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Oxidative Dimerization of 1*H*-Benzo[*f*]chromenes: Synthesis of Benzannulated Analogues of Spirobiflavonoids Welwitschins E and F

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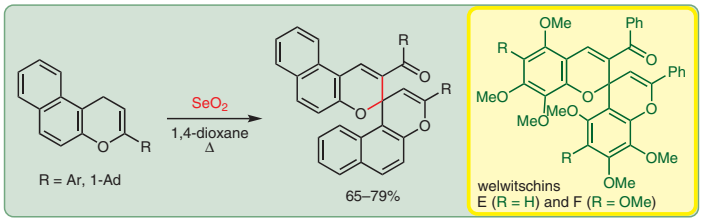

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Abstract A new oxidative transformation of 1*H*-benzo[*f*]chromenes into spirodimers under the action of selenium dioxide was discovered, leading to spirodimers, which are dibenzannulated analogues of naturally occurring welwitschins E and F. In the reaction, both MnO_2 and I_2O_5 can also be used as an oxidant. The protocol has advantages of mild reaction conditions and simple operation. At the same time, oxidation of 1*H*-benzo[*f*]chromenes with (diacetoxyiodo)benzene is accompanied by the formation of 3,3′-bibenzo[*f*]chromene as a dimer of a different structure. It was also found that 4*H*-chromenes under the action of various oxidants are cleaved to give chalcone.

Key words oxidation, dimerization, 1*H*-benzo[*f*]chromenes, spirobiflavonoids, welwitschins, selenium dioxide, (diacetoxyiodo)benzene, 4*H*-chromenes

The biflavonoids are widely distributed in the plant kingdom and display a broad variety of biological activities. However, their use as pharmaceuticals has been limited due to the following reasons: low abundance in the plant material and their unavailability, inseparable mixtures, tedious purification techniques which often include extraction with large quantities of solvents and multiple chromatographic separations. One of the possible solutions of these problems is the development of efficient synthetic methodologies, which can produce not only the natural products but also their synthetic analogues for medicinal applications.

Spirobiflavonoids, which contain a spiro C-atom, are relatively recently discovered members of the flavonoid class.[1] They are of interest due to the fact that two new racemic products welwitschins E and F have been isolated from the roots of *Uvaria welwitschii*, whose extracts possess antileukemic action (Scheme 1).[2] In addition, it turned out that welwitschin E has a strong antiplasmoid activity.[3] Based on the biflavonoid isolated from *Reineckia carnea*, widely used in Chinese traditional medicine, a drug was proposed for the treatment of renal carcinoma.[4] On the other hand, condensed spiropyrans can be used as effective molecular switches that are sensitive to the pH of the medium (**A**), temperature (**B**), or UV-light (**C**).[5] Under the action of external factors, the pyran rings open with the formation of a polyene or zwitterionic structure, which closes back into a cyclic structure under other conditions (Scheme 1). In this regard, it is of practical interest to develop a method for the synthesis of these compounds and their analogues.

Chromenes with various levels of saturation and oxidation are ubiquitous motifs frequently found in natural products and biologically active compounds. Chromenes themselves can be used as starting compounds for the preparation of flavonoids including such outstanding ones as flav-2-enes **D** (2-aryl-4*H*-chromenes) and their benzocondensed analogues. Being enol ethers, they possess high chemical reactivity and easily undergo different oxidative transformations. There is a limited number of oxidative transformations of flav-2-enes, many of which are not selective or are represented by single examples. The opening of the pyran ring of 2-aryl-4*H*-chromenes is observed upon oxidation with monoperoxyphthalic acid or OsO_4 with the formation of α,β-dihydro-α-hydroxychalcones **E** and 2-alkoxy-3-hydroxyflavans **F** in the presence of alcohols (Scheme 2).[6] Benzopyrylium salts **G** were obtained by oxidative dehydrogenation of 4*H*-chromenes with Koser's reagent[7] or trityl perchlorate,[6a,8] as well as by decarboxylation of 4-carboxyflav-2-enes with $Pb(OAc)_4$.[9] Flavones **H** were obtained from flav-2-enes under the action of $Tl(NO_3)_3{\cdot}5H_2O$ (TTN)[10] or $KMnO_4$.[11] In the presence of Brønsted or Lewis acids, 2-aryl-4*H*-chromenes undergo disproportionation to form 2-arylchromanes **I** and 2-arylbenzopyrylium salts **G**.[12] Previously, we disclosed that 1,3-diarylbenzo[*f*]chromenes rearrange into 2-acylnaphthofurans **J** under the action of SeO_2.[13] At the same time, the similar oxidation of 2,4-diaryl-4*H*-chromenes

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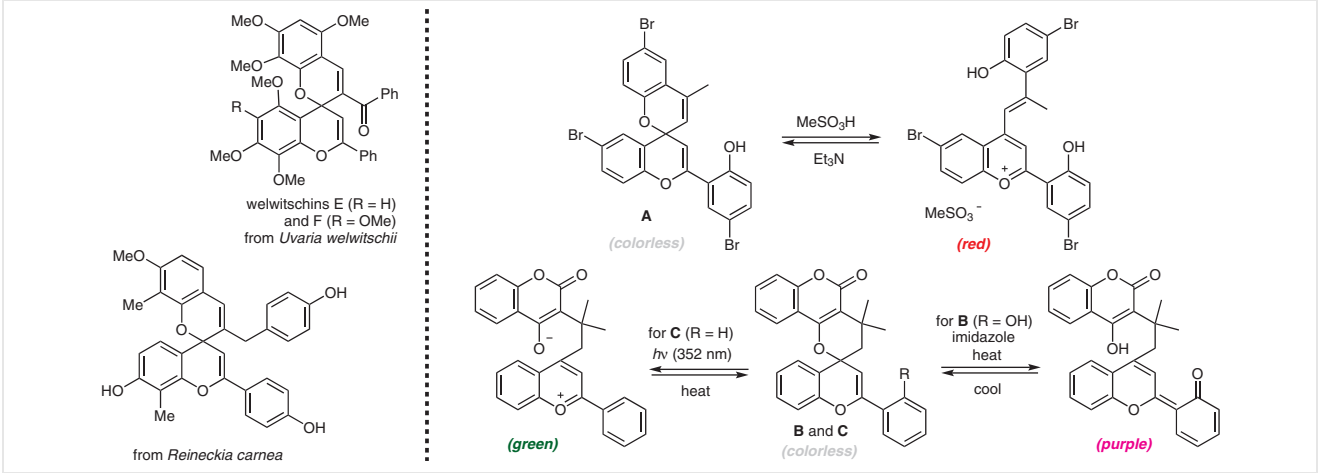
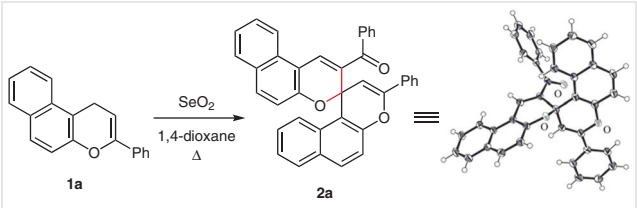


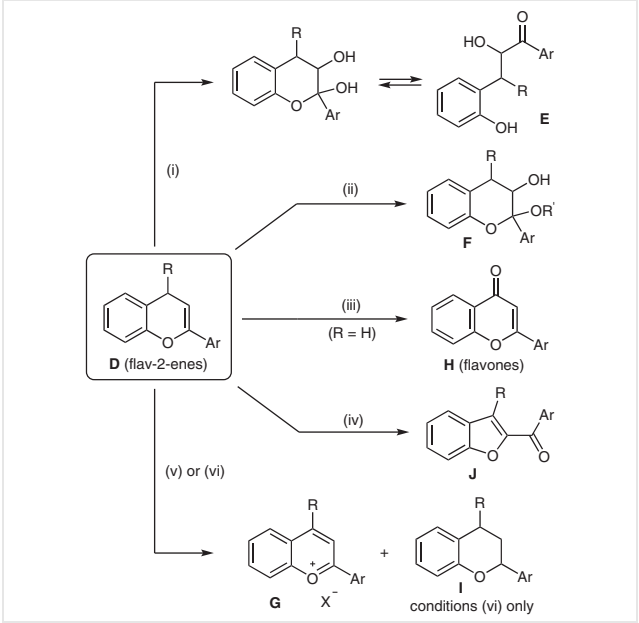
Scheme 1 Spiropyrans as natural products and molecular switchers

with $Pb(OAc)_4$ is not selective and leads to 2-acylbenzofurans in low yields.[14]

In continuation of our studies on the reactivity of 4*H*-chromenes, we carried out the oxidation of 3-phenyl-1*H*-benzo[*f*]chromene (**1a**) with a widely used reagent in organic synthesis: selenium dioxide.[15] The product formed in this reaction contained a double set of equally integrated signals in the aromatic region, which indicated the dimeric structure of the product. At the same time, the presence of the signal of the quaternary carbon atom at 77.4 ppm in the ^{13}C NMR spectrum suggested the spirocyclic structure of the product. These assumptions were confirmed by the X-ray analysis; the product **2a** turned out to be a dibenzocondensed analogue of the welwitschins E and F (Scheme 3).



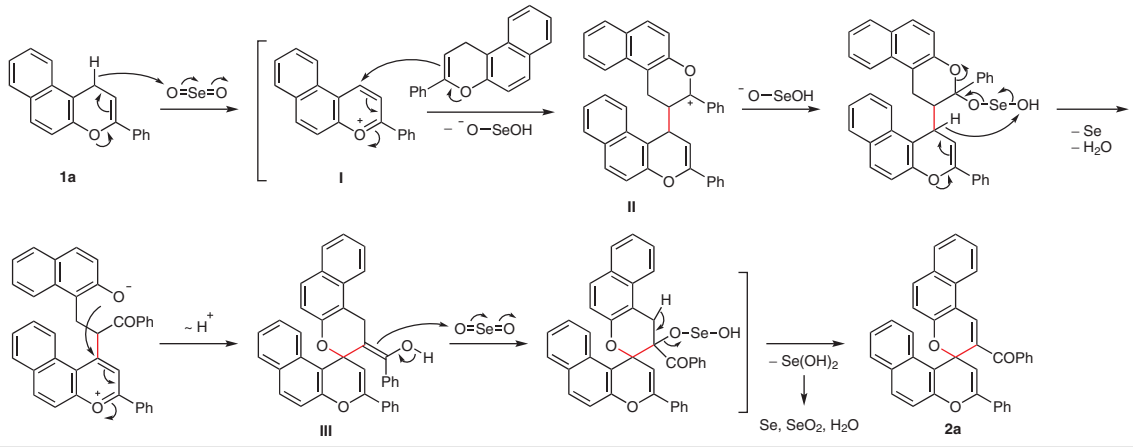
Scheme 3 Synthesis and structure of 1,3′-spirobi(benzo[*f*]chromene) **2a**



Scheme 2 Known oxidative transformations of flav-2-enes. *Reagents and conditions*: (i) RCO_3H or OsO_4, then H_2O; (ii) RCO_3H, R′OH; (iii) TTN or $KMnO_4$; (iv) SeO_2 or $Pb(OAc)_4$; (v) Koser's reagent or trityl perchlorate, or $Pb(OAc)_4$; (vi) Brønsted or Lewis acid.

Allegedly, the mechanism of formation of spirodimer **2a** includes intermolecular hydride transfer from chromene **1a** to selenium dioxide with the formation of naphthopyrylium salt **I**, which as a Michael acceptor adds the second molecule of starting benzochromene **1a** to form dimeric resonance-stabilized carbocation **II**. Further reductive elimination of selenium followed by intramolecular cyclization lead to spirodimer **III**, which undergoes subsequent dehydrogenation under the action of SeO_2 with the formation of the final product (Scheme 4).

The structural similarity of the spirodimer **2a** and welwitschins E and F allowed us to assume that the discovered oxidative spirodimerization can provide access to the carbon skeleton of the latter, the synthetic approaches to which have not been described to date. In this regard, we decided to study the synthesis of the dimer **2a** from benzochromene **1a** as a model reaction (Table 1). Initially, we determined the effect of the amount and nature of oxidant on the product yield. The use of 0.5 equivalent of SeO_2 resulted to the spirodimer in 51% yield (Table 1, entry 1), while increasing the amount of oxidant to stoichiometric led to the product **2a** in 74% yield (entry 2). This observation is consistent with the proposed mechanism, according to which



Scheme 4 Proposed mechanism for the spirodimerization of benzo[*f*]chromene **1a**

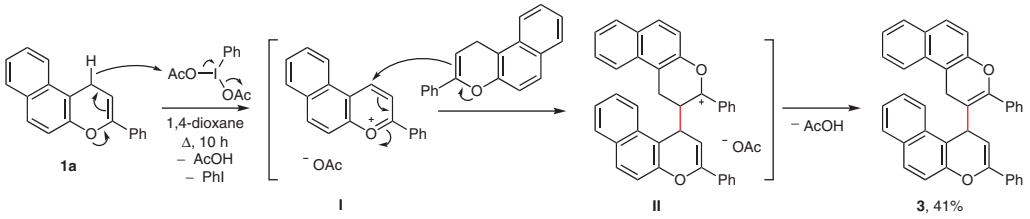
benzochromene **1a** and SeO_2 react in equimolar amounts. The use of an excess of SeO_2 also leads to a decrease in the yield of the product, apparently due to its subsequent oxidation (entry 3). In order to evaluate the limits of the reaction, we examined several other oxidants. We found that by treating of benzochromene **1a** with manganese dioxide we could obtain the desired product in 52% yield (entry 4). However, despite the use of excess of the oxidizing agent (5 equiv), the reaction required a longer time to complete (15 h). This can be explained by both the lower reactivity of manganese dioxide in comparison with selenium dioxide and its poor solubility in 1,4-dioxane. Further reaction screening using various oxidants did not reveal more suitable ones. Thus, only traces of the dimeric product were found when using the molybdenum oxide (entry 5). Such oxidants as Ag_2O, TeO_2, HgO, and $K_3[Fe(CN)_6]$ (entries 6–9) showed complete inertness in this reaction. In contrast, hypervalent iodine-based oxidants were found to be reactive towards benzochromene **1a**. To our delight, its oxidation with a stoichiometric amount of iodine pentoxide was successful and resulted in a spirodimer **2a** in 68% yield (entry 10). Oxidation of chromene **1a** with PIFA [phenyliodine(III) bis(trifluoracetate)] was nonselective and led to the formation of a complex mixture of unidentified products (entry 11).

Interestingly, the use of phenyliodine(III) diacetate (PIDA) (1.0 equiv) in the reaction with benzochromene **1a** allowed us to obtain 1,2′-bibenzo[*f*]chromene **3** as a dimeric product of different structure in 41% yield. The mechanism of this oxidative coupling is partially similar to that for the spirodimer **2a**. Initially, benzochromene **1a** undergoes hydride transfer to (diacetoxyiodo)benzene to form naphthopyrylium acetate **I**, which is converted into cation **II** due to conjugated addition of another benzochromene molecule. The deprotonation of the latter leads to 1,2′-dimer (Scheme 5).

Table 1 Optimization of the Reaction Conditions[a]

Entry	Oxidant	Time (h)	Yield of **2a** (%)
1	SeO_2, 0.5 equiv	8	51
2	SeO_2, 1.0 equiv	8	74
3	SeO_2, 1.5 equiv	8	63
4	MnO_2, 5.0 equiv	15	52
5	$MoO_3 \cdot H_2O$, 5.0 equiv	15	trace
6	Ag_2O, 2.0 equiv	10	–
7	TeO_2, 2.0 equiv	10	–
8	HgO, 2.0 equiv	10	–
9	$K_3[Fe(CN)_6]$, 2.0 equiv	10	–
10	I_2O_5, 1.0 equiv	1.5	68
11	PIFA, 1.0 equiv	3	complex mixture

[a] Reaction were performed in anhyd 1,4-dioxane under reflux.

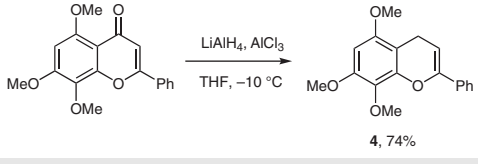


Scheme 5 Proposed mechanism for the formation of dimer **3**

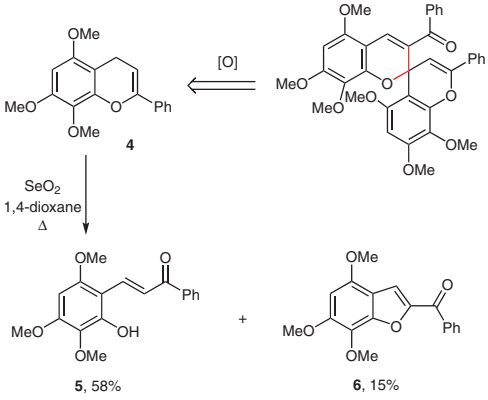
It should be noted that with a further increase in the amount of PIDA to 1.5 equivalents, the yield of dimer **3** decreases to 26%.

The ^{1}H NMR spectrum of product **3** shows characteristic doublets at 3.86 and 3.06 ppm with the geminal coupling constant ^2J = 19.8 Hz attributed to diastereotopic methylene protons. Protons H-1 and H-2 of another pyran fragment display two doublets at 5.27 and 5.72 ppm, respectively, with the vicinal coupling constant ^3J = 5.2 Hz. A distinguishing resonance at 21.6 ppm for methylene carbon, and 98.6 ppm and for methine carbon C-2 at double bond of pyran cycle are observed in the ^{13}C NMR spectrum of dimer **3**.

Inspired by these results, we decided to synthesize welwitschin E. We hypothesized that 4*H*-chromenes have similar reactivity towards oxidants as 1*H*-benzo[*f*]chromenes under mentioned conditions, which should have provided access to the welwitschins E and F. We assumed that welwitschin E could be obtained from 5,7,8-trimethoxyflav-2-ene **4** by its oxidative spirodimerization. Based on the availability of the starting materials, we prepared it from the previously described 5,7,8-trimethoxyflavone[16] by its reduction with a mixture of $LiAlH_4$ and $AlCl_3$ in Et_2O (Scheme 6).[17] However, the oxidation of 5,7,8-trimethoxyflav-2-ene **4** with SeO_2 under optimized conditions did not lead to the desired welwitschin E. Instead, chalcone **5** and 4,6,7-trimethoxy-2-benzoylbenzofuran (**6**) were isolated (Scheme 7). It is worth noting that the conversion of 4*H*-chromenes into benzofurans under action of selenium dioxide has recently been described,[7] while the oxidative cleavage of the 4*H*-chromenes into chalcones, to the best of our knowledge, is unprecedented.

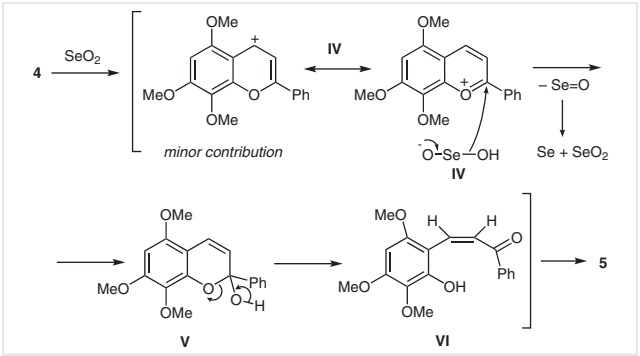


Scheme 6 Synthesis of 4*H*-chromene **4**



Scheme 7 Oxidation of the 4*H*-chromene **4**

The mechanism for the formation of chalcone **5** presumably includes hydride transfer from 4*H*-chromene **4** to selenium dioxide, addition of negatively charged oxygen atom of the $HSeO_2^-$ anion to the resulting benzopyrylium salt **IV** followed by elimination of selenium monoxide to give 2-hydroxy-2*H*-chromene **V**. Subsequent ring-opening and thermal isomerization of the resulting (*Z*)-chalcone **VI** lead to chalcone **5** (Scheme 8).



Scheme 8 Proposed mechanism for the formation of chalcone **5**

Due to this failure, we decided to carry out an additional screening of oxidants for 4*H*-chromene spirodimerization (Table 2). Oxidation of flavene **4** with selenium dioxide at lower temperatures (Table 2, entries 2, 3) or I_2O_5, Ag_2O, MoO_3, MnO_2 did not lead to the formation of benzofuran **6**, but the main product in all cases remained chalcone **5**. At the same time, HgO and TeO_2 appeared inert under the reaction conditions.

Table 2 Optimization of the Reaction Conditions[a]

Entry	Oxidant and temperature	Time (h)	Yield of **5** (%)
1	SeO_2, 1.0 equiv, 100 °C	4	58 + 15 of **6**
2	SeO_2, 1.0 equiv, 50 °C	4	66
3	SeO_2, 1.0 equiv, 25 °C	8	32
4	I_2O_5, 1.0 equiv, 100 °C	1	61
5	Ag_2O, 2.0 equiv, 100 °C	8	73
6	$MoO_3{\cdot}H_2O$, 5.0 equiv, 100 °C	15	70
7	MnO_2, 5.0 equiv, 100 °C	10	complex mixture
8[b]	HgO, 4.0 equiv, 100 °C	15	–
9[b]	TeO_2, 2.0 equiv, 100 °C	15	–

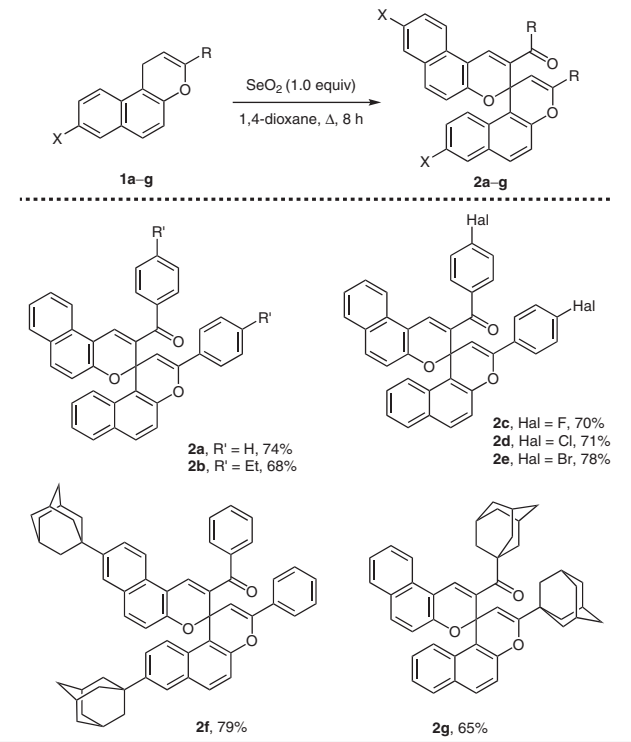
[a] Reactions were performed in anhyd 1,4-dioxane.
[b] Unreacted starting flavene **4** was recovered.

According to the proposed mechanism (Scheme 4), spirodimerization is possible in the case of sufficiently high electrophilicity of the γ-position in the pyrylium salts, which allows to attack it with the second molecule of starting chromene. It seems obvious that the positive charge at the γ-position of benzopyrylium salt **IV** is reduced com-

pared to that in naphthopyrylium salt **I** due to the double +M effect of two methoxy groups at C5 and C7. This leads to the localization of the positive charge at α-position with its subsequent attack by the $HSeO_2^-$ anion, transformation into 2*H*-chromene **V** and then into chalcone **5** (Scheme 7) instead of the desired spirodimerization.

We have also tried to introduce into this reaction 2-phenyl-4*H*-chromene and 2-(3,4,5-trimethoxyphenyl)-4*H*-chromene, which were obtained analogously to flavene **4** from 3′,4′,5′-trimethoxyflavone.[17] However, their oxidation with SeO_2 leads to a complex mixture of unidentified products in both cases.

Getting back to Table 1, the conditions as listed in entry 2 was chosen as the optimal condition for the oxidation of 1*H*-benzo[*f*]chromenes to spirodimers. We have successfully extended this approach to several other 3-arylbenzo[*f*]-chromenes **1b–f** and 3-(adamantan-1-yl)benzochromene **1g**. As shown in Scheme 9, spirodimers **2** were prepared in 65–79% yields. All reactions were carried out using equimolar ratio of benzochromene **1** and SeO_2.



Scheme 9 Substrate scope

The structures of all spirodimers were confirmed on the basis of their analytical data. The IR spectra show the presence of a carbonyl group (1647–1665 cm^{-1}). The characteristic feature of the ^{13}C NMR spectra is the presence of signal of quaternary carbon atom in the region 77.3–77.7 ppm.

In conclusion, we have developed an effective route to benzannulated analogues of naturally occurring spirobiflavonoids welwitschins E and F via oxidative dimerization of 3-aryl-substituted 1*H*-benzo[*f*]chromenes. It was found that the reaction of 3-phenyl-1*H*-benzo[*f*]chromene with (diacetoxyiodo)benzene leads to the formation of different dimeric product 1,2′-bibenzo[*f*]chromene. In addition, a new oxidative cleavage of 5,7,8-trimethoxy-2-phenyl-4*H*-chromene into chalcone under action of various oxidants has been discovered.

Melting points were determined by capillary method on a SRS OptiMelt MPA100 apparatus and are uncorrected. FTIR spectra were taken on a Shimadzu IR Affinity-1 spectrophotometer with single-reflection ATR accessory and are reported in cm^{-1}. ^1H, ^{19}F, and ^{13}C NMR spectra were recorded on a JEOL JNM-ECX 400 spectrometer (400, 376, and 100 MHz, respectively) in DMSO-d_6 or $CDCl_3$ solutions at ambient temperature, unless otherwise noted, relative to residual solvent signal [$CHCl_3$ δ = 7.26 (^1H), $CDCl_3$ δ = 77.0 (^{13}C); DMSO-d_6 δ = 2.50 (^1H), δ = 39.5 (^{13}C)] or to $CFCl_3$ (^{19}F) as internal standard. Chemical shifts and coupling constants were recorded in units of parts per million and hertz (Hz), respectively. Elemental analyses were carried out on a Euro Vector EA-3000 automatic CHNS analyzer. The reaction progress was monitored by TLC on aluminum foil-backed silica gel plates (Merck, Kieselgel 60 F254), visualization under UV light and in I_2 vapor. Organic solutions were concentrated under reduced pressure on a rotary evaporator. All commercial solvents and reagents were used without additional purification.

1,3′-Spirobi(benzo[*f*]chromenes) 2; General Procedure

1*H*-Benzo[*f*]chromene **1** (1.0 mmol) and SeO_2 (0.11 g, 1.0 mmol) were refluxed for 8 h in anhyd 1,4-dioxane (8 mL). After completion of the reaction, the mixture was cooled, and the precipitated Se was filtered off. The solvent was evaporated in vacuo. The crude product was purified by column chromatography (silica gel, $CHCl_3/CCl_4$ 1:1) and recrystallized (MeOH/THF 7:1).

Phenyl[3-phenyl-1,3′-spirobi(benzo[*f*]chromen)-2′-yl]methanone (2a)[18]

Yield: 196 mg (74%); yellow solid; mp 253–254 °C (dec.).

IR (ATR): 3059, 1667, 1641, 1622, 1599, 1562, 1447, 1435, 1337, 1298, 1276, 1236, 1211, 1194, 1080, 1026, 949, 866, 839, 812, 745, 723, 689 cm^{-1}.

^1H NMR (DMSO-d_6 at 80 °C, 400 MHz): δ = 8.75 (d, *J* = 8.5 Hz, 1 H), 8.01–7.82 (m, 8 H), 7.64 (d, *J* = 7.1 Hz, 2 H), 7.57–7.33 (m, 11 H), 7.10 (d, *J* = 9.0 Hz, 1 H), 6.39 (s, 1 H).

^{13}C NMR (DMSO-d_6 at 80 °C, 100 MHz): δ = 192.5 (C), 151.5 (C), 150.1 (C), 146.8 (C), 138.0 (C), 134.53 (C), 134.49 (CH), 132.9 (C), 132.6 (CH), 131.7 (2 C), 131.3 (CH), 130.8 (C), 130.1 (CH), 130.0 (CH), 129.85 (2 × CH), 129.79 (C), 129.3 (2 × CH), 129.1 (2 × CH), 128.8 (2 × CH), 128.5 (CH), 127.2 (CH), 126.5 (CH), 125.7 (2 × CH), 124.9 (CH), 124.8 (CH), 121.8 (CH), 118.7 (CH), 118.0 (CH), 112.8 (C), 112.6 (C), 98.8 (CH), 77.4 (C).

Anal. Calcd for $C_{38}H_{24}O_3$: C, 86.34; H, 4.58. Found: C, 86.23; H, 4.52.

(4-Ethylphenyl)[3-(4-ethylphenyl)-1,3′-spirobi(benzo[*f*]chromen)-2′-yl]methanone (2b)

Yield: 199 mg (68%); yellow solid; mp 228–230 °C (dec.).

IR (ATR): 2965, 1665, 1641, 1624, 1605, 1564, 1514, 1458, 1410, 1339, 1298, 1256, 1237, 1126, 1018, 1001, 947, 922, 866, 835, 816, 744 cm^{-1}.

^1H NMR (DMSO-d_6 at 120 °C, 400 MHz): δ = 8.74 (d, *J* = 8.7 Hz, 1 H), 8.01–7.83 (m, 6 H), 7.70 (d, *J* = 7.4 Hz, 2 H), 7.57–7.53 (m, 3 H), 7.47–7.41 (m, 3 H), 7.35–7.31 (m, 3 H), 7.23 (d, *J* = 8.7 Hz, 2 H), 7.20 (d, *J* = 8.5 Hz, 2 H), 7.08 (d, *J* = 8.9 Hz, 1 H), 6.28 (s, 1 H), 2.65–2.60 (m, 4 H), 2.19–2.14 (m, 6 H).

^{13}C NMR (DMSO-d_6 at 120 °C, 100 MHz): δ = 192.1 (C), 151.4 (C), 150.1 (C), 148.9 (C), 147.1 (C), 146.2 (C), 135.8 (C), 135.1 (C), 134.2 (CH), 131.9 (C), 131.8 (C), 131.2 (CH), 130.9 (C), 130.6 (C), 130.0 (2 × CH), 129.9 (C), 129.3 (CH), 129.2 (CH), 129.0 (CH), 128.45 (2 × CH), 128.43 (C), 128.41 (CH), 128.1 (2 × CH), 127.0 (CH), 126.5 (CH), 125.8 (2 × CH), 124.8 (CH), 124.7 (CH), 121.8 (CH), 118.7 (CH), 117.9 (CH), 112.8 (C), 98.4 (CH), 77.7 (C), 28.5 (CH_2), 28.4 (CH_2), 15.4 (CH_3), 15.1 (CH_3).

Anal. Calcd for $C_{42}H_{32}O_3$: C, 86.27; H, 5.52. Found: C, 86.37; H, 5.47.

(4-Fluorophenyl)[3-(4-fluorophenyl)-1,3′-spirobi(benzo[*f*]chromen)-2′-yl]methanone (2c)

Yield: 198 mg (70%); yellow solid; mp 271–273 °C (dec.).

^1H NMR (DMSO-d_6, 400 MHz): δ = 8.75 (d, *J* = 8.5 Hz, 1 H), 8.12 (d, *J* = 8.2 Hz, 1 H), 8.00–7.75 (m, 9 H), 7.57–7.34 (m, 5 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 7.21 (d, *J* = 8.2 Hz, 2 H), 7.12 (d, *J* = 8.7 Hz, 2 H), 6.44 (s, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 191.1 (C), 165.0 (d, $J_{C,F}$ = 249.8 Hz, C), 163.4 (d, $J_{C,F}$ = 246.0 Hz, C), 151.4 (C), 149.9 (C), 145.7 (C), 134.4 (CH), 134.2 (d, $J_{C,F}$ = 2.9 Hz, C), 134.0 (C), 133.0 (d, $J_{C,F}$ = 9.5 Hz, 2 × CH), 131.6 (C), 131.4 (CH + C), 130.8 (C), 130.5 (CH), 129.7 (C), 129.5 (CH), 129.3 (CH), 129.2 (d, $J_{C,F}$ = 2.9 Hz, C), 128.5 (CH), 128.1 (d, $J_{C,F}$ = 8.6 Hz, 2 × CH), 127.4 (CH), 126.6 (CH), 125.0 (CH), 124.9 (CH), 122.3 (CH), 118.8 (CH), 118.0 (CH), 116.2 (d, $J_{C,F}$ = 14.3 Hz, 2 × CH), 116.0 (d, $J_{C,F}$ = 14.3 Hz, 2 × CH), 113.0 (C), 112.3 (C), 98.4 (CH), 77.1 (C).

^{19}F NMR (DMSO-d_6, 376 MHz): δ = –111.4, –106.9.

Anal. Calcd for $C_{38}H_{22}F_2O_3$: C, 80.84; H, 3.03. Found: C, 80.92; H, 2.98.

(4-Chlorophenyl)[3-(4-chlorophenyl)-1,3′-spirobi(benzo[*f*]chromen)-2′-yl]methanone (2d)

Yield: 212 mg (71%); yellow solid; mp 250–251 °C (dec.).

IR (ATR): 1667, 1643, 1622, 1582, 1562, 1516, 1493, 1456, 1346, 1327, 1298, 1238, 1126, 1084, 1015, 947, 920, 866, 854, 814, 802, 745, 698 cm^{-1}.

^1H NMR (DMSO-d_6 at 120 °C, 400 MHz): δ = 8.72 (d, *J* = 8.7 Hz, 1 H), 8.06 (d, *J* = 8.5 Hz, 1 H), 7.98–7.93 (m, 3 H), 7.90–7.82 (m, 4 H), 7.64 (d, *J* = 8.2 Hz, 2 H), 7.59–7.55 (m, 1 H), 7.49–7.40 (m, 7 H), 7.37–7.33 (m, 1 H), 7.09 (d, *J* = 8.9 Hz, 1 H), 6.40 (s, 1 H).

^{13}C NMR (DMSO-d_6 at 120 °C, 100 MHz): δ = 191.3 (C), 151.5 (C), 150.0 (C), 146.1 (C), 137.7 (C), 136.8 (C), 135.0 (C), 134.6 (CH), 134.3 (C), 131.95 (C), 131.85 (C), 131.8 (C), 131.5 (2 × CH), 131.4 (CH), 130.9 (C), 130.1 (CH), 129.9 (C), 129.33 (CH), 129.28 (CH), 129.2 (2 × CH), 128.9 (2 × CH), 128.5 (CH), 127.6 (2 × CH), 127.2 (CH), 126.4 (CH), 124.89 (CH), 124.87 (CH), 122.0 (CH), 118.7 (CH), 117.8 (CH), 112.8 (C), 112.6 (C), 99.4 (CH), 77.3 (C).

Anal. Calcd for $C_{38}H_{22}Cl_2O_3$: C, 76.39; H, 3.71. Found: C, 76.32; H, 3.75.

(4-Bromophenyl)[3-(4-bromophenyl)-1,3′-spirobi(benzo[*f*]chromen)-2′-yl]methanone (2e)

Yield: 268 mg (78%); yellow solid; mp 248–250 °C (dec.).

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.76 (d, *J* = 8.5 Hz, 1 H), 7.93 (d, *J* = 8.5 Hz, 1 H), 7.89 (d, *J* = 9.2 Hz, 1 H), 7.84 (d, *J* = 8.7 Hz, 2 H), 7.83 (s, 1 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.67 (d, *J* = 8.3 Hz, 2 H), 7.59–7.40 (m, 10 H), 7.35–7.31 (m, 1 H), 7.13 (d, *J* = 9.0 Hz, 1 H), 6.26 (s, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 191.5 (C), 151.7 (C), 150.2 (C), 146.6 (C), 136.5 (C), 134.6 (C), 134.3 (CH), 132.1 (C), 131.8 (C), 131.63 (2 × CH), 131.59 (2 × CH), 131.5 (C), 131.3 (2 × CH), 131.2 (CH), 130.5 (C), 129.7 (CH), 129.6 (C), 129.3 (CH), 129.2 (CH), 128.1 (CH), 127.2 (2 × CH), 127.1 (C), 126.6 (CH), 126.0 (CH), 124.6 (CH), 124.5 (CH), 123.7 (C), 121.0 (CH), 119.0 (CH), 117.8 (CH), 112.4 (C), 111.7 (C), 97.9 (CH), 77.3 (C).

Anal. Calcd for $C_{38}H_{22}Br_2O_3$: C, 66.49; H, 3.23. Found: C, 66.40; H, 3.27.

[8,8′-Di(adamantan-1-yl)-3-phenyl-1,3′-spirobi(benzo[*f*]chromen)-2′-yl](phenyl)methanone (2f)

Yield: 315 mg (79%); yellow solid; mp 266–268 °C (dec.).

IR (ATR): 3051, 2980, 1667, 1643, 1630, 1598, 1552, 1495, 1459, 1326, 1298, 1256, 1221, 1146, 1020, 992, 950, 922, 840, 811, 754 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.72 (d, *J* = 9.0 Hz, 1 H), 7.89–7.78 (m, 6 H), 7.72 (s, 1 H), 7.67–7.62 (m, 4 H), 7.51–7.32 (m, 8 H), 7.10 (d, *J* = 8.7 Hz, 1 H), 6.26 (s, 1 H), 2.16–1.73 (m, 30 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 192.7 (C), 151.3 (C), 149.9 (C), 147.5 (C), 147.4 (C), 147.0 (C), 138.1 (C), 135.1 (C), 134.0 (CH), 133.4 (C), 131.88 (CH), 131.85 (C), 131.0 (CH), 129.9 (2 × CH), 129.8 (CH), 129.7 (C), 129.6 (C), 129.3 (CH), 128.7 (C), 128.4 (2 × CH), 128.1 (2 × CH), 126.0 (CH), 125.9 (CH), 125.6 (2 × CH), 124.5 (CH), 124.3 (CH), 124.2 (CH), 120.9 (CH), 118.9 (CH), 117.5 (CH), 112.4 (C), 111.8 (C), 97.7 (CH), 77.7 (C), 43.2 (3 × CH_2), 43.1 (3 × CH_2), 36.9 (6 × CH_2), 36.2 (C), 36.1 (C), 29.0 (6 × CH).

Anal. Calcd for $C_{58}H_{52}O_3$: C, 87.40; H, 6.58. Found: C, 87.52; H, 6.66.

(Adamantan-1-yl)[3-(adamantan-1-yl)-1,3′-spirobi(benzo[*f*]chromen)-2′-yl]methanone (2g)

Yield: 210 mg (65%); yellow solid; mp 238–240 °C.

IR (ATR): 2983, 1689, 1647, 1619, 1580, 1550, 1525, 1493, 1456, 1343, 1320, 1270, 1222, 1196, 1099, 1015, 947, 915, 879, 860, 832, 814, 755, 690 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.62 (d, *J* = 8.2 Hz, 1 H), 8.04 (d, *J* = 8.4 Hz, 1 H), 7.84–7.81 (m, 2 H), 7.80 (d, *J* = 8.9 Hz, 1 H), 7.76 (d, *J* = 8.5 Hz, 2 H), 7.62 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1 H), 7.43 (ddd, *J* = 7.8, 6.6, 0.7 Hz, 1 H), 7.38–7.30 (m, 2 H), 7.26 (d, *J* = 8.4 Hz, 1 H), 7.07 (d, *J* = 8.7 Hz, 1 H), 5.44 (s, 1 H), 2.00 (br s, 3 H), 1.91–1.50 (m, 27 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 204.5 (C), 156.7 (C), 150.5 (C), 150.3 (C), 135.9 (C), 132.4 (CH), 131.7 (C), 131.4 (C), 130.4 (CH), 130.3 (C), 129.5 (C), 129.1 (CH), 128.7 (CH), 127.6 (CH), 127.3 (CH), 126.0 (CH), 124.0 (CH), 123.9 (CH), 121.5 (CH), 120.9 (CH), 119.2 (CH), 117.9 (CH), 112.3 (C), 111.7 (C), 95.4 (CH), 77.8 (C), 47.3 (C), 39.9 (3 × CH_2), 39.5 (3 × CH_2), 36.9 (3 × CH_2), 36.5 (3 × CH_2), 36.4 (C), 28.33 (3 × CH), 28.27 (3 × CH).

Anal. Calcd for $C_{46}H_{44}O_3$: C, 85.68; H, 6.88. Found: C, 85.77; H, 6.95.

3,3′-Diphenyl-1*H*,1′*H*-1,2′-bibenzo[*f*]chromene (3)

1*H*-Benzo[*f*]chromene **1a** (400 mg, 1.55 mmol) and $PhI(OAc)_2$ (500 mg, 1.55 mmol) were refluxed for 10 h in anhyd 1,4-dioxane (8 mL). After completion of the reaction, the mixture was cooled, and the solvent was evaporated in vacuo. The crude product was purified by column chromatography (silica gel, CCl_4), and recrystallized (*i*-PrOH/$CHCl_3$ 5:1); yield: 164 mg (41%); colorless solid; mp 250–251 °C.

IR (ATR): 3057, 2922, 1670, 1624, 1599, 1516, 1466, 1400, 1354, 1325, 1283, 1227, 1173, 1159, 1085, 1003, 1016, 808, 769, 752, 700, 692 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.89–7.85 (m, 4 H), 7.78–7.75 (m, 2 H), 7.71 (d, *J* = 8.0 Hz, 1 H), 7.67–7.55 (m, 5 H), 7.49–7.45 (m, 3 H), 7.42–7.30 (m, 6 H), 7.13 (d, *J* = 9.0 Hz, 1 H), 5.72 (d, *J* = 5.2 Hz, 1 H), 5.27 (d, *J* = 5.2 Hz, 1 H), 3.86 (d, *J* = 19.8 Hz, 1 H), 3.06 (d, *J* = 19.8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 150.7 (C), 150.5 (C), 148.0 (C), 144.4 (C), 135.2 (C), 133.9 (C), 132.0 (C), 131.9 (C), 130.9 (C), 130.2 (C), 129.4 (CH), 129.1 (3 × CH), 128.93 (2 × CH), 128.90 (CH), 128.6 (2 × CH), 128.5 (CH), 128.2 (CH), 127.8 (CH), 126.5 (CH), 126.4 (CH), 124.9 (2 × CH), 124.4 (CH), 124.1 (CH), 123.4 (CH), 122.6 (CH), 117.8 (CH), 117.5 (CH), 112.6 (C), 111.4 (C), 111.1 (C), 98.6 (CH), 35.0 (CH_2), 21.6 (CH_2).

Anal. Calcd for $C_{38}H_{26}O_2$: C, 88.69; H, 5.09. Found: C, 88.79; H, 5.15.

5,7,8-Trimethoxy-2-phenyl-4*H*-chromene (4)[17]

A solution of 5,7,8-trimethoxyflavone[16] (2.2 g, 7.1 mmol) in anhyd THF (35 mL) was added dropwise over 30 min into a stirred mixture of $AlCl_3$ (6.54 g, 49.2 mmol) and $LiAlH_4$ (0.94 g, 24.7 mmol) in anhyd THF (25 mL) under argon atmosphere, maintaining the temperature in the range of –5 to –0 °C. Stirring was continued for another 20 min after the addition, then wet EtOAc was added dropwise to the solution until the evolution of H_2 ceased and diluted with H_2O. The product was extracted with EtOAc, the combined organic layers were washed with H_2O, aq $NaHCO_3$ and brine, and dried (anhyd Na_2SO_4). The solvent was evaporated in vacuo and the residue was recrystallized from MeOH; yield: 1.57 g (74%); colorless solid; mp 125–126 °C.

IR (ATR): 2953, 1665, 1589, 1522, 1489, 1435, 1417, 1342, 1231, 1130, 982, 937, 841, 785, 758, 696 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.73–7.70 (m, 2 H), 7.40–7.36 (m, 2 H), 7.34–7.29 (m, 1 H), 6.20 (s, 1 H), 5.56 (t, *J* = 3.9 Hz, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.80 (s, 3 H), 3.38 (d, *J* = 3.9 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.9 (C), 151.9 (C), 148.2 (C), 146.2 (C), 134.5 (C), 131.6 (C), 128.4 (2 × CH), 128.3 (CH), 124.5 (2 × CH), 102.4 (C), 96.7 (CH), 91.2 (CH), 61.5 (OCH_3), 56.6 (OCH_3), 55.8 (OCH_3), 19.7 (CH_2).

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.40; H, 6.04.

Oxidation of 4*H*-Chromene 4

5,7,8-Trimethoxy-2-phenyl-4*H*-chromene (**4**; 1.0 mmol) and SeO_2 (0.11 g, 1.0 mmol) were refluxed for 4 h in anhyd 1,4-dioxane (8 mL). After completion of the reaction, the mixture was cooled, and the precipitated Se was filtered off. The solvent was evaporated in vacuo. The products were separated by column chromatography (silica gel, $CHCl_3$) and purified by recrystallization (MeOH).

(*E*)-3-(2-Hydroxy-3,4,6-trimethoxyphenyl)-1-phenylprop-2-en-1-one (5)

Yield: 0.09 g (58%); orange solid; mp 142–143 °C (Lit.[19] mp 140–141 °C).

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.22 (d, *J* = 15.8 Hz, 1 H), 8.03–8.01 (m, 2 H), 7.97 (d, *J* = 15.8 Hz, 1 H), 7.54–7.44 (m, 3 H), 6.65 (s, 1 H), 6.07 (s, 1 H), 3.91 (s, 3 H), 3.87 (s, 3 H), 3.85 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 192.0 (C), 157.0 (C), 154.1 (C), 150.7 (C), 139.2 (C), 135.9 (CH), 132.2 (CH), 129.8 (C), 128.6 (2 × CH), 128.5 (2 × CH), 122.6 (CH), 105.3 (C), 88.3 (CH), 61.4 (OCH_3), 56.03 (OCH_3), 55.96 (OCH_3).

Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.70; H, 5.81.

Phenyl(4,6,7-trimethoxybenzofuran-2-yl)methanone (6)

Yield: 0.02 g (15%); yellow solid; mp 132–134 °C.

IR (ATR): 2856, 1638, 1591, 1552, 1514, 1479, 1412, 1375, 1318, 1256, 1228, 1180, 1152, 1032, 1014, 995, 941, 872, 853, 736, 694 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.00–7.98 (m, 2 H), 7.60 (tt, *J* = 7.3, 1.4 Hz, 1 H), 7.54 (s, 1 H), 6.40 (s, 1 H), 4.08 (s, 3 H), 3.97 (s, 3 H), 3.92 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 183.5 (C), 152.9 (C), 151.4 (C), 150.2 (C), 149.6 (C), 137.7 (C), 132.6 (CH), 129.4 (2 × CH), 129.2 (C), 128.5 (2 × CH), 115.3 (CH), 113.4 (C), 93.1 (CH), 61.4 (OCH_3), 57.5 (OCH_3), 56.0 (OCH_3).

Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.29; H, 5.13.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

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