether). $[\alpha]_D^{24}$= -51.36˚ (c 1.46, $CHCl_3$). IR (KBr) cm^{-1}: 1589, 757, 712. ^{1}H-NMR ($CDCl_3$) δ: 7.59 (t, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 5.79 (s, 1H), 3.79 (dd, *J* = 3.1 Hz, 8.1 Hz, 1H), 3.29 (d, *J* = 14.2 Hz, 1H), 2.83 (d, *J* = 14.2 Hz, 1H), 2.53 (s, 3H), 2.02 (m, 1H), 1.71-1.78 (m, 3H), 1.54 (m, 1H), 1.45 (s, 3H), 1.02-1.09 (m, 2H), 0.96 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ : 157.70, 157.16, 136.89, 122.53, 117.89, 85.53, 84.36, 46.74, 45.54, 42.14, 37.87, 34.38, 29.64, 27.25, 24.35, 23.37, 20.42. *Anal.* Calcd for $C_{17}H_{23}NOS$: C, 70.54; H, 8.01; N, 4.84. Found : C, 70.27; H, 8.26; N, 4.88. Ms *m/z* : 289 (M^+).

(1*R*,3*R*,5*S*,8*S*)-11,11-Dimethyl-4-oxa-5-pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (14).

Obtained (71 mg, 96%) as a white solid, mp 123 °C (hexane-ether). $[\alpha]_D^{24}$= -50.80˚ (c 1.24, $CHCl_3$). IR (KBr) cm^{-1}: 1590, 748, 719. ^{1}H-NMR ($CDCl_3$) δ: 8.54 (d, *J* = 3.4 Hz, 1H), 7.66-7.76 (m, 2H), 7.21 (m, 1H), 5.97 (s, 1H), 3.95-4.02 (m, 1H), 3.26 (d, *J* = 14.2 Hz, 1H), 2.72 (m, 1H), 2.56 (d, *J* = 14.2 Hz, 1H), 2.28 (m, 1H), 1.69-1.77 (m, 2H), 1.25-1.47 (m, 2H), 1.20 (dd, *J* = 4.8 Hz, 13.5 Hz, 1H), 0.97 (s, 3H), 0.96 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ : 157.69, 148.62, 136.64, 123.00, 121.17, 85.77, 84.37, 47.03, 44.80, 44.35, 34.36, 32.94, 27.87, 25.84, 19.58, 18.64. *Anal.* Calcd for $C_{16}H_{21}NOS$: C, 69.78; H, 7.69; N, 5.09. Found : C, 69.50; H, 7.88; N, 5.04. Ms *m/z* : 275 (M^+).

(1*R*,3*R*,5*S*,8*S*)-11,11-Dimethyl-4-oxa-5-(6-methyl)pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (15).

Obtained (61 mg, 78%) as a colorless oil. $[\alpha]_D^{24}$= -47.77˚ (c 0.9, $CHCl_3$). IR (film) cm^{-1}: 1594. ^{1}H-NMR ($CDCl_3$) δ: 7.62 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 5.91 (s, 1H), 3.96 (m, 1H), 3.24 (d, *J* = 14.2 Hz, 1H), 2.69 (m, 1H), 2.54 (d, *J* = 14.2 Hz, 1H), 2.54 (s, 3H), 2.26 (m, 1H),

1.74-1.77 (m, 2H), 1.30-1.46 (m, 2H), 1.18 (dd, *J* = 4.7 Hz, 13.8 Hz, 1H), 0.96 (s, 3H), 0.95 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ : 157.35, 157.25, 137.02, 122.80, 118.22, 86.26, 84.43, 47.11, 44.91, 44.45, 34.50, 33.11, 28.00, 25.98, 24.47, 19.70, 18.74. Ms *m/z* : 289 (M^+). HRMS calcd for $C_{17}H_{23}NOS$: 289.1500, found : 289.1518.

(1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-(6-hydroxymethyl)pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]-undecane (16).

Obtained (64 mg, 78%) as a white solid, mp 120 °C (hexane-ether). $[\alpha]_D^{24}$= -55.00˚ (c 1.0, $CHCl_3$). IR (KBr) cm^{-1}: 1591, 759, 718. ^{1}H-NMR ($CDCl_3$) δ : 7.71 (t, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 5.83 (s, 1H), 4.73 (br s, 2H), 3.80 (dd, *J* = 3.1 Hz, 7.9 Hz, 1H), 3.70 (br s, 1H), 3.30 (d, *J* = 14.2 Hz, 1H), 2.84 (d, *J* = 14.2 Hz, 1H), 2.04 (m, 1H), 1.70-1.82 (m, 3H), 1.54 (m, 1H), 1.45 (s, 3H), 0.99-1.09 (m, 2H), 0.96 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ : 158.10, 157.54, 137.60, 119.89, 119.89, 85.67, 84.08, 64.01, 46.84, 45.59, 42.24, 37.92, 34.39, 29.58, 27.28, 23.38, 20.45. *Anal.* Calcd for $C_{17}H_{23}NO_2S$: C, 66.85; H, 7.59; N, 4.59. Found : C, 66.56; H, 7.61; N, 4.31. Ms *m/z* : 305 (M^+).

(1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-(6-*tert*-butyldimethylsilyloxymethyl)pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (17).

To a mixture of **16** (64 mg, 0.21 mmol) and imidazole (108 mg, 1.59 mmol) in dry dichloromethane (3 mL) was added TBDMSCl (100 mg, 0.67 mmol) at rt and the reaction mixture was stirred at same temperature for 1.5 h. The solvent was evaporated under a reduced pressure and the residue was subjected to column chromatography on silica gel with hexane/AcOEt (5 : 1) as an eluent to give a white solid (**17**) (67 mg) in 76% yield. mp 71 ˚C (hexane-ether). $[\alpha]_D^{24}$= -36.89˚ (c 1.03, $CHCl_3$). IR (KBr) cm^{-1}: 1592, 778, 755. ^{1}H-NMR ($CDCl_3$) δ : 7.73 (t, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 2H), 5.78 (s, 1H), 4.82 (s, 2H), 3.79 (dd, *J* = 3.0 Hz, 7.9 Hz, 1H), 3.29 (d, *J* = 14.2 Hz, 1H), 2.83 (d, *J* = 14.4 Hz, 1H), 1.98-2.08 (m, 1H), 1.74-1.81 (m, 3H), 1.59 (m, 1H), 1.45 (s, 3H), 0.98-1.09 (m, 1H), 0.96 (s, 3H), 0.95 (s, 9H), 0.85-0.94 (m, 1H), 0.11 (s, 6H). ^{13}C-NMR ($CDCl_3$) δ : 160.53, 157.43, 137.54, 119.32, 119.16, 85.70, 84.38, 66.01, 46.84, 45.64, 42.24, 37.94, 34.45, 29.68, 27.31, 25.93, 23.42, 20.47, 18.36, -5.37. *Anal.* Calcd for $C_{23}H_{37}NO_2SSi$: C, 65.82; H, 8.89; N, 3.34. Found : C, 65.61; H, 9.16; N, 3.07. Ms *m/z* :

419 (M^+).

(1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-(6-*tert*-butyldiphenylsilyloxymethyl)pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (18).

To a mixture of **16** (64 mg, 0.21 mmol) and imidazole (43 mg, 0.63 mmol) in dry dichloromethane (3 mL) was added TBDPSCl (115 mg, 0.42 mmol) at rt and the reaction mixture was stirred at rt for 24 h. The solvent was evaporated under a reduced pressure and the residue was subjected to column chromatography on silica gel with hexane/AcOEt (5 : 1) as an eluent to give a light yellow oil (**18**) (63mg) in 55% yield. $[\alpha]_D^{24}$= -31.03˚ (c 1.45, $CHCl_3$). IR (KBr) cm^{-1}: 1595, 758, 703. ^{1}H-NMR ($CDCl_3$) δ: 7.61-7.80 (m, 6H), 7.31-7.47 (m, 7H), 5.73 (s, 1H), 4.86 (s, 2H), 3.76 (dd, *J* = 3.1 Hz, 7.9 Hz, 1H), 3.25 (d, *J* = 14.2 Hz, 1H), 2.80 (d, *J* = 14.4 Hz, 1H), 1.97-2.06 (m, 1H), 1.68-1.80 (m, 3H), 1.47-1.67 (m, 1H), 1.45 (s, 3H), 1.13 (s, 9H), 1.06 (m, 1H), 0.90-1.01 (m, 4H). ^{13}C-NMR ($CDCl_3$) δ : 160.09, 157.47, 137.59, 135.48, 134.78, 133.19, 133.16, 129.75, 129.72, 129.59, 127.74, 127.73, 127.68, 119.25, 119.16, 85.65, 84.31, 66.65, 46.79, 45.59, 42.18, 37.89, 34.39, 29.62, 27.26, 26.88, 26.53, 23.38, 20.42, 19.32. Ms *m/z* : 543 (M^+). HRMS calcd for $C_{33}H_{41}NO_2SSi$: 543.2628, found : 543.2675.

(1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-[6-(*R*)-1-hydroxypropyl]pyridinyl-6-thiatricyclo-[6.2.1.0^{3,8}]undecane (19a) and (1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-[6-(*S*)-1-hydroxypropyl]-pyridinyl-6-thiatricyclo[6.2.1.0^{3,8}]undecane (19b).

(*1S*)-(-)-10-Mercaptoisoborneol (**8**) (100 mg, 0.54 mmol), aldehyde (**7**) (90 mg, 0.60 mmol), *p*-toluenesulfonic acid monohydrate (20 mg, 0.11 mmol) and benzene (10 mL) were placed in a flask equipped with a Dean-Stark trap. The mixture was refluxed for 12 h. The solvent was evaporated under a reduced pressure and the residue was purified by preparative TLC (hexane : ether = 10 : 1) to give pure **19a** (40 mg, 22%) and **19b** (58 mg, 32%). **19a** : A white solid. mp 96-98 °C (hexane-ether). $[\alpha]_D^{24}$= -50.45˚ (c 1.1, $CHCl_3$). IR (KBr) cm^{-1}: 3428, 1591. ^{1}H-NMR ($CDCl_3$) δ: 7.71 (t, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 5.83 (s, 1H), 4.67 (dd, *J* = 4.9 Hz, 11.7 Hz, 1H), 4.07 (d, *J* = 5.4 Hz, 1H), 3.81 (dd, *J* = 3.1 Hz, 7.9 Hz, 1H), 3.31 (d, *J* = 14.2 Hz, 1H), 2.84 (d, *J* = 14.2 Hz, 1H), 2.02 (m, 1H), 1.50-1.91 (m, 6H), 1.46 (s, 3H), 0.99-1.12 (m, 2H), 0.96 (s, 3H), 0.94 (t, *J* = 7.4 Hz,

3H). ^{13}C-NMR ($CDCl_3$) δ : 161.05, 157.20, 137.58, 119.78, 119.78, 85.61, 84.04, 73.61, 46.83, 45.59, 42.20, 37.91, 34.38, 31.31, 29.55, 27.28, 23.36, 20.44, 9.41. *Anal.* Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16; N, 4.20. Found : C, 68.20; H, 7.86; N, 4.15. Ms *m/z* : 333 (M^+). **19b** : A white solid. mp 127 °C (hexane-ether). $[\alpha]_D^{24}$= -59.09˚ (c 1.2, $CHCl_3$). IR (KBr) cm^{-1}: 3292, 1596. ^{1}H-NMR ($CDCl_3$) δ: 7.70 (t, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 5.84 (s, 1H), 4.67 (dd, *J* = 4.6 Hz, 7.1 Hz, 1H), 4.16 (br s, 1H), 3.81 (dd, *J* = 3.0 Hz, 7.9 Hz, 1H), 3.30 (d, *J* = 14.2 Hz, 1H), 2.84 (d, *J* = 14.2 Hz, 1H), 2.02 (m, 1H), 1.66-1.89 (m, 5H), 1.55 (m,1H), 1.46 (s, 3H), 0.98-1.12 (m, 2H), 0.96 (s, 3H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ : 160.99, 157.16, 137.52, 119.79, 119.77, 85.64, 84.14, 73.49, 46.85, 45.62, 42.25, 37.95, 34.41, 31.27, 29.57, 27.30, 23.39, 20.46, 9.40. *Anal.* Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16; N, 4.20. Found : C, 68.15; H, 8.19; N, 4.12. Ms *m/z* : 333 (M^+).

X-Ray crystal structure determination of 19b.

A single crystal with sizes of 0.35 x 0.2 x 0.08 mm was mounted on a Rigaku/MSC Mercury CCD diffractometer using MoKα radiation (λ = 0.71069 Å) at the temperature of -50°C. Crystal data are as follows; MF = $C_{19}H_{27}NO_2S$, MW = 333.49, monoclinic, $P2_1$, a = 9.086(3), b = 6.553(2), c = 16.058(6) Å, β = 106.726(5) °, V=915.7(5) Å ^{3}, Z=2, D(calcd)=1.209g/cm^3. A total of 6943 intensity data were measured up to 2θ = 55°, of which 3875 reflections including Freidel pairs were assigned as unique reflections(Rint = 0.022). The structure was solved by the direct method and refined by the full-matrix least-squares method. Final refinement for all non-hydrogen atoms anisotropically and all hydrogen atoms fixed isotropically were converged to give R of 0.046 and Rw of 0.047 for 3459 observed data [Io > 3σ(Io)], and GOF of 1.61. The flack parameter indicating the correctness of absolute configuration is 0.05(7). The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC 186853) in CIF format.

Typical procedure of Pd-catalyzed asymmetric allylation of (±)-1,3-diphenyl-2-propenyl acetate (20) with dimethyl malonate.

A mixture of the ligands (**12-19a,b**) [0.02 mmol (5 mol%) or 0.0084 mmol (2.1 mol%)] and [PdCl(η^3-C_3H_5)]$_2$ (0.01 mmol or 0.0042 mmol), respectively, in dry dichloromethane (1 mL) was stirred at room

temperature for 1 h and the resulting yellow solution was added to a mixture of acetate (**20**) (100 mg, 0.40 mmol) and potassium acetate (0.8 mg, 0.008 mmol) in dry dichloromethane (1 mL), followed by the addition of dimethyl malonate (160 mg, 1.2 mmol) and BSA (240 mg, 1.2 mmol). The reaction was carried out an ambient temperature. The reaction mixtures were diluted with ether and quenched with sat. NH_4Cl. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated under a reduced pressure and the residue was purified by preparative TLC (hexane : ether = 5 : 1) to give a pure product (**21**). The enantiomeric excess was determined by HPLC (Chiralcel OD-H, 0.5 mL/min, hexane : 2-propanol = 98 : 2). The absolute configuration was determined by the specific rotation.[2a,b,e]

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