products (29% yield) were obtained along with the recovered starting material (46% yield) (entry 7). On the other hand, (*S*)-verbenol showed better reactivity and selectivity, *i.e.* alcohol oxidation predominates over the olefin epoxidation to provide enone and epoxy ketone in 67% and 20% yield, respectively. This preference could be explained by assuming the difficulty of the catalyst approaching to the sterically congested trisubstituted C=C bond in (*S*)-verbenol.

This reaction is considered to proceed via electrophilic Mn^{V}=O intermediate, which is proposed in the related epoxidation chemistry (Scheme 1).[9] The active Mn=O species abstract H atom next to hydroxy group, which is followed by the rebound of manganese hydroxide to the radical or cationic intermediate. This rebound step should be very fast, considering that no cyclopropyl rearranged product was observed in the oxidation of 1-phenyl-1-cyclopropanemehanol (see entry 2 in Table 2). In addition, the low reactivity of the primary alcohols could be ascribed to the low electron density around α-carbon to hydroxy group. Studies on the further reaction mechanism are in progress.

We have shown that the (salen)Mn(III) complex **1** can be used as a catalyst for the oxidation of various alcohols. This oxidation is effected under mild reaction conditions utilizing bleach (aq. NaOCl) as the oxidant. Due to its simple waste disposal together with low toxicity and cost, NaOCl consists of a favorable oxidant over the other typical oxidants such as Cr(VI) and Mn(VI).[10] This work introduces a new method which can utilize a commercial bleach as an oxidant for the oxidation of alcohols. Easy preparation and handling of the catalyst **1** coupled with practical reaction conditions will make this procedure useful in organic synthesis.

Acknowledgment. The authors wish to acknowledge the financial support of the Korea Research Foundation made in the program year of 1997.

References

1. (a) Zhang, W.; Leobach, J. L.; Wilson, R. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (b) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R. *J. Am. Chem. Soc.* **1991**, *113*, 7063. (c) Katsuki, T. *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 940. (d) Pospisil, P. J.; Carsten, D. H.; Jacobsen, E. N. *Chem. Eur. J.* **1996**, *2*, 974 and references cited therein.
2. (a) For the oxidation of sulfides, see: Palucki, M.; Hanson, P.; Jacobsen, E. N. *Tetrahedron Lett.* **1992**, *33*, 7111. (b) For the hydroxylation, see: Katsuki, T.; Irie, R.; Hamachi, K. *Tetrahedron Lett.* **1996**, *37*, 4979. (c) For the aziridination, see: Nishikori, H.; Katsuki, T. *Tetrahedron Lett.* **1996**, *37*, 9245.
3. Lee, N. H.; Lee, C-S.; Jung, D-S. *Tetrahedron Lett.* **1998**, *39*, 1385.
4. Zhang, W.; Jacobsen, E. N. *J. Org. Chem.* **1991**, *56*, 2296.
5. These complexes were prepared from the racemic trans-1,2-diaminocyclohexane and the corresponding salicylaldehydes according to the literature procedure, see: Larrow, J. F.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X.; Zepp, C. M. *J. Org. Chem.* **1994**, *59*, 1939.
6. Jacobsen, E. N.; Zhang, W.; Guler, M. L. *J. Am. Chem. Soc.* **1991**, *113*, 6703.
7. Hughes, D. L.; Smith, G. B.; Liu, J.; Dezeny, G. C.; Senayake, C. H.; Larson, R. D.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1997**, *62*, 2222.
8. Typical experimental procedure is as follows: to a solution of 1-phenylethanol (61 mg, 0.5 mmol) and (salen) Mn complex **1** (16 mg, 0.04 mmol) in CH_2Cl_2 (1.5 mL) was added 1.4 mL (2.0 mmol) of NaOCl solution (1.4 M). The resulting reaction mixture was stirred at 0 °C for 3 hrs. After the reaction was quenched by adding diethyl ether (20 mL), the organic layer was washed with brine solution and dried with anhydrous sodium sulfate. After being concentrated, the mixture was analyzed by GC and GC-MSD spectrometer and purified by flash column chromatography to give the acetophenone (55 mg, 91% yield).
9. (a) Fu, H.; Look, G.; Zhang, W.; Jacobsen, E. N.; Wong, C-H. *J. Org. Chem.* **1991**, *56*, 6497. (b) Norrby, P-O.; Linde, C.; Akermark, B. *J. Am. Chem. Soc.* **1995**, *117*, 11035.
10. *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons: Chichester, England, 1995; Vol. 7, p 4580.

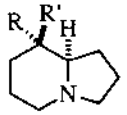
Synthesis of (+)-Tashiromine and (+)-5-Epitashiromine Utilizing the Diastereoselective Alkylation of (S)-4-Carbethoxymethyl-2-oxazolidinone

Deok-Chan Ha*, Sung-Ho Park, Kwang-Sun Choi, and Chang-Soo Yun

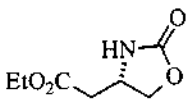
Department of Chemistry, Korea University, 5-1-2 Anam-Dong, Seoul 136-701, Korea
Received April 2, 1998

Tashiromine (**1**) is an indolizidine alkaloid isolated from subtropical Asian deciduous shrub, *Maackia tashiroi*.[1] The optical rotation was not measured due to the shortage of the isolated material and, thus, the absolute stereochemistry remains unknown. Although racemic[2] and (-)-tashiromine[3] were synthesized by several research groups, synthesis of the (+)-enantiomer has not been reported.

In our previous report, we studied the diastereoselective



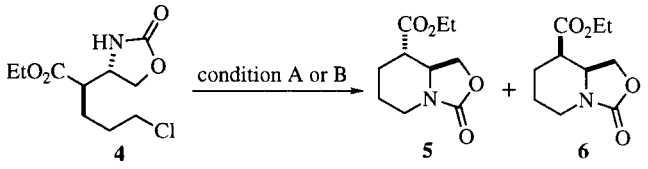
1: R=CH_2OH, R'=H
2: R=H, R'=CH_2OH



3

alkylation of (*S*)-4-carbethoxymethyl-2-oxazolidinone (**3**) with 1-chloro-3-iodopropane to give 97 : 3 diastereomeric mixture of **4** in 80% yield.[4,5] This paper describes the diasteroselective synthesis of (+)-tashiromine (**1**) and (+)-5-epitashiromine (**2**) from the chromatographically inseparable mixture **4**.[6]

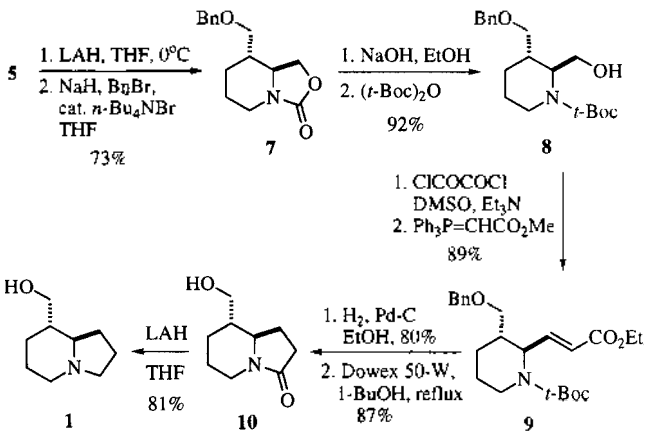
When the cyclic carbamate **4** was heated at reflux with DBU and catalytic amounts of *n*-Bu_4NI in THF, the cyclized and isomerized *trans* carbamate **5** (68%) was obtained together with the *cis* product **6** (5%) which was easily separable by silica gel chromatography. To minimize the isomerization at the C-5 position, K_2CO_3 was used instead of DBU to provide the *cis* product **6** (73%) and *trans* product **5** (16%). These cyclizations provide a divergent approach to *cis* and *trans* bicyclic carbamate **5** and **6** from a diastereomeric mixture of **4**.



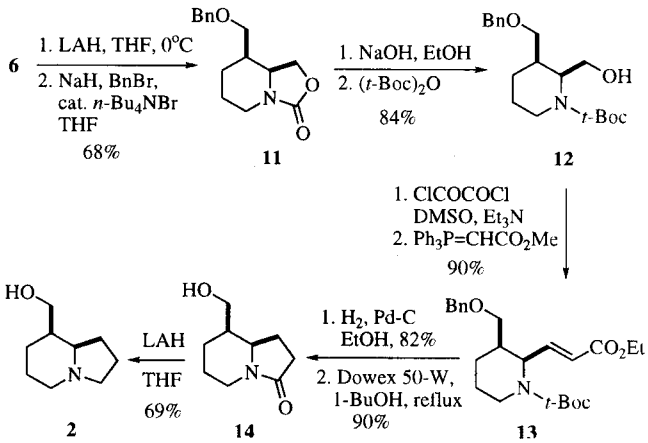
4 **5** **6**

condition A: DBU, *n*-Bu_4NI, THF, reflux **5** (68%) + **6** (5%)
condition B: K_2CO_3, *n*-Bu_4NI, THF, reflux **5** (16%) + **6** (73%)

Synthesis of (+)-tashiromine from *trans*-carbamate **5** is shown in Scheme 1. Selective reduction of the ester moiety of **5** with lithium aluminum hydride at 0 °C in THF followed by conversion to benzyl ether of the resulting hydroxy group gave **7** in 73% combined yield. To construct the second ring of **1**, the carbamate **7** was hydrolyzed in refluxing ethanolic NaOH and the resulting piperidine was selectively protected with *t*-Boc group to give **8** (92% from **7**). Swern oxidation of the alcohol **8** followed by Wittig reaction of the resulting crude aldehyde provided the unsaturated ester **9** in 89% yield. Hydrogenolysis of the benzyl ether with concomitant reduction of the double bond of



Scheme 1



Scheme 2

9 under atmospheric hydrogen pressure was accomplished in 80% yield to give the corresponding saturated hydroxy ester. Removal of *t*-Boc group of the piperidine ring and cyclization of the resulting aminoester to **10** proceeded smoothly in 87% yield in a single step using Dowex 50-W acidic resin in *n*-BuOH heated at reflux. Finally, LAH reduction of **10** in THF heated at reflux gave (+)-tashiromine (**1**) in 81% yield (mp 40-41 °C) after silica gel chromatography (MeOH : NH_4OH=100 : 1) followed by Kugelrohr distillation. The spectral data (IR, mass, ^1H- and ^{13}C NMR) of **1** are identical with those reported.[2c]

The ^1H- and ^{19}F NMR spectra of the Mosher's esters of **1** and **10** showed only a single diasteroisomer, respectively. Also, the specific rotation of **1** measured in chloroform ($[\alpha]^{20}_D$=+43.4, c 0.53) and ethanol ($[\alpha]^{20}_D$=+42.9, c 2.35) was higher than that of (-)-tashiromine synthesized before.[3]

The same synthetic approach was also applied to *cis*-carbamate **6** for the synthesis of oily (+)-5-epitashiromine **2** without any difficulty (Scheme 2).[2c] Though the ^1H- and ^{19}F NMR spectra displayed that the Mosher's esters of **2** and **14** are diastereomerically pure, the specific rotation of **2** ($[\alpha]^{20}_D$ =+1.6, in H_2O and +1.1 in EtOH) changed slowly from a positive to a negative value by possible contamination with the corresponding amine *N*-oxide. Constant optical rotation ($[\alpha]^{20}_D$=+29.1, c 0.45, EtOH) was obtained by HCl salt formation of **2**.

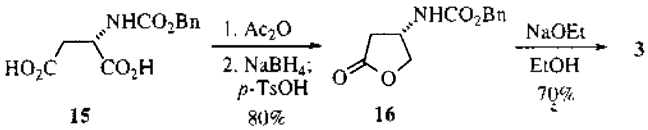
In conclusion, we described the first synthesis of enantiomerically pure (+)-tashiromine from chiral 2-oxazolidinone **3** using an eleven-step reaction sequence in 18% overall yield. Also, (+)-5-epitashiromine was synthesized using the same strategy in 15% overall yield. This synthetic strategy using the 2-oxazolidinone intermediates derived from aspartic acid can provide straightforward approaches to diverse nitrogen-containing mono- and bicyclic alkaloids.

Acknowledgment. This research was financially supported by the Basic Science Research Institute Program (BSRI-97-3406) and the Organic Chemistry Research Center-KOSEF.

References

1. Ohmiya, S.; Kubo, H.; Otomasu, H.; Saito, K.; Murakoshi, I. *Heterocycles* **1990**, *30*, 537.
2. (a) Beckwith, A. L. J.; Westwood, S. W. *Tetrahedron* **1989**, 706. (b) Haddad, M.; Celerier, J. P.; Haviari, G.;

Lhommet, G. *Heterocycles* **1990**, *31*, 1251. (c) Paulvannan, K.; Stille, J. R. *J. Org. Chem.* **1994**, *59*, 1613.
3. (a) Nagao, Y.; Dai, W.-M.; Ochiai, M.; Tsukagoshi, S.; Fujita, E. *J. Am. Chem. Soc.* **1989**, *110*, 289. (b) Nagao, Y.; Dai, W.-M.; Ochiai, M.; Tsukagoshi, S.; Fujita, E. *J. Org. Chem.* **1990**, *55*, 1148. (c) Gage, J. L.; Branchaud, B. P. *Tetrahedron Lett.* **1997**, *38*, 7007.
4. Ha, D.-C.; Kil, K.-E.; Choi, K.-S.; Park, H.-S. *Tetrahedron Lett.* **1996**, *37*, 5723.
5. (a) McGarvey, G. J.; Williams, J. M.; Hiner, R. N.; Matsubara, Y.; Oh, T. *Tetrahedron Lett.* **1983**, *24*, 2733. (b) McGarvey, G. J.; Williams, J. M.; Hiner, R. N.; Matsubara, Y.; Oh. T. *J. Am. Chem. Soc.* **1986**, *108*, 4943.
6. In our previous communication, we reported the specific rotation of **4** to be +8.5 (c 2.4, $CHCl_3$).[4] But, we found partial racemization observed during the removal of acetic acid under elevated temperatureafter the anhydride formation from **15**. Evaporation with dioxane below 40 °C under reduced pressure to remove acetic anhydride and acetic acid provided optically pure anhydride which was reduced to **16**.[5b] Lactone **16** was converted to oxazolidinone **3**, and the specific rotation of **4** from **3** was +11.7 (c 2.4, $CHCl_3$).



7. Spectroscopic data for **5**: colorless oil; R_f=0.60 (EtOAc); $[\alpha]^{20}_D$=+100.9 (c 0.54, $CHCl_3$); IR (CH_2Cl_2, cm^{-1}) 1748, 1437, 1231; ^1H NMR (300 MHz, $CDCl_3$) δ 4.54 (dd, *J*= 9.2, 8.2 Hz, 1H), 4.16 (q, *J*=7.1 Hz, 2H), 4.06 (dd, *J*= 9.2, 6.4 Hz, 1H), 3.89 (m, 1H), 3.78 (m, 1H), 2.80 (m, 1H), 2.31 (m, 2H), 1.78 (m,1H), 1.52 (m, 2H), 1.26 (t, *J* =7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 23.6, 26.4, 40.8, 46.4,55.3, 61.2, 67.7, 156.7, 171.8; HRMS *m/z* calcd. for $C_{10}H_{15}NO_4$ 213.1001, found 213.1002. **6**: colorless oil; R_f=0.36 (EtOAc); $[\alpha]^{20}_D$=+10.5 (c 0.44, $CHCl_3$); IR (CH_2Cl_2, cm^{-1}) 1744, 1439, 1244; ^1H NMR (300 MHz, $CDCl_3$) δ 4.36 (t, *J*=9.1 Hz, 1H), 4.14 (m, 3H), 3.95-3.82 (m, 2H), 2.85 (dt, *J*=12.4, 4.0 Hz, 1H), 2.66 (m, 1H), 2.16 (m, 1H), 1.82-1.63 (m, 2H), 1.49 (m, 1H), 1.23 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.4, 19.1, 25.2, 39.9, 40.1, 53.6, 59.9, 64.5, 156.2, 171.0; HRMS *m/z* calcd. for $C_{10}H_{15}NO_4$ 213.1001, found 213.1001.

Conversion of Carboxylic Acids into Aldehydes by Oxidation of Alkoxyaluminum Intermediate with Pyridinum Chlorochromate or Pyridinium Dichromate

Jin Soon Cha*, Jong Mi Kim, Joong Hyun Chun, Oh Oun Kwon, and Jae Cheol Lee†

Department of Chemistry, Yeungnam University, Kyongsan 712-749, Korea
†Department of General Education, Samchok National University, Samchok 245-080, Korea
Received April 8, 1998

Very recently, we reported that primary and secondary alcohols are readily converted into the corresponding aldehydes and ketones in essentially quantitative yields by oxidation of trialkoxyaluminum with pyridinium chlorochromate (PCC) at room temperature.[1] The reaction proceeds in a similar fashion where alcohols are converted into carbonyl compounds by oxidation of trialkyl borates with PCC,[2] however the reaction conditions appear to be much milder presumably due to the bigger atomic size of aluminum than that of boron. From this point of view, we decided to extend this procedure to the transformation of carboxylic acids into the corresponding aldehydes, similar to the case in which carboxylic acids are converted into aldehydes by oxidation of trialkoxyboroxine with PCC.[3]

Carboxylic acids are readily reduced to the corresponding alcohols with immediate evolution of 1 equiv hydrogen by aluminum hydride at 0 °C[4] (Eq. 1). The initial reaction product in such reduction has not been identified, but we believe that it could be a kind of alkoxyaluminum (**1**). As the facile conversion of primary alcohols to aldehydes by oxidation of trialkoxyaluminum by PCC as already reported,[1] we undertook to explore the practicality of a simple one-pot conversion of carboxylic acids into aldehydes. Herein, we describe such transformation by oxidation of the alkoxyaluminum intermediate (**1**) with PCC or pyridinium dichromate (PDC).

$$\mathrm{RCOOH} \xrightarrow[0^\circ]{\mathrm{AlH_3}} \mathrm{RCOOAlH_2} + 1/2\ \mathrm{H_2}\uparrow$$
$$\mathrm{RCOOAlH_2} \xrightarrow[0^\circ]{} \underset{\mathbf{1}}{[\mathrm{RCH_2O\text{-}Al<}]} \xrightarrow{\mathrm{H_3O^+}} \mathrm{RCH_2OH} \quad (1)$$

The method involves the rapid reduction of carboxylic acid with aluminum hydride, followed by oxidation of the resultant alkoxyaluminum intermediate (**1**) (without isolation) with PCC or PDC at room temperature (Eq. 2).

$$\mathbf{1} \xrightarrow[\text{RT, 3~12 h}]{\text{PCC or PDC}} \underset{\sim 100\%}{\mathrm{RCHO}} \quad (2)$$