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# Brønsted acid TfOH-mediated reactions of 2-(arylmethylene)cyclopropylcarbinols with acetonitrile

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**Abstract**—We report herein Brønsted acid TfOH-mediated reactions of 2-(arylmethylene)cyclopropylcarbinols with acetonitrile to give the corresponding ring-enlarged *N*-(3-arylmethylidenecyclobutyl)acetamides in moderate to good yields under mild conditions. A plausible mechanism is proposed on the basis of previous investigations.


Methylenecyclopropanes (MCPs) are highly strained but readily accessible molecules that serve as useful building blocks in organic synthesis. MCPs undergo a variety of ring-opening reactions because the relief of ring strain provides a potent thermodynamic driving force.[1] Transition-metal (such as Pd, Rh, Ru and Pt)-catalyzed reactions of MCPs with various reactants have attracted much attention.[2,3] Recently, we reported that in the presence of Brønsted acid trifluoromethanesulfonic acid $CF_3SO_3H$ (TfOH), methylenecyclopropanes react with nitriles to give [3+2] cycloaddition products in good to high yields along with Ritter reaction products.[4] In this letter, we wish to report Brønsted acid TfOH-mediated reactions of 2-(arylmethylene)cyclopropylcarbinols **1**,[5] another kind of MCPs bearing a hydroxymethyl group, with acetonitrile to give the corresponding *N*-(3-arylmethylidenecyclobutyl)acetamides **2** in moderate to good yields at 60 °C.

At the outset of our investigations, the reaction of 2-(phenylmethylene)cyclopropylcarbinol *E*-**1a** with acetonitrile was chosen as a model reaction and was carried out in the presence of various Brønsted acids and under different reaction conditions to develop the optimum reaction conditions. Table 1 shows the representative results. After several trials and errors, we were pleased to find out that the reaction of *E*-**1a** with acetonitrile in the presence of TfOH (0.12–1.20 equiv) produced the corresponding ring-enlarged *N*-(3-phenylmethylidenecyclobutyl)acetamide **2a** in 37–76% yields at 60 °C within 5 h (Table 1, entries 1–8). Traces of **2a** were obtained at room temperature under otherwise identical conditions (Table 1, entry 2). Other Brønsted acids such as methanesulfonic acid and trifluoroacetic acid (TFA) did not promote this reaction (Table 1, entries 9 and 10). In the presence of sulfuric acid (0.7 equiv), **2a** was obtained in a 20% yield under the standard conditions (Table 1, entry 11). Therefore, the best reaction conditions are to carry out the reaction in acetonitrile in the presence of TfOH (0.7 equiv) at 60 °C. It should be emphasized here that using fresh TfOH as a catalyst, the corresponding **2a** was obtained in a lower yield under identical conditions.[6]

With the optimal conditions in hand, we next carried out the reactions of various 2-(arylmethylene)cyclopropylcarbinols **1** with acetonitrile in the presence of TfOH (0.7 equiv). All reactions proceeded smoothly to give the corresponding ring-enlarged products **2** in moderate to good yields (Table 2). For 2-(arylmethylene)-cyclopropylcarbinols *E*-**1b**, *E*-**1c** and *E*-**1e**–**i** having an electron-withdrawing group on the benzene ring, the corresponding ring-enlarged products **2b**, **2c** and **2e**–**i** were obtained in a good yields (60–73% yields) (Table 2, entries 2, 3 and 5–9). For 2-(4-methylphenylmethylene)cyclopropylcarbinol *E*-**1d** having a moderately electron-donating methyl group on the benzene ring, the corresponding ring-enlarged product **2d** was obtained in 31% yield along with many unidentified products

*Keywords*: 2-(Arylmethylene)cyclopropylcarbinols; Brønsted acid; Ring-enlarging reaction; Acetonitrile; Trifluoromethanesulfonic acid; *N*-(3-Arylmethylidenecyclobutyl)acetamides.
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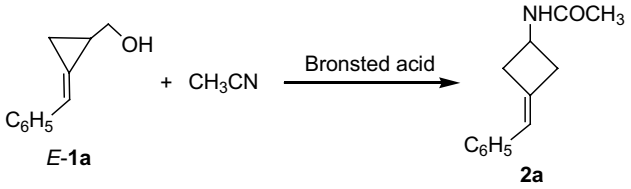
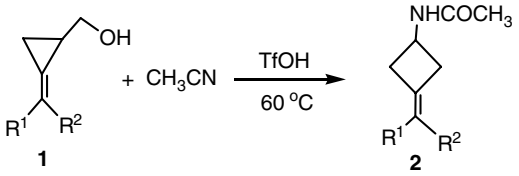
**Table 1.** Brønsted acids-mediated reactions of 2-(phenylmethylene)-cyclopropylcarbinol *E*-**1a** with acetonitrile




| Entry[a] | Brønsted acid (equiv) | Temperature (°C) | **2a**, Yield[b] (%) |
|---|---|---|---|
| 1 | TfOH (0.12) | 60 | 37 |
| 2 | TfOH (0.34) | rt | Trace |
| 3 | TfOH (0.34) | 60 | 56 |
| 4 | TfOH (0.5) | 60 | 71 |
| 5 | TfOH (0.7) | 60 | 76 |
| 6 | TfOH (0.8) | 60 | 65 |
| 7 | TfOH (1.0) | 60 | 63 |
| 8 | TfOH (1.2) | 60 | 62 |
| 9 | $CH_3SO_3H$ (0.7) | 60 | — |
| 10 | TFA (0.7) | 60 | — |
| 11 | $H_2SO_4$ (0.7) | 60 | 20 |

[a] All reactions were carried out in 2.0 mL of $CH_3CN$ for 5 h.
[b] Isolated yields by alumina ($Al_2O_3$) column chromatography.

**Table 2.** Brønsted acids-mediated reactions of 2-(arylmethylene)cyclopropylcarbinol **1** with acetonitrile




| Entry[a] | $R^1/R^2$ | **2a**, Yield (%)[b] |
|---|---|---|
| 1 | $C_6H_5$/H **1a** | **2a**, 76 |
| 2 | 4-$BrC_6H_4$/H **1b** | **2b**, 65 |
| 3 | 2-$BrC_6H_4$/H **1c** | **2c**, 73 |
| 4 | 4-$MeC_6H_4$/H **1d** | **2d**, 31 |
| 5 | 4-$ClC_6H_4$/H **1e** | **2e**, 68 |
| 6 | 3-$FC_6H_4$/H **1f** | **2f**, 66 |
| 7 | 4-$FC_6H_4$/H **1g** | **2g**, 60 |
| 8 | 2,3-$Cl_2C_6H_3$/H **1h** | **2h**, 64 |
| 9 | 2,4-$Cl_2C_6H_3$/H **1i** | **2i**, 71 |
| 10 | H/4-$ClC_6H_4$/H **1j** | **2e**, 33 |
| 11 | H/H **1k** | **2k**, 43 |

[a] All reactions were carried out in the presence TfOH (0.7 equiv) in 2.0 mL of $CH_3CN$ for 5 h.
[b] Isolated yields by alumina column chromatography.

presumably due to its high reactivity (Table 2, entry 4). For *Z*-2-(4-chlorophenylmethylene)cyclopropylcarbinol **1j** and aliphatic methylenecyclopropylcarbinol **1k**, the corresponding ring-enlarged products **2e** and **2j** were obtained in 33% and 34% yields, respectively, also along with many unidentified products (Table 2, entries 10 and 11). These results suggest that the stability of cationic intermediate and steric effect of aromatic group play a key role in this reaction.

The structures of products **2** were determined by $^1H$ NMR and $^{13}C$ NMR spectroscopic data, microanalyzes and HRMS (see the Supporting Information). The structure of **2a** was confirmed ambiguously by an X-ray diffraction.[7] The ORTEP drawing of **2a** is shown in Figure 1.

A plausible mechanism is shown in Scheme 1 on the basis of our previous investigations[4] and Ritter reaction mechanism.[8] In the presence of Brønsted acid TfOH, 2-(arylmethylene)cyclopropylcarbinol **1** first produces a non-classic carbocation: bicyclobutonium ion **A**[9,10] due to the neighbouring-group participation of the cyclopropyl ring after dehydration (Scheme 1). Then, the corresponding cationic intermediate **B** is formed from the reaction of cationic intermediate **A** with acetonitrile, which affords the corresponding *N*-(3-arylmethylidenecyclobutyl)acetamide **2** via a Ritter reaction pathway.

In conclusion, we have found an interesting Brønsted acid TfOH-mediated reaction of 2-(arylmethylene) cyclopropylcarbinols **1** with acetonitrile to give the corresponding ring-enlarged *N*-(3-arylmethylidenecyclobutyl)acetamides **2** in moderate to good yields under mild conditions.[11] Since aliphatic methylenecyclopropylcarbinols are difficult to be prepared at the present stage, we are unable to examine them under the standard conditions in this letter. A plausible

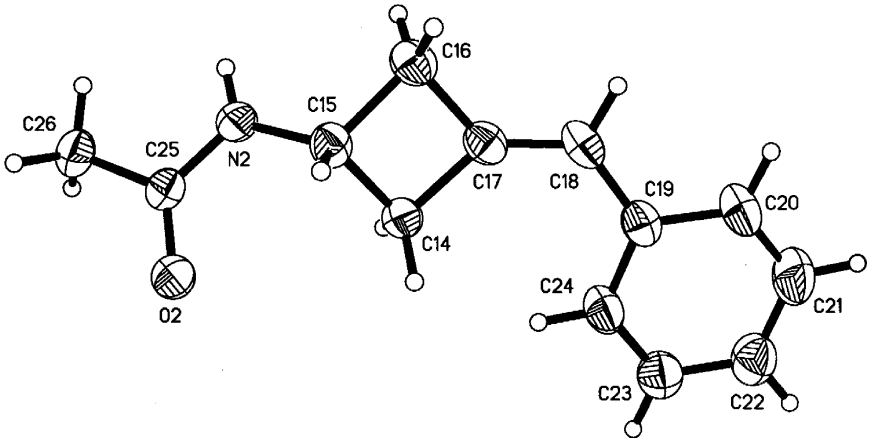
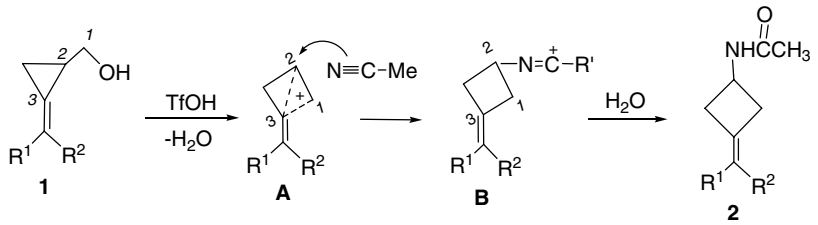



**Figure 1.** ORTEP drawing of **2a**.




**Scheme 1.** Proposed mechanism for the formation of *N*-(3-arylmethylidnecyclobutyl)acetamides **2**.

reaction mechanism has been proposed on the basis of previous investigations and Ritter reaction pathway. In addition, scope and limitations of this reaction has been disclosed. Efforts are under way to elucidate the mechanistic details and subsequent transformation. Work along these lines is currently in progress.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.09.063.

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