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A new combination reagent system (AlCl₃-NaI-CH₃CN) was devised for selective demethylation of aliphatic methyl ether in the presence of aromatic methyl ether under mild conditions. This reagent system cleaved the methyl ether of primary alcohol faster than that of secondary alcohol. The order of reactivity of ethers is aliphatic benzyl ether > aromatic benzyl ether, aliphatic methyl ether (primary > secondary) > aromatic methyl ether. Benzyl ester and ethylene acetal were deprotected but methyl ester, acetate, lactone, and α,β-unsaturated ketone remained intact.

**KEY WORDS:** Aluminum chloride / Sodium iodide / Acetonitrile / Selective dealkylation / Methyl ether / Benzyl ether / Ethylene acetal / Benzyl ester / Hard acid / Soft nucleophile

The concept of "Hard" and "Soft" was introduced in chemistry in 1963 by Pearson and used to classify the various acids and bases. The HSAB principle is an expression on reactivity that a hard acid combines with a hard base and a soft acid does with a soft base preferentially. Although the use of this principle had been limited only in inorganic chemistry in the early stage, this was also well recognized in the organic chemistry after the expansion into organic chemistry in 1967. A chemical bond has the hard-soft dissymmetry as well as the charge dissymmetry. Thus, a combination system of a hard acid and a soft nucleophile may cleave the bond which consists of a hard base and a soft acid. Previously we have developed various combination systems of a hard Lewis acid and a thiol or a sulfide as a soft nucleophile for C-O bond cleavage reactions of methyl ethers, benzyl ethers, esters, and lactones, according to the general concept as shown in Fig. 1.

To avoid foul smell of a thiol or a sulfide, we have devised a new combination system (AlCl₃-NaI-acetonitrile), where a thiol or a sulfide is replaced by iodide ion...
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Fig. 1 Carbon-Oxygen Bond Cleavage Reaction

as a soft nucleophile. Here we will discuss the selectivities on dealkylation of methyl and benzyl ethers, and benzyl ester with AlCl₃-NaI-acetonitrile system.

Results and Discussion

Acetonitrile is a solvent of choice because it donates the electrons of the nitrogen to aluminum chloride to make a weak Lewis acid so that it dissolves aluminum chloride and also sodium iodide very well. Results of the demethylation of methyl ethers with this new combination system are listed in Table 1. Aliphatic primary and secondary methyl ethers 1a - 6a were easily cleaved by the present system at ambient temperature. The starting material 7a was recovered in 98% yield at room temperature for 24 h. Refluxing temperature was required for demethylation of aromatic methyl ethers 7a and 8a. The observed difference in reactivity between aliphatic methyl ethers and aromatic methyl ethers indicates that the selective

<table>
<thead>
<tr>
<th>Compound (mmol)</th>
<th>AlCl₃ (mmol)</th>
<th>NaI (mmol)</th>
<th>Cosolvent</th>
<th>Temp.</th>
<th>Time, h</th>
<th>Product (Yield, %) a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a (0.2)</td>
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<td>none</td>
<td>r. t.</td>
<td>8</td>
<td>1b (89)</td>
</tr>
<tr>
<td>2a (0.1)</td>
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<td>1.1</td>
<td>CH₂Cl₂</td>
<td>r. t.</td>
<td>9</td>
<td>2b (90)</td>
</tr>
<tr>
<td>3a (0.026)</td>
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<td>0.36</td>
<td>CH₂Cl₂</td>
<td>r. t.</td>
<td>20</td>
<td>3b (93)</td>
</tr>
<tr>
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<td>2.0</td>
<td>CH₂Cl₂</td>
<td>r. t.</td>
<td>6</td>
<td>4b (91)</td>
</tr>
<tr>
<td>5a (0.2)</td>
<td>0.7</td>
<td>1.2</td>
<td>none</td>
<td>r. t.</td>
<td>5</td>
<td>5b (95)</td>
</tr>
<tr>
<td>6a (0.1)</td>
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<td>1.0</td>
<td>none</td>
<td>r. t.</td>
<td>8</td>
<td>6b (95)</td>
</tr>
<tr>
<td>7a (0.2)</td>
<td>2.0</td>
<td>2.2</td>
<td>CH₂Cl₂</td>
<td>reflux</td>
<td>7</td>
<td>7b (92)</td>
</tr>
<tr>
<td>8a (0.2)</td>
<td>2.0</td>
<td>2.1</td>
<td>CH₂Cl₂</td>
<td>reflux</td>
<td>5</td>
<td>8b (86)</td>
</tr>
<tr>
<td>9a (0.1)</td>
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<td>1.0</td>
<td>CH₂Cl₂</td>
<td>r. t.</td>
<td>5.5</td>
<td>9b (87)</td>
</tr>
<tr>
<td>10a (0.25)</td>
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<td>1.6</td>
<td>none</td>
<td>r. t.</td>
<td>5</td>
<td>10b (83)</td>
</tr>
<tr>
<td>11a (0.6)</td>
<td>3.1</td>
<td>3.4</td>
<td>none</td>
<td>r. t.</td>
<td>5</td>
<td>11b (69) 11c (27)</td>
</tr>
</tbody>
</table>

a) Isolated yield. b) An 8% yield of starting material was recovered. c) A 15% yield of diol was obtained.
demethylation of aliphatic methyl ether in the presence of aromatic methyl ether can be performed simply by controlling the reaction temperature. This idea was realized in selective demethylation of dimethyl ethers 9a and 10a. No report has been published on the selective demethylation of aliphatic methyl ether in the presence of the aromatic methyl ether in the same molecule, except for an example of estradiol dimethyl ether (9a) with a thiol–boron trifluoride etherate system. Chemoselectivities observed with this reagent system were as follows. The acetate group in 3a was not affected as the same with the aluminum chloride–thiol system. Although the acetal group was deblocked to the corresponding carbonyl group, methyl ester and lactone remained intact under the reaction conditions, as shown in the case of 6a. The α, β-unsaturated ketone in 5a survived under the reaction conditions, which were not tolerated on the aluminum chloride–thiol system. It is worthy to point out the selective demethylation of the methyl ether of primary alcohol in the presence of that of the secondary alcohol in the case of 11a. This differentiable ability of the new reagent system is very unique. There has been only one example of selective demethylation at a primary position in a permethylated thiglycoside reported by Hanessian.

The benzyl ethers and esters are commonly used as the protective group of alcohols and carboxylic acids. These were also cleaved smoothly to give the parent alcohols, phenols or carboxylic acids in high yields as listed in Table 2. Generally, the debenzylation was proceeded more quickly than the demethylation. This is presumably due to the overlap of the p-orbital of benzene ring into the antibonding of AlCl₃-activated carbon–oxygen bond to facilitate the cleavage of C-O bond. This reagent system is especially useful for debenzylation of 5c, for which the usual hydrogenolysis can not be used. The selective aliphatic benzyl ether cleavage was observed in the presence of the aromatic benzyl ether 9c. The preferential debenzylation of benzyl ether of primary alcohol was performed cleanly in the presence of aromatic methyl ether in the case of 10c. The selective benzyl ether deprotection of 12a was proceeded to give 12b. The same selective debenzylation on the ester 14a was disclosed.

<table>
<thead>
<tr>
<th>Compound (mmol)</th>
<th>AlCl₃ (mmol)</th>
<th>Nal (mmol)</th>
<th>Temp.</th>
<th>Time, h</th>
<th>Product (yield, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1c (0.2)</td>
<td>2.0</td>
<td>2.2</td>
<td>r. t.</td>
<td>1.5</td>
<td>1b (92)</td>
</tr>
<tr>
<td>4c (0.1)</td>
<td>1.0</td>
<td>1.1</td>
<td>r. t.</td>
<td>1.5</td>
<td>4c (86)</td>
</tr>
<tr>
<td>5c (0.1)</td>
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<td>1.3</td>
<td>r. t.</td>
<td>1.0</td>
<td>5c (76)</td>
</tr>
<tr>
<td>9c (0.1)</td>
<td>1.0</td>
<td>1.0</td>
<td>0 °C</td>
<td>2.0</td>
<td>9d (71)</td>
</tr>
<tr>
<td>10c (0.13)</td>
<td>1.5</td>
<td>1.4</td>
<td>r. t.</td>
<td>1.3</td>
<td>10b (87)</td>
</tr>
<tr>
<td>12a (0.04)</td>
<td>0.44</td>
<td>0.44</td>
<td>0 °C</td>
<td>3.5</td>
<td>12b (71)</td>
</tr>
<tr>
<td>13a (0.33)</td>
<td>3.2</td>
<td>3.2</td>
<td>r. t.</td>
<td>3.0</td>
<td>13b (98)</td>
</tr>
<tr>
<td>14a (1.0)</td>
<td>10.4</td>
<td>10.8</td>
<td>r. t.</td>
<td>0.7</td>
<td>14b (86)</td>
</tr>
<tr>
<td>15a (0.43)</td>
<td>4.3</td>
<td>4.4</td>
<td>r. t.</td>
<td>4.0</td>
<td>15b (94)</td>
</tr>
</tbody>
</table>

a) Isolated yield. b) Estradiol (7%) and the starting material (21%) were obtained. c) Androsterone-3,17-diol (13%) and the starting material (16%) were obtained.
Ethylene acetal was deprotected as shown in 6a, another ethylene acetal 16a\(^{11}\) also gave the parent carbonyl compound 16b in 90\% yield, in which naphthyl ester and naphthol remained intact.

The possible mechanism for this dealkylation is shown on demethylation in Chart 1. Lewis acidity of aluminum chloride is decreased to some extent by the coordination with acetonitrile to form a complex A (eq. 1). Addition of a methyl ether into the mixture attains the equilibrium (eq. 2), in which the bias depends upon the basicity of the oxygen atom. Because of the inductive effect of the phenyl ring and delocalization of the lone pair electrons on the oxygen over the aromatic ring, the basicity of the oxygen on the aromatic ring is somewhat decreased as compared to that of aliphatic ethers. As a result, the equilibrium shown in eq. 2 is

\[
\text{CH}_3\text{CN} + \text{AlCl}_3 \rightarrow \text{CH}_3\text{C}=\text{N}^-\text{AlCl}_3 (A) \quad (1)
\]

\[
\text{R}-\text{O}-\text{Me} + \text{CH}_3\text{C}=\text{N}^-\text{AlCl}_3 \rightleftharpoons \text{CH}_3\text{CN} + \text{R}^-\text{O}^-\text{AlCl}_3 (B) \quad (2)
\]

\[
\text{R}^-\text{O}^-\text{AlCl}_3 + \text{I}^- \rightarrow \text{R}-\text{O}^-\text{AlCl}_3 + \text{MeI} (C) \quad (3)
\]
shifted to the right in aliphatic methyl ethers and to the left in aromatic methyl ethers. The oxonium ion B thus formed is attacked by iodine ion at the less hindered methyl group followed by hydrolysis of the resulting C to complete demethylation (eq. 3).

Conclusion

A key feature of the hard acid and soft nucleophile system involves an easy control of the dealkylating ability by the combination of a hard acid and a soft nucleophile as well as the using of dichloromethane as a co-solvent. Thus a balancing of the pulling factor and the pushing factor described in Fig. 1 makes it possible to dealkylate selectively. The pulling factor of hard acid is decreased in this new reagent system by the coordination with acetonitrile. This reagent system for dealkylation is characterized by followings. (1) The methyl ether of primary alcohol was demethylated preferentially to that of secondary alcohol. (2) Aliphatic methyl ether was exclusively deprotected in the presence of the aromatic methyl ether at room temperature. Refluxing condition was required for the demethylation of aromatic methyl ether. (3) Benzyl protective group of alcohols and carboxylic acids were selectively cleaved in the presence of the corresponding methyl protecting group. The order of reactivity of ethers is aliphatic benzyl ether > aromatic
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benzyl ether, aliphatic methyl ether (primary > secondary) > aromatic methyl ether.

(4) Aliphatic methyl ether, benzyl ether, benzyl ester, and ethylene acetal were
dealkylated, but methyl ester, acetate, lactone and \( \alpha \beta \)-unsaturated ketone remained
intact. (5) Each component of the reagent system is inexpensive and readily
available in laboratory and is easy to handle without any stench.

This new reagent system was already applied to the demethylation of methylated
sugar in which the anchimeric effect was observed\(^{12}\).

Acknowledgment

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Experimental

**General** Melting points were taken with a micro hot-stage apparatus (Yanagimoto)
and were uncorrected. The infrared spectra were recorded with a JASCO A–
202 diffraction grating infrared spectrophotometer and \(^1\)H–NMR spectra were
obtained with a JEOL JNM–FX–100 spectrometer or a Varian XL–300 or a JEOL
JNM–GX–400 spectrometer in CDCl\(_3\) with trimethylsilylane as an internal standard.
Mass spectra were determined on a JEOL JMS–DX 300 or a Hitachi M–80 mass
spectrometer. Kieselgel 60 (70–230 mesh Merck) was used for column chromatography,
and Kieselger 60 F–254 plates (Merck) for thin layer chromatography
(TLC) and preparative TLC (PTLC).

**Materials** Methyl ethers 2a\(^{8}\), 3a\(^{13}\), 4a\(^{8}\), 6a\(^{14}\), 7a\(^{15}\), 9a\(^{8}\), 10a\(^{8}\), 11a\(^{13}\) and benzyl
ethers 4c\(^{16}\), 5c\(^{17}\), 9c\(^{16}\), 14a\(^{19}\) were prepared according to the literatures. Methyl ether
8a and benzyl ether 15a are commercially available.

2-(2-Naphthyl)ethyl Methyl Ether (1a) To a solution of 2-(2-naphthyl)
ethanol (861 mg, 5.0 mmol) in N, N-dimethylformamide (DMF) was added sodium
hydride (60% in mineral oil) (456 mg, 11.4 mmol) at 0 °C. After being stirred for 30
min methyl iodide (1.0 ml, 11.6 mmol) was added and stirred for 30 min at room
temperature. The reaction mixture was poured into ice–water, acidified with dilute
hydrochloric acid, extracted with ether, and followed by usual work–up. Purification
by silica gel column chromatography gave 1a (845 mg, 91%) as colorless oil: \(^1\)H NMR
\( \delta \) 7.84 – 7.60 (m, 4 H, aromatic), 7.50 – 7.26 (m, 3 H, aromatic), 3.67 (t, \( J = 7 \) Hz, 2 H),
3.34 (s, 3 H), 3.03 (t, \( J = 7 \) Hz, 2 H); IR (CDCl\(_3\)) 1605, 1515 cm\(^{-1}\); high–resolution
MS calcld for C\(_{13}\)H\(_{14}\)O (M\(^+\)) 186.108, found 186.106.

2-(2-Naphthyl)ethyl Benzyl Ether (1c) To a solution of 2-(2-naphthyl)
ethanol (344 mg, 2.0 mmol) in DMF was added sodium hydride (60% in mineral oil)
(400 mg, 10 mmol) at 0 °C. After being stirred for 30 min, benzyl chloride (0.3 ml, 2.6
mmol) was added and stirred for 4 h at room temperature. The reaction mixture
was poured into ice–water, acidified with dilute hydrochloric acid, extracted with
ether and followed by usual work–up. Purification by silica gel column chromatography
gave 1c (476 mg, 91%) as colorless powder: mp 41.0 – 41.3 °C (MeOH); \(^1\)H

(313)
NMR δ 7.84 - 7.60 (m, 4 H, aromatic), 7.48 - 7.32 (m, 3 H, aromatic), 7.25 (bs, 5 H), 4.52 (s, 2 H), 3.76 (t, J = 7 Hz, 2 H), 3.08 (t, J = 7 Hz, 2 H); IR (CHCl₃) 1602, 1360, 1095 cm⁻¹; MS 262 (M⁺). Anal. Calcd for C₁₉H₁₈O: C, 86.98; H, 6.91. Found: C, 87.09; H, 6.95.

**Testosterone Methyl Ether** (5a) To a solution of testosterone ethylene acetal (166 mg, 0.5 mmol) in DMF was added sodium hydride (60% in mineral oil) (275 mg, 6.9 mmol) at 0 °C. After being stirred for 10 min methyl iodide (0.5 ml, 8.0 mmol) was added and stirred for 100 min at room temperature. The reaction mixture was poured into ice-water, acidified with dilute hydrochloric acid, extracted with ether and followed by usual work-up. To an acetone (20 ml) solution of this residue 5% hydrochloric acid (10 ml) was added and stirred for 13 h at room temperature. Extraction with dichloromethane and purification by silica gel column chromatography gave 5a (133 mg, 88%) as colourless powder: mp 126.0 - 126.5 °C (MeOH); ¹H NMR δ 5.70 (bs, 1 H), 3.31 (s, 3 H), 3.22 (t, J = 8 Hz, 1 H), 1.18 (s, 3 H), 0.79 (s, 3 H); IR (CHCl₃) 1660, 1095 cm⁻¹; MS 302 (M⁺). Anal. Calcd for C₂₀H₃₀O₂: C, 79.42; H, 10.00. Found: C, 79.22; H, 9.86.

**Preparation of 10c** To a solution of methyl O-methylpodocarpate (302 mg, 1.0 mmol) in ether was added lithium aluminum hydride (190 mg, 5.0 mmol) at 0 °C and stirred for 21 h at room temperature. The reaction mixture was poured into ice-water and acidified with dilute hydrochloric acid and extracted with ether then followed by usual work-up. To a solution of the residue in DMF (10 ml) were added sodium hydride (60% in mineral oil) (470 mg, 11.8 mmol) and benzyl chloride (1.0 ml, 8.7 mmol) at 0 °C. After being stirred for 20 h at room temperature, the reaction mixture was poured into ice-water and acidified with dilute hydrochloric acid and extracted with ether and worked up as usual. Purification by silica gel column chromatography gave 10c (267 mg, 73%) as a colorless oil; ¹H NMR δ 7.36 - 7.12 (bs, 5 H, aromatic), 6.88 (d, J = 8 Hz, 1 H, aromatic), 6.74 (d, J = 3 Hz, 1 H, aromatic), 6.58 (dd, J = 8 and 3 Hz, 1 H, aromatic), 4.45 (s, 2 H), 3.69 (s, 3 H), 2.58 and 2.32 (ABq, J = 9 Hz, each 1 H), 1.12 (s, 3 H), 1.08 (s, 3 H); IR (CHCl₃) 1610, 1555 cm⁻¹; high-resolution MS calcd for C₂₅H₃₂O₂ (Mt) 364.240, found 364.237.

**Preparation of 17-Methoxyandrostanyl Benzyl Ether** (12a) To a solution of androsterone 17 (236 mg, 0.85 mmol) in dichloromethane (12 ml) were added dihydropyran (0.12 ml, 1.3 mmol) and pyridinium p-toluenesulfonate (PPTS) (44 mg, 0.17 mmol) at room temperature and stirred for 6 h. The reaction mixture was poured into ice-water and extracted with dichloromethane and followed by usual work-up. Purification by silica gel column chromatography gave tetrahydropyranyl androsterone 18 (288 mg, 92%). To a solution of crude 19 in DMF (5 ml) were added sodium borohydride (0.12 ml, 1.3 mmol) and pyridinium p-toluenesulfonate (PPTS) (44 mg, 0.17 mmol) at room temperature and stirred for 1.5 h. The reaction mixture was poured into ice-water and extracted with dichloromethane and followed by usual work-up to give crude 19.

To a solution of tetrahydropyranyl androsterone 18 (176 mg, 0.48 mmol) in methanol (5 ml) was added sodium borohydride at room temperature. After being stirred for 1.5 h, the reaction mixture was poured into ice-water and extracted with dichloromethane and followed by usual work-up to give crude 19.

To a solution of crude 19 in DMF (5 ml) were added sodium hydride (60% in mineral oil) (201 mg, 5.0 mmol) and methyl iodide (0.15 ml, 2.4 mmol) at 0 °C. After being stirred for 3 h at room temperature, the reaction mixture was poured into ice-
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water and extracted with ether and followed by the usual work-up to afford crude 20. One drop of 10% hydrochloric acid was added to a solution of the obtained 20 in methanol (6 ml) then stirred for 2.5 h at room temperature. The reaction mixture was poured into ice-water and extracted with dichloromethane and worked up as usual. Purification by silica gel column chromatography gave 12b (121 mg, 83%), which was recrystallized from dichloromethane–methanol to afford analytical sample: colorless powder; mp 169.0–169.5 °C (CH₂Cl₂–MeOH); ¹H NMR δ 4.02 (bs, 1 H), 3.32 (s, 3 H), 3.22 (t, J= 8 Hz, 1 H), 0.74 (s, 3 H), 0.78 (s, 3 H); MS 306 (M⁺). Anal. Calcd for C₂₀H₃₄O₂: C, 78.38; H, 11.18. Found; C, 78.10; H, 10.95.

To a solution of 12b (110 mg, 0.36 mmol) in DMF (5 ml) were added sodium hydride (60 % in mineral oil) (164 mg, 4.1 mmol) and benzyl chloride (0.2 ml, 1.7 mmol) at 0 °C. After being stirred for overnight at room temperature, the reaction mixture was poured into ice-water and acidified with diluted hydrochloric acid, extracted with dichloromethane, worked up as usual. Purification by silica gel column chromatography gave 12a (103 mg, 72%), which was recrystallized from ethyl acetate–methanol to afford colorless powder: mp 80.0–80.2 °C (AcOEt–MeOH); ¹H NMR δ 7.30 (s, 5 H), 4.44 (s, 2 H), 3.62 (bs, 1 H), 3.32 (s, 3 H), 3.20 (t, J= 8 Hz, 1 H), 0.78 (s, 3 H), 0.74 (s, 3 H); MS 396 (M⁺). Anal. Calcd for C₂₇H₄₀O₂: C, 81.76; H, 10.17. Found; C, 82.08; H, 10.01.

Benzyl Naphthoate (13a) To a solution of naphthoic acid (1.72 g, 10.0 mmol) in benzene (30 ml) were added thionyl chloride (6 ml, 82 mmol) and several drops of DMF and stirred for 5 h at room temperature. After concentration of the solvent under the reduced pressure, dichloromethane (30 ml), benzyl alcohol (3 ml, 29 mmol) and triethylamine (3 ml, 22 mmol) were added to the obtained residue and stirred for 3 h. The reaction mixture was poured into ice-water and extracted with dichloromethane and worked up as usual. Purification by silica gel column chromatography gave 13a (2.62 g, 100%) as colorless oil: ¹H NMR δ 8.90 (dd, J= 8 and 2 Hz, 1 H, aromatic), 8.20 – 7.20 (m, 11 H, aromatic), 5.36 (s, 2 H); IR (CHCl₃) 1705, 1515 cm⁻¹; high-resolution MS calcd for C₁₈H₁₄O₂ (M⁺) 262.099, found 262.099.

General Procedure for Carbon–Oxygen Bond Cleavage Reaction with Aluminum Chloride–Sodium Iodide–Acetonitrile System

To a solution of a substrate (0.1 mmol) in acetonitrile (4 ml) and dichloromethane (2 ml) were added aluminum chloride and sodium iodide at 0 °C under nitrogen, the reaction mixture was stirred under the conditions described in Table 1 and 2. The reaction was followed by thin layer chromatography (TLC). The reaction mixture was poured into ice-water and extracted with dichloromethane. The organic layer was washed with aqueous sodium thiosulfate and brine, dried over sodium sulfate or magnesium sulfate, then concentrated in vacuo. Purification by silica gel column chromatography or preparative TLC gave the product which was identified with the authentic sample except for the case of unknown products.

Demethylation of 3a. To a solution of 3a (9.5 mg, 0.026 mmol) in acetonitrile (0.5 ml) and dichloromethane (0.1 ml) were added aluminum chloride (46.2 mg, 0.35 mmol) and sodium iodide (54.6 mg, 0.36 mmol) at 0 °C then stirred for overnight at ambient temperature. According to the general procedure 3b (8.5 mg, 94%) was ob-
M. Node, T. Kajimoto, K. Nishide, E. Fujita and K. Fuji
tained as colorless powder: mp 190.0-190.2 °C (Et₂O); ¹H NMR δ 4.90 (dd, J = 6 and
4 Hz, 1 H), 3.72 (dd, A part of ABX, J = 11 and 5 Hz, 1 H), 3.46 (dd, B part of ABX,
J = 11 and 9 Hz, 1 H), 2.38 (bs, 1 H), 2.07 (s, 3 H), 1.04 (s, 3 H), 0.85 (s, 3 H),
0.80 (s, 3 H); IR (CHCl₃) 3450, 1710, 1260 cm⁻¹; MS 348 (M⁺). Anal. Calcd for
C₂₂H₃₆O₃: C, 75.81; H, 10.41. Found; C, 75.66; H, 10.54.

Data for 6b: colorless powder; mp 229.8-230.3 °C (MeOH); ¹H NMR δ 4.44 and
4.04 (ABq, J = 10 Hz, each 1 H), 4.31 (m, 1 H), 3.65 (s, 3 H), 1.32 (s, 3 H), 1.21 (s,
3 H). IR (CHCl₃) 3620, 1770, 1715, 1240 cm⁻¹; high-resolution MS calcd for C₂₀H₂₈O₆
(M⁺) 364.189, found 364.192.

Demethylation of 11a. To a solution of 11a (197.1 mg, 0.59 mmol) in acetonitrile
(4.0 ml) and dichloromethane (0.5 ml) were added aluminum chloride (410.5 mg, 3.08
mmol) and sodium iodide (513.6 mg, 3.42 mmol) at 0 °C than stirred for 2 h at
ambient temperature. According to the general procedure 11b (131.1 mg, 69%) and
11c (50.8 mg, 27%) were obtained, which were recrystallized from methanol.

11b: colorless powder; mp 114.0-114.5 °C (MeOH); ¹H NMR δ 3.98 (dd, J = 12 and
6 Hz, 1 H), 3.87 (t, A part of ABX, 1 H), 3.59-3.30 (m, B part of ABX, 1 H),
3.34 (s, 3 H), 1.10 (s, 3 H), 0.84 (s, 3 H), 0.79 (s, 3 H); IR (CHCl₃) 3530, 1460,
1100 cm⁻¹; MS 320 (M⁺). Anal. Calcd for C₂₁H₃₆O₂: C, 78.69; H, 11.32. Found; C,
78.65; H, 11.17.

11c: colorless powder; mp 84.5-85.5 °C (MeOH); ¹H-NMR δ 4.42 (dd, J = 10 and
7 Hz, 1 H), 3.70 (dd, A part of ABX, J = 12 and 8 Hz, 1 H), 3.42-3.28 (m, B part of
ABX, 1 H), 3.36 (s, 3 H), 1.02 (s, 3 H), 0.84 (s, 3 H), 0.79 (s, 3 H); IR (CHCl₃)
3550, 1090 cm⁻¹; MS 320 (M⁺). Anal. Calcd for C₂₁H₃₆O₂: C, 78.69; H, 11.32. Found; C,
78.81; H, 11.52.

(S)-2'-Hydroxyl-1,1'-binaphthalen-2-yl 2-cyclohexanonecarboxylate (16b)
A Mixture of (S)-2'-hydroxyl-1,1'-binaphthalen-2-yl 2,2-ethylenedioxy-cyclo-
hexanecarboxylate 16a (263 mg, 0.58 mmol), aluminum chloride (770 mg, 5.8 mmol),
sodium iodide (869 mg, 5.8 mmol) in acetonitrile (6.0 ml) was stirred for 1.5 h. The
reaction mixture was extracted with dichloromethane (50 ml, twice), and followed
by the work-up described in the general procedure. (S)-2'-Hydroxy-1,1'-binaphtha-
len-2-yl 2-cyclohexanecarboxylate (16b) (213 mg, 90%) was obtained as a 1 : 1
mixture with its enol form: ¹H NMR δ 11.56 (s, 0.5 H, OH), 8.10-7.81 (m, 4 H), 7.55-
7.45 (m, 2 H), 7.40-7.20 (m, 5 H), 7.08-7.01 (m, 1 H), 5.25 (brs, 0.5 H, OH),
5.20 (brs, 0.5 H, OH), 3.24-3.19 (m, 0.5 H), 2.26-2.12 (m, 2 H); MS (20 eV) 410
(M⁺, 0.2), 287 (22), 286 (100), 257 (12), 239 (6), 115 (6); high-resolution MS
caled for C₂₇H₂₂O₄ (M⁺) 410.152, found 410.152.

References
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11) Preparation of acetal 16a will be published elsewhere.


