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Ring-enlargement of Cyclopropylacylsilanes with Sulfuric or Triflic Acid. Selective Formation of Cyclobutanones or 2-Silyl-4,5-dihydrofurans.

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Abstract: Reaction of cyclopropylacylsilanes with sulfuric or triflic acid in aprotic solvent affords the corresponding cyclobutanone or 2-silyl-4,5-dihydrofuran derivatives, depending upon the substituents on the three-membered ring or acid used. The use of triflic acid results in the selective formation of the dihydrofurans.

Opening of the three-membered ring of cyclopropyl ketones and cyclopropylcarbinyl compounds under acidic conditions followed by attack of a nucleophile is an area of considerable interest in organic synthesis.^{1,2} The chemical behavior of cyclopropylacylsilanes, however, has not yet been fully clarified because of their synthetic difficulty.³ Previously, we presented that a series of cyclopropylacylsilanes (1) reacted with hydrogen chloride or halogenated Lewis acids under milder conditions than their non-silylated counterparts to give the corresponding γ -halogenoacylsilanes or 2-silyl-4,5-dihydrofurans, depending upon the substituents on the three-membered ring of 1 or the acids used.⁴ However, there have been few reports on the formation of dihydrofurans from cyclopropyl ketones under acidic conditions.⁵ Furthermore, Danheiser et al. observed the isomerization of 1-methylcyclopropylacylsilane to 2-methyl-2-silylcyclobutanone in the presence of TiCl.⁶

In connection with the above observations, we report here that cyclopropylacylsilanes (1) react with *strong* acids having low nucleophilic counter anion in aprotic solvents to yield two types of ring-enlargement products, cyclobutanones (2) or 2-silyl-4,5-dihydrofuran derivatives (3), depending upon the substituents on the threemembered ring of 1 or the acids used. The results were summarized in Table 1,^{7,8}

At first, the reaction of 2-arylcyclopropylacylsilanes (1) with H_3SO_4 in THF or dimethoxyethane (DME) at



 60° C proceeded with the exclusion of the silvl group to give the corresponding 2-arylcyclobutanones (2) as sole isolable product. In this reaction, the use of DME as solvent increased the yield of 2.⁹ This result is in contrast to the previous studies^{1b,10} that cyclopropylcarbinyl-cyclobutyl ring-enlargement under acidic conditions is facilitated by the presence of electron donating substituent on 1-position of the three-membered ring.

In contrast, a similar reaction of 2,2-dimethylcyclopropylacylsilane (1d) with H_2SO_4 in THF at 20°C afforded 5,5-dimethyl-2-silyl-4,5-dihydrofuran (3d) as sole isolable product, and that of 1e resulted in the formation of a mixture of the corresponding dihydrofuran (3) and its hydrated product (3'). Incidentally, a similar reaction of 1 with H_2SO_4 in methanol was found to give the corresponding ring opening products, γ -methoxyacylsilanes (4) in high yield, regardless of substituents on the cyclopropyl ring of 1.

| | A | cylsilane | | Solvent | Molar | Temp | Time | | Proc | lucts and Yie | eld ²⁾ |
|----|----------------|-----------------------------------|----------------|---------|---------|------|------|-----|------|---------------|-------------------|
| _1 | R ¹ | R ² | R ³ | | ratio1) | (°C) | (h) | 2 (| (%) | 3 (3')(%) | 4 (%) |
| 1a | Н | Ph | Н | THF | Α | 60 | 9 | 2a | 51 | | - |
| | | | | DME | Α | 60 | 2 | | 63 | - | - |
| | | | | DME | в | 60 | 2 | | 70 | - | - |
| 1b | Н | p-MeC ₆ H ₄ | Н | DME | в | 60 | 1 | 2b | 85 | - | - |
| 1c | Н | p-CIC ₆ H ₄ | Н | DME | в | 60 | 7 | 2c | 63 | - | - |
| 1a | Н | Ph | Н | MeOH | Α | 20 | 2 | | - | - | 4a 94 |
| 1d | Me | e Me | Н | DME | Α | 0 | 0.5 | | - | 3d 69 | - |
| | | | | MeOH | Α | 20 | 3 | | - | - | 4d 96 |
| 1e | Н | -(CH ₂) | 4- | THF | Α | 20 | 5 | | - | 3e 20 (10) | - |
| | | | | MeOH | Α | 20 | 6 | | - | | 4e 95 |

Table 1. Reaction of Cyclopropylacylsilanes (1) with Sulfuric Acid

1) A; 1:H₂SO₄:solvent=1:1:40~100, B; 1:H₂SO₄:solvent=1:2.5:100. 2) Based on 1 and determined by GC.

Interestingly, the selective conversion of 1 to dihydrofurans 3 was achieved by use of triflic acid (TfOH) in DME at -20°C or trimethylsilyl triflate (TfOSiMe₃) in CH_2Cl_2 at -80°C. The results were shown in Table 2.^{7,8} In these reactions, the use of excess amounts of the acid in low concentration was effective for the formation of 3, and no cyclobutanones and acyclic products were detected.

| Acylsilane | Acid | Molar | Temp | Time | Products and Yield 2) | | |
|------------|----------------------|---------|------|-------|-----------------------|-----|--|
| 1 | | ratio1) | (°C) | (min) | 3 | (%) | |
| 1a | TfOH | Α | -20 | 15 | 3a | 75 | |
| | TfOSiMe ₃ | В | -80 | 5 | | >99 | |
| 1b | TfOH | Α | -20 | 15 | 3b | 62 | |
| 1c | TfOH | Α | -20 | 120 | 3c | 47 | |
| 1d | TfOH | Α | -20 | 15 | 3d | 52 | |
| | TfOSiMe ₃ | В | -80 | 5 | | >99 | |
| 1e | TfOH | Α | -20 | 15 | 3e | 81 | |
| | TfOSiMe ₃ | в | -80 | 5 | | >99 | |

 Table 2.
 Selective Conversion of Cyclopropylacylsilanes (1) with Triflic Acid or Trimethylsilyl Triflate into 2-Silyl-4,5-dihydrofurans (3)

1) A; 1:TfOH:DME=1:10:400. B; 1:TfOSiMe₃:CH₂CH₂=1:50:200.

2) Isolated yield based on 1

In order to elucidate the reaction mechanism based on the facts that 1a (*trans*) was obtained quantitatively by the isomerization of the *cis* isomer (1a') with acids¹¹ and that dihydrofurans (3) were labile under acidic or high temperature conditions, we next measured changes of the products distribution in the reaction of 2-phenylcyclopropylacylsilane (1a/1a'=30/70) with an equivalent of H_2SO_4 in DME at 20°C. As shown in Figure 1, 1a' rearranged rapidly to 1a in the initial stage of reaction, and the amount of 3areached a maximum after 20 min and then decreased gradually with a concomitant accumulation of 2a. In addition, we confirmed separately that 3a reacted with an equivalent of H_2SO_4 in DME at 60°C to give 2a in ca 50 % yield.



Figure 1. The Reaction of 2-Phenylcyclopropylacylsilane (1a/1a'=30/70) with H_2SO_4 in DME at 20°C. [Molar ratio; $1:H_2SO_4:DME=1:1:40$]

A reasonable reaction pathways are shown in Scheme 2. The initial reaction with sulfuric acid involves the protonation of carbonyl group of the acylsilanes (1) followed by a series of cationic migrations involving ring opening of cyclopropyl group to form the four intermediary cationic species (**B**, **C**, **D** and **E**) in equilibrium. In the reaction of 2-arylcyclopropylacylsilanes ($1a \sim c$) with H_2SO_4 , cyclobutyl cation **D** rearranged to cation **E** in which the cation center is stabilized by the adjacent aryl group and by β -silicon effect.¹² Subsequent desilylation with ⁻OSO₃H proceeds irreversively¹³ and results in the formation of 2-arylcyclobutanones $2a \sim c$ through the unstable cyclobutenol **F**. In the case of acylsilanes bearing alkyl substituents on 2-positions of the three-memberd ring, the equilibrium may be lain to 1-oxacyclopent-2-enyl cation species (**C**) followed by work-up with water to give the 2-silyldihydrofurans (**3**) or by the rearrangement to 1-oxacyclopent-1-enyl cation (**C**')^{2a,2d} to give 2-hydroxy-2-silyloxolanes (**3**'). The exclusive formation of **3** in the reaction with TfOH or TfOSiMe₃ suggests that the exclusion of the silyl group from the cation species **E** does not proceed owing to the lower nucleophilicity of ⁻OTf compared with ⁻OSO₃H.

On the other hand, the reaction in the presence of methanol proceeds through acyclic cation B or C' to give the corresponding γ -methoxyacylsilanes (4) due to the highly nucleophilic nature of methanol.



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- 7. General procedure for the reaction. To a solution of cyclopropylacylsilanes (1, 0.5 mmol) in THF or DME (2 mL) was added a solution of excess amounts (1~40 equivalents) of concentrated H₂SO₄ or TfOH in the solvent dropwise at a given temperature. After being stirred until 1 was almost consumed, the resulting mixture was poured into icewater containing NaHCO₃, washed with brine and extracted with ether. The extract was concentrated and distilled *in vacuo* to give 2 or 3.
- 8. The selected physical data for 2 and 3 are as follows. 2a: bp. $72^{\circ}C$ (0.5 Torr). ¹H-NMR and IR were in accord with the reported data.¹⁵ ¹³C-NMR (CDCl₃) δ 17.6 (t, ¹J_{CH}=140Hz), 44.8 (t, ¹J_{CH}=143Hz), 64.4 (d, ¹J_{CH}=132Hz), 126.9 (d, ¹J_{CH}=158Hz), 128.6 (d, ¹J_{CH}=160Hz), 136.4 (s), 207.7 (s). 2b: bp. 102°C (0.3 Torr). ¹H-NMR (CDCl₃) δ 2.1~ 2.7 (m, 2H), 2.3 (s, 3H), 3.0~3.3 (m, 2H), 4.5 (t, *J*=9.2Hz, 1H), 7.13 (m, 4H). IR(cm⁻¹) 1780, 1510, 1460, 1175, 1140, 805. 2c: bp. 104°C (0.5 Torr). ¹H-NMR (CDCl₃) δ 2.0~2.8 (m, 2H), 2.8~3.4 (m, 2H), 4.5 (t, *J*=9.2Hz, 1H), 6.9~7.5 (m, 4H). IR(cm⁻¹) 1780, 1620, 1495, 1400, 1095, 1015, 820. 3a: bp. 85°C (0.3 Torr). ¹H-NMR (CDCl₃) δ 0.20 (s, 9H), 2.54 (ddd, *J*=2.6, 7.7, 15.7Hz, 1H), 3.11 (ddd, *J*=2.6, 10.8, 15.7Hz, 1H), 5.15 (t, *J*= 2.6Hz, 1H), 5.51 (dd, *J*=7.7, 10.8Hz, 1H), 7.25~7.34 (m, 5H). IR(cm⁻¹) 1600, 1500, 1100, 840. 3b: bp. 100°C (0.3 Torr). ¹H-NMR (CDCl₃) δ 0.20 (s, 9H), 2.33 (s, 3H), 2.53 (ddd, *J*=2.6, 7.8, 15.7Hz, 1H), 3.08 (ddd, *J*=2.6, 10.6, 15.7Hz, 1H), 5.14 (t, *J*=2.6Hz, 1H), 5.47 (dd, *J*=7.8, 10.6Hz, 1H), 7.25~7.34 (m, 5H). IR(cm⁻¹) 1600, 1250, 1100, 850. 3c: bp. 105~110°C (0.3 Torr). ¹H-NMR (CDCl₃) δ 0.20 (s, 9H), 2.49 (ddd, *J*=2.5, 7.7, 15.6Hz, 1H), 3.18 (ddd, *J*=2.5, 10.8, 15.6Hz, 1H), 5.14 (t, *J*=2.6Hz, 1H), 5.14 (t, *J*=2.5Hz, 1H), 5.48 (dd, *J*=7.7, 10.8Hz, 1H), 7.15~7.35 (m, 5H). IR(cm⁻¹) 1600, 1250, 1100, 850. 3c: bp. 105~110°C (0.3 Torr). ¹H-NMR (CDCl₃) δ 0.20 (s, 9H), 2.39 (ddd, *J*=7.7, 10.8Hz, 1H), 7.15~7.35 (m, 5H). IR(cm⁻¹) 1604, 1250, 1100, 850. 3d: bp. 55 °C (40 Torr). ¹H-NMR (CDCl₃) δ 0.11 (s, 9H), 1.31 (s, 3H), 2.37 (d, *J*=2.5Hz, 2H), 5.0 (t, *J*=2.5Hz, 1H). IR(cm⁻¹) 1450, 1250, 1090, 840. 3e: bp. 38°C (0.2 Torr). ¹H-NMR (CDCl₃) δ 0.11 (s, 9H), 1.31 (s, 3H), 2.37 (d, *J*=2.5Hz, 2H), 5.0 (t, *J*=2.5Hz, 1H). IR(cm⁻¹) 1450, 1250, 1090, 840. 3e: bp. 38°C (0.2 Torr). ¹H-NMR (CDCl₃) δ 0.14 (s, 9H), 1.0~2.1 (m, 8H), 2.5~2.8 (m, 1H), 4.3
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