Lewis Acid-Induced Ring-Opening of
2, 4-Dioxaspiro [5.5] undecan-7-one

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In a previous paper\textsuperscript{10}, we reported that the cyclohexanone ring-opening reaction of 2,4-dioxaspiro [5.5] undecan-7-one\textsuperscript{10} with lead tetraacetate carried out to know organoleptic properties of the products having 1,3-dioxane moiety. This paper will report on 1,3-dioxane ring-opening of the above spiro-ketone with Lewis acids (MX\textsubscript{n}, n=2–4) in acetic anhydride (Ac\textsubscript{2}O); the experiments were undertaken in order to clarify the effects of Lewis acid and reaction variables.

Result and Discussion

The 1,3-dioxane ring-opening reactions of 2,4-dioxaspiro [5.5] undecan-7-one (1) with various Lewis acids, such as SnCl\textsubscript{4}, BF\textsubscript{3}(OEt\textsubscript{2}), ZnCl\textsubscript{2}, FeCl\textsubscript{3}, CuCl\textsubscript{2} and AlCl\textsubscript{3}, were performed in Ac\textsubscript{2}O under reflux to give 1-acetoxymethyl-3,5-dioxabicyclo [4.4.0] decan-6-ene (2), 2-acetoxymethyl-2-hydroxymethylcyclohexanone (3), 1-acetoxymethyl-3-oxabicyclo [3.3.1] nonan-9-one (4), 2,2-diacetoxymethylcyclohexanone (5), 2-[(acetoxymethoxy) methyl]-2-acetoxymethyl-cyclohexanone (6) and 1,5-diacetoxymethyl-3-oxabicyclo [3.3.1] nonan-9-one (7). The reactions in acetic acid (AcOH) were also attempted to clear the cleavage mechanism, however, proceeded hardly at all to afford only small amounts of 2, 3 and 5. The results are summarized in the Table.

\begin{center}
\begin{tabular}{ccc}

\includegraphics[width=0.3\textwidth]{image.png}

1 & 2 & 3 & 4 & 5 & 6 & 7
\end{tabular}
\end{center}
Table. Reaction of 2, 4-Dioxaspiro[5.5]undecan-7-one with various Lewis acids in Ac$_2$O or AcOH

Spiro-ketone (1) 11.8 mmol (2.00g); Lewis acid 1.1 mmol; Ac$_2$O or AcOH 9.8 mmol, 19.6 mmol

Reaction conditions: Reflux, 3 h

<table>
<thead>
<tr>
<th>Lewis acid</th>
<th>Yield (g)</th>
<th>Reaction mixture</th>
<th>Component ratio (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1$^*$</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>in Ac$_2$O</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SnCl$_4$</td>
<td>2.51(2.98)</td>
<td>13( 1)</td>
<td>7(—)</td>
</tr>
<tr>
<td>BF$_3$$^b$</td>
<td>2.52(2.89)</td>
<td>25(—)</td>
<td>t(—)</td>
</tr>
<tr>
<td>ZnCl$_2$</td>
<td>2.02(2.31)</td>
<td>80( 2)</td>
<td>—(—)</td>
</tr>
<tr>
<td>FeCl$_3$</td>
<td>2.27(2.61)</td>
<td>72(11)</td>
<td>—( t)</td>
</tr>
<tr>
<td>CuCl$_2$</td>
<td>2.92(2.85)</td>
<td>60(—)</td>
<td>10( 3)</td>
</tr>
<tr>
<td>AlCl$_3$</td>
<td>1.67(1.03)</td>
<td>47(15)</td>
<td>10(15)</td>
</tr>
<tr>
<td>in AcOH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SnCl$_4$</td>
<td>2.14(2.35)</td>
<td>83(64)</td>
<td>6(13)</td>
</tr>
<tr>
<td>BF$_3$$^b$</td>
<td>2.21(1.47)</td>
<td>83(61)</td>
<td>—( t)</td>
</tr>
<tr>
<td>ZnCl$_2$</td>
<td>1.01(0.75)</td>
<td>100(100)</td>
<td>—(—)</td>
</tr>
<tr>
<td>FeCl$_3$</td>
<td>2.16(2.03)</td>
<td>96(88)</td>
<td>—(—)</td>
</tr>
<tr>
<td>CuCl$_2$</td>
<td>1.31(1.09)</td>
<td>90(95)</td>
<td>t( t)</td>
</tr>
<tr>
<td>AlCl$_3$</td>
<td>2.09(2.43)</td>
<td>72(68)</td>
<td>t( t)</td>
</tr>
</tbody>
</table>

a) Determined by GLC. The value in the parentheses show the ratio in the case of using 19.6 mmol Ac$_2$O or AcOH.  
b) Etherate  
* : Unreacted  
 t : Trace

It has generally been called$^b$ that the order of Lewis acids catalyst activities in Friedel-Crafts reactions is AlCl$_3$ > FeCl$_3$ > BF$_3$ > ZnCl$_2$ > SnCl$_4$ > CuCl$_2$. While in the reaction with 1 having both ethereal and carbonyl oxygens, the order of their reactivities in 9.8 mmol Ac$_2$O revealed SnCl$_4$ > BF$_3$ > AlCl$_3$ > CuCl$_2$ > FeCl$_3$ > ZnCl$_2$ on the basis of the unreacted 1. By use of double the molar quantity of Ac$_2$O, each reactivity so remarkably increased that the order cannot be compared.

When the results of the reactions using 19.6 mmol Ac$_2$O were aligned as is shown in Table, we found that the Lewis acids are classified into two groups according to tendency for formation of the products, that is, AlCl$_3$ and CuCl$_2$ belong to the IInd group, and SnCl$_4$, BF$_3$, ZnCl$_2$ and FeCl$_3$ are included in the IInd group. The reactions of both the groups gave 5 as a common product. In addition, the former group afforded the acetoxymethoxymethyl compound (6) as the characteristic product with a small amounts of 2. On the other hand, in the presence of the latter group, the reactions gave the oxabicyclo compound (4) in substantial
quantity together with 7 analogous to 4.

It seems that these reactions are at first induced by either the acylum ion
\[(CH_3\overset{\delta^+}{C}=O \cdot MX_{n+1}; CH_3CO_2MX_{n-1})\] or the oxonium compound \[(CH_3\overset{\delta^-}{C}=O \cdot MX_n)\]
which may be formed by the reaction of Lewis acid with Ac_2O. In the 1,3-dioxane
ring-opening, both the acylum ion and the oxonium compound ought to provide an
intermediate having carbonium ion respectively. On the basis
of such a concept, the reaction mechanism can be explained
as follows.

i) : It is obvious that the common product 5 was formed by the following deforma-
ylation and acetoxylation from the carbonium ion. ii) : In the reaction of the acylum
ion bearing a strong reactivity, the carbonium ion was directly acetoxylated into 6
in preference to the deformatylation. Since 6 gradually changed to 2 on standing at
room temperature, it is assumed that 2 was produced through a kind of intramole-
cular acetalation with the elimination of acetyl group from 6. iii) : In the case of
the oxonium compound less polarized than the acylum ion, the same carbonium
ion mildly cyclized with the activated methylene adjacent to the carbonyl group
to give 4. The similar cyclization was caused in concert to afford 7 with 5 via
bimolecular condensation of the carbonium ion intermediates, followed by cleavage
of ether linkage. iv) : The formation of the hydroxy compound (3) is due to AcOH
produced as by-product in these reactions.

These results suggest that the Lewis acids of Ist and IInd groups, respectively,
participated in the reaction as the acylum ion and the oxonium compound.

Experimental

The melting point is uncorrected. IR spectra were measured with a JASCO
model IRA-1 spectrometer. ^1H-NMR and ^13C-NMR spectra were recorded with
JEOL JNM-MH-60-II and JNM-FX 100 spectrometers using tetramethysilane as an
internal standard, respectively. Mass spectra were determined on a JEOL JMS-D
300 spectrometer. GLC were performed using Yanaco model G-180 gas chromato-
graphs equipped with a 3mm x 75cm Silicone OV-1 (3%) column.

Preparation of 2,4-dioxaspiro [5.5] undecan-7-one (1)

2,4-dioxaspiro [5.5] undecan-7-one was prepared according to the procedure
described in a previous paper\(^3\).
A typical procedure

A mixture of 1 (11.8 mmol, 2.00 g), SnCl₄ (1.1 mmol) and Ac₂O (9.8 mmol) was refluxed with stirring at 110°C for 3 h. The cooled mixture was extracted with chloroform, and the solution was washed with brine, sodium carbonate solution and water, dried over sodium sulfate, and concentrated in vacuo to viscous oil, whose GLC (Silicone OV-1, 150°C, N₂ 0.4 kg/cm² and H₂ 0.6 kg/cm² of carrier gas) shows seven major peaks with Rt 1.3, 2.7, 3.1, 3.8, 5.6, 11.3 and 22.5 min in a relative intensity of 13:7:4:24:18:9:25 for unreacted 1, 1-acetoxyethyl-3,5-dioxabicyclo[4.4.0]decan-6-ene (2), 2-acetoxyethyl-2-hydroxymethylcyclohexanone (3), 1-acetoxyethyl-3-oxabicyclo[3.3.1]nonan-9-one (4), 2, 2-diaceotoxyethylcyclohexanone (5), 2-[(acetoxymethoxy) methyl]-2-acetoxymethylcyclohexanone (6) and 1, 5-diacetoxyethyl-3-oxabicyclo[3.3.1]nonan-9-one (7). The viscous oil was chromatographed on silica gel, using hexane-acetone-ether (40:2:1 in volume), hexane-acetone-ethyl acetate (45:4:3), hexane-acetone-ethyl acetate (30:1:1), hexane-ether-chloroform (10:8:1), hexane-ether (1:1) and hexane-acetone (7:1) as the eluent, to afford 1, 2, 3, 4, 5, 6 and 7, respectively. The structures of the products were confirmed on the basis of the IR, ¹H-NMR, ¹³C-NMR and Mass spectra.

In a similar manner, the reactions of 1 with various Lewis acids were examined. Spectral data of the products are given below.

2: Colorless oil; nD²⁵ : 1.4903; IR (neat): 2920, 2850, 2760, 1755, 1670, 1450, 1365, 1195, 1160, 1130, 1090, 1050, 1030 cm⁻¹; ¹H-NMR(CDCls): δ 1.45–2.19 (m, 6H, CH₂×3), 2.16 (s, 3H, OCOCH₃), 3.75 (s, 4H, CH₂O + CH₂OCO), 4.77 (AB-q, J=6Hz, 2H, OCH₂O), 5.48 (t, J=4Hz, 1H, =CH); ¹³C-NMR(CDCls): δ 169.3 (s, OC=O), 146.6 (s, OC=O), 119.8 (d, =CH), 93.6 (t, OCH₂O), 72.4 (t, CH₂O×2), 38.4 (s, C), 29.8 (t, CH₂), 24.1 (t, CH₂), 20.9 (q, CH₃), 18.1 (t, CH₂); EIMS (70eV): m/e 170 (17%), 152(21), 140(12), 122(25), 110(100), 95(24), 79(25), 67(29), 55(17), 44(76); CIMS (200eV): m/e Isobutane 213 (M+H)⁺, Ammonia 230 [(M+NH₄)⁺, 100%]

3: Colorless oil; nD²⁵ : 1.4842; IR (neat): 3450, 2910, 2840, 1730, 1700, 1440, 1370, 1220, 1030 cm⁻¹; ¹H-NMR(CDCls): δ 1.28–2.08 (m, 7H, CH₂×3+OH), 2.04 (s, 3H, OCOCH₃), 2.24–2.52 (m, 2H, CH₂C=O), 3.54–4.04 (m, 2H, CH₂OH), 4.26 AB-q, J=12Hz, 2H, CH₂OCO); ¹³C-NMR(CDCls): δ 212.4 (s, C=O), 170.7 (s, OC=O), 64.7 (t, CH₂OCO), 63.7 (t, CH₂OH), 53.8 (s, C), 39.6 (t, CH₃), 31.5 (t, CH₂), 27.0 (t, CH₂), 20.8 (t, CH₂), 20.7 (q, COCH₃); EIMS (22eV): m/e 200 (M⁺, 3%), 158(34), 140(59), 123(51), 95(100), 94(34), 43(86); CIMS (200eV): m/e Isobutane 201 [(M+H)⁺, 100%]
4: Colorless oil; n_25^\circ: 1.4371; IR (neat): 2910, 2835, 1735, 1720, 1450, 1360, 1225, 1130, 1035 cm^{-1}; ^1\text{H}-\text{NMR (CDCl}_3): \delta 0.97-2.04 (m, 6H, CH_2\times3), 2.05 (s, 3H, OCOCH_3), 2.32-2.51 (m, 1H, CHC=O), 3.95 (AB-q, J=12Hz, 2H, CH_2O), 4.06 (s, 2H, CH_2OCO), 4.07 (AB-q, J=11Hz, 2H, CH_2O); ^13\text{C}-\text{NMR (CDCl}_3): \delta 212.7 (s, C=O), 170.1 (s, OC=O), 76.4 (t, CH_2O), 74.8 (t, CH_2O), 64.9 (t, CH_2OCO), 51.4 (s, C), 49.2 (d, CH), 37.0 (t, CH_2), 34.1 (t, CH_2), 20.6 (t, CH_2), 20.6 (q, CH_3); EIMS (22eV): m/e 212 (M^+, 6%), 170(7), 152(100), 140(11), 122(59), 111(20), 95(17), 79(9)

5: Colorless oil; n_25^\circ: 1.4650; IR (neat): 2925, 2850, 1730, 1700, 1365, 1220 cm^{-1}; ^1\text{H}-\text{NMR (CDCl}_3): \delta 1.57-1.94 (m, 6H, CH_2\times3), 1.98 (s, 6H, OCOCH_3\times2), 2.19-2.60 (m, 2H, CH_2C=O), 4.13 (AB-q, J=12Hz, 4H, CH_2OCO\times2); ^13\text{C}-\text{NMR (CDCl}_3): \delta 209.4 (s, C=O), 170.3 (s, OC=O\times2), 64.4 (t, CH_2O\times2), 51.7 (s, C), 39.1 (t, CH_2), 32.2 (t, CH_2), 26.8 (t, CH_2), 20.8 (t, CH_2), 20.8 (q, COCH_3\times2); EIMS (22eV): m/e 242(M^+, 2%), 182(7), 140 (100), 122(59), 111(20), 95(17), 79(9)

6: Colorless oil; n_25^\circ: 1.4659; IR (neat): 2920, 1740, 1725, 1700, 1440, 1358, 1225, 1150 cm^{-1}; ^1\text{H}-\text{NMR (CDCl}_3): \delta 1.19-1.93 (m, 6H, CH_2\times3), 2.02 (s, 3H, OCOCH_3), 2.08 (s, 3H, OCOCH_3), 1.68-2.67 (m, 2H, CH_2C=O), 3.83 (AB-q, J=10Hz, 2H, CH_2OCO), 4.30 (AB-q, J=12Hz, 2H, CH_2OCOCH_2), 5.22 (s, 2H, OCH_2); ^13\text{C}-\text{NMR (CDCl}_3): \delta 210.4 (s, C=O), 170.4 (s, OC=O), 170.1 (s, OC=O), 89.1 (t, OCH_2), 70.9 (t, CH_2O), 64.6 (t, CH_2O), 52.6 (s, C), 39.3 (t, CH_2), 32.3 (t, CH_2), 27.0 (t, CH_2), 20.9 (q,COCH_3), 20.7 (t, CH_2), 20.7 (q, COCH_3); EIMS (22eV): m/e 182(15%), 170 (10), 152(68), 140(61), 122(100), 110(61), 94 (36); CIMS (200eV): m/e Ammonia 290 [(M+NH_4)^+, 100%], 213 [(M+H–AcOH)^+, 75%]

7: White crystals; mp: 93.5-95.0°C (from ether); IR (KBr): 2900, 2815, 1720, 1715, 1685, 1425, 1350, 1225, 1155, 1025 cm^{-1}; ^1\text{H}-\text{NMR (CDCl}_3): \delta 1.41-2.46 (m, 6H, CH_2\times3), 2.04 (s, 6H, OCOCH_3\times2), 3.96 (AB-q, J=12Hz, 4H, CH_2O\times2), 4.09 (s, 4H, CH_2OCO\times2); ^13\text{C}-\text{NMR (CDCl}_3): \delta 211.2 (s, C=O), 170.3 (s, OC=O), 76.6 (t, CH_2O\times2), 64.7 (t, CH_2OCO\times2), 51.0 (s, C\times2), 37.1 (t, CH_2\times2), 20.8 (q, CH_2\times2), 20.0 (t, CH_2); EIMS (22eV): m/e 294 (M^+, 2%), 224(49), 195(23), 182(26), 164(86), 151(40), 136(100), 134(91), 122(26), 108(27)

References