

Article

Cross-Coupling as a Key Step in the Synthesis and Structure Revision of the Natural Products Selagibenzophenones A and B

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Abstract: Selagibenzophenone A (**1**) and its isomer selagibenzophenone B (**2**) were recently described as natural products from *Selaginella* genus plants with PDE4 inhibitory activity. Herein, we report the first total syntheses of both compounds. By comparing spectroscopic data of the synthetic compounds with reported data for the isolated material, we demonstrate that the structure of one of the two natural products was incorrectly assigned, and that in fact isolated selagibenzophenone A and selagibenzophenone B are identical compounds. The synthetic strategy for both **1** and **2** is based on a cross-coupling reaction and on the addition of organometallic species to assemble the framework of the molecules. Identifying a suitable starting material with the correct substitution pattern is crucial because its pattern is reflected in that of the targeted compounds. These syntheses are finalized via global deprotection. Protecting the phenols as methoxy groups provides the possibility for partial control over the selectivity in the demethylation thanks to differences in the reactivity of the various methoxy groups. Our findings may help in future syntheses of derivatives of the biologically active natural product and in understanding the structure–activity relationship.

Keywords: cross-coupling; natural products; structure revision



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1. Introduction

Plants from the genus *Selaginella* (*Selaginellaceae*) are used in traditional medicine in China, India, and Colombia to treat various ailments such as asthma, dysmenorrhea, or traumatic injuries [1,2]. Species from this genus are sources of structurally diverse natural products, including various bioflavonoids and alkaloids, which can be isolated from different sources as well. Several polyphenolic compounds have been isolated exclusively from species of the *Selaginella* genus, including selagibenzophenones A (**1**) [2] and B [3] (**2**; also referred to as selaphenin A [4] in the literature); selaginpulvilin (**3**) [5,6], which contains a rather rare bisaryl fluorene motif; and selaginellin (**4**) [7] (Figure 1). These compounds have shown various biological activities, including antimicrobial [8], cytotoxic [9], antidiabetic [10], anticancer [4], and phosphodiesterase-4 (PDE4) inhibitory properties [2,11].

Several approaches have been developed to synthesize selaginpulvilins, including our formal syntheses of selaginpulvilins C and D [12–17], as well as other unnatural derivatives containing the characteristic diaryl acetylene motif [18]. Syntheses of polyarylated benzophenone containing natural products have not been described yet.

Selagibenzophenone A (**1**) is a naturally occurring benzophenone derivative, which was recently isolated from *Selaginella pulvinata* [2]. The determination of the structure revealed that the natural product contains three 4'-hydroxyphenyl rings in positions 2, 4, and 6 of one of the benzophenone rings, the aromatic ring B (Figure 1, **1**). The compound has demonstrated inhibitory activity against PDE4, with a promising EC₅₀ value of 1.04 μM.

Enzyme PDE4 is involved in the regulation of cyclic adenosine monophosphate (cAMP), and therefore in the modulation of cellular processes [18]. As such, PDE4 is a key target in various indications, including inflammation or memory enhancement (cognitive function stimulation) [19]. Nevertheless, little is known about the other biological properties of selagibenzophenone A (1).

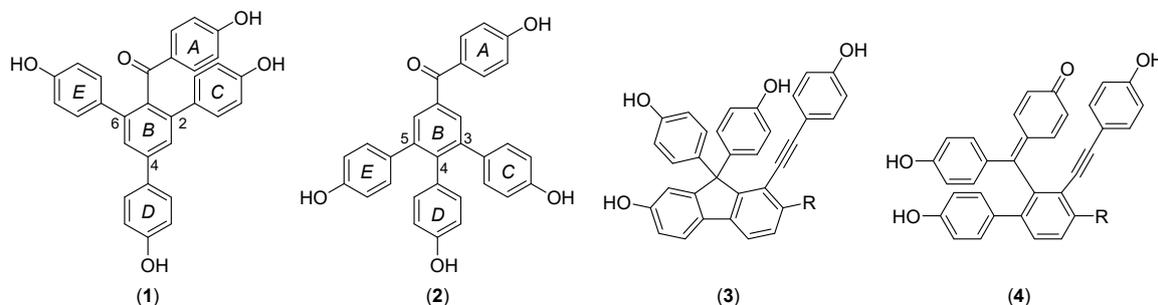


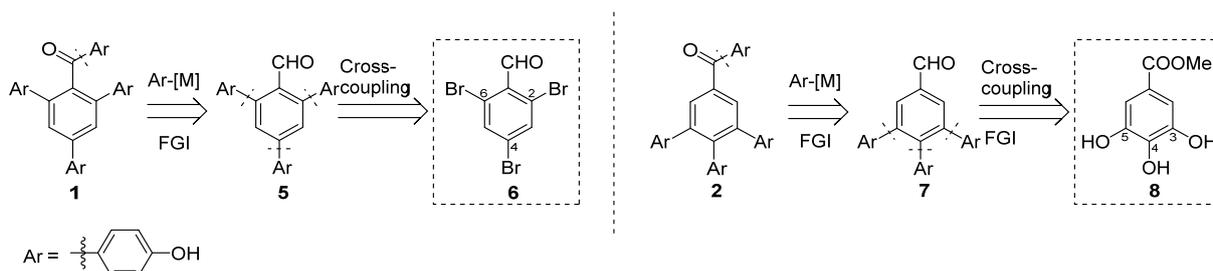
Figure 1. Examples of natural products isolated from *Selaginella* plants.

Liang and Wang [4] in 2018, and later Xu and Tan [3] in 2020, reported the isolation of a novel benzophenone analogue, selagibenzophenone B (2) (referred to as selaphenin A by Liang and Wang), with potential anticancer activity. The authors proposed that compound 2 differed from selagibenzophenone A (1) in the position of the substitution of the benzophenone core. Benzophenone 1 contains three 4'-hydroxyphenyl rings in positions 2, 4, and 6 of aromatic ring B, whereas selagibenzophenone B (2) has 4'-hydroxyphenyl rings in positions 3, 4, and 5 (Figure 1, 2).

A closer analysis of the reported ^1H and ^{13}C NMR spectra of isolated selagibenzophenone A (1) and selagibenzophenone B (2) showed their striking similarity. We put forth two explanations for this similarity: (a) their origin is coincidental, and both compounds actually display similar spectral characteristics; or more likely, (b) only one natural product exists in nature and the structure of the other one was assigned incorrectly. It is not uncommon for the structure of a natural product to be incorrectly solved, as shown by the numerous examples of synthetic work published in the literature that have resulted in subsequent corrections to previously proposed structures of isolated compounds [20,21]. Therefore, we decided to synthesize both molecules. Based on the comparison of spectroscopic data of synthetic and isolated materials, we shed light on this discrepancy in this study. The synthesis and our findings are summarized in the following discussion.

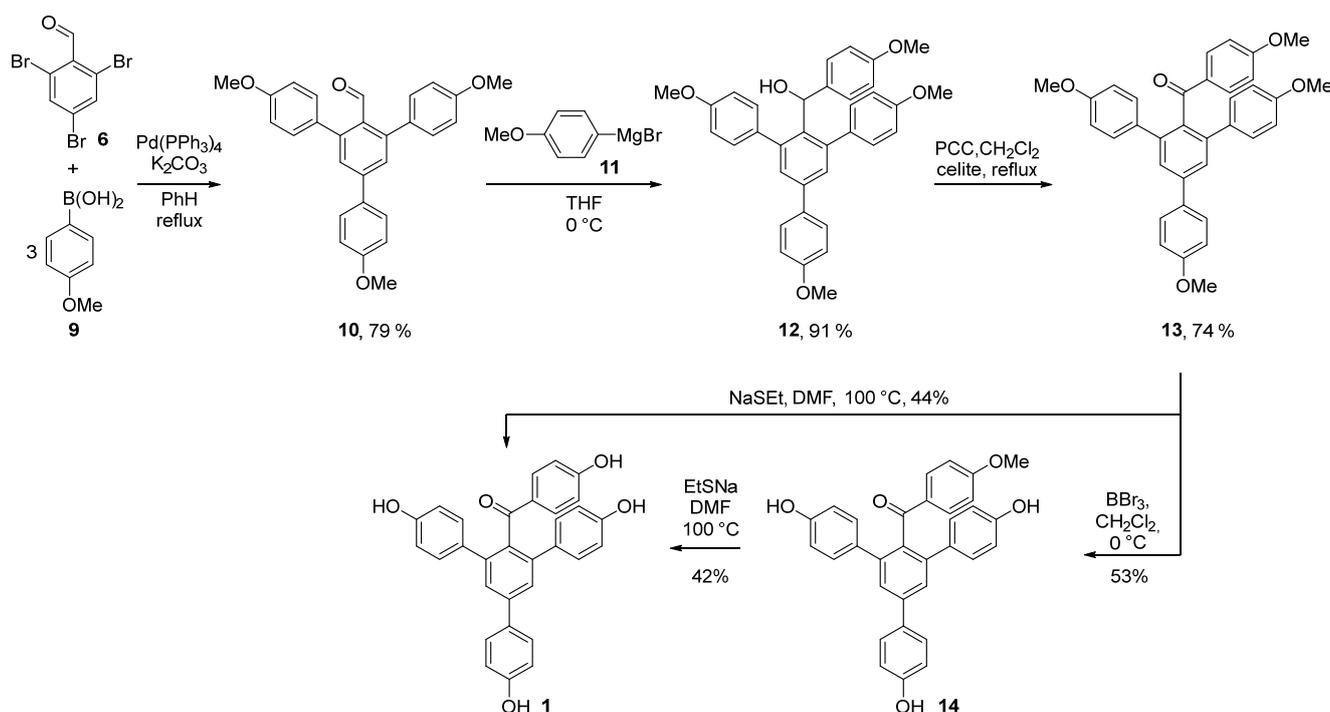
2. Results and Discussion

Our synthetic strategy relied on the formation of a benzophenone moiety in both cases via an addition of organometallic species to an aldehyde, followed by re-oxidation to a ketone and a cross-coupling reaction with a suitably substituted starting material. The substitution pattern of the starting aromatic synthon is crucial because it will be reflected in the final substitution pattern of compounds 1 and 2. We identified commercially available 2,4,6-tribromobenzaldehyde (6) and methyl gallate (8) as suitable starting materials for compounds 1 and 2, respectively (Scheme 1).



Scheme 1. Retrosynthetic analysis and identification of suitable starting materials (6 and 8).

The synthesis of selagibenzophenone A (**1**) commenced with the Suzuki cross-coupling reaction of 2,4,6-tribromobenzaldehyde (**6**) with a three-fold excess of boronic acid **9** (Scheme 2). In the presence of tetrakis(triphenylphosphine)palladium (0) and potassium carbonate, this reaction provided benzaldehyde **10** in 79% yield. In the next step, aldehyde **10** was subjected to the Grignard reaction with 4-methoxyphenylmagnesium bromide (**11**) to furnish secondary alcohol **12** in 91% yield. Further oxidation of the alcohol led to the formation of ketone **13** in 74% yield.



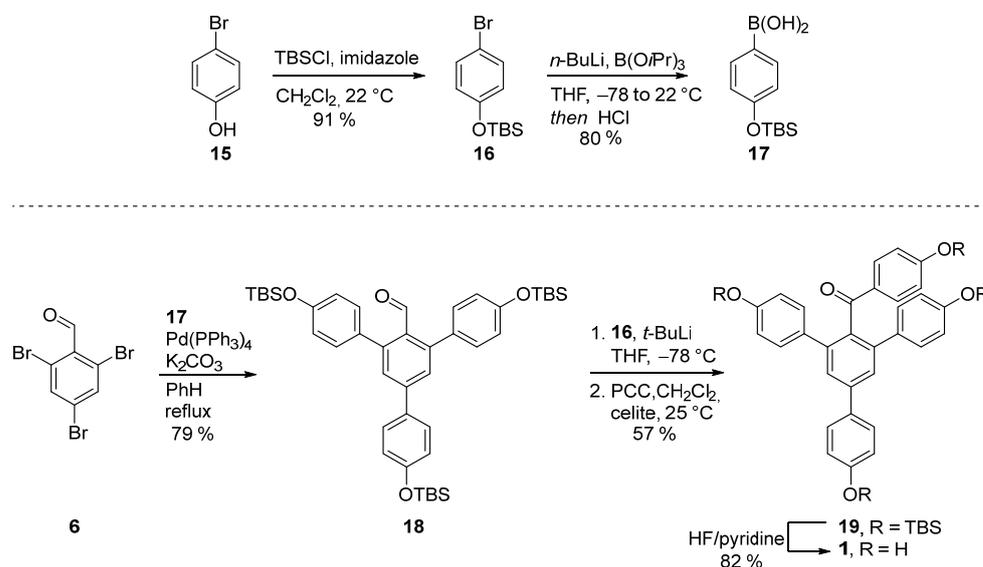
Scheme 2. Synthesis of selagibenzophenone A (**1**).

Our attempts to demethylate anisole moieties led to an unexpected outcome. Using conditions commonly applied for demethylation of methylphenyl ethers and employing boron tribromide [22,23] in CH_2Cl_2 at $0\text{ }^\circ\text{C}$, a new product was formed in 53% yield and with a significantly higher polarity, indicating the formation of free phenols. However, NMR analysis revealed the presence of one remaining methoxy group at the aromatic ring A, as depicted in the structure of compound **14** (Scheme 2). The resistance of this methoxy group to demethylation can be explained by the decrease in the Lewis basicity of this particular methoxy group, which was caused by the electron-withdrawing effect of the carbonyl moiety in the para position, thus decreasing the reactivity towards boron tribromide. Such a reactivity has already been described in the literature for similar systems [24]. Despite the fact that such a selectivity in the deprotection step can be beneficial in the synthesis of derivatives of this natural product for medicinal chemistry purposes and for understanding the structure–activity relationship, this approach is not applicable for the synthesis of the natural product. Increasing the reaction temperature to $25\text{ }^\circ\text{C}$ or to a refluxing temperature did not change the outcome of the reaction either. In addition, applying harsh conditions, as described in the synthesis of related selaginpulvilins C and D, namely using neat MeMgI at $160\text{ }^\circ\text{C}$ [12,15], led to the decomposition of the material and to the formation of a complex mixture of products.

Considering the above, we hypothesized that the remaining methoxy group could also be cleaved using nucleophilic instead of electrophilic conditions. Indeed, when applying sodium ethanethiolate in DMF at $100\text{ }^\circ\text{C}$ [24], the remaining methoxy group was cleaved and tetraphenol **1** was formed in 42% yield. Moreover, subjecting the fully protected compound **13** to the same reaction conditions resulted in the cleavage of all methoxy

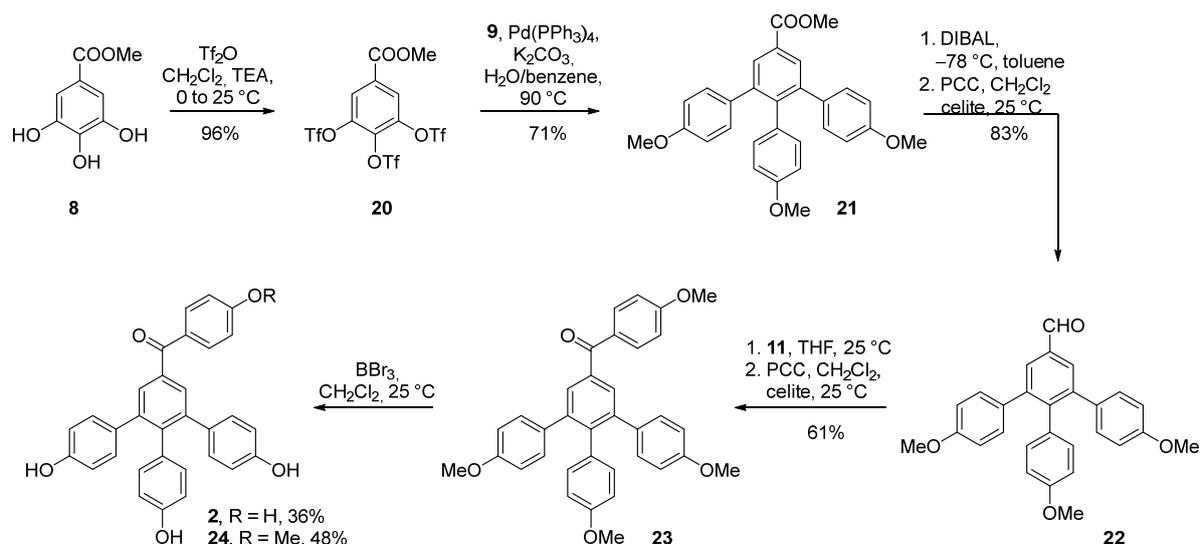
groups and in the formation of the desired product **1** in 44% yield (Scheme 2). However, we found that this demethylation was not reproducible despite extensive research. The reasons for the lack of reproducibility of this protocol remain elusive.

These unsatisfactory results, combined with the unpractical use of a large excess of sodium ethylthiolate, which has an unpleasant odor, prompted us to develop a more reliable route to compound **1**, employing an alternative and easily removable *tert*-butyldimethyl silyl (TBS) protective group. Therefore, the second-generation synthesis began with the synthesis of boronic acid **17** from 4-bromophenol (**15**), which was achieved in two steps, namely protection of the phenol moiety, yielding 91% of bromide **16**; and introduction of boronic acid via lithium-halogen exchange, reaction with isopropyl borate, and in situ hydrolysis. Suzuki coupling of aldehyde **6** and boronic acid **17** under similar conditions to those applied in the previous synthesis provided aldehyde **18** in 79% yield. In the next step, aryl bromide **16** was treated with *t*-butyl lithium and the resulting organolithium species reacted with aldehyde **18**. The immediate oxidation of the crude reaction mixture provided ketone **19** in 57% yield over two steps. Global deprotection of TBS groups employing HF-pyridine resulted in the formation of the natural product (**1**) in 82% yield (Scheme 3).



Scheme 3. Improved synthesis of selagibenzophenone A (**1**).

In the synthesis of selagibenzophenone B (**2**), the hydroxy groups of gallate **8** were converted into triflates in a reaction with triflic anhydride in the presence of triethylamine (Scheme 4). This reaction provided the desired triflate **20** in 96% yield. Suzuki cross-coupling of compound **20** and 3.15 equivalents of 4-methoxyphenyl boronic acid (**9**) proceeded smoothly and furnished the trisarylated aromatic ester **21** in 71% yield. Reduction of the ester moiety in compound **21** was pursued next. When using DIBAL-H at -78°C , this reaction resulted in the formation of the desired aldehyde, albeit with partial overreduction to alcohol. Therefore, the crude reaction mixture was subjected to re-oxidation with pyridinium chlorochromate (PCC) to provide aldehyde **22** in 83% yield. Alternatively, LiAlH_4 can be used for a complete reduction of the ester to primary alcohol, and after re-oxidation with PCC, aldehyde **22** was obtained in 72% overall yield. The aromatic ring D was introduced into the structure via Grignard reaction with 4-methoxyphenylmagnesium bromide. The resulting alcohol was subjected to the PCC-mediated oxidation without further purification and yielded the desired ketone **23** in 61% yield (over two steps). To our delight, subjecting compound **23** to BBr_3 in CH_2Cl_2 at room temperature resulted in the formation of the desired polyphenol **2** in 36% yield along with monomethoxy derivative **24** in 48% yield (Scheme 4).



Scheme 4. Synthesis of selagibenzophenone B (2).

Having both desired compounds **1** and **2** in hand, we compared their analytical data. The spectra of the synthetic compounds **1** and **2** are clearly different (Figure 2). In fact, the change in the chemical shifts of corresponding protons of these molecules in the ¹H NMR spectra are more significant than it appears at first glance. The chemical shift in the signals of aromatic rings A and D in both compounds are strongly influenced by the anisotropic effect of aromatic rings C and E. In compound **1**, protons H^A and H^B (ring A) are shielded by aromatic rings C and E and shifted upfield relative to protons H^A and H^B in compound **2** (**1**: H^A = 7.42 ppm and H^B = 6.60 ppm; **2** H^A = 7.78 ppm and H^B = 6.76 ppm). Conversely, in compound **2**, the shielding zone of rings C and E affects the protons of the aromatic ring D, meaning the signals H^C and H^D are shifted upfield in compound **2** relative to those in compound **1** (**1**: H^C = 7.58 ppm and H^D = 6.90 ppm; **2** H^C = 6.66 ppm and H^D = 6.48 ppm). The effect is most significant on proton H^C, for which the difference in chemical shift is nearly one ppm. Similarly, in both compounds, protons H^E and H^F from rings C and E are affected by the anisotropic shielding of either conjugated system of the carbonyl group together with ring A in compound **1** or by aromatic ring D in compound **2**. The chemical shifts of protons H^E (**1**: 7.11 ppm; **2** 6.90 ppm) clearly show that the shielding of the aromatic ring D in **2** is stronger than that of the conjugated carbonyl–aromatic ring A system in **1**.

Based on the findings described above, the coincidental similarity for the spectra of isolated selagibenzophenones A and B was ruled out. Consequently, the structure of one of the isolated compounds was incorrectly assigned. For this reason, we compared the spectra of both synthetic compounds **1** and **2** with the spectra of the isolated selagibenzophenones reported in the literature. The chemical shift in the signals observed in ¹H and ¹³C NMR spectra are summarized in Table S1 (see supplementary information). The reported spectra of both isolated compounds correspond to the spectra of synthetic compound **1**. As such, the structure of the isolated selagibenzophenone B was assigned incorrectly and the compound previously reported as selagibenzophenone B was in fact selagibenzophenone A.

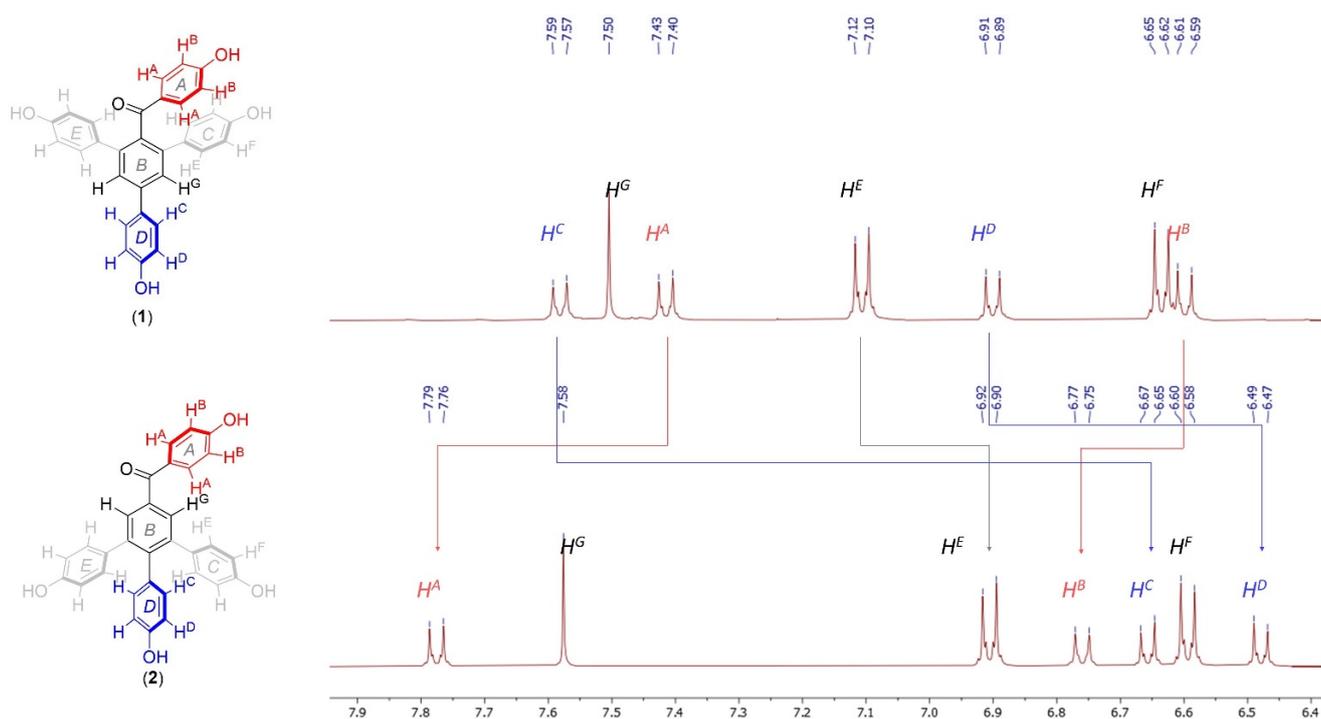


Figure 2. Comparison of the ^1H NMR spectra of synthetic compounds **1** and **2**.

3. Materials and Methods

3.1. General

All of the chemicals were purchased from the common sources, namely Merck KGaA (Darmstadt, Germany), Acros Organics (part of Thermo Fisher, Geel, Belgium), Alfa Aesar (part of Thermo Fisher, Kandel, Germany), Strem Chemicals (Kehl, Germany), PENTA Chemicals (Prague, Czech Republic), Fluorochem (Headfield, UK), and Cambridge Isotope Laboratories (Tewksbury, MA, USA), Inc. All of the reagents were used without further purification unless otherwise noted. Solvents used in the reactions were distilled and dried prior the use. The reactions were monitored by TLC using Merck TLC (Merck KGaA, Darmstadt, Germany) silica gel 60 F254 plates, using UV lamp (254 nm) detection and Hanessian's stain (CAM). NMR spectra were recorded on a Bruker Avance III spectrometer (Bruker, Billerica, MA, United States, 400 MHz and 600 MHz for ^1H NMR and 100 MHz and 150 MHz for ^{13}C NMR, respectively) and Varian NMR Solutions 300 (Varian, Inc., Palo Alto, CA, USA, 300 MHz for ^1H NMR and 75 MHz for ^{13}C NMR). All chemical shifts δ are reported in ppm with a reference to a residual solvent. Mass spectrometry was performed on a VG-Analytical ZAB SEQ (VG Analytical, Manchester, UK). Infrared spectrum were measured in KBr with a Thermo Nicolet AVATAR 370 FT-IR spectrometer (Thermo Fisher Scientific Inc., Waltham, MA, USA). Melting points were determined using a MXBAOHENG Melting Point Apparatus with Microscope X-4 (MRC laboratory-instruments, Harlow, UK). Unless otherwise stated, for reactions that required heating, these were carried out using the oil bath as the heat source. Copies of the NMR spectra are available in supplementary information.

3.2. Synthesis

3.2.1. Synthesis of 4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-2'-carbaldehyde (**10**)

2,4,6-Tribromobenzaldehyde **6** (0.73 mmol, 250 mg), $\text{Pd}(\text{PPh}_3)_4$ (0.037 mmol, 5 mol%, 42 mg), K_2CO_3 (2.56 mmol, 353 mg), and (4-methoxyphenyl)boronic acid **9** (2.3 mmol, 355 mg) were dissolved in a degassed mixture of benzene and H_2O (5:1, 6 mL). The reaction was heated in a closed vial at 90°C for 16 h. Then, the reaction mixture was concentrated

and the product was purified with column chromatography (EA:Hex 1:6 to 1:4). The reaction yielded 574 mg (93%) of product in the form of a yellow glassy oil. $R_f = 0.3$ [EA:Hex (1:4)]; IR (KBr) 3033, 2999, 2954, 2933, 2906, 2835, 2754, 1693, 1608 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.97 (s, 1H), 7.70–7.59 (m, 2H), 7.54 (s, 2H), 7.41–7.32 (m, 4H), 7.10–6.91 (m, 6H), 3.88 (s, 6H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 193.4, 160.2, 159.4 (2C), 145.1 (2C), 143.9, 132.3 (2C), 132.0, 131.3, 131.0 (4C), 128.6 (2C), 128.4 (2C), 114.6 (2C), 113.8 (4C), 55.5 (3C); HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{25}\text{O}_4$ (MS + H^+): 425.1747; found 425.1746.

3.2.2. Synthesis of (4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanol (**12**)

A solution of (4-methoxyphenyl)magnesium bromide **11** (1 M in THF, 0.1 mmol, 0.1 mL) was added in a dropwise manner to a solution of 4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-2'-carbaldehyde **10** (0.071 mmol, 34 mg) in THF (1 mL) at 0 °C. After stirring the reaction in the ice bath for 40 min, it was quenched with saturated NH_4Cl solution (3 mL). The product was extracted with EA (3 \times 5 mL). Combined organic phases were dried over Na_2SO_4 , then filtered and concentrated. The product was purified by column chromatography (gradient eluent EA:Hex 1:6 to 1:4). The reaction yielded 30 mg (79%) of product in the form of a colorless glassy oil. $R_f = 0.2$ [EA:Hex (1:4)]; IR (KBr) 3556, 3033, 2999, 2952, 2933, 2906, 2835, 2044, 1888, 1736, 1608 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.62–7.56 (m, 2H), 7.43 (s, 2H), 7.13 (d, $J = 7.9$ Hz, 4H), 6.99–6.93 (m, 2H), 6.91–6.85 (m, 2H), 6.84–6.78 (m, 4H), 6.73–6.67 (m, 2H), 5.95 (d, $J = 9.2$ Hz, 1H), 3.84 (s, 3H), 3.81 (s, 6H), 3.77 (s, 3H), 2.14 (d, $J = 10.1$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.5, 158.9 (2C), 158.1, 142.8 (2C), 139.1, 138.0 (2C), 134.0 (2C), 132.7, 130.8 (4C), 128.8 (2C), 128.2 (2C), 126.7 (2C), 114.4 (2C), 113.5 (4C), 113.2 (2C), 72.3, 55.5, 55.4 (3C); HRMS (ESI) calculated for $\text{C}_{35}\text{H}_{31}\text{O}_4$: 515.2217; found 515.2219.

3.2.3. Synthesis of (4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone (**13**)

PCC (0.483 mmol, 104 mg), (4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanol **12** (0.4 mmol, 214 mg), and Celite[®] (214 mg) were suspended in DCM (15 mL) and refluxed for 24 hours. Then reaction mixture was filtered through a plug of Celite[®] and concentrated. On TLC, the conversion was visible only when the plate was stained with Hanessian's stain (CAM). The product was purified by column chromatography (EA:Hex 1:6 to 1:4). Reaction yielded 156 mg (74%) of product in the form of a colorless glassy oil. $R_f = 0.2$ [EA:Hex (1:4)]; mp = 180–182 °C (DCM:MeOH), lit. 173–174 °C [25] (AcOH); IR (KBr) 3033, 3001, 2956, 2933, 2908, 2835, 2048, 1660, 1606, 1597 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.67–7.61 (m, 2H), 7.58–7.53 (m, 4H), 7.26–7.22 (m, 4H), 7.03–6.98 (m, 2H), 6.79–6.73 (m, 4H), 6.70–6.64 (m, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.74 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.9, 163.2, 159.7, 158.9 (2C), 141.2, 140.9, 136.9 (2C), 133.1 (2C), 132.8, 131.9, 131.7 (2C), 130.4 (4C), 128.4 (2C), 127.2 (2C), 114.5 (2C), 113.7 (4C), 113.4 (2C), 55.5, 55.4, 55.3 (2C); HRMS (ESI) calculated for $\text{C}_{35}\text{H}_{31}\text{O}_5$ (M + H): 531.2166; found 531.2167.

3.2.4. Synthesis of (4,4''-dihydroxy-5'-(4-hydroxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone (**14**)

BBr_3 solution (1 M in heptane, 0.415 mmol, 0.415 mL) was added into a solution of (4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone (0.094 mmol, 50 mg) in DCM (2 mL) in a dropwise manner at 0 °C. The reaction was stirred at room temperature for 16 h. The reaction mixture was quenched with a solution of NaHSO_3 (50%, 5 mL), then extracted with EA (3 \times 7 mL). Organic phases were combined, washed with brine (5 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The product was purified by column chromatography (EA:Hex 1:4 to 1:1). The reaction yielded 24 mg (53%) of product in the form of a colorless glassy oil. $R_f = 0.2$ [EA:Hex (1:1)]; IR (KBr) 3323, 3070, 3033, 3014, 2964, 2935, 2839, 2044, 1894, 1643, 1610,

1591 cm^{-1} ; ^1H NMR (600 MHz, $\text{MeOD-}d_4$) δ 7.59–7.56 (m, 2H), 7.51–7.48 (m, 4H), 7.12–7.08 (m, 4H), 6.92–6.88 (m, 2H), 6.78–6.74 (m, 2H), 6.64–6.60 (m, 4H), 3.77 (s, 3H); ^{13}C NMR (150 MHz, $\text{MeOD-}d_4$) δ 200.7, 165.2 (2C), 158.8, 157.9 (2C), 143.1, 142.4 (2C), 137.5, 133.2 (2C), 133.1, 132.7, 132.6, 131.5 (4C), 129.3 (2C), 127.6 (2C), 116.8 (2C), 115.9 (4C), 114.5 (2C), 56.0; HRMS (ESI) calculated for $\text{C}_{32}\text{H}_{25}\text{O}_5$ (M + H): 489.1697; found 489.1697.

3.2.5. Synthesis of (4,4''-dihydroxy-5'-(4-hydroxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-hydroxyphenyl)methanone—selagibenzophenone A (1)

Procedure A: A solution of (4,4''-dihydroxy-5'-(4-hydroxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone **13** (0.01 mmol, 5 mg) and NaSEt (0.24 mmol, 20 mmol) in DMF (0.8 mL, anhydrous) was heated in a vial at 100 °C. After 10 h, the reaction mixture was cooled down and diluted with an aqueous HCl (1 M, 8 mL). The product was extracted with EA (3 \times 10 mL). Combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced vacuum. The product was purified by preparative TLC with EA:Hex (1:2 \times 3). The reaction yielded 2 mg (42%) of product in the form of an off-white glassy oil.

Procedure B: A solution of (4,4''-dimethoxy-5'-(4-methoxyphenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone **14** (0.038 mmol, 20 mg) and NaSEt (0.667 mmol, 56 mg) in DMF was loaded into a vial, closed, and heated at 100 °C. After 18 h, the reaction mixture was cooled down and diluted with HCl solution (1 M, 15 mL). The product was extracted with EA (3 \times 20 mL). Organic phases were washed with brine (1 \times 4 mL), dried over Na_2SO_4 , filtered, and concentrated. The product was purified using column chromatography (EA:Hex, 1:4 to 2:1). The reaction yielded 8 mg (44%) of product in the form of an off-white glassy oil.

Procedure C: Olah's reagent ($\text{HF}\cdot\text{pyridine}$, 12 mmol, 0.3 mL) was added to a solution of (4,4''-bis((tert-butyl)dimethylsilyloxy)-5'-(4-((tert-butyl)dimethylsilyloxy)phenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-((tert-butyl)dimethylsilyloxy)phenyl)methanone (**19**) (0.02 mmol, 20 mg) in THF (5 mL) in a plastic flask and stirred at 22 °C for 2 h. Then, the reaction mixture was quenched with saturated solution NaHCO_3 (5 mL) and extracted with EA (3 \times 10 mL). Combined organic layers were washed with HCl (1M, 1 \times 20 mL), dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure. The selagibenzophenone A (**1**) was purified with column chromatography (DCM:MeOH 20:1). The reaction yielded 8.4 mg (82%) of product in the form of a slightly yellow solid. $R_f = 0.1$ [1:1 (EA:Hex)]; ^1H NMR (600 MHz, $\text{MeOD-}d_4$) δ 7.60–7.56 (m, 2H), 7.50 (s, 2H), 7.43–7.39 (m, 2H), 7.12–7.09 (m, 4H), 6.92–6.88 (m, 2H), 6.65–6.62 (m, 4H), 6.61–6.58 (m, 2H); ^{13}C NMR (150 MHz, $\text{MeOD-}d_4$) δ 200.7, 163.8, 158.8, 157.9 (2C), 143.0, 142.4 (2C), 137.6, 133.5 (2C), 133.2 (2C), 132.8, 131.6, 131.5 (4C), 129.3 (2C), 127.6 (2C), 116.8 (2C), 116.0 (2C), 115.8 (4C). The recorded values are in a good agreement with the published data [2].

3.2.6. Synthesis of (4-bromophenoxy)(tert-butyl)dimethylsilane (16)

Tert-butyl dimethyl silyl chloride (104 mmol, 16 g) and imidazole (104 mmol, 7.5 g) were added to a solution of a 4-bromophenol **15** (87 mmol, 15.5 g) in DCM (80 mL) at 0 °C. After 16 hours of stirring at 22 °C, the reaction mixture was filtered through a short pad of silica gel and washed with hexanes (200 mL). The product was used in the next reaction without additional purification. The reaction yielded 22.5 g (91%) of product in the form of a transparent oil. $R_f = 0.4$ [Hex]; ^1H NMR (400 MHz, CDCl_3) δ 7.37–7.34 (m, 2H), 6.77–6.74 (m, 2H), 1.03 (s, 9H), 0.23 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 155.0, 132.4 (2C), 122.0 (2C), 113.8, 25.8 (3C), 18.3, −4.4 (2C). The recorded values are in good agreement with the published data [26].

3.2.7. Synthesis of (4-((tert-butyl)dimethylsilyloxy)phenyl)boronic acid (17)

A solution of *n*-BuLi (1.6 M in hexane, 3.8 mmol, 2.4 mL) was slowly added to a solution of (4-bromophenoxy)(tert-butyl)dimethylsilane (**16**) (3.5 mmol, 1 g) in THF (10 mL) at −78 °C. After 30 min, triisopropyl borate (10.5 mmol, 2.3 mL) was added in

a dropwise manner at $-78\text{ }^{\circ}\text{C}$ and the reaction was then allowed to warm to $22\text{ }^{\circ}\text{C}$ and stirred for 16 h. The reaction mixture was acidified with HCl (1 M, 3 mL). Then, the organic layer was washed with brine ($1 \times 5\text{ mL}$), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The product was purified with column chromatography (DCM to DCM:MeOH 20:1). The reaction yielded 700 mg (80%) of product in the form of an off-white solid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.13–8.11 (m, 2H), 6.97–6.95 (m, 2H), 1.02 (s, 9H), 0.26 (s, 6H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 159.9, 137.6 (2C), 123.1, 119.9 (2C), 25.9 (3C), 18.5, -4.2 (2C). The recorded values are in good agreement with the published data [26].

3.2.8. Synthesis of 4,4''-bis((tert-butyl dimethylsilyl)oxy)-5'-(4-((tert-butyl dimethylsilyl)oxy)phenyl)-[1,1':3',1''-terphenyl]-2'-carbaldehyde (18)

2,4,6-Tribromobenzaldehyde **6** (0.29 mmol, 100 mg), $\text{Pd}(\text{PPh}_3)_4$ (0.029 mmol, 10 mol%, 34 mg), K_2CO_3 (1.02 mmol, 140 mg), and (4-methoxyphenyl)boronic acid **9** (0.92 mmol, 140 mg) were dissolved in a degassed mixture of benzene and H_2O (5:1, 2.2 mL). The reaction was heated in a closed vial at $90\text{ }^{\circ}\text{C}$ for 16 h. Then, the reaction mixture was concentrated and the product was purified with column chromatography (EA:Hex 1:20 to 1:4). The reaction yielded 166 mg (79%) of product in the form of a yellow glassy oil. $R_f = 0.14$ [EA:Hex (1:30)]; IR (KBr) 3033, 2956, 2858, 2540, 1699, 1604, 1508, 1263, 914, 837, 781 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.96 (s, 1H), 7.57 (d, $J = 8.6\text{ Hz}$, 2H), 7.52 (s, 2H), 7.30–7.22 (m, 4H), 6.96–6.86 (m, 6H), 1.02 (s, 18H), 1.00 (s, 9H), 0.25 (s, 12H), 0.23 (s, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 193.5, 156.4, 155.6 (2C), 145.1 (2C), 143.8, 132.9 (2C), 132.7, 131.3, 130.9 (4C), 128.6 (2C), 128.4 (2C), 120.7 (2C), 119.8 (4C), 25.8 (9C), 18.4 (3C), -4.2 (6C); HRMS (ESI) calculated for $\text{C}_{43}\text{H}_{61}\text{O}_4\text{Si}_3$ ($\text{MS} + \text{H}^+$): 725.3872; found 725.3895.

3.2.9. Synthesis of (4,4''-bis((tert-butyl dimethylsilyl)oxy)-5'-(4-((tert-butyl dimethylsilyl)oxy)phenyl)-[1,1':3',1''-terphenyl]-4'-yl)(4-((tert-butyl dimethylsilyl)oxy)phenyl)methanone (19)

A solution of *t*-BuLi (1.7 M in heptane, 0.25 mmol, 0.16 mL) was added in a dropwise manner to a solution of (4-bromophenoxy)(tert-butyl)dimethylsilane (**16**, 0.25 mmol, 70 mg) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$. After 20 min, a solution of 4,4''-bis((tert-butyl dimethylsilyl)oxy)-5'-(4-((tert-butyl dimethylsilyl)oxy)phenyl)-[1,1':3',1''-terphenyl]-2'-carbaldehyde (**18**, 0.18 mmol, 130 mg) in THF (3 mL) was added and the reaction was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 h. The reaction mixture was warmed up to room temperature, quenched with water (10 mL), and extracted with EA ($3 \times 20\text{ mL}$). Combined organic layers were dried over MgSO_4 , filtered, and concentrated. The resulting crude product was redissolved in DCM (10 mL) and Celite[®] (200 mg) and PCC (0.4 mmol, 90 mg) was added to it. After 16 h, the reaction mixture was filtered through a pad of Celite[®]. The product was purified with column chromatography (DCM:Hex, 1:3 to 1:1). The reaction yielded 96 mg (57%) of product in the form of a yellow oil. $R_f = 0.2$ [DCM:Hex (1:2)]; IR (KBr) 2966, 2929, 2887, 2858, 1666, 1597, 1508, 1263 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CD_3OD) 7.59–7.57 (m, 2H), 7.55 (s, 2H), 7.44–7.42 (m, 2H), 7.17–7.15 (m, 4H), 6.94–6.92 (m, 2H), 6.68–6.66 (m, 4H), 6.59–6.57 (m, 2H), 1.01 (s, 9H), 0.94 (s, 27H), 0.24 (s, 6H), 0.16 (s, 6H), 0.13 (s, 12H). $^{13}\text{C NMR}$ (100 MHz, CD_3OD) δ 197.9, 159.8, 155.9, 155.1 (2C), 141.3, 141.1 (2C), 136.9, 133.8 (2C), 133.5, 132.4, 131.7 (2C), 130.5 (4C), 128.4 (2C), 127.2 (2C), 120.6 (2C), 119.8 (4C), 119.4 (2C), 25.9 (3C), 25.8 (6C), 25.7 (3C), 18.4, 18.3 (3C), -4.2 (2C), -4.3 (2C), -4.3 (4C); HRMS (ESI) calculated for $\text{C}_{55}\text{H}_{78}\text{O}_5\text{Si}_4$ ($\text{MS} + \text{H}^+$): 931.4999; found 931.5030.

3.2.10. Synthesis of Methyl 3,4,5-tris(((trifluoromethyl)sulfonyl)oxy)benzoate (20)

In a flame-dried flask, methyl gallate (7.6 mmol, 1.5 g) was dissolved in CH_2Cl_2 (20 mL) under an inert atmosphere. Triethyl amine (24.2 mmol, 3.4 mL) was added, whereupon the suspension dissolved. The mixture was cooled to $0\text{ }^{\circ}\text{C}$ and Tf_2O (24.2 mmol, 4.07 mL) was added. The mixture was heated to the room temperature and stirred for 5 minutes. After this, the reaction was quenched via the addition of 5% HCl (20 mL). The organic phase was separated and washed with NaHCO_3 (15 mL) and brine (15 mL). The organic phase was dried with MgSO_4 and concentrated under reduced pressure. The

mixture was used without further purification for the next step. $R_f = 0.3$ [EA:Hex (1:10)]; mp = 49–51 °C (DCM); IR (KBr) 3116, 2968, 2682, 2355, 1728, 1597, 1435, 1321 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.20 (s, 2H), 4.02 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 162.7, 142.4, 132.1, 125.1, 124.1, 120.8, 120.7, 116.6, 116.4, 112.3, 53.8; HRMS (ESI) calculated for $\text{C}_{11}\text{H}_9\text{F}_9\text{NO}_{11}\text{S}_3$ ($\text{MS} + \text{NH}_4^+$): 597.9198; found 597.9192.

3.2.11. Synthesis of Methyl 4,4''-dimethoxy-6'-(4-methoxyphenyl)-[1,1':2',1''-terphenyl]-4'-carboxylate (**21**)

Aldehyde **20** (2.60 mmol, 1.49 mg), $\text{Pd}(\text{PPh}_3)_4$ (0.26 mmol, 10 mol%, 300 mg), K_2CO_3 (9.1 mmol, 1.25 mg), and (4-methoxyphenyl)boronic acid **9** (8.20 mmol, 1.24 mg) were dissolved in a degassed mixture of benzene and H_2O (5:1, 20 mL). The reaction was heated in a closed vial at 90 °C for 16 h. Then, the reaction mixture was concentrated and the product was purified with column chromatography (EA:Hex 1:99 to 1:10). The reaction yielded 865 mg (71%) of product in the form of a yellow glassy oil. $R_f = 0.15$ [EA:Hex (1:4)]; mp = 133–136 °C (DCM); IR (KBr) 3066, 3005, 2993, 2935, 2839, 2065, 1716, 1608, 1514, 1435 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.04 (s, 2H), 7.03–6.96 (m, 4H), 6.80–6.68 (m, 6H), 6.61–6.54 (m, 2H), 3.94 (s, 3H), 3.76 (s, 6H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 158.3 (2C), 158.0, 143.4, 142.2, 133.8, 132.5 (2C), 131.4, 131.0 (4C), 130.4 (2C), 128.8, 113.3 (4C), 113.1 (2C), 55.3, 55.1, 52.3; HRMS (ESI) calculated for $\text{C}_{29}\text{H}_{27}\text{O}_5$ ($\text{MS} + \text{H}^+$): 455.1853; found 455.1853.

3.2.12. Synthesis of 4,4''-dimethoxy-6'-(4-methoxyphenyl)-[1,1':2',1''-terphenyl]-4'-carbaldehyde (**22**)

A solution of LiAlH_4 (1M in THF, 1.6 mmol, 1.6 mL) was added dropwise into a solution of methyl 4,4''-dimethoxy-6'-(4-methoxyphenyl)-[1,1':2',1''-terphenyl]-4'-carboxylate (**21**) (0.82 mmol, 400 mg) in THF (10 mL) at 0 °C. After 1 h, the reaction mixture was quenched with Na_2SO_4 (300 mg), filtered through a pad of Celite[®], then the filtrate was concentrated under reduced pressure. The crude mixture was then dissolved in DCM (10 mL). After adding Celite[®] (400 mg) and PCC (1.6 mmol, 356 mg), the reaction mixture was left to stir for 16 h. Then, it was filtered through a plug of Celite[®], the filtrate was concentrated, and the product was purified with column chromatography (EA:Hex 1:5). The reaction yielded 270 mg (72%) of product in the form of a yellow glassy oil. $R_f = 0.2$ [EA:Hex (1:4)]; IR (KBr) 3032, 2999, 2956, 2933, 2835, 2729, 2536, 2044, 1888, 1695, 1512, 1441 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.09 (s, 1H), 7.86 (s, 2H), 7.00–6.98 (m, 4H), 6.74–6.72 (m, 6H), 6.59–6.57 (m, 2H), 3.77 (s, 6H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 192.3, 158.5 (2C), 158.2, 145.1, 142.9 (2C), 135.2, 133.5 (2C), 132.4 (2C), 131.2, 130.9 (4C), 130.6 (2C), 113.4 (4C), 113.2 (2C), 55.3 (2C), 55.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{25}\text{O}_4$ ($\text{MS} + \text{H}^+$): 425.1747; found 425.1749.

3.2.13. Synthesis of (4,4''-dimethoxy-6'-(4-methoxyphenyl)-[1,1':2',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone (**23**)

A solution of (4-methoxyphenyl)magnesium bromide (1M in THF, 1 mL, 1 mmol) was added in a dropwise manner to a solution of 4,4''-dimethoxy-6'-(4-methoxyphenyl)-[1,1':2',1''-terphenyl]-4'-carbaldehyde (**22**, 0.64 mmol, 270 mg) in THF (10 mL) at 0 °C. After 16 h, the reaction was quenched with a saturated solution of NH_4Cl (20 mL) and extracted with EA (3 \times 30 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and evaporated. The crude mixture was then dissolved in DCM (20 mL) and Celite[®] (240 mg) and PCC (0.9 mmol, 196 mg) was added to it. After 16 h, the reaction mixture was filtered over a Celite[®] pad and the filtrate was concentrated. The product was purified with column chromatography (EA:Hex 1:10 to 4:1). The reaction yielded 141 mg (70%) of product in the form of a slightly yellow solid. $R_f = 0.2$ [EA:Hex (1:5)]; mp = 77–78 °C (DCM); IR (KBr) 3032, 3001, 2956, 2931, 2908, 2835, 1510, 1250, 1034, 831 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.95–7.93 (m, 2H), 7.75 (s, 2H), 7.01–6.97 (m, 6H), 6.77–6.70 (m, 2H), 6.72–6.70 (m, 4H), 6.60–6.57 (m, 2H), 3.89 (s, 3H), 3.76 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.4,

163.4, 158.3 (2C), 158.1, 142.4, 141.9 (2C), 137.1, 133.9 (2C), 132.7 (2C), 132.6 (2C), 131.5, 131.1 (4C), 130.7 (2C), 130.4, 113.8 (2C), 113.3 (4C), 113.1 (2C), 55.6, 55.3(2C), 55.2; HRMS (ESI) calculated for $C_{35}H_{31}O_5$ (MS + H^+): 531.2166; found 531.2161.

3.2.14. Synthesis of (4,4''-dihydroxy-6'-(4-hydroxyphenyl)-[1,1':2',1''-terphenyl]-4'-yl)(4-hydroxyphenyl)methanone—selagibenzophenone B (2)

A solution of a BBr_3 (1M in heptane, 0.2 mmol, 0.2 ml) was added in a dropwise manner to a solution of the (4,4''-dimethoxy-6'-(4-methoxyphenyl)-[1,1':2',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone (**23**, 0.026 mmol, 14 mg) in DCM (2 mL) at room temperature. After 16 h, the reaction was quenched with a saturated solution of NH_4Cl (5 mL) and extracted with EA (3×10 mL). Combined organic phases were dried over Na_2SO_4 , filtered, and evaporated. The product was purified with preparative TLC (DCM:MeOH, 20:1). The reaction yielded 6 mg of the monomethoxy derivative (4,4''-dihydroxy-6'-(4-hydroxyphenyl)-[1,1':2',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone (48% yield) and 6 mg of the selagibenzophenone B (**2**) in the form yellow solids (36% yield). Selagibenzophenone B (**2**): $R_f = 0.2$ [DCM:MeOH 20:1]; mp = 250 °C (decomp.); IR (KBr) 3459, 2927, 2792, 1587, 1342 cm^{-1} ; 1H NMR (600 MHz, $MeOD-d_4$) δ 7.79–7.55 (m, 2H), 7.58 (s, 2H), 6.93–6.88 (m, 4H), 6.77–6.74 (m, 2H), 6.77–6.74 (m, 2H), 6.61–6.58 (m, 4H), 6.50–6.46 (m, 2H); ^{13}C NMR (150 MHz, $MeOD-d_4$) δ 197.5, 170.5, 157.2 (2C), 156.9, 143.7, 143.4 (2C), 138.8, 134.6 (2C), 134.2, 133.7 (2C), 132.1 (4C), 131.9, 131.0 (2C), 126.5, 118.2 (2C), 115.6 (4C), 115.4 (2C). HRMS (ESI) calculated for $C_{31}H_{23}O_5$ (MS + H^+): 475.1540, found 475.1545.

3.2.15. Synthesis of (4,4''-dihydroxy-6'-(4-hydroxyphenyl)-[1,1':2',1''-terphenyl]-4'-yl)(4-methoxyphenyl)methanone—(monomethoxy-selagibenzophenone B) (**24**)

$R_f = 0.4$ [DCM:MeOH 20:1]; mp = 253–254 °C (DCM); IR (KBr) 3302, 3032, 2958, 2841, 1888, 1699, 1595, 1512, 1419, 1342, 1257 cm^{-1} ; 1H NMR (400 MHz, CD_3OD) δ 7.90–7.88 (m, 2H), 7.62 (s, 2H), 7.07–7.05 (m, 2H), 6.90–6.88 (m, 4H), 6.66–6.64 (m, 2H), 6.60–6.58 (m, 4H), 6.49–6.47 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 197.5, 165.2, 157.2 (2C), 156.9, 144.4, 143.7 (2C), 137.8, 134.0, 133.7 (3C), 133.7 (2C), 132.0 (4C), 131.7, 131.3 (2C), 131.2, 115.6 (4C), 115.4 (2C), 114.9 (2C), 56.1; HRMS (ESI) calculated for $C_{32}H_{25}O_5$ (MS + H^+): 489.1697 found 489.1691.

4. Conclusions

In conclusion, we accomplished the total synthesis of the natural product selagibenzophenone A (**1**), comprising a Suzuki coupling and an addition of an organometallic aromatic compound to a carbonyl moiety to assemble the backbone of the natural product. Further adjustment of the oxidation state and liberation of the phenols led to the synthesis of selagibenzophenone A (**1**) and to confirmation of the proposed structure. The synthesis was performed using two different protecting group strategies. In the first, the phenols were protected as methoxy groups and partial control over the selectivity of the deprotection was gained, depending on the deprotection method used. This will be useful in the future synthesis of derivatives of the natural product and determination of the structure–activity relationship. However, the protocol leading to the formation of the desired natural product lacked reproducibility, which prompted us to develop a second-generation synthesis procedure, using easily removable TBS protecting groups. This approach allowed us to achieve the first reliable total synthesis of selagibenzophenone A (**1**).

In addition, we achieved the total synthesis of compound **2**, which had been described as a natural product known as selagibenzophenone B by Xu and Tan [3] and by Liang and Wang [4]. Our synthetic studies and comparison of our data with previously reported data revealed that the structure of the isolated material, described as selagibenzophenone B, is in fact misassigned and that the isolated compound is selagibenzophenone A. This finding is important not only for natural product chemists but also for the medicinal chemistry community because several biological activities have been reported for selagibenzophenone B (**2**) when they should be instead ascribed to selagibenzophenone A (**1**).

Currently, follow-up studies are being conducted in our laboratory and in the laboratories of our collaborators, where natural and unnatural selaginbenzophenones are being prepared and assessed for their biological effects.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/catal11060708/s1>: Figure S1: Numbering of selaginbenzophenones A and B and key HMBC correlations for selaginbenzophenone B; Table S1: Comparison of NMR shifts of synthetic and isolated selaginbenzophenones A and B; Figure S2: ^1H NMR spectra of compound **10** in CDCl_3 (400 MHz); Figure S3: ^{13}C NMR spectra of compound **10** in CDCl_3 (100 MHz); Figure S4: ^1H NMR spectra of compound **12** in CDCl_3 (400 MHz); Figure S5: ^{13}C NMR spectra of compound **12** in CDCl_3 (100 MHz); Figure S6: ^1H NMR spectra of compound **13** in CDCl_3 (400 MHz); Figure S7: ^{13}C NMR spectra of compound **13** in CDCl_3 (100 MHz); Figure S8: ^1H NMR spectra of compound **14** in $\text{MeOD-}d_4$ (600 MHz); Figure S9: ^{13}C NMR spectra of compound **14** in $\text{MeOD-}d_4$ (150 MHz); Figure S10: ^1H NMR spectra of selaginbenzophenone A (**1**) in $\text{MeOD-}d_4$ (400 MHz); Figure S11: ^{13}C NMR spectra of selaginbenzophenone A (**1**) in $\text{MeOD-}d_4$ (100 MHz); Figure S12: COSY spectra of selaginbenzophenone A (**1**) in $\text{MeOD-}d_4$; Figure S13: HSQC spectra of selaginbenzophenone A (**1**) in $\text{MeOD-}d_4$; Figure S14: HSQC spectra of selaginbenzophenone A (**1**) in $\text{MeOD-}d_4$; Figure S15: ^1H NMR spectra of compound **18** in CDCl_3 (400 MHz); Figure S17: ^1H NMR spectra of compound **19** in CDCl_3 (400 MHz); Figure S18: ^{13}C NMR spectra of compound **19** in CDCl_3 (100 MHz); Figure S19: ^1H NMR spectra of compound **20** in CDCl_3 (300 MHz); Figure S20: ^{13}C NMR spectra of compound **20** in CDCl_3 (75 MHz); Figure S21: ^1H NMR spectra of compound **21** in CDCl_3 (400 MHz); Figure S22: ^{13}C NMR spectra of compound **21** in CDCl_3 (100 MHz); Figure S23: ^1H NMR spectra of compound **22** in CDCl_3 (400 MHz); Figure S24: ^{13}C NMR spectra of compound **22** in CDCl_3 (100 MHz); Figure S25: ^1H NMR spectra of compound **23** in CDCl_3 (400 MHz); Figure S27: ^1H NMR spectra of selaginbenzophenone B (**2**) in $\text{MeOD-}d_4$ (400 MHz); Figure S28: ^{13}C NMR spectra of selaginbenzophenone B (**2**) in $\text{MeOD-}d_4$ (100 MHz); Figure S29: COSY spectra of selaginbenzophenone B (**2**) in $\text{MeOD-}d_4$; Figure S30: HSQC spectra of selaginbenzophenone B (**2**) in $\text{MeOD-}d_4$; Figure S31: HMBC spectra of selaginbenzophenone B (**2**) in $\text{MeOD-}d_4$; Figure S32: ^1H NMR spectra of monomethoxy-selaginbenzophenone B **24** in $\text{MeOD-}d_4$ (400 MHz); Figure S33: ^{13}C NMR spectra of monomethoxy-selaginbenzophenone B **24** in $\text{MeOD-}d_4$ (100 MHz); Figure S34: COSY spectra of monomethoxy-selaginbenzophenone B **24** in $\text{MeOD-}d_4$ (100 MHz).

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