Ring Opening of Cyclic Ethers by Sulfuric Acid - Acetic Anhydride

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Cyclic ethers such as tetrahydrofuran or tetrahydropyran were easily cleaved at room temperature by sulfuric acid - acetic anhydride providing the corresponding diacetoxyalkanes in good yield. The ring opening was applicable to saturated cyclic ethers, regardless of the presence of substituent groups.

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Introduction.

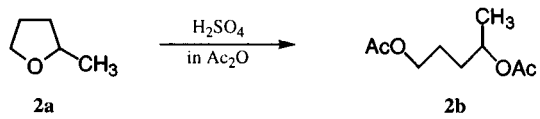
The cleavage of ethers is an important and versatile reaction in organic synthesis. The ring opening of cyclic ethers has been accomplished using a variety of agents [1]. For example, tetrahydrofuran and 2-methyltetrahydrofuran have been opened with zinc chloride/acetic anhydride ($ZnCl_2/Ac_2O$) [2], tosylacetate (AcOTs) [3], bromotrimethylsilane (Me_3SiBr) [4], iodotrimethylsilane (Me_3SiI) [5,6], alkanoyl chloride/palladium(II)/trialkyltin halide ($RCOCl/Pd(II)/R_3SnX$) [7], tribromoborane (BBr_3) [8], alkanoyl chloride/platinum(II) (RCOCl/Pt(II)) [9], tetrabutylammonium iodide/trifluoroborane in diethylether (n-$Bu_4NI/BF_3{\bullet}Et_2O$) [10], bromodimethylborane (Me_2BrB) [11], lithium tri-*tert*-butoxyaluminum hydride/triethylborane ($Li(t\text{-}BuO)_3AlH/Et_3B$) [12], tetrabutylammonium bromide/trifluoroborane in diethylether (n-$Bu_4NBr/BF_3{\bullet}Et_2O$) [13], aluminum trichloride/sodium iodide ($AlCl_3$/NaI) [14]. However, most of these reagents except for zinc chloride/acetic anhydride ($ZnCl_2/Ac_2O$) and tosyl acetate (AcOTs) gave halogen alcohols, halogen esters, or halogen ethers.

In the course of our study on ring opening of a compound having a tetrahydrofuran ring, we have found that a sulfuric acid - acetic anhydride combination system opened the ring to give a corresponding diacetoxyalkane. We now report a convenient ring opening of cyclic ethers by this system.

Results and Discussion.

Treatment of 2-methyltetrahydrofuran (**2a**) with sulfuric acid in acetic anhydride at room temperature gave 1,4-diacetoxypentane (**2b**) as shown in Scheme 1. In an attempt to examine the reaction system, the reaction of **2a** with sulfuric acid - acetic anhydride was carried out under several conditions.

Scheme 1



2a **2b**

First, sulfuric acid was changed from 0.01 to 2 molar amounts; the results are listed in Table 1. These results suggest that the reaction system requires 1 molar equivalent of sulfuric acid to the substrate.

Table 1
Amount of Sulfuric Acid for Ring Opening of 2-Methyltetrahydrofuran (**2a**)

Entry	H_2SO_4/Molar Amount	Yield/%
1	0.01	7
2	0.1	22
3	0.2	38
4	0.5	56
5	1.0	70
6	2.0	51

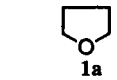
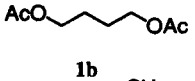
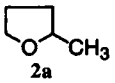
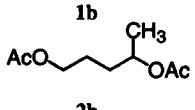
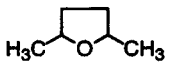
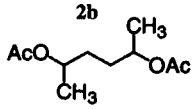
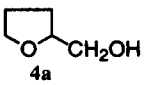
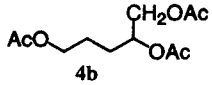
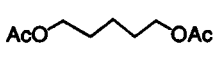
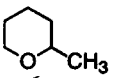
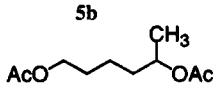
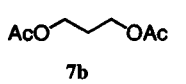
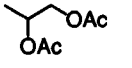
We next examined the reaction time at room temperature for the ring opening. The time was changed from 15 minutes to 68 hours as shown in Table 2. The ring opening requires 20 hours.

Table 2
Time for Ring Opening of 2-Methyltetrahydrofuran (**2a**)

Entry	Time/Hours	Yield/%
1	0.25	38
2	1	45
3	5	55
4	10	63
5	20	70
6	68	70

This ring opening was applied to other cyclic ethers (**1a-8a**) as shown in Table 3. Tetrahydrofuran (**1a**) (entry 1) gave 1,4-diacetoxybutane (**1b**) in 98% yield. Paul [2] has also reported that treatment of **1a** with $ZnCl_2$-Ac_2O at 230 °C for 8 hours gave **1b**, but the yield was 66%. The ring opening of 2-hydroxymethyltetrahydrofuran (**4a**) (entry 4) afforded 1,2,5-triacetoxypentane (**4b**) in 88% yield. Grummitt and coworkers [15] have also described the cleavage of **4a** with $ZnCl_2$-Ac_2O under reflux for 24 hours to give **4b** in yields ranging from 87 to 90%.

Table 3
Ring Opening of Various Cyclic Ethers

Entry	Cyclic Ether	Product	Yield/%
1	 **1a**	 **1b**	99
2	 **2a**	 **2b**	70
3	 **3a**	 **3b**	70
4	 **4a**	 **4b**	88
5	 **5a**	 **5b**	89
6	 **6a**	 **6b**	39
7	 **7a**	 **7b**	69
8	 **8a**	 **8b**	49

As shown in Table 3, this reaction was applicable to the ring opening of saturated cyclic ethers, regardless of the presence of substituent groups, to give the corresponding diacetoxyalkanes. However, unsaturated cyclic ethers such as 2,3-dihydrofuran or 2,3-dihydropyran underwent polymerization. Such polymerization was rapid even at lower temperatures.

Conclusions.

A novel ring opening of cyclic ethers by sulfuric acid - acetic anhydride system has been devised. The system requires 1 molar amount of sulfuric acid and 20 hours at room temperature. The ring opening is applicable to saturated cyclic ethers to give the corresponding diacetoxyalkanes.

EXPERIMENTAL

Unless otherwise noted all materials were reagent grade and were used without further purification. The ^1H and ^{13}C nmr spectra were taken on a JEOL JNM-A500 spectrometer in $CDCl_3$ solutions, unless otherwise specified, using TMS and $CDCl_3$ as internal standards, respectively. The EI mass spectra and FAB mass spectra (in a matrix of glycerin) for 1,4-diacetoxypentane (**2b**) were performed with a JEOL JMS-DX 300 mass spectrometer, but no parent peak was observed. The ir spectra were obtained using a Shimadzu IR 470 spectrometer. For preparative column chromatography, Wakogel C-200 silica gel was employed. Micro vacuum distillation was performed with a Vidrex semimicro distilling apparatus type I.

General Procedure for the Ring Opening of Cyclic Ethers.

The ring opening of 2-methyltetrahydrofuran (**2a**) is described as a typical example. To a solution of sulfuric acid (1.87 ml, 34.8 mmoles) and acetic anhydride (10 ml) was added dropwise 2-methyltetrahydrofuran (**2a**) (3.49 ml, 34.8 mmoles) at room temperature and the mixture was stirred at room temperature for 20 hours. The reaction mixture was diluted with water (50 ml) and extracted with chloroform (3 x 50 ml). The extract was washed with brine (50 ml) and dried with anhydrous sodium sulfate. The solvent was evaporated *in vacuo* and the crude product was chromatographed on silica gel with chloroform to give 4.62 g (70%) of 1,4-diacetoxypentane (**2b**) as a colorless liquid which was further purified by micro vacuum distillation (53-54 °C/0.24 x 133.32 Pa, lit. bp [16] 110-115 °C/17 x 133.32 Pa); ir (KBr): ν 1734 (C=O), 1375, 1245, 1037 cm^{-1}; ^1H nmr: δ 1.23 (d, J = 6.4 Hz, 3H, CH_3), 1.65 (m, 4H, CH_2), 2.04 (s, 3H, CH_3COO), 2.05 (s, 3H, CH_3COO), 4.07 (t, J = 6.3 Hz, 2H, $AcOCH_2$), 4.93 (m, 1H, CH); ^{13}C nmr: δ 19.85 (CH_3), 20.84 (CH_3COO), 21.21 (CH_3COO), 24.57 (CH_2), 32.24 (CH_2), 64.05 ($AcOCH_2$), 70.32 (CH), 170.61 (C=O), 171.01 (C=O).

Ring Opening of Tetrahydrofuran (**1a**).

Reaction under the usual conditions gave 1,4-diacetoxybutane (**1b**) in 98% yield; bp 82-83 °C/1.6 x 133.32 Pa, lit. bp [17] 106 °C/15 x 133.32 Pa; ir (KBr): ν 1736 (C=O), 1367, 1241, 1046 cm^{-1}; ^1H nmr: δ 1.71 (m, 4H, $ArOCH_2CH_2$), 2.05 (s, 6H, CH_3COO), 4.09 (t, J = 6.1 Hz, 4H, $AcOCH_2$); ^{13}C nmr: δ 20.83 (CH_3), 25.16 ($AcOCH_2CH_2$), 63.83 ($AcOCH_2$), 170.99 (C=O).

Ring Opening of 2,5-Dimethyltetrahydrofuran (**3a**).

Reaction under the usual conditions gave 2,5-diacetoxyhexane (**3b**) in 70% yield; bp 55-56 °C/0.23 x 133.32 Pa, lit. bp [18] 88-91 °C/2 x 133.32 Pa; ir (KBr): ν 1733 (C=O), 1373, 1245, 1050, 1025 cm^{-1}; ^1H nmr: δ 1.22 (d, J = 6.4 Hz, 6H, CH_3), 1.56 (m, 4H, CH_2), 2.03 (s, 6H, CH_3COO), 4.90 (m, 2H, CH); ^{13}C nmr: δ 19.83 (CH_3), 21.22 (CH_3COO), 31.56 (CH_2), 70.43 (CH), 170.60 (C=O).

Ring Opening of 2-Hydroxymethyltetrahydrofuran (**4a**).

Reaction under the usual conditions gave 1,2,5-triacetoxypentane (**4b**) in 88% yield; bp 107-108 °C/0.24 x 133.32 Pa, lit. bp [15] 155-165 °C/14 x 133.32 Pa; ir (KBr): ν 1736 (C=O), 1371, 1240, 1048 cm^{-1}; ^1H nmr: δ 1.68 (m, 4H, CH_2), 2.05 (s, 3H, CH_3COO), 2.07 (s, 3H, CH_3COO), 2.08 (s, 3H, CH_3COO), 4.15 (m, 4H, $AcOCH_2$), 5.10 (m, 1H, CH); ^{13}C nmr: δ 20.61 (CH_3COO), 20.78 (CH_3COO), 20.88 (CH_3COO), 24.31 (CH_2), 27.22 (CH_2), 63.72 ($AcOCH_2$), 64.77 ($AcOCH_2$), 70.86 (CH), 170.41 (C=O), 170.59 (C=O), 170.93 (C=O).

Ring Opening of Tetrahydropyran (**5a**).

Application of the usual conditions with the exception that **5a** was added at 0 °C gave 1,5-diacetoxypentane (**5b**) in 89% yield; bp 66-68 °C/0.24 x 133.32 Pa, lit. bp [19] 244 °C; ir (KBr): ν 1737 (C=O), 1367, 1240, 1037 cm^{-1}; ^1H nmr: δ 1.43 (m, 2H, CH_2), 1.67 (q, J = 7.6 Hz, 4H, CH_2), 2.05 (s, 6H, CH_3COO), 4.07 (t, J = 6.7 Hz, 4H, $AcOCH_2$); ^{13}C nmr: δ 20.83 (CH_3COO), 22.35 (CH_2), 28.13 (CH_2), 64.11 ($AcOCH_2$), 171.00 (C=O).

Ring Opening of 2-Methyltetrahydropyran (**6a**).

The reaction was carried out under similar conditions of the ring opening of **5a** to give 1,5-diacetoxyhexane (**6b**) in 39% yield; bp 69-70 °C/0.33 x 133.32 Pa; ir (KBr): ν 1736 (C=O), 1371, 1248, 1043 cm^{-1}; ^1H nmr: δ 1.21 (d, J = 6.1 Hz, 3H, CH_3), 1.63 (m, 6H, CH_2), 2.03 (s, 3H, CH_3COO), 2.04 (s, 3H, CH_3COO), 4.06 (t, J = 6.7 Hz, 2H, $AcOCH_2$), 4.90 (m, 1H, CH); ^{13}C nmr: δ 19.76 (CH_3), 20.77 (CH_3COO), 21.14 (CH_3COO), 21.71 (CH_2), 28.26 (CH_2), 35.32 (CH_2), 64.07 ($AcOCH_2$), 70.49 (CH), 170.51 (C=O), 170.92 (C=O).

Ring Opening of Trimethylene Oxide (**7a**).

Application of the usual conditions with the exception that **7a** was added at -50 °C gave 1,3-diacetoxypropane (**7b**) in 69% yield; bp 112-113 °C/30 x 133.32 Pa, lit. bp [20] 88-90 °C/10 x 133.32 Pa; ir (KBr): ν 1736 (C=O), 1369, 1235, 1053 cm^{-1}; ^1H nmr: δ 1.98 (quintet, J = 6.4 Hz, 2H, CH_2), 2.06 (s, 6H, CH_3COO), 4.15 (t, J = 6.4 Hz, 2H, $AcOCH_2$); ^{13}C nmr: δ 20.69 (CH_3COO), 27.75 (CH_2), 60.89 ($AcOCH_2$), 170.83 (C=O).

Ring Opening of Propylene Oxide (**8a**).

The reaction was carried out under similar conditions of the ring opening of **7a** to give 1,2-diacetoxypropane (**8b**) in 47% yield; bp 99-100 °C/32 x 133.32 Pa, lit. bp [21] 190-191 °C/762 x 133.32 Pa; ir (KBr): ν 1738 (C=O), 1374, 1232, 1050 cm^{-1}; ^1H nmr: δ 1.25 (d, J = 6.7 Hz, 3H, CH_3), 2.06 (s, 3H, CH_3COO), 2.07 (s, 3H, CH_3COO), 4.11 (m, 2H, CH_2), 5.12 (m, 1H, CH); ^{13}C nmr: δ 16.26 (CH_3), 20.55 (CH_3COO), 20.94 (CH_3COO), 65.89 (CH_2), 68.03 (CH), 170.20 (C=O), 170.51 (C=O).

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