# Synthesis and Characterization of Novel Chiral 1,2-Diamines Derived from α-Pinene

Toshiaki Suzuki, Akira Shibata, Naoya Morohashi,* and Yoshihiro Ohba*
*Department of Chemistry and Chemical Engineering, Faculty of Engineering, Yamagata University, 4-3-16 Yonezawa, Yamagata 992-8510*

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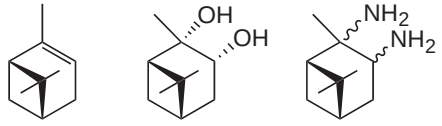
Direct diazidation of α-pinene (**1**) followed by reduction gave two novel 1,2-diamines (**2a** and **2b**) whose absolute configuration were determined by 2D $^1$H NMR and X-ray crystallography.

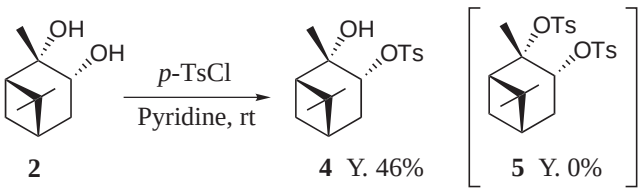
Enatiomeric 1,2-diamines have been known as an efficient chiral auxiliary in various kinds of chiral catalysts and reagents. Despite the many existing chiral 1,2-diamines, the design of new and improved enatiomerically enriched compounds is still sought. On the other hand, α-pinene (**1**) is a very useful chiral source because of its easily availability as an enantiomeric pure sample and ease of chemical modification. Therefore, its derivatives such as 2-hydroxypinan-3-one,[1] pinanediol (e.g. 2),[2] and 3-amino-2-hydroxypinane[3] have been widely applied in use as chiral source of asymmetric catalyst. Surprisingly, it appears that there is no report up until now about free 1,2-diamine (**3**) based on α-pinene.[4] Herein, we report the preparation of unsymmetrical 1,2-diamine (**3**) based on commercially available α-pinene and the analysis of their absolute configuration by 2D $^1$H NMR and X-ray crystallography (Scheme 1).




**Scheme 1.**

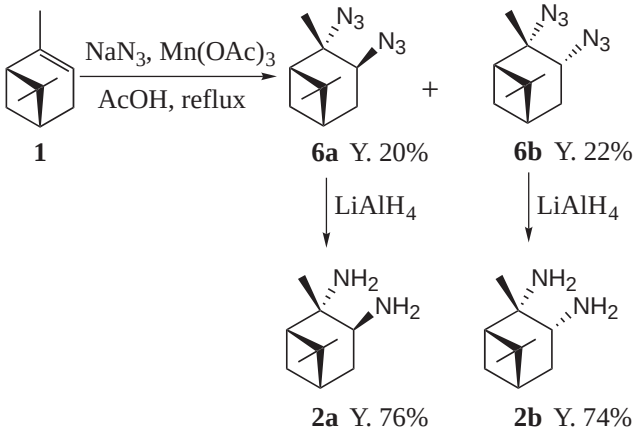
It is well known that the general synthetic method of chiral 1,2-diamine from alkene is as follows: alkene is converted to chiral 1,2-diol by asymmetric dihyroxylation,[5] and diazidation of ditosylate of diol followed by reduction give corresponding chiral 1,2-dimaine. Unfortunately, it was very difficult to synthesize ditosylate from **2** because of low reactivity of the tertiary OH group (Scheme 2).

Therefore, **1** was converted to the corresponding diazide according to direct diazidation of alkenes reported by Fristad et al.[6] Thus, **1** was treated with $NaN_3$ in the presence of $Mn(OAc)_3 \cdot 2H_2O$ in acetic acid under reflux condition to give pinane diazide **6** (Scheme 3).[7,8] The FAB-MS and NMR spectra of reaction mixture indicated the presence of small amount of several monoazide compounds. However, it was very difficult to isolate and identify these monoazide compounds. The TLC and $^1$H NMR revealed that **6** consisted of only two diastereomers, suggesting that this diazidation occurred diastereoselectively. Fortunately, these diastereomers could be separated by column chromatography on silica gel to afford **6a** (the first eluted compound) and **6b** (the second eluted compound) in almost the same yields. The infrared spectra of both **6a** and **6b** display absorption at ca. 2100 $cm^{-1}$ assignable to the azide groups. The absolute configurations of these diastereomers were determined by 2D $^1$H NMR. Cross peaks were observed at 8-H/9-H in the NOESY spectrum of both diastereomers, suggesting that both **6a** and **6b** have 2*S* configuration (Figure 1). Furthermore, we observed a cross peaks at 3-H/4-$H_b$ and 4-$H_a$/9-H in **6a**, in which no cross peaks between 3-H and 9-H was observed, indicating that two azide groups are anti configuration to each other. In **6b**, two azide groups are syn configuration because of cross peaks of 3-H/8-H and 3-H/9-H. These results indicate that **6a** and **6b** have (2*S*, 3*S*), (2*S*, 3*R*) configuration, respectively.




**Scheme 2.**

On reduction with $LiAlH_4$ in diethyl ether, the diazide **6a** and **6b** afforded the corresponding 2,3-pinane diamine **2a** and




**Scheme 3.**

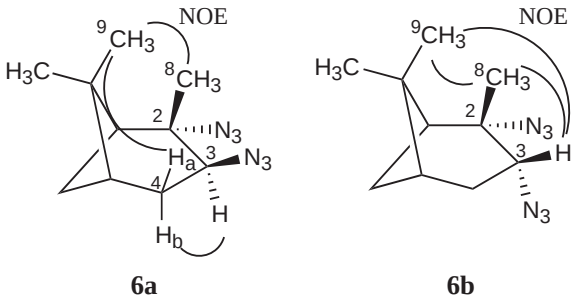



**Figure 1.** NOE correlation of pinane diazide **6a** and **6b**.

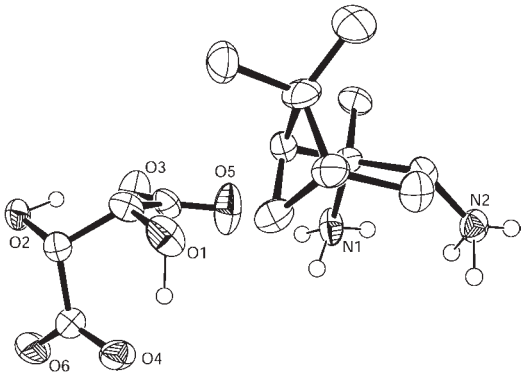



**Figure 2.** X-ray structure of **2b**·L-(+)-tartrate. The thermal ellipsoids are drawn at 50% probability. Water molecule and hydrogen atoms except of OH and $NH_3$ are omitted for clarity.

**2b**, respectively.[9] The infrared spectrum of both **2a** and **2b** displays an absorption at ca. 3360 $cm^{-1}$ assignable to the amino groups. Specific rotation $[\alpha]_D$ of **2a** and **2b** were measured to be +22 and −38°, respectively.

In order to confirm the structure and absolute configuration of the obtained diamines, **2a** and **2b** were converted to salt with tartaric acid for preparation of a single crystal suitable for X-ray analysis.[10] A single crystal of 1:1 complex of **2b**·L-(+)-tartrate was obtained by recrystallization from $H_2O$–MeOH solution.[11] Without any doubt, **2b** has (1*S*, 2*S*, 3*R*, 5*S*) configuration (Figure 2). Unfortunately, a single crystal of salt of **2a** with tartaric acid could not be obtained.

In conclusion, we showed the first example of conversion of α-pinene **1** to free 2,3-pinane diamine **2a** and **2b**, whose absolute configurations are (2*S*, 3*S*), (2*S*, 3*R*), respectively. Application of these new diamines for asymmetric synthesis is under current investigation.

**References and Notes**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7 α-Pinene **1** (3.0 g, 22 mmol) was resolved in acetic acid (56 mL) containing $Mn(OAc)_3 \cdot 2H_2O$ (15.8 g, 66 mmol) and $NaN_3$ (22 g, 0.33 mol). The mixture was refluxed under nitrogen for 2 h. After cooling, water was added and extracted with petroleum ether. The organic layer was washed with sat. $NaHCO_3$ (aq), dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by column chromatography on silica gel with hexane as the eluent to give **6a** (0.97 g, 20%) and **6b** (1.1 g, 22%). **6a**: $[\alpha]_D = +2.9°$ (*c* 3.5, $CHCl_3$); IR ($cm^{-1}$): 2100 (-$N_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 0.94 (s, 3H, C*H*$_3$), 1.27 (s, 3H, C*H*$_3$), 1.47 (d, 1H, *J* = 11 Hz, C*H*), 1.51 (s, 3H, C*H*$_3$), 1.79 (dd, 1H, *J* = 13.5, 7.5 Hz, C*H*), 1.97 (q, 1H, *J* = 5.4 Hz, C*H*), 2.05 (t, 1H, *J* = 5.4 Hz, C*H*), 2.21–2.26 (m, 1H, C*H*), 2.41–2.47 (m, 1H, C*H*), 3.86 (dd, 1H, *J* = 10.5, 7.5 Hz, C*H*); $^{13}$C NMR ($CDCl_3$) δ: 21.1, 22.8, 26.0, 27.4, 32.1, 39.0, 39.3, 51.5, 62.3, 70.8. **6b**: $[\alpha]_D = +115°$ (*c* 3.1, $CHCl_3$); IR ($cm^{-1}$): 2102 (-$N_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 1.03 (s, 3H, C*H*$_3$), 1.31 (s, 3H, C*H*$_3$), 1.43 (d, 1H, *J* = 10.5 Hz, C*H*), 1.50 (s, 3H, C*H*$_3$), 1.94 (dd, 1H, *J* = 13.5, 8.3 Hz, C*H*), 2.05–2.21 (m, 2H, C*H*), 2.28–2.33 (m, 1H, C*H*), 2.36–2.40 (m, 1H, C*H*), 3.80 (t, 1H, *J* = 8.3 Hz, C*H*); $^{13}$C NMR ($CDCl_3$) δ: 23.7, 25.6, 28.0, 29.8, 32.8, 38.7, 40.2, 52.4, 60.7, 68.5.

8 Diazidation reaction of **1** was examined at several conditions with changing equiv. of $NaN_3$ and $Mn(OAc)_3$ and concentration. However, it was very difficult to separate **6** and monoazide compounds under the conditions, in which the conversion yield of **6** from **1** is low.

9 To a vigorously stirred suspension of $LiAlH_4$ (120 mg, 2.8 mmol) in ether (5 mL), a solution of **6a** (156 mg, 0.7 mmol) was added dropwise. The mixture was heated under reflux for 2 h, and the complexes were decomposed by addition of $NaOH_{(aq)}$. The layers were separated, and the aqueous phase was washed with ether. Mixed ether extracts were washed with brine and dried over $Na_2SO_4$. The solvent was evaporated, and the solid residue was recrystallized from hexane to give **2a** (90 mg, 76%). From **6b**, **2b** (74%) was obtained in a similar manner. **2a**: mp 77–79 °C; $[\alpha]_D = +22°$ (*c* 1.0, $CHCl_3$); IR ($cm^{-1}$): 3367 (-$NH_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ (ppm): 0.85 (s, 3H, C*H*$_3$), 1.08 (s, 3H, C*H*$_3$), 1.16 (s, 3H, C*H*$_3$), 1.18 (s, 4H, N*H*$_2$), 1.39 (m, 2H, C*H*), 1.69 (t, 1H, *J* = 5.5 Hz, C*H*), 1.85 (dd, 1H, *J* = 10, 5.5 Hz, C*H*), 2.05 (m, 1H, C*H*), 2.18 (m, 1H, C*H*), 2.99 (t, 1H, *J* = 9.0 Hz, C*H*); $^{13}$C NMR ($CDCl_3$) δ: 23.5, 24.0, 25.0, 28.0, 35.0, 39.6, 40.4, 54.3, 56.7, 57.3. **2b**: mp 74–76 °C; $[\alpha]_D = -38°$ (*c* 1.0, $CHCl_3$); IR ($cm^{-1}$); 3359 (-$NH_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 0.97 (s, 3H, C*H*$_3$), 1.10 (s, 3H, C*H*$_3$), 1.15 (d, 1H, *J* = 10 Hz, C*H*), 1.19 (s, 3H, C*H*$_3$), 1.22 (s, 4H, N*H*$_2$), 1.31 (ddd, 1H, *J* = 13.5, 7.5, 2 Hz, C*H*), 1.77–1.84 (m, 2H, C*H*), 2.09–2.14 (m, 1H, C*H*), 2.28–2.34 (m, 1H, C*H*), 3.15 (dd, 1H, *J* = 9.5, 7.5 Hz, C*H*); $^{13}$C NMR ($CDCl_3$) δ: 24.1, 28.4, 29.8, 31.2, 39.4, 39.9, 40.8, 50.7, 55.0, 55.7.

10 Diamine **2b** in EtOH was mixed with L-(+)-tartaric acid, and the mixture was refluxed for 30 min. The white precipitate was separated by filtration to give **2b**·L-(+)-tartrate 1:1 complex (92%).

11 Crystal data: $C_{14}H_{26}N_2O_6 \cdot (H_2O)_{0.5}$, fw 647.36, colorless, crystal dimensions 0.40 × 0.30 × 0.20 $mm^3$, orthorhombic, space group $P2_12_12$ (No. 18), $a = 11.580(3)$, $b = 11.629(3)$, $c = 12.682(4)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 1707(3)$ Å$^3$, $Z = 4$, Cu Kα radiation ($\lambda = 1.5419$ Å), $D_{calcd} = 2.517$ g $cm^{-3}$, $T = 296$ K, $\mu$(Cu Kα) = 2.639 $cm^{-1}$, Rigaku RAXIS RAPID imaging plate diffractometer, 14595 measured reflections, 1794 unique reflections ($R_{int} = 0.077$), 755 observed reflections ($I > 3.00\sigma(I)$), 202 parameters, $R = 0.059$, $wR = 0.066$, refined against $|F|$, GOF = 1.456. Crystallographic data for this crystal has been deposited with the Cambridge Crystallographic Date Centre as supplementary publication No. CCDC 263943. Copies of the data can be obtained free of charge (via http://www.ccdc.cam.ac.uk/conts/retrieving.html) on application to CCDC, 12, Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).


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