

## Regular Article

## Ring-Opening Cyclization of Spirocyclopropanes Using Sulfoxonium Ylides

Yuta Onuki, Hisanori Nambu,\* and Takayuki Yakura\*

Faculty of Pharmaceutical Sciences, University of Toyama; Sugitani, Toyama 930–0194, Japan.

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**Ring-opening cyclization of cyclohexane-1,3-dione-2-spirocyclopropanes using dimethylsulfoxonium methylide proceeded regioselectively to produce 2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-ones in good to high yields. The reactions of cycloheptane- and cyclopentane-1,3-dione-2-spirocyclopropanes could construct [7.6]- and [5.6]-fused ring systems. This reaction was also carried out using sulfoxonium ethylide, butylide, and benzylide, resulting in the formation of the corresponding 2,3-*trans*-disubstituted products in good to high yields, and it was shown that the dimethyl group can act as a dummy substituent. It was found that the 2- and 3-phenylhexahydrobenzopyran-5-ones can be readily converted into 5-hydroxyflavan and 5-hydroxyisoflavan, respectively.**

**Key words** sulfoxonium ylide; spirocyclopropane; ring-opening cyclization; flavan; isoflavan

## Introduction

In the 1960s, Corey and Chaykovsky developed the reaction of sulfur ylides, such as sulfonium ylide **1** and sulfoxonium ylide **2**, with carbonyl compounds, which became known as the Corey–Chaykovsky reaction.<sup>1,2</sup> Both **1** and **2** react with either aldehydes or ketones in the same way to give the corresponding epoxides. However, when reacted with enones, they behave differently. For example, dimethylsulfonium methylide (**1a**) reacts with calcone to afford epoxide in 87% yield, whereas dimethylsulfoxonium methylide (**2a**) produces cyclopropane in 95% yield<sup>3</sup> (Chart 1). Using density functional theory calculations, Yu and colleagues recently reported that these different reaction outcomes can be attributed to thermodynamics, as sulfonium ylide **1a** is less stable, and therefore more highly reactive, than sulfoxonium ylide **2a**.<sup>4</sup> To date, sulfur ylides **1a** and **2a** have been widely used in the synthesis of various epoxides,<sup>5,6</sup> cyclopropanes,<sup>7,8</sup> and heterocyclic compounds.<sup>9–11</sup>

Doubly-activated cyclopropanes are versatile intermediates for the synthesis of a wide range of carbocycles<sup>12</sup> and heterocycles.<sup>13</sup> With this in mind, regioselective ring-opening cyclizations of cyclohexane-1,3-dione-2-spirocyclopropanes **3** have been developed for the synthesis of indole<sup>14–16</sup> and benzofuran.<sup>17,18</sup> Furthermore, we recently reported that the regio- and diastereoselective ring-opening cyclization of spirocyclopropanes **3** with electron-withdrawing group (EWG)-substituted sulfonium ylides **1b** affords 2,3-*trans*-disubstituted 2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-ones **4** in high yields<sup>19</sup> (Chart 2A). The reaction proceeds through nucleophilic attack of the carbanion in **1b** to the electrophilic cyclopropane carbon possessing an R<sup>1</sup> substituent in **3**. Subsequently, an S<sub>N</sub>2-type cyclization occurs to afford the product **4** with the concomitant release of dimethyl sulfide. This was the first example of the ring opening of cyclopropanes using a sulfonium ylide as a carbon nucleophile. However, sulfonium ylides used in this reaction were limited to EWG-stabilized ones **1b**. Since sulfur ylides with various reactivities have been used in organic synthesis,<sup>5–11</sup> this study focused on the reaction between different sulfur ylides and spirocyclopropanes. Herein, the ring-opening cyclization of spirocyclopropanes **3** using

non-, alkyl-, and phenyl-substituted sulfoxonium ylides **2** as a carbon nucleophile is reported (Chart 2B).

## Results and Discussion

Initially, the reaction was carried out using highly reactive dimethylsulfonium methylide (**1a**), which was prepared *in situ* from trimethylsulfonium iodide (**6**) (Chart 3). After treatment of sulfonium salt **6** using sodium hydride in dimethylsulfoxide (DMSO) at room temperature for 0.5 h,<sup>3</sup> the produced sulfonium ylide **1a** was reacted with 2'-phenylspirocyclopropane **3a**.<sup>20</sup> Unfortunately, reaction at room temperature for 24 h gave only decomposition products, indicating that the reactivity of **1a** is too high to induce a ring-opening cyclization reaction.

Next, the reaction of the lower reactive sulfoxonium ylide **2a** with **3a** was examined (Table 1). When the dimethylsulfoxonium methylide (**2a**), which was prepared *in situ* from 2.1 eq of trimethylsulfoxonium iodide (**7a**) using 2.0 eq of sodium hydride in DMSO at room temperature for 0.5 h,<sup>3</sup> reacted with **3a**, the desired ring-opening cyclization proceeded regioselectively at room temperature within 8 h to afford 3-phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (**5a**) in 68% yield (entry 1). Trimethylsulfoxonium chloride (**7b**) proved to be a more suitable sulfoxonium ylide precursor than **7a**, leading to a higher yield of **5a** (76%, entry 2), presumably because side reactions caused by the presence of the highly nucleophilic iodide ion are prevented when switching to the lower nucleophilic chloride ion.<sup>18</sup> Changing the solvent from DMSO to *N,N*-dimethylformamide (DMF) led to a decrease in the product yield to 71% (entry 3). However, neither CH<sub>2</sub>Cl<sub>2</sub> nor toluene<sup>21</sup> were found to be suitable solvents, leading to the recovery of **3a** (entries 4 and 5). In contrast, when tetra-

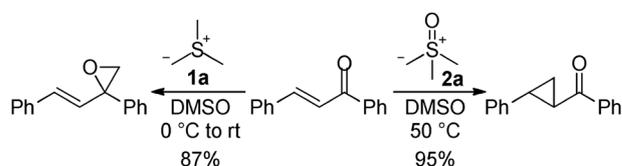
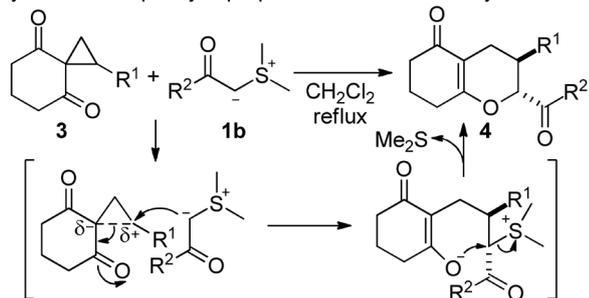


Chart 1. The Corey–Chaykovsky Reaction

\* To whom correspondence should be addressed. e-mail: nambu@pha.u-toyama.ac.jp; yakura@pha.u-toyama.ac.jp

**A. Previous work:** Regio- and diastereoselective ring-opening cyclization of spirocyclopropanes **3** with sulfonium ylides **1b**



**B. This work:** Ring-opening cyclization of spirocyclopropanes **3** with sulfoxonium ylides **2**

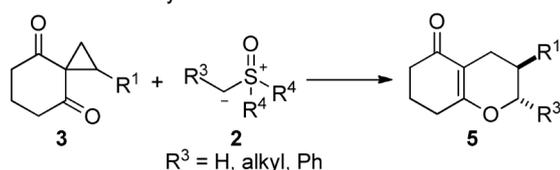


Chart 2. Ring-Opening Cyclization of Spirocyclopropanes **3** with Sulfur Ylides **1** and **2**

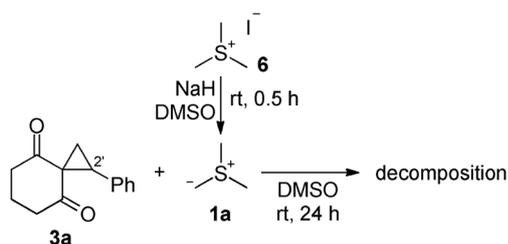


Chart 3. The Reaction of Spirocyclopropane **3a** with Sulfonium Ylide **1a** Prepared from Sulfonium Salt **6**

Table 1. The Reaction of Spirocyclopropane **3a** with Sulfoxonium Ylide **2a** Prepared from Sulfoxonium Salts **7a** and **7b**<sup>a)</sup>

Entry	<b>7</b> (eq)	Base (eq)	Solvent	Time (h)	Yield (%)
1	<b>7a</b> (2.1)	NaH (2.0)	DMSO	8	68
2	<b>7b</b> (2.1)	NaH (2.0)	DMSO	8	76
3	<b>7b</b> (2.1)	NaH (2.0)	DMF	8	71
4 <sup>b)</sup>	<b>7b</b> (2.1)	NaH (2.0)	CH <sub>2</sub> Cl <sub>2</sub>	24	NR
5 <sup>b)</sup>	<b>7b</b> (2.1)	NaH (2.0)	Toluene	24	NR
6 <sup>b)</sup>	<b>7b</b> (2.1)	NaH (2.0)	THF	8	75
7 <sup>b)</sup>	<b>7b</b> (2.1)	<sup>t</sup> BuOK (2.0)	THF	8	74
8	<b>7b</b> (2.1)	NaH (1.5)	DMSO	12	79
9	<b>7b</b> (1.5)	NaH (1.2)	DMSO	12	82
10	<b>7b</b> (1.2)	NaH (1.1)	DMSO	12	68
11 <sup>c)</sup>	<b>7b</b> (1.5)	NaH (1.2)	DMSO	12	72

a) All reactions were performed on a 0.3 mmol scale. b) Sulfoxonium ylide **2a** was prepared by heating at reflux for 3 h. c) The reaction was carried out at 50°C.

hydrofuran (THF) was used as a solvent (at reflux for 3 h), the reaction with **3a** gave the product **5a** in 75% yield (entry 6). Changing the base from sodium hydride to potassium *tert*-butoxide<sup>22)</sup> (<sup>t</sup>BuOK in THF at reflux for 3 h) led to a similar product yield of **5a** in both cases (74%, entry 7). For ylide preparation in THF, the reaction required 3 h at reflux, whereas in DMSO it required only 0.5 h at room temperature. For this reason, DMSO was chosen as a solvent. Next, an attempt was made to reduce the amount of **7b** and base used (entries 8–10), where 1.5 eq of **7b** and 1.2 eq of sodium hydride were found to give the best result. Moreover, increasing the reaction temperature to 50°C led to a lower product yield (72%, entry 11). Finally, 1.5 eq of **7b** and 1.2 eq of sodium hydride in DMSO at room temperature were chosen as the optimized conditions.

Next, the reactions of a range of spirocyclopropanes **3b–i**, **8**, and **10** with sulfoxonium salt **7b** were investigated (Table 2). Under the previously stated optimized conditions, dimedone-derived spirocyclopropane **3b** gave the corresponding hexahydrobenzopyran-5-one **5b** in 83% yield (entry 1). The reaction of aryl-substituted spirocyclopropanes **3c** and **3d** bearing *p*-methyl or *p*-bromo substituents on their benzene rings afforded products **5c** and **5d** in 82 and 71% yields, respectively (entries 2 and 3). It was also possible to use 2',3'-nonsubstituted spirocyclopropanes **3e–h**<sup>23)</sup> in this reaction, furnishing the corresponding products **5e–h** in 71–78% yields (entries 4–7). The reaction of *n*-butyl-substituted spirocyclopropane **3i** was then investigated (entry 8). Unexpectedly, the 4-butyl-substituted product **5i'** was obtained together with 3-butyl-substituted **5i**, where the combined yield of these products was 83% and the ratio of **5i** to **5i'** was determined to be 76:24 from <sup>1</sup>H-NMR analysis of the crude product. Since the butyl-substituted carbocation, formally formed by the cleavage of cyclopropane, is less stable than phenyl-substituted one, it is speculated that the sulfoxonium ylide **2a** would partially attack to the less hindered carbon atom on cyclopropane in **3i** to produce the regioisomer **5i'** as a minor product. Next, the reactions of spirocyclopropanes **8** and **10** derived from cycloheptane- and cyclopentane-1,3-diones were investigated (entries 9 and 10). Although the yields of the corresponding products **9** and **11** decreased to 64 and 41%, respectively, it was discovered that the present reaction can also be used to construct [7.6]- and [5.6]-fused ring systems.

In addition, the reaction of non-spirocyclopropane was examined under the optimized conditions (Chart 4). The reaction of 1,1-diacetyl-2-phenylcyclopropane (**12**) with sulfoxonium salt **7b** in the presence of sodium hydride in DMSO at room temperature for 12 h resulted in the formation of only decomposition products, suggesting that a spiro-type structure is crucial for successful ring-opening cyclization to occur. It is clear that the spirocyclopropane is more reactive than non-spiro one, probably due to its higher ring strain energy.

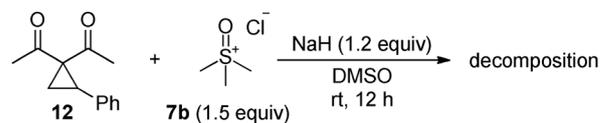
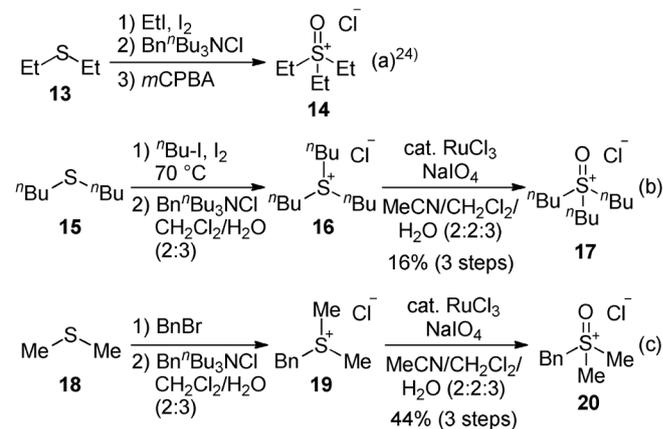
As an extension of the present method, the reaction was carried out using sulfoxonium ethylide, butylide, and benzylide. Initially, the corresponding sulfoxonium salts were prepared as sulfoxonium ylide precursors (Chart 5). Since the Shea group has already proven that triethylsulfoxonium chloride (**14**) is a precursor of sulfoxonium ethylide **2b**,<sup>24)</sup> salt **14** was prepared from diethyl sulfide (**13**) according to their reported procedure. Ethylation of **13** with iodoethane and iodine, anion exchange with benzyltributylammonium chloride, and oxida-

Table 2. The Reaction of Spirocyclopropanes **3**, **8** and **10** with Sulfoxonium Salt **7b**<sup>a)</sup>

Entry	Substrate	Product	Yield (%)
1			83
2	<b>3c</b> : R = Me	<b>5c</b> : R = Me	82
3	<b>3d</b> : R = Br	<b>5d</b> : R = Br	71
4			78
5			74
6	<b>3g</b> : R = Me	<b>5g</b> : R = Me	74
7	<b>3h</b> : R = Ph	<b>5h</b> : R = Ph	71
8			83
			( <b>5i</b> : <b>5i'</b> = 76:24) <sup>b)</sup>
9			64
10			41

<sup>a)</sup> All reactions were performed on a 0.3 mmol scale. After preparation of sulfoxonium ylide **2a** from 1.5 eq of sulfoxonium salt **7b** with 1.2 eq of sodium hydride in DMSO for 0.5 h *in situ*, spirocyclopropane **3**, **8** or **10** was added to the reaction mixture. <sup>b)</sup> The ratio of **5i** to **5i'** was determined from <sup>1</sup>H-NMR analysis of the crude product.

tion using *m*-chloroperoxybenzoic acid (*m*CPBA) resulted in the formation of sulfoxonium salt **14** (Chart 5a). Next, tributylsulfoxonium chloride (**17**) was prepared according to the same procedure. Alkylation of dibutyl sulfide

Chart 4. The Reaction of Cyclopropane **12** with Sulfoxonium Salts **7b**Chart 5. Preparation of the Sulfoxonium Salts **14**, **17** and **20**

anion exchange reaction gave tributylsulfoxonium chloride (**16**). However, the oxidation of **16** with *m*CPBA was not successful. As a result of the testing of different oxidation conditions, it was found that the Sharpless oxidation (cat. RuCl<sub>3</sub>, NaIO<sub>4</sub>)<sup>25</sup> could be applied to this step, resulting in the formation of sulfoxonium salt **17** in 16% yield from **15** (Chart 5b). Because of the difficulty in synthesizing the tribenzylsulfoxonium salt, benzyldimethylsulfoxonium chloride (**20**) was successfully prepared as an alternative. Although the sulfoxonium ylide precursor **20** has the potential to form methylene in addition to benzylyde, it was expected that the deprotonation of **20** would proceed at the most basic benzylic position. Alkylation of dimethyl sulfide (**18**) with benzyl bromide and a subsequent anion exchange reaction gave benzyldimethylsulfoxonium chloride (**19**). Finally, the Sharpless oxidation of **19** provided the corresponding sulfoxonium salt **20** in 44% yield from benzyl bromide (Chart 5c).

Using these sulfoxonium ylide precursors, the reactions of spirocyclopropanes with sulfoxonium ethylide **2b**, butylide **2c**, and benzylide **2d** were investigated (Chart 6). After treatment of triethylsulfoxonium chloride (**14**) under the aforementioned optimized conditions, spirocyclopropane **3a** was added. The reaction proceeded at room temperature within 12 h, affording 2-methyl-3-phenylhexahydrobenzopyran-5-one (**5j**) in 73% yield (Chart 6a). From this result, it was found that sulfoxonium ethylide **2b** was generated from **14** under these conditions.<sup>26</sup> The stereochemistry of **5j** was determined from <sup>1</sup>H nuclear Overhauser effect experiments to be 2,3-*trans* (see Supplementary materials), as in previous results.<sup>19</sup> Tributylsulfoxonium chloride (**17**) was determined to be a very good precursor in the formation of sulfoxonium butylide **2c** to furnish the final *trans*-3-phenyl-2-propyl-substituted product **5k** in 72% yield (Chart 6b). Next, the reaction of **3a** with benzyldimethylsulfoxonium chloride (**20**) was examined under the same conditions, which was found to proceed smoothly to afford *trans*-2,3-diphenyl-substituted **5l** as the sole product in 90% yield (Chart 6c). This result clearly implies that

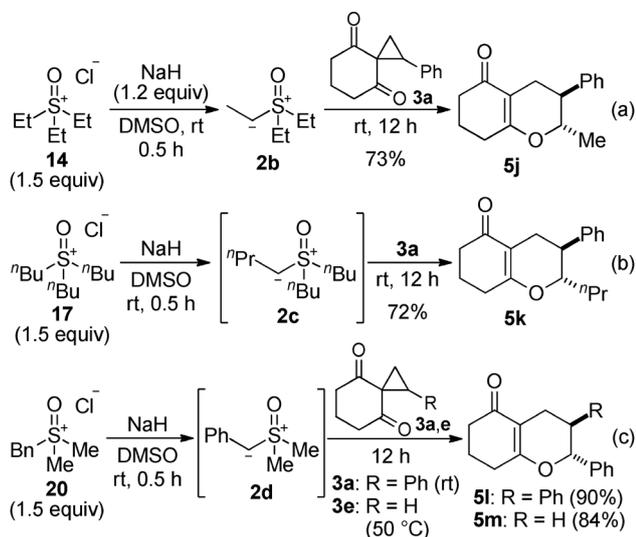


Chart 6. Reaction of Spirocyclopropanes **3a** and **3e** with Sulfoxonium Ylides **2b–d** Prepared from Sulfoxonium Salts **14**, **17** and **20**

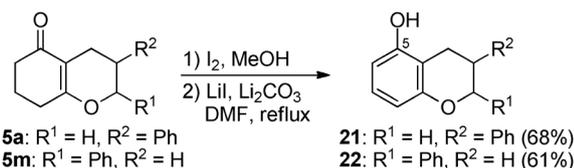


Chart 7. Conversion of Hexahydrobenzopyran-5-ones **5a** and **5m** into 5-Hydroxyisoflavan (**21**) and 5-Hydroxyflavan (**22**)

the corresponding sulfoxonium benzylide **2d** was formed as expected. The reaction of 2',3'-nonsubstituted spirocyclopropane **3e** with **20** proceeded at 50°C, providing the 2-phenyl-substituted product **5k**<sup>27,28</sup> in 84% yield (Chart 6c). In the case of the reactions of **14** and **17**, either diethyl sulfoxide or dibutyl sulfoxide are expelled as by-products in the cyclization step. However, the reaction of **20** produces dimethyl sulfoxide as a leaving group. It is very interesting and useful in terms of atom economy that the dimethyl group in **20** can act as a dummy substituent.

To demonstrate the utility of this reaction, the conversions of hexahydrobenzopyran-5-ones **5a** and **5m** into isoflavan and flavan derivatives **21** and **22** were carried out (Chart 7), because isoflavan and flavan are structural motifs found in a number of biologically active natural products.<sup>29–32</sup> On the basis of a reported procedure for the aromatization of cyclohexenone,<sup>33</sup> reaction of **5a** and **5m** with iodine in methanol followed by aromatization using a combination of LiI and Li<sub>2</sub>CO<sub>3</sub> afforded 5-hydroxyisoflavan (**21**) and 5-hydroxyflavan (**22**) in 68 and 61% yields, respectively.

In conclusion, a regioselective ring-opening cyclization of spirocyclopropanes with dimethylsulfoxonium methylide has been developed, which affords 2-nonsubstituted hexahydrobenzopyran-5-ones in up to 83% yields. Spirocyclopropanes derived from cycloheptane- and cyclopentane-1,3-diones could be applied to this reaction. It was also found that sulfoxonium ethylide, butylide, and benzylide can be used in the present protocol. Moreover, it was shown that the dimethyl group can act as a dummy substituent. The obtained products were readily converted into flavan and isoflavan derivatives. Further

application of the present method in the synthesis of a variety of flavan- and isoflavan-based natural products is currently in progress.

## Experimental

**General** Melting points are uncorrected. IR spectra were recorded on a JASCO FT/IR-460 Plus spectrophotometer and absorbance bands are reported in wavenumber (cm<sup>-1</sup>). All NMR spectra were recorded using a JEOL JNM-ECX400P spectrometer. <sup>1</sup>H-NMR spectra were recorded at 400 or 500 MHz. Chemical shifts are reported relative to internal standard (tetramethylsilane at δ<sub>H</sub> 0.00, CDCl<sub>3</sub> at δ<sub>H</sub> 7.26, or (CD<sub>3</sub>)<sub>2</sub>SO at δ<sub>H</sub> 2.50). Data are presented as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, m = multiplet), coupling constant and integration. <sup>13</sup>C-NMR spectra were recorded at 100 or 126 MHz. The following internal reference was used (CDCl<sub>3</sub> at δ<sub>C</sub> 77.0 or (CD<sub>3</sub>)<sub>2</sub>SO at δ<sub>C</sub> 39.5). All <sup>13</sup>C-NMR spectra were determined with complete proton decoupling. High-resolution mass spectra (HR-MS) were determined with JEOL JMS-GCmate II instrument [electron ionization (EI)] and Thermo Scientific LTQ Orbitrap XL ETD [electrospray ionization (ESI)]. Column chromatography was performed on Silica Gel 60 PF<sub>254</sub> (Nacalai Tesque, Kyoto, Japan) and Kanto silica gel 60N (63–210 mesh) under pressure. Analytical TLC was carried out on Merck Kieselgel 60F<sub>254</sub> plates. Visualization was accomplished with UV light and phosphomolybdic acid stain solution followed by heating.

Reagents were used as received unless otherwise noted. Sodium hydride (60% dispersion in mineral oil) was washed with three portions of dry hexane to remove the mineral oil and the remaining sodium hydride was dried *in vacuo*. Dehydrated DMSO, DMF, CH<sub>2</sub>Cl<sub>2</sub>, toluene, THF, acetonitrile, and methanol were purchased from Kanto Chemical Co., Inc. (Tokyo, Japan) and Wako Pure Chemical Corporation (Osaka, Japan). 1-Phenylspiro[2.5]octane-4,8-dione (**3a**),<sup>20</sup> 6,6-dimethyl-1-phenylspiro[2.5]octane-4,8-dione (**3b**),<sup>20</sup> 1-(4-methylphenyl)-spiro[2.5]octane-4,8-dione (**3c**),<sup>20</sup> 1-(4-bromophenyl)-spiro[2.5]octane-4,8-dione (**3d**),<sup>20</sup> spiro[2.5]octane-4,8-dione (**3e**),<sup>23</sup> 6,6-dimethylspiro[2.5]octane-4,8-dione (**3f**),<sup>23</sup> 6-methylspiro[2.5]octane-4,8-dione (**3g**),<sup>23</sup> 6-phenylspiro[2.5]octane-4,8-dione (**3h**),<sup>23</sup> 1-butylspiro[2.5]octane-4,8-dione (**3i**),<sup>17</sup> 1-phenylspiro[2.4]heptane-4,7-dione (**10**),<sup>20</sup> 1,1-diacetyl-2-phenylcyclopropane (**12**),<sup>23</sup> and triethylsulfoxonium chloride (**14**)<sup>24</sup> were prepared according to literature procedures.

**Typical Procedure for the Ring-Opening Cyclization of Spirocyclopropane **3** with Sulfoxonium Salt **7**: 3-Phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (**5a**) (Table 1, Entry 9)** Trimethylsulfoxonium chloride (**7b**) (58 mg, 0.45 mmol) was added to a suspension of sodium hydride (8.6 mg, 0.36 mmol) in DMSO (1.5 mL) at room temperature. After stirring for 30 min, 1-phenylspiro[2.5]octane-4,8-dione (**3a**) (64 mg, 0.30 mmol) was added to the mixture. After stirring at room temperature for 12 h, the reaction was quenched with water (3 mL) and the whole mixture was extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine (10 mL) and dried over anhydrous MgSO<sub>4</sub>. The filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, 30% EtOAc in hexane) to provide **5a** (56 mg, 82%) as a white solid: mp 117.0–117.5°C; IR (KBr, cm<sup>-1</sup>) 2949, 1640, 1617, 1398, 1379, 1215, 1188, 1129,

1008, 981, 764, 702; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.34 (t, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 2H), 4.32 (ddd, *J* = 10.8, 4.0, 2.0 Hz, 1H), 3.90 (td, *J* = 10.8, 2.8 Hz, 1H), 3.04 (tt, *J* = 10.8, 4.0 Hz, 1H), 2.73 (ddd, *J* = 16.4, 4.0, 2.0 Hz, 1H), 2.46–2.29 (m, 5H), 2.04–1.92 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 198.1, 171.0, 140.6, 128.7, 127.3, 127.1, 111.6, 71.4, 37.8, 36.6, 28.4, 24.9, 20.8; HR-MS (EI) *m/z* Calcd for C<sub>15</sub>H<sub>16</sub>O<sub>2</sub> (M<sup>+</sup>) 228.1150. Found 228.1142.

**7,7-Dimethyl-3-phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5b)** (Table 2, Entry 1) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5b** was prepared from **3b** (73 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 25% EtOAc in hexane) to provide **5b** (64 mg, 83%) as a white solid: mp 92.0–92.5°C; IR (KBr, cm<sup>-1</sup>) ν 2952, 1651, 1624, 1455, 1395, 1377, 1215, 1168, 1125, 1026, 765, 702; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 2H), 4.31 (ddd, *J* = 10.4, 4.0, 2.4 Hz, 1H), 3.92 (t, *J* = 10.4 Hz, 1H), 3.04 (tt, *J* = 10.4, 4.0 Hz, 1H), 2.74 (m, 1H), 2.38–2.22 (m, 5H), 1.09 (s, 3H), 1.08 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 197.7, 169.2, 140.6, 128.7, 127.3, 127.1, 110.2, 71.4, 50.5, 42.1, 37.7, 32.1, 29.0, 27.7, 24.5; HR-MS (EI) *m/z* Calcd for C<sub>17</sub>H<sub>20</sub>O<sub>2</sub> (M<sup>+</sup>) 256.1463. Found 256.1450.

**3-(4-Methylphenyl)-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5c)** (Table 2, Entry 2) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5c** was prepared from **3c** (68 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 30% EtOAc in hexane) to provide **5c** (60 mg, 82%) as a white solid: mp 72.5–73.0°C; IR (KBr, cm<sup>-1</sup>) ν 2940, 1645, 1620, 1518, 1463, 1395, 1213, 1186, 1128, 1080, 1009, 980, 817; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.14 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 4.29 (ddd, *J* = 10.8, 4.0, 2.4 Hz, 1H), 3.86 (t, *J* = 10.8 Hz, 1H), 3.00 (tt, *J* = 10.8, 4.0 Hz, 1H), 2.71 (ddq, *J* = 16.4, 5.6, 1.6 Hz, 1H), 2.45–2.38 (m, 4H), 2.33 (s, 3H), 2.31 (m, 1H), 2.05–1.91 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 198.0, 170.9, 137.4, 136.7, 129.4, 127.1, 111.6, 71.4, 37.3, 36.6, 28.3, 24.8, 21.0, 20.8; HR-MS (EI) *m/z* Calcd for C<sub>16</sub>H<sub>18</sub>O<sub>2</sub> (M<sup>+</sup>) 242.1307. Found 242.1340.

**3-(4-Bromophenyl)-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5d)** (Table 2, Entry 3) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5d** was prepared from **3d** (88 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **5d** (65 mg, 71%) as a white solid: mp 125.0–125.5°C; IR (KBr, cm<sup>-1</sup>) ν 2939, 1645, 1619, 1489, 1462, 1395, 1214, 1187, 1130, 1106, 1072, 1008, 978, 825; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.46 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 4.28 (ddd, *J* = 10.4, 3.2, 2.4 Hz, 1H), 3.87 (t, *J* = 10.4 Hz, 1H), 3.01 (tt, *J* = 10.4, 3.2 Hz, 1H), 2.71 (dd, *J* = 16.4, 3.2 Hz, 1H), 2.45–2.35 (m, 4H), 2.29 (dd, *J* = 16.4, 10.4 Hz, 1H), 2.04–1.93 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 197.9, 170.9, 139.5, 131.8, 129.0, 120.9, 111.3, 71.0, 37.2, 36.6, 28.3, 24.7, 20.8; HR-MS (EI) *m/z* Calcd for C<sub>15</sub>H<sub>15</sub>BrO<sub>2</sub> (M<sup>+</sup>) 306.0255. Found 306.0235.

**2,3,4,6,7,8-Hexahydro-5H-1-benzopyran-5-one (5e)** (Table 2, Entry 4) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5e** was prepared from **3e** (41 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The

crude product was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **5e** (35 mg, 78%) as a white solid: mp 41.5–42.0°C; IR (KBr, cm<sup>-1</sup>) ν 2941, 1644, 1617, 1399, 1275, 1228, 1178, 1131, 1092, 964, 859; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 4.10 (t, *J* = 5.2 Hz, 2H), 2.39–2.35 (m, 4H), 2.24 (t, *J* = 6.4 Hz, 2H), 1.95 (quint, *J* = 6.4 Hz, 2H), 1.90–1.84 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 198.2, 171.5, 111.6, 67.3, 36.6, 28.6, 21.4, 20.8, 17.5; HR-MS (EI) *m/z* Calcd for C<sub>9</sub>H<sub>12</sub>O<sub>2</sub> (M<sup>+</sup>) 152.0837. Found 152.0801.

**7,7-Dimethyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5f)** (Table 2, Entry 5) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5f** was prepared from **3f** (50 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 25% EtOAc in hexane) to provide **5f** (40 mg, 74%) as a colorless oil: IR (film, cm<sup>-1</sup>) ν 2955, 1654, 1626, 1397, 1372, 1270, 1232, 1200, 1165, 1125, 1089, 1065, 960; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ: 4.10 (t, *J* = 5.0 Hz, 2H), 2.26–2.23 (m, 6H), 1.87 (quint, *J* = 5.0 Hz, 2H), 1.06 (s, 6H); <sup>13</sup>C-NMR (126 MHz, CDCl<sub>3</sub>) δ: 197.9, 169.7, 110.2, 67.4, 50.5, 42.4, 31.9, 28.5, 28.3, 21.4, 17.2; HR-MS (EI) *m/z* Calcd for C<sub>11</sub>H<sub>16</sub>O<sub>2</sub> (M<sup>+</sup>) 180.1150. Found 180.1146.

**7-Methyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5g)** (Table 2, Entry 6) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5g** was prepared from **3g** (46 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **5g** (37 mg, 74%) as a white solid: mp 76.0–76.5°C; IR (KBr, cm<sup>-1</sup>) ν 2948, 1644, 1615, 1396, 1298, 1225, 1134, 1066, 964, 916; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 4.17 (dt, *J* = 10.8, 6.4 Hz, 1H), 4.02 (ddd, *J* = 10.8, 7.6, 4.0 Hz, 1H), 2.44 (m, 1H), 2.36 (dd, *J* = 15.6, 2.4 Hz, 1H), 2.31–2.01 (m, 5H), 1.93–1.81 (m, 2H), 1.06 (d, *J* = 5.6 Hz, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 198.2, 170.9, 111.1, 67.4, 45.0, 36.7, 28.4, 21.4, 21.0, 17.4; HR-MS (EI) *m/z* Calcd for C<sub>10</sub>H<sub>14</sub>O<sub>2</sub> (M<sup>+</sup>) 166.0994. Found 166.0998.

**7-Phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5h)** (Table 2, Entry 7) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5h** was prepared from **3h** (64 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 30% EtOAc in hexane) to provide **5h** (48 mg, 71%) as a white solid: mp 78.0–78.5°C; IR (KBr, cm<sup>-1</sup>) ν 2944, 1647, 1613, 1398, 1276, 1182, 1128, 1091, 1062, 964, 763, 704; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.34 (t, *J* = 7.2 Hz, 2H), 7.25–7.23 (m, 3H), 4.22 (m, 1H), 4.05 (td, *J* = 10.4, 3.6 Hz, 1H), 3.34 (tt, *J* = 11.6, 4.4 Hz, 1H), 2.71–2.54 (m, 4H), 2.36–2.21 (m, 2H), 1.91–1.90 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ: 197.2, 170.6, 143.0, 128.7, 126.9, 126.6, 111.4, 67.6, 43.7, 38.9, 36.1, 21.4, 17.5; HR-MS (EI) *m/z* Calcd for C<sub>15</sub>H<sub>16</sub>O<sub>2</sub> (M<sup>+</sup>) 228.1150. Found 228.1147.

**3-Butyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5i)** and **4-Butyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5i')** (Table 2, Entry 8) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5i** and **5i'** were prepared from **3i** (58 mg, 0.30 mmol) with **7b** (58 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 15% EtOAc in hexane) to provide **5i** (38 mg, 62%) as a colorless oil and **5i'** (13 mg, 21%) as a colorless oil. **5i**: IR (neat, cm<sup>-1</sup>) ν 2929, 1655, 1625, 1395, 1377, 1215, 1188, 1132, 1006, 754; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)

$\delta$ : 4.15 (ddd,  $J=10.4, 3.6, 2.4$ Hz, 1H), 3.59 (t,  $J=10.4$ Hz, 1H), 2.49 (ddd,  $J=15.2, 4.4, 2.0$ Hz, 1H), 2.42–2.30 (m, 4H), 2.01–1.89 (m, 2H), 1.87–1.70 (m, 2H), 1.46–1.19 (m, 6H), 0.90 (t,  $J=7.2$ Hz, 3H);  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ )  $\delta$ : 198.3, 171.3, 111.1, 71.5, 36.6, 31.5, 31.4, 28.7, 28.4, 24.1, 22.7, 20.8, 13.9; HR-MS (EI)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{20}\text{O}_2$  ( $\text{M}^+$ ) 208.1463. Found 208.1445. **5i**: IR (neat,  $\text{cm}^{-1}$ )  $\nu$  2952, 1653, 1615, 1396, 1372, 1277, 1182, 1124, 1083, 1022;  $^1\text{H-NMR}$  (400MHz,  $\text{CDCl}_3$ )  $\delta$ : 4.18 (dtd,  $J=10.8, 4.0, 1.2$ Hz, 1H), 4.03 (td,  $J=10.8, 4.0$ Hz, 1H), 2.61 (m, 1H), 2.43–2.27 (m, 4H), 1.92 (quint,  $J=6.4$ Hz, 2H), 1.81–1.70 (m, 2H), 1.61 (m, 1H), 1.38–1.23 (m, 4H), 1.11 (tdd,  $J=9.2, 8.4, 5.2$ Hz, 1H), 0.89 (t,  $J=6.4$ Hz, 3H);  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ )  $\delta$ : 197.7, 170.7, 116.1, 63.5, 37.2, 33.5, 29.4, 28.8, 26.7, 24.7, 22.7, 20.9, 14.1; HR-MS (EI)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{20}\text{O}_2$  ( $\text{M}^+$ ) 208.1463. Found 208.1483.

**Preparation of 1-Phenylspiro[2.6]nonane-4,9-dione (8) (Table 2, Entry 9)** According to our reported procedure for the synthesis of spirocyclopropanes from cycloalkane-1,3-diones with sulfonium salt,<sup>20</sup> **8** was prepared from cycloheptane-1,3-dione with (2-bromo-1-phenylethyl)-dimethylsulfonium bromide. Powdered  $\text{K}_2\text{CO}_3$  (726mg, 3.00mmol) and cycloheptane-1,3-dione (221mg, 1.75mmol) were added to a suspension of the sulfonium salt (857mg, 2.63mmol) in EtOAc (17.5mL). After stirring at room temperature for 8h, the sulfonium salt (286mg, 0.87mmol) and powdered  $\text{K}_2\text{CO}_3$  (242mg, 1.75mmol) were further added to the reaction mixture. After stirring at room temperature for 2h, the reaction mixture was filtered through a Celite pad and the filter cake was rinsed with EtOAc (100mL). Combined filtrates were washed with water (30mL) and the aqueous layer was extracted with EtOAc ( $2 \times 15$ mL). The combined organic layer was washed with brine (30mL) and dried over anhydrous  $\text{MgSO}_4$ . The filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, 1:1 Et<sub>2</sub>O/hexane) to provide **8** (332mg, 83%) as a white solid: mp 76.5–77.0°C; IR (KBr,  $\text{cm}^{-1}$ )  $\nu$  2945, 1701, 1677, 1496, 1457, 1333, 1221, 1205, 1127, 1110, 966, 948, 897, 782, 754;  $^1\text{H-NMR}$  (400MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.28–7.19 (m, 3H), 7.12–7.09 (m, 2H), 3.37 (t,  $J=8.0$ Hz, 1H), 2.73 (m, 1H), 2.64 (dt,  $J=12.8, 4.4$ Hz, 1H), 2.39 (dd,  $J=8.0, 4.0$ Hz, 1H), 2.32 (m, 1H), 2.03–1.86 (m, 4H), 1.81 (m, 1H), 1.71 (dd,  $J=8.8, 4.4$ Hz, 1H);  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ )  $\delta$ : 206.0, 205.3, 133.9, 128.3, 128.2, 127.4, 52.4, 41.9, 41.8, 38.7, 24.0, 22.3, 20.8; HR-MS (EI)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{16}\text{O}_2$  ( $\text{M}^+$ ) 228.1150. Found 228.1163.

**3-Phenyl-3,4,6,7,8,9-hexahydrocyclohepta[b]pyran-5(2H)-one (9) (Table 2, Entry 9)** According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **9** was prepared from **8** (68mg, 0.30mmol) with **7b** (58mg, 0.45mmol). The crude product was purified by column chromatography (silica gel, 20% EtOAc in hexane) to provide **9** (47mg, 64%) as a colorless oil: IR (film,  $\text{cm}^{-1}$ )  $\nu$  2939, 1639, 1611, 1455, 1375, 1349, 1235, 1195, 1182, 1152, 1107, 1029, 995, 956, 757, 700;  $^1\text{H-NMR}$  (400MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.33 (t,  $J=7.2$ Hz, 2H), 7.27–7.19 (m, 3H), 4.28 (dt,  $J=10.4, 4.0$ Hz, 1H), 3.84 (t,  $J=10.4$ Hz, 1H), 2.96 (tt,  $J=10.4, 4.0$ Hz, 1H), 2.81 (dd,  $J=16.4, 4.0$ Hz, 1H), 1.80 (m, 1H), 2.63–2.59 (m, 3H), 2.32 (dd,  $J=16.8, 10.4$ Hz, 1H), 1.92–1.75 (m, 4H);  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ )  $\delta$ : 201.3, 171.4, 140.9, 128.7, 127.3, 127.0, 114.0, 71.3, 41.2, 37.7, 32.1, 27.5, 23.5, 21.1;

HR-MS (EI)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{18}\text{O}_2$  ( $\text{M}^+$ ) 242.1307. Found 242.1320.

**3-Phenyl-3,4,6,7-tetrahydrocyclopenta[b]pyran-5(2H)-one (11) (Table 2, Entry 10)** According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **11** was prepared from **10** (60mg, 0.30mmol) with **7b** (58mg, 0.45mmol). The crude product was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **11** (26mg, 41%) as a white solid: mp 107.5–108.0°C; IR (KBr,  $\text{cm}^{-1}$ )  $\nu$  2932, 1681, 1625, 1460, 1402, 1237, 1116, 956, 768, 708;  $^1\text{H-NMR}$  (400MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.36 (t,  $J=7.2$ Hz, 2H), 7.28 (t,  $J=7.2$ Hz, 1H), 7.21 (d,  $J=7.2$ Hz, 2H), 4.44 (ddd,  $J=10.8, 4.0, 2.0$ Hz, 1H), 4.09 (t,  $J=10.8$ Hz, 1H), 3.06 (tt,  $J=10.8, 4.4$ Hz, 1H), 2.63–2.55 (m, 3H), 2.51–2.48 (m, 2H), 2.36 (m, 1H);  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.5, 183.9, 139.8, 128.9, 127.4, 115.3, 73.3, 37.5, 33.7, 26.2, 23.4; HR-MS (EI)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{14}\text{O}_2$  ( $\text{M}^+$ ) 214.0994. Found 214.1007.

**Preparation of Tributylsulfonium Chloride (17) (Chart 5)** Dibutyl sulfide (**15**) (920mg, 5.00mmol), butyl iodide (805mg, 5.50mmol) and iodine (635mg, 2.50mmol) were heated at 70°C and stirred in the dark for 24h. The resulting mixture was then transferred to a flask containing water (15mL) and  $\text{CH}_2\text{Cl}_2$  (10mL). After the addition of benzyltributylammonium chloride (1.56g, 5.00mmol), the reaction mixture was stirred at room temperature for 24h. The aqueous layer was separated from the reaction mixture and washed with  $\text{CH}_2\text{Cl}_2$  ( $5 \times 10$ mL). Evaporation of water *in vacuo* furnished the crude product **16** (1.05g, approx. 4.40mmol) as a colorless oil, which was used in the next step without further purification.

$\text{RuCl}_3$  (46mg, 0.22mmol) was added to a biphasic solution of crude product **16** in acetonitrile (6.3mL),  $\text{CH}_2\text{Cl}_2$  (6.3mL), and water (9.4mL). The mixture was stirred vigorously at room temperature for 10min and then  $\text{NaIO}_4$  (3.77g, 17.6mmol) was added in 5 portions over 10min to the brown colored solution. After stirring at room temperature for 12h, the reaction was quenched with MeOH (20mL) and the resulting suspension was filtered through a Celite pad, and the filter cake was rinsed with MeOH (20mL). The filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, 4:4:1  $\text{CH}_2\text{Cl}_2$ /hexane/MeOH) to provide **17** (206mg, 18% from **15**) as a white solid: mp 99.0–99.5°C; IR (KBr,  $\text{cm}^{-1}$ )  $\nu$  2960, 2872, 1469, 1385, 1183, 1091, 936, 750;  $^1\text{H-NMR}$  (400MHz,  $\text{CDCl}_3$ )  $\delta$ : 4.39 (t,  $J=7.6$ Hz, 6H), 1.93 (quint,  $J=7.6$ Hz, 6H), 1.60 (sext,  $J=7.6$ Hz, 6H), 1.03 (t,  $J=7.6$ Hz, 9H);  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ )  $\delta$ : 49.6, 22.0, 21.6, 13.5; HR-MS (ESI+)  $m/z$  Calcd for  $\text{C}_{24}\text{H}_{54}\text{ClO}_2\text{S}_2$  [ $^t\text{Bu}_3\text{SO}^+\text{Cl}^-$ ] 473.3248. Found 473.3261.

**Preparation of Benzyldimethylsulfonium Chloride (20) (Chart 5)** Dimethyl sulfide (**18**) (1.86g, 30.0mmol) and benzyl bromide (855mg, 5.00mmol) were stirred at room temperature for 24h. The resulting white precipitate was collected by suction, washed with Et<sub>2</sub>O (10mL), dried *in vacuo*, and then dissolved in water (15mL) and  $\text{CH}_2\text{Cl}_2$  (10mL). After the addition of benzyltributylammonium chloride (1.56g, 5.00mmol), the reaction mixture was stirred at room temperature for 24h. The aqueous layer was separated from the reaction mixture and washed with  $\text{CH}_2\text{Cl}_2$  ( $5 \times 10$ mL). Evaporation of water *in vacuo* furnished the crude product **19** (630mg, approx. 3.34mmol) as a colorless oil, which was used in the next step without further purification.

RuCl<sub>3</sub> (35 mg, 0.17 mmol) was added to a biphasic solution of crude product **19** in acetonitrile (4.8 mL), CH<sub>2</sub>Cl<sub>2</sub> (4.8 mL), and water (7.1 mL). The mixture was stirred vigorously at room temperature for 10 min and then NaIO<sub>4</sub> (2.86 g, 13.4 mmol) was added in 5 portions over 10 min to the brown colored solution. After stirring at room temperature for 12 h, the reaction was quenched with MeOH (20 mL) and the resulting suspension was filtered through a Celite pad, and the filter cake was rinsed with MeOH (20 mL). The filtrate was concentrated *in vacuo* and the crude solid was purified by recrystallization from MeOH/CHCl<sub>3</sub> to provide **20** (446 mg, 44% from benzyl bromide) as a white solid: mp 162.5–163.0°C; IR (KBr, cm<sup>-1</sup>)  $\nu$  2962, 2878, 1496, 1236, 1050, 958, 776, 700; <sup>1</sup>H-NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$ : 7.56–7.50 (m, 5H), 5.76 (s, 2H), 3.91 (s, 6H); <sup>13</sup>C-NMR (100 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$ : 131.8, 130.3, 129.4, 123.8, 56.5, 36.4; HR-MS (EI) *m/z* Calcd for C<sub>9</sub>H<sub>13</sub>ClO<sub>5</sub> (M<sup>+</sup>) 204.0376. Found 204.0390.

**rel-(2R,3S)-2-Methyl-3-phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5j)** (Chart 6) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5j** was prepared from **3a** (64 mg, 0.30 mmol) with **14**<sup>24</sup> (77 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **5j** (53 mg, 73%) as a white solid: mp 131.5–132.0°C; IR (KBr, cm<sup>-1</sup>)  $\nu$  2930, 1646, 1616, 1455, 1392, 1378, 1244, 1227, 1188, 1100, 1030, 987, 865, 758, 702; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.31 (t, *J* = 7.2 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 2H), 4.12 (dq, *J* = 10.0, 6.4 Hz, 1H), 2.68 (dd, *J* = 16.0, 5.2 Hz, 1H), 2.60 (td, *J* = 10.0, 5.2 Hz, 1H), 2.45–2.37 (m, 4H), 2.31 (dd, *J* = 16.0, 11.2 Hz, 1H), 2.06–1.92 (m, 2H), 1.14 (d, *J* = 6.4 Hz, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 198.0, 171.0, 141.7, 128.7, 127.7, 127.0, 111.9, 77.7, 45.2, 36.6, 28.5, 26.8, 20.9, 19.2; HR-MS (EI) *m/z* Calcd for C<sub>16</sub>H<sub>18</sub>O<sub>2</sub> (M<sup>+</sup>) 242.1307. Found 242.1303.

**rel-(2R,3S)-2-Propyl-3-phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5k)** (Chart 6) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5k** was prepared from **3a** (64 mg, 0.30 mmol) with **17** (115 mg, 0.45 mmol). The crude product was purified by column chromatography (silica gel, 30% EtOAc in hexane) to provide **5k** (58 mg, 74%) as a colorless oil: IR (neat, cm<sup>-1</sup>)  $\nu$  2957, 1652, 1624, 1392, 1223, 1187, 1112, 959, 760, 702; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.31 (t, *J* = 7.2 Hz, 2H), 7.24 (tt, *J* = 7.2, 1.6 Hz, 1H), 7.12 (dd, *J* = 7.2, 1.6 Hz, 2H), 4.03 (ddd, *J* = 8.8, 7.6, 4.0 Hz, 1H), 2.72–2.65 (m, 2H), 2.45–2.37 (m, 4H), 2.30 (ddt, *J* = 17.2, 12.0, 2.0 Hz, 1H), 2.04–1.93 (m, 2H), 1.51 (m, 1H), 1.41–1.26 (m, 3H), 0.82 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 198.0, 171.1, 142.0, 128.7, 127.7, 126.8, 111.7, 80.9, 43.3, 36.6, 34.8, 28.5, 27.0, 20.9, 18.1, 13.8; HR-MS (EI) *m/z* Calcd for C<sub>18</sub>H<sub>22</sub>O<sub>2</sub> (M<sup>+</sup>) 270.1620. Found 270.1620.

**rel-(2R,3S)-2,3-Diphenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5l)** (Chart 6) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5l** was prepared from **3a** (43 mg, 0.20 mmol) with **20** (61 mg, 0.30 mmol). The crude product was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **5l** (55 mg, 90%) as a white solid: mp 127.0–127.5°C; IR (KBr, cm<sup>-1</sup>)  $\nu$  2931, 1645, 1617, 1455, 1391, 1340, 1227, 1189, 1128, 1092, 1008, 982, 764; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.19–7.07 (m, 8H), 6.95 (d, *J* = 6.8 Hz, 2H), 4.94 (d, *J* = 10.0 Hz, 1H), 3.05 (dt, *J* = 10.0, 5.2 Hz, 1H), 2.79 (dd, *J* = 16.8, 5.2 Hz, 1H),

2.59–2.38 (m, 5H), 2.04 (quint, *J* = 6.0 Hz, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 198.0, 171.0, 140.4, 138.3, 128.3, 128.1, 128.0, 127.9, 127.0, 126.7, 112.0, 83.8, 45.2, 36.6, 28.5, 26.3, 20.9; HR-MS (EI) *m/z* Calcd for C<sub>21</sub>H<sub>20</sub>O<sub>2</sub> (M<sup>+</sup>) 304.1463. Found 304.1488.

**2-Phenyl-2,3,4,6,7,8-hexahydro-5H-1-benzopyran-5-one (5m)**<sup>27,28</sup> (Chart 6) According to the typical procedure for the ring-opening cyclization of **3a** with **7b**, **5m** was prepared from **3e** (41 mg, 0.30 mmol) with **20** (92 mg, 0.45 mmol) at 50°C. The crude product was purified by column chromatography (silica gel, 8:1.5:0.5 CH<sub>2</sub>Cl<sub>2</sub>/hexane/EtOAc) to provide **5m** (57 mg, 84%) as a colorless oil: IR (neat, cm<sup>-1</sup>)  $\nu$  2943, 1651, 1622, 1394, 1293, 1181, 1073, 759, 700; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.41–7.32 (m, 5H), 4.94 (dd, *J* = 10.4, 2.4 Hz, 1H), 2.52–2.35 (m, 5H), 2.28 (m, 1H), 2.17 (m, 1H), 2.05–1.97 (m, 2H) 1.90 (m, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 198.2, 171.5, 140.3, 128.6, 128.2, 125.9, 111.6, 79.1, 36.7, 29.1, 28.7, 20.9, 18.1.

**Typical Procedure for the Synthesis of Isoflavan and Flavan Derivatives: 5-Hydroxy-3-phenyl-3,4-dihydro-2H-1-benzopyran (21)** (Chart 7) Iodine (228 mg, 0.90 mmol) was added to a solution of **5a** (68 mg, 0.30 mmol) in MeOH (1.5 mL) at room temperature. After stirring for 3 h, the reaction mixture was quenched by addition of saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (3 mL), and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), and dried over anhydrous MgSO<sub>4</sub>. Filtration and evaporation *in vacuo* furnished the crude product (152 mg), which was used in the next step without further purification.

LiI (24 mg, 0.33 mmol) and Li<sub>2</sub>CO<sub>3</sub> (44 mg, 0.33 mmol) were added to a solution of crude product in DMF (3.0 mL). After stirring at reflux for 2.0 h, the reaction was cooled to room temperature and diluted with 20% EtOAc in hexane (3 mL). The reaction mixture was quenched by addition of saturated aqueous NH<sub>4</sub>Cl (3 mL), and the resulting mixture was extracted with 20% EtOAc in hexane (3 × 10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), and dried over anhydrous MgSO<sub>4</sub>. Filtration was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **21** (46 mg, 68%) as a pale yellow solid: mp 79.5–80.0°C; IR (KBr, cm<sup>-1</sup>)  $\nu$  3400, 2925, 1707, 1616, 1595, 1496, 1470, 1460, 1329, 1276, 1234, 1091, 1073, 1029, 980, 774, 757, 700; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.36 (t, *J* = 7.6 Hz, 2H), 7.29–7.24 (m, 3H), 6.99 (t, *J* = 8.4 Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 6.37 (d, *J* = 8.4 Hz, 1H), 4.87 (s, 1H), 4.35 (dq, *J* = 10.4, 1.6 Hz, 1H), 4.00 (t, *J* = 10.4, 1H), 3.22 (tt, *J* = 10.8, 4.0 Hz, 1H), 3.07 (ddd, *J* = 16.4, 5.6, 1.6 Hz, 1H), 2.80 (dd, *J* = 16.4, 12.4 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 155.5, 154.0, 141.3, 128.8, 127.4, 127.2, 127.1, 109.7, 109.1, 106.7, 70.4, 38.1, 26.6; HR-MS (EI) *m/z* Calcd for C<sub>15</sub>H<sub>14</sub>O<sub>2</sub> (M<sup>+</sup>) 226.0994. Found 226.0999.

**5-Hydroxy-2-phenyl-3,4-dihydro-2H-1-benzopyran (22)** (Chart 7) According to the typical procedure for the synthesis of **21**, **22** was prepared from **5m** (57 mg, 0.25 mmol). The crude product was purified by column chromatography (silica gel, 20% EtOAc in hexane) to provide **22** (34 mg, 61%) as a pale yellow solid: mp 103.5–104.0°C; IR (KBr, cm<sup>-1</sup>)  $\nu$  3404, 2925, 1704, 1616, 1592, 1496, 1465, 1339, 1278, 1201, 1055, 1017, 774, 758, 700; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.44–7.37

(m, 4H), 7.32 (t,  $J=7.2$  Hz, 1H), 6.99 (t,  $J=8.0$  Hz, 1H), 6.55 (d,  $J=8.0$  Hz, 1H), 6.37 (d,  $J=8.0$  Hz, 1H), 5.01 (dd,  $J=10.4$ , 2.4 Hz, 1H), 4.77 (s, 1H), 2.86–2.72 (m, 2H), 2.25 (m, 1H), 2.07 (m, 1H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 156.3, 153.9, 141.5, 128.5, 127.9, 127.2, 126.0, 109.6, 109.4, 106.6, 77.4, 29.3, 19.4; HR-MS (EI)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{14}\text{O}_2$  ( $\text{M}^+$ ) 226.0994. Found 226.1004.

**Conflict of Interest** The authors declare no conflict of interest.

**Supplementary Materials** The online version of this article contains supplementary materials.

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