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# A novel transformation of 1-*exo*-substituted 2a-aroyl-1,2,2a, 8b-tetrahydro-3*H*-benzo[*b*]cyclobuta[*d*]pyran-3-ones with sulfoxonium ylide to highly strained 2a-(1-arylethenyl)-1,2,2a,7b-tetrahydrocyclobuta[*b*]benzofurans

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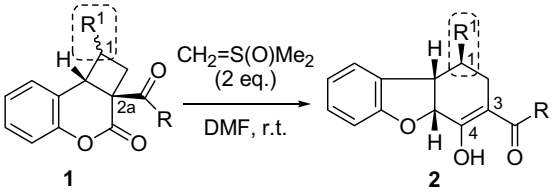
**Abstract**

When 1-substituted 2a-aroyl-1,2,2a,8b-tetrahydro-3*H*-benzo[*b*]cyclobuta[*d*]pyran-3-ones (**1**) were treated with dimethylsulfoxonium methylide, 1-*endo* isomers (*endo*-**1**) gave 1-substituted 3-aroyl-1,2,4a,9b-tetrahydrodibenzofuran-4-ols (**2**) exclusively as expected. On the other hand, 1-*exo* isomers (*exo*-**1**) underwent a novel transformation to 1-substituted 2a-(1-arylethenyl)-1,2,2a,7b-tetrahydrocyclobuta[*b*]benzofurans (**3**), together with **2**.


*Keywords:* Sulfur ylide; 3*H*-Benzo[*b*]cyclobuta[*d*]pyran; Cyclobuta[*b*]benzofuran; Tetrahydrodibenzofuran; Skelton transformation

Dimethylsulfoxonium methylide is well known as a reagent for methylene transfer reactions such as methylation, epoxidation of ketones and aldehydes, and cyclopropanation of α,β-unsaturated carbonyl compounds.[1] We have reported an interesting reaction of coumarins having an electron-withdrawing group at the 3-position with dimethylsulfoxonium methylide[2] and a stereoconvergent transformation reaction of 1,2a-disubstituted benzo[*b*]-cyclobuta[*d*]pyranones (**1**) with dimethylsulfoxonium methylide to 1,3-disubstituted tetrahydrodibenzofuranols (**2**) regardless of the stereochemistry of the 1-substituent group in **1** (Scheme 1).[3]




Scheme 1.

In a continuation of the latter study, we noted that only the 2a-benzoyl derivative (**1a**) gave a small amount of a by-product (**3a**) together with **2a** (Scheme 2). In this Letter, we describe a novel transformation of 1-substituted 2a-aroylbenzo[*b*]cyclobuta[*d*]pyranones (**1**) with dimethylsulfoxonium methylide to 2a-(1-arylethenyl)-1,2,2a,7b-tetrahydrocyclobuta[*b*]benzofurans (**3**).

The molecular formula of the by-product (**3a**) was found to be $C_{24}H_{20}O$ on the basis of high-resolution MS and

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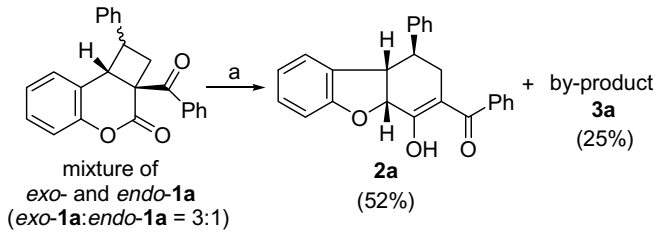
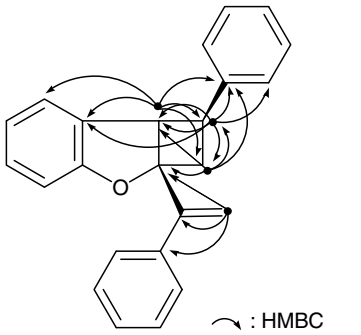



Scheme 2. Reagents and conditions: (a) $CH_2$=S(O)$Me_2$ (2 equiv), DMF, rt.

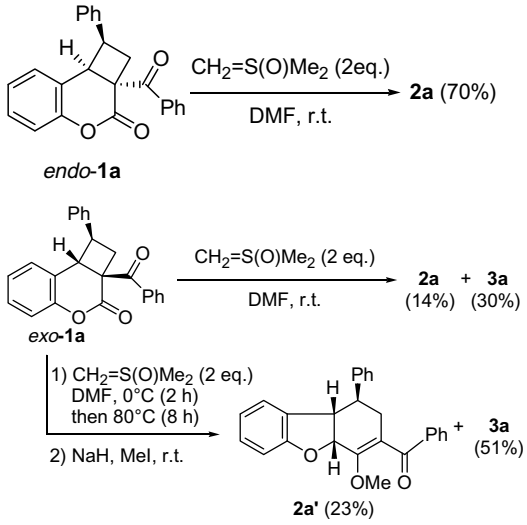
elemental analysis, and the structure of **3a** was confirmed as 1-phenyl-2a-(1-phenylethenyl)-1,2,2a,7b-tetrahydrocyclobuta[*b*]benzofuran on the basis of NMR spectral data including detailed analysis of the heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple bond coherence (HMBC) spectra (Fig. 1).[4] In nuclear Overhauser enhancement and exchange spectroscopy (NOESY) spectra of **3a**, an NOE was observed between the terminal olefinic proton $H_a$ and $C_{7b}$–H, but not between $H_a$ and $C_1$–H. Therefore, the stereochemistry of **3a** should be as that shown in Figure 1.

Judging from the stereochemistry of **3a**, we hypothesized that **3a** was derived from *exo*-**1a**. To verify this assumption, the diastereomeric isomers (*exo*-**1a** and *endo*-**1a**) were separated using medium-pressure liquid chromatography (MPLC) and their stereochemistries were confirmed on the basis of $^1$H NMR spectra.[5] Each of *exo*- and *endo*-**1a** was treated with 2 equiv of sulfoxonium methylide. *Endo*-**1a** gave only **2a** in 70% yield.[3b,c] On the other hand, *exo*-**1a** gave a mixture of **2a** and **3a** in 14% and 30% yields, respectively (Scheme 3). Several reaction conditions were




**3a** : 1-phenyl-2a-(1-phenylethenyl)-1,2,2a,7b-tetrahydrocyclobuta[*b*]benzofuran

Fig. 1. Structure and selected HMBC and NOESY correlations in **3a**.



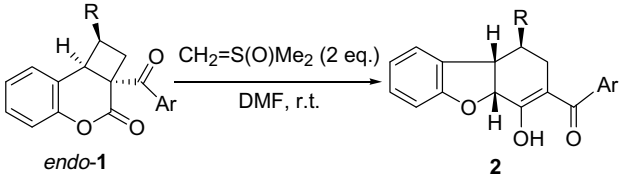

Scheme 3.

examined to optimize the yield of **3a**, improving it to 51% by treating *exo*-**1a** with 2 equiv of sulfoxonium methylide at 0 °C for 2 h then at 80 °C for 8 h (Scheme 3).[6] Under these conditions, **2a**′ (the methylated **2a**) was isolated after treatment with methyl iodide and sodium hydride.

Next, the generality of these reactions was examined. Several cyclobutane compounds (**1b–k**) were prepared[5] and each of the diastereomers (*exo*-**1** and *endo*-**1**) was separated. Each diastereomer was subjected to react with sulfoxonium methylide. The results are summarized in Tables 1 and 2.

In cases of *endo*-**1b–k**, **2b–k** were obtained in 40–83% yields without production of any amount of **3** except for **1i** (Table 1). On the other hand, in all cases of *exo*-**1b–k**,

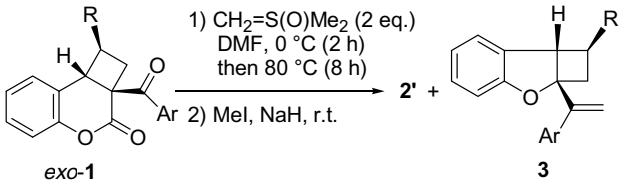
Table 1
The reaction of *endo*-**1** and $CH_2$=S(O)$Me_2$




| Run | | Starting material | | Product |
|---|---|---|---|---|
| | | Ar | R | Isolated yield (%) |
| 1 | *endo*-**1a**: | Ph | Ph | **2a**: 70 |
| 2 | *endo*-**1b**: | Ph | 2-Pyridyl | **2b**: 60 |
| 3 | *endo*-**1c**: | Ph | 4-Br–$C_6H_4$ | **2c**: 56 |
| 4 | *endo*-**1d**: | Ph | 4-MeO–$C_6H_4$ | **2d**: 83 |
| 5 | *endo*-**1e**: | Ph | *n*-Bu | **2e**: 74 |
| 6 | *endo*-**1f**: | Ph | $AcOCH_2$ | **2f**: 68 |
| 7 | *endo*-**1g**: | Ph | Cyclohexyl | **2g**: 71 |
| 8 | *endo*-**1h**: | 4-F–$C_6H_4$ | Ph | **2h**: 66 |
| 9 | *endo*-**1i**: | 4-$CF_3$–$C_6H_4$ | Ph | **2i**: 68[a] |
| 10 | *endo*-**1j**: | 4-MeO–$C_6H_4$ | Ph | **2j**: 53 |
| 11 | *endo*-**1k**: | 3,4,5-$(MeO)_3$–$C_6H_2$ | Ph | **2k**: 40 |

[a] A corresponding **3i** (1-*epi*-**3i**) was obtained in 15% yield.

Table 2
The reaction of *exo*-**1** and $CH_2$=S(O)$Me_2$

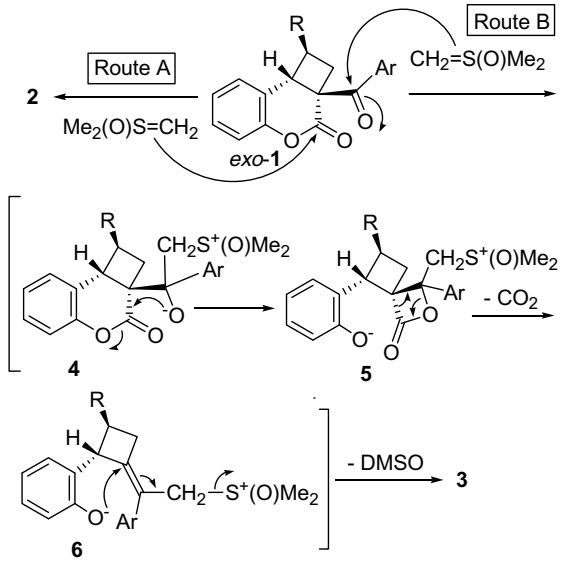



| Run | | Starting material | | Product | |
|---|---|---|---|---|---|
| | | Ar | R | Isolated yield[a] (%) | |
| 1 | *exo*-**1a**: | Ph | Ph | **2a′**: 23 (14) | **3a**: 51 (30) |
| 2 | *exo*-**1b**: | Ph | 2-Pyridyl | **2b′**: 16 | **3b**: 22 |
| 3 | *exo*-**1c**: | Ph | 4-Br–$C_6H_4$ | **2c′**: 21 | **3c**: 25 |
| 4 | *exo*-**1d**: | Ph | 4-MeO–$C_6H_4$ | **2d′**: 23 (22) | **3d**: 31 (26) |
| 5 | *exo*-**1e**: | Ph | *n*-Bu | **2e′**: 34 (23) | **3e**: 28 (30) |
| 6 | *exo*-**1f**: | Ph | $AcOCH_2$ | **2f′**: 18 (16) | **3f**: 29 (26) |
| 7 | *exo*-**1g**: | Ph | Cyclohexyl | **2g′**: 19 (19) | **3g**: 37 (33) |
| 8 | *exo*-**1h**: | 4-F–$C_6H_4$ | Ph | **2h′**: 10 | **3h**: 26 |
| 9 | *exo*-**1i**: | 4-$CF_3$–$C_6H_4$ | Ph | **2i′**: 11 (0) | **3i**: 61 (50) |
| 10 | *exo*-**1j**: | 4-MeO–$C_6H_4$ | Ph | **2j′**: 6 (13) | **3j**: 22 (23) |
| 11 | *exo*-**1k**: | 3,4,5-$(MeO)_3$–$C_6H_2$ | Ph | **2k′**: 20 (25) | **3k**: 24 (26) |

[a] The figure in parentheses is the yield of **2** and **3** when the reaction was performed at rt.

**3b–k** were obtained in 22–61% yields together with **2b′–k′** (Table 2).

We propose a plausible reaction mechanism as shown in Scheme 4. First attack of sulfoxonium methylide to the carbonyl carbon of the coumarin ring in *exo*-**1** and *endo*-**1** affords **2** (Route A in Scheme 4).[3b,c] In *exo*-**1**, the methylide might first attack the carbonyl carbon of the aroyl group to produce **3** (Route B in Scheme 4). The reactivity toward nucleophilic attack of the methylide would be higher at the carbonyl carbon of the coumarin ring than at that of the aroyl group, and the methylide would attack from convex direction. The conformation of the aroyl group in *exo*-**1a** was similar to that of *endo*-**1a** on the basis of their X-ray analyses,[5] and the phenyl ring of their aroyl groups located over the carbonyl group of the coumarin ring. Since the aroyl group of *endo*-**1** would be relatively flexible, the attack of the methylide at the carbonyl carbon of the coumarin ring would precede. On the other hand, because the aroyl group of *exo*-**1** would be rather rigid due of the substituent group at the 1 position, the attack at the aroyl carbon would also occur. When the electrophilicity at the aroyl carbon increased, the yield of **3i** rose to 61% (Run 9 in Table 2). Furthermore, a corresponding **3i** (1-*epi*-**3i**) was obtained even in *endo*-type (*endo*-**1i**) (Run 9 in Table 1).[7]




Scheme 4. A plausible reaction mechanism.

In conclusion, we have investigated the novel transformation of 1-*exo* substituted 2a-aroyl-1,2,2a,8b-tetrahydro-3*H*-benzo[*b*]cyclobuta[*d*]pyran-3-ones (**1**) to 1-substituted 2a-(1-arylethenyl)-1,2,2a,7b-tetrahydrocyclobuta[*b*]benzofurans (**3**) together with the formation of 1-substituted 3-aroyl-1,2,4a,9b-tetrahydrodibenzofuran-4-ols (**2**). The optimization of the reaction, elucidation of detailed reaction mechanism, and synthetic application of **3** are now in progress.

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4. Compound **3a**: Colorless plates (*n*-hexane), mp 55.0–56.9 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 2.76 (1H, ddd, $J = 13.8$, 7.0, 2.0 Hz, 2-$CH_2$), 3.18 (1H, ddd, $J = 13.8$, 9.7, 1.3 Hz, 2-$CH_2$), 3.55 (1H, ddd, $J = 9.7$, 7.0, 4.8 Hz, 1-CH), 4.15 (1H, br d, $J = 4.8$ Hz, 7b-CH), 5.44 (1H, d, $J = 0.5$ Hz, –CPh=C$H_2$), 5.54 (1H, d, $J = 0.5$ Hz, –CPh=C$H_2$), 6.88–6.91 (2H, m, Ar-H), 7.16–7.23 (5H, m, Ar-H), 7.27–7.35 (5H, m, Ar-H), 7.47–7.51 (2H, m, Ar-H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$: 40.9, 44.0, 54.1, 91.0, 110.3, 115.3, 120.8, 124.1, 126.4, 126.6, 127.4, 127.7, 128.2, 128.5, 128.6, 131.2, 138.2, 144.0, 148.0, 160.6. IR ($CHCl_3$): 1597 cm$^{-1}$. LR-FABMS *m*/*z*: 325 $(M+H)^+$, 220 (100). HR-FABMS calcd for $C_{24}H_{20}O + H$: 325.1592. Found: 325.1599. Anal. Calcd for $C_{24}H_{20}O$: C, 88.85; H, 6.21. Found: C, 88.72; H, 6.26.
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6. The selectivity of **2** and **3** at 0 °C was moderate, but the reaction time was long. Though its selectivity at 80 °C was low, the reaction time was short. Therefore, this reaction condition was chosen in consideration for product ratio and time.
7. The reason why this reaction occur in only 1-*exo*-**1** of which substituent groups at the 2a position is the aroyl group is not clear. The theoretical calculation will disclose this result.