Study on FeCl₃ Induced Rearrangement Reaction of Bicyclic Acetal Compound

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Lewis acid induced C-O bond cleavage has been well documented because it is not only important but also variable depending on the structure of starting materials. In our laboratory, we explored Lewis acid systems for the specific transformation of bicyclic acetal 1 to other important structures in unique one-flask reactions. Recently, we reported an interesting transformation reaction of acetal 1 to monoacetate 2, diacetate 3 and enone 4 as 37%, 16% and 16% yield, respectively by using AcCl-NaI (Scheme 1). We proposed the transformation mechanism (Scheme 2) and selectively obtained the monoacetate 2 in 85% yield as a single product by using MgBr₂·Ac₂O-NaOAc system. We now wish to report the production of the diacetate 3 selectively.

Ether cleavage and acylation with ferric chloride/acetic anhydride have been reported. On the other hand, ferric chloride on silica gel has been used in dehydration of alcohols, cleavage of acetals and in coupling of phenol ethers. Also, ferric chloride in acetic acid has been used in acetylation of alcohols, ethers and acetals.

We have extended the use of FeCl₃ as a Lewis acid to the one pot conversion of bicyclic acetal to the corresponding diketone by rearrangement reactions. Sharma used FeCl₃ in AcOH for the acetylation of acetal and we adopted this method for the acetylation of bicyclic acetal. The acetal 1 was refluxed overnight with FeCl₃ (0.3 equiv)-AcOH (3 equiv) in CH₂Cl₂ to produce the mixture of 1,5-diketone 5 (54%) and cyclohexenone 6 (7%) as shown in Scheme 3. The mechanism for the 1,5-diketone 5 should be similar to AlCl₃ case. The C (5)-O (6) bond cleavage followed by 1,2-hydride shift via an epoxide intermediate produced the diketone 5, and further reaction proceeded to afford the cyclohexenone 6 as aldol product (Scheme 4). The addition of NaI (1 equiv) in the reaction produced only the diketone in 68% yield. The reaction mechanism of NaI in the reaction was not exactly known, but it prohibited the aldol condensation as shown in TMSCl-NaI system.

The substitution of AcOH to acetic anhydride in the reaction produced the expected diacetate 3 (Scheme 5). Thus, the acetal 1 was refluxed overnight with FeCl₃ (0.3 equiv)-Ac₂O (3 equiv) in CH₂Cl₂ and yielded the diacetate 3 in 84% yield.
as a single product. Addition of NaI (1 equiv) in the reaction produced only the monoacetate 2 in 60% yield. From the results, we can propose the role of NaI in the reaction as a diminishing the nucleophilicity of acetate anion, but increasing the basicity.

In conclusion, the diacetate 3 was selectively obtained from the acetal 1 by using FeCl3 with Ac2O in CH2Cl2, while the monoacetate 2 was also obtained selectively by the addition of NaI in the reaction. But, the best way to make the monoacetate will be the use of MgBr2-2Ac2O-NaOAc system.

**Experimental Section**

All chemicals were used purchased from commercial sources and used as received unless otherwise stated. NMR spectra were recorded on Varian Gemini-400 MHz FT-NMR for 1H and 100 MHz for 13C, with the chemical shifts (δ) reported in parts per million (ppm) relative to TMS and the coupling constants (J) quoted in Hz. CDCl3 was used as a solvent and an internal standard. Infrared spectra were recorded on a Shimadzu IR-435 spectrometer. GC-MS analyses were performed using a HP-5890/JMS-AM 150, JEOL. Flash chromatography was carried out using silica gel Merck 60 (230-400 mesh). Thin-layer chromatography (TLC) was performed on DC-Plastikfolien 60, F254 (Merck, layer thickness 0.2 mm) plastic-backed silica gel plates with visualization by UV light (254 nm) or by treatment with p-anisaldehyde.

**Procedure by using FeCl3-AcOH.** To a solution of FeCl3 (50 mg, 0.19 mmol) and AcOH (0.11 mL, 1.92 mmol) in methylene chloride (10 mL) under nitrogen atmosphere was added bicyclic acetal 1 (0.10 g, 0.64 mmol) and refluxed for 15 hr. The reaction was quenched by the addition of 10% aqueous sodium hydroxide solution (10 mL). The organic product was extracted with diethyl ether, washed with brine, dried and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc, 2:1) to give the 1,5-diketone 5 (54 mg, 54%, Rf 0.38) and the cyclohexene-one 6 (7 mg, 7%, Rf 0.69).

**Procedure by using FeCl3-AcOH-NaI.** To a solution of FeCl3 (50 mg, 0.19 mmol), NaI (100 mg, 0.64 mmol) and AcOH (0.11 mL, 1.92 mmol) under nitrogen atmosphere was added bicyclic acetal 1 (0.10 g, 0.64 mmol) and refluxed for 15 hr. The reaction was quenched by the addition of 10% aqueous sodium hydroxide solution (10 mL). The organic product was extracted with diethyl ether, washed with brine, dried and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc, 2:1) to give 7-methyloctane-2,6-dione (5) (68 mg, 68%, Rf 0.38); 1H NMR (CDCl3): δ 2.58 (1H, m, H-7), 2.49 (2H, t, J = 7 Hz, COCH3), 2.46 (2H, t, J = 7 Hz, COCH3), 2.13 (3H, s, CH3CO), 1.83 (2H, quintet, J = 7 Hz, CH2) 1.09 (6H, d, J = 7 Hz, 2 x CH3); 13C NMR (CDCl3): δ 214.2 (s), 208.4 (s), 42.6 (t), 40.8 (d), 39.0 (t), 29.8 (q), 18.2 (q, 2 x Me), 17.8 (t); IR (neat): 2963, 1709 (br), C=O; HRMS calcd for C9H16O2 (M+) 156.1150, found 156.1148.

**Procedure by using FeCl3-Ac2O.** To a solution of FeCl3 (30 mg, 0.01 mmol) and Ac2O (0.10 mL, 0.96 mmol) in methylene chloride (10 mL) under nitrogen atmosphere was added bicyclic acetal 1 (0.05 g, 0.32 mmol) and refluxed for 15 hr. The reaction was quenched by the addition of 10% aqueous sodium hydroxide solution (10 mL). The organic product was extracted with diethyl ether, washed with brine, dried and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc, 2:1) to give 6,7-diacetoxy-7-methyl-2-octanone (3) (42 mg, 84%, Rf 0.32); 1H NMR (CDCl3): δ 5.15 (1H, m, H-6), 2.43 (2H, m, COCH3), 2.12 (3H, s, CH3CO), 2.08 (3H, s, OCOCH3), 1.94 (3H, s, OCOCH3), 1.7-1.5 (4H, m, CH2CH2), 1.43 (3H, s, CH3), 1.40 (3H, s, CH3), 134.1 (s), 122.5 (s), 101.2 (s), 82.4 (s), 76.2 (d), 42.7 (t), 29.8 (q), 28.1 (t), 22.1 (t), 22.0 (t), 20.8 (q), 19.7 (q); IR (neat): 1690 (br, C=O), 1351, 1220, 1130, 1010 cm⁻¹; Ms m/z 157 (M'⁻CH2CO-OOH), 141, 115, 97, 51, 43 (base); HRMS calcd for C9H17O2 (M'⁻CH2CO-OOH) 157.1229, found 157.1201.

**Procedure by using FeCl3-Ac2O-NaI.** To a solution of FeCl3 (30 mg, 0.01 mmol), NaI (50 mg, 0.32 mmol) and Ac2O (0.10 mL, 0.96 mmol) in methylene chloride (10 mL) under nitrogen atmosphere was added bicyclic acetal 1 (0.05 g, 0.32 mmol) and refluxed for 15 hr. The reaction was quenched by the addition of 10% aqueous sodium hydroxide solution (10 mL). The organic product was extracted with diethyl ether, washed with brine, dried and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc, 2:1) to give 6-acetoxy-7-methyl-7-octen-2-one (2) (30 mg, 60%, Rf 0.32); 1H NMR (CDCl3): δ 5.14 (1H, t, J = 5.5 Hz, H-6), 4.93 (1H, br s, C=CH), 4.87 (1H, br s, C=CH), 2.43 (2H, t, J = 7 Hz, COCH3), 2.12 (3H, s, CH3CO), 2.04 (3H, s, OCOCH3), 1.70 (3H, br s, CH3C=CH), 1.7-1.5 (4H, m, CH2CH2); 13C NMR (CDCl3): δ 208.3 (s, C=O), 170.2 (s, ester C=O), 142.8 (s, C=CH), 112.8 (t, CH3C=CH), 76.8 (d, OCOCH3), 43.0 (t, COCH3), 31.9 (t, CH3C=OAc), 29.8 (q, CH3CO), 21.1 (q, CH3COO), 19.4 (t, CH2CH2CH3), 18.0 (q, CH3C=CH); IR (neat): 1695 (br, C=O), 1351, 1225, 1012 cm⁻¹; Ms m/z 156 (M'⁻CH2CO), 138, 95, 81, 71, 58, 43 (base); HRMS calcd for C9H19O2 (M'⁻CH2CO) 156.1150, found 156.1151.

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**References**


