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Synthesis of (+)-Varitriol Analogues via Novel and Versatile Building Blocks Based on Julia Olefination

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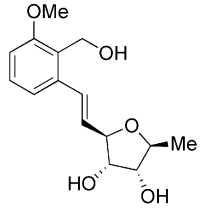
Dedicated to Professor G. C. Kulkarni on the occasion of his 60th birthday

Keywords: Natural products / Varitriol analogues / Julia olefination / Sulfones

The synthesis of (+)-varitriol (**1**) analogues was achieved through the use of Julia olefination. The potential anticancer properties of **1** coupled with our interest in developing building blocks that enable olefin formation under the Julia protocol constitute the basis of our research project. Efforts are aimed at the synthesis of building blocks **2** and **3** and to explore their use towards the synthesis of (+)-varitriol analogues. Herein, we would like to present the synthesis of building block **3** and its ability to react with variety of substituted aromatic-, heterocyclic- and carbohydrate-derived aldehydes to yield alkene **6** in moderate to good yields with *E* as the major isomer. The successful coupling of **2** with (furanoside moieties) aldehydes **5k**, **5m** and **5n** in particular and the obtainment of compound **23** reflect the promise associated with the new strategy.

Introduction

(+)-Varitriol (**1**, Figure 1), a natural product isolated from the marine strain of the fungus *Emericella variecolor* in 2002,[1] has attracted the attention of synthetic organic chemists due to its potential anticancer properties.[2] Jennings[3] first synthetic efforts towards **1**, using D-ribose for the furanoside part of **1**, led to the synthesis of its enantiomer, which not only established the configuration of the natural product but also laid the basis for their argument towards the possible synthesis of **1** through the use of expensive L-ribose. Subsequent to this, Taylor[4] also achieved the synthesis of **1** along with other analogues by making use of the Ramberg–Backlund reaction for the C–C bond formation between the aromatic and furanoside parts. The first total synthesis of **1** was presented by Shaw,[5] and it involved the use of olefin cross metathesis for the same C–C connectivity between the aromatic and furanoside parts. Although the elegant use of methyl α-D-mannopyranoside as the starting material for the furanoside part of **1** obviated the need for expensive L-ribose, the synthetic route became lengthy and the yield in the olefin cross metathesis step was modest. Simultaneously, Nagarapu[6] also used the olefin cross metathesis strategy for the synthesis of novel analogues of **1** and evaluated their cytotoxicity. In the absence of detailed investigations, initial studies indicated that too much variation in the aromatic ring was unfavourable.



(+)-Varitriol (**1**)

Figure 1. Structure of (+)-varitriol (**1**).

Given the fact that (+)-varitriol (**1**) has an impressive biological activity against several tumours and awaits elucidation of its mode of action, synthetic pursuits towards analogues in particular becomes necessary and justified. In this context, a synthetic strategy based on the disconnection *X* was envisaged (Figure 2). The conceived synthetic route was designed to retain the aromatic residue needed in natural product **1**, while allowing the flexibility of altering the furanoside part by coupling with a variety of functionalized aldehydes, particularly from the domain of carbohydrates. The proposed synthetic equivalent for synthon **A** towards this objective was **2**. The envisaged C–C bond formation for the proposed disconnection was based on the efficiency of the Julia olefination in the literature (Figure 2).[7] While this exploration was underway, another synthesis of (+)-varitriol (**1**) by Gracza appeared, wherein the requisite

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furanoside part of the natural product had been synthesized from dimethyl L-tartrate and appended to the aromatic aldehyde through the Kocieński–Julia protocol.[8]

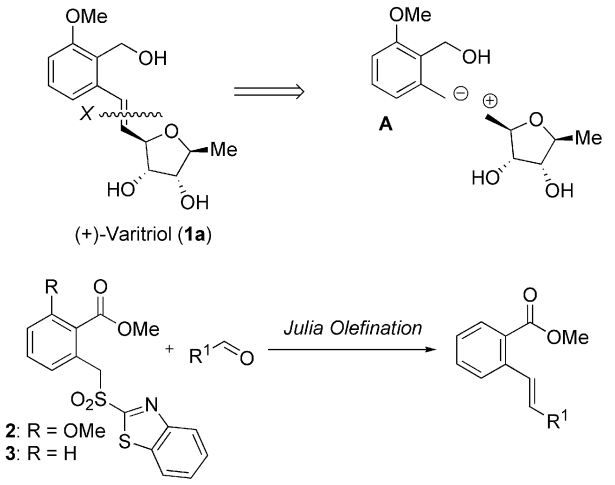
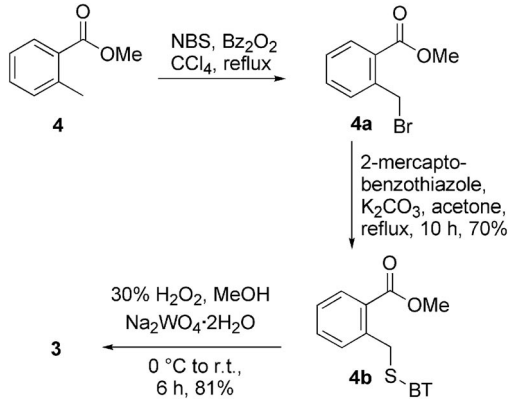


Figure 2. Retroanalysis of (+)-varitriol (**1**) and novel building blocks **2** and **3**.

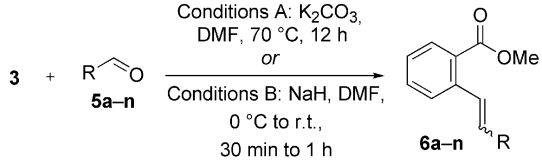
Results and Discussion

Towards model studies, synthesis of ester sulfone **3** and its reaction with the aldehyde functionality was planned. Sulfone **3**, hitherto unknown in the literature, could be easily synthesized in three steps from methyl *o*-toluate (**4**). It involved bromination of the benzylic site in **4** with *N*-bromosuccinimide (NBS) to give known ester bromide **4a**.[9] Nucleophilic substitution of benzyl bromide **4a** with 2-mercaptobenzothiazole (HS–BT) occurred in the presence of anhydrous K_2CO_3 in acetone at reflux to furnish sulfide **4b** in 70% yield. Sulfide **4b** was then oxidized to sulfone **3** by 30% H_2O_2 in the presence of sodium tungstate at 0 °C in 81% yield (Scheme 1).



Scheme 1. Synthesis of building block **3** for model studies.

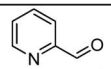
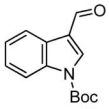
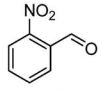
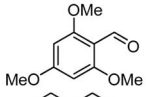
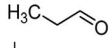
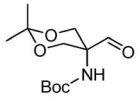
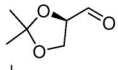
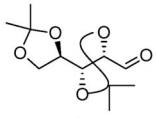
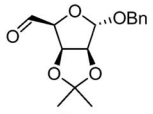
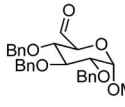
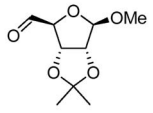
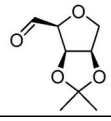
With the use of anhydrous K_2CO_3 as base in dry DMF at 70 °C, the benzylic carbanion was formed and treated with a variety of substituted aromatic and heterocyclic aldehydes **5a**–**h** in excellent yields over a 10–12 h reaction period (Scheme 2). Olefinated products **6a**–**h** were formed either exclusively as the *E* isomer or as an *E*/*Z* mixture (Table 1). All the products were characterized by ^1H and ^{13}C NMR spectroscopy and mass spectrometry. To preclude any possible decomposition of sensitive carbohydrate-derived aldehydes under the reaction conditions, which involved heating at 70 °C, the use of sodium hydride as a base in dry DMF at ambient or low temperature was explored (Scheme 2). To our satisfaction and delight, a clean reaction ensued with a variety of carbohydrate-derived aldehydes **5i**–**n**[10] at 0 °C (Table 1). Successful synthesis of sulfone **3** and its facile reaction with a variety of aldehydes offered proof of concept for the proposed new strategy towards the synthesis of (+)-varitriol (**1**) analogues through the disconnection *X*. The focus and objective of this new strategy for analogues is to bring variation into the furanoside part while retaining the aromatic structural features of the natural product intact.



Scheme 2. Model studies on the reactivity of building block **3**.

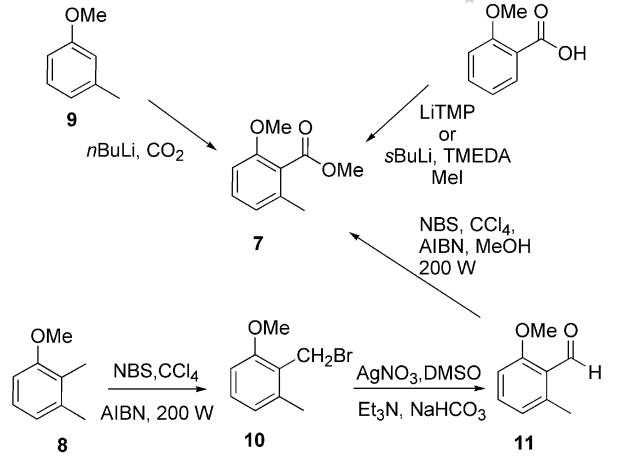
With successful model studies in the background, the synthesis of the key building block **2** was initiated by using the same protocol as that described for the synthesis of **3**. This demanded ester **7** as the necessary starting material. Although commercially available, it is prohibitively expensive and therefore merited an efficient and convenient synthetic route from cheap starting materials as an alternative. A literature survey (Scheme 3) revealed the use of 2,3-dimethyl anisole (**8**) or 3-methylanisole (**9**) as the starting material towards this end. The use of the former[11] involves regioselective oxidation of the methyl group at the C-2 position and the latter[12] uses heteroatom-directed lithiation for introduction of the carboxyl group at the C-2 position. Stringent reaction conditions and nonexclusive lithiation at C-2 with *n*BuLi for subsequent carboxylation by using carbon dioxide as the electrophile made the use of 3-methylanisole as the starting material deter. The regioselective oxidation of **8** is based on exclusive benzylic bromination at the C-2 methyl with 1 equivalent of NBS, under the influence of a 200-W light source and AIBN (azobisisobutyronitrile) as the radical initiator. Further oxidation of benzylic bromide intermediate **10** to aldehyde **11** by using $AgNO_3$ as an oxidant, followed by second oxidation with NBS under radical conditions paves the way for **7**. Recently, regioselective lithiation[13] of *o*-anisic acid with the use of lithium

Table 1. Formation of olefins **6a**–**n** by reaction of sulfone **3** with aldehydes **5a**–**n**.

Entry		Aldehyde R^1CHO	Olefin (% yields)	*E*/*Z* ratio[c]
1	**5a**		**6a** (87)[a]	*E* only
2	**5b**		**6b** (75)[a]	4:1
3	**5c**		**6c** (79)[a]	4:1
4	**5d**		**6d** (80)[a]	*E* only
5	**5e**		**6e** (75)[a]	4:1
6	**5f**		**6f** (86)[a]	24:1
7	**5g**		**6g** (84)[a]	1:1
8	**5h**		**6h** (80)[a]	*E* only
9	**5i**		**6i** (65)[b]	4.8:1
10	**5j**		**6j** (64)[b]	15.7:1
11	**5k**		**6k** (65)[b]	5.6:1
12	**5l**		**6l** (50)[b]	*E* only
13	**5m**		**6m** (56)[b]	*E* only
14	**5n**		**6n** (75)[b]	*E* only

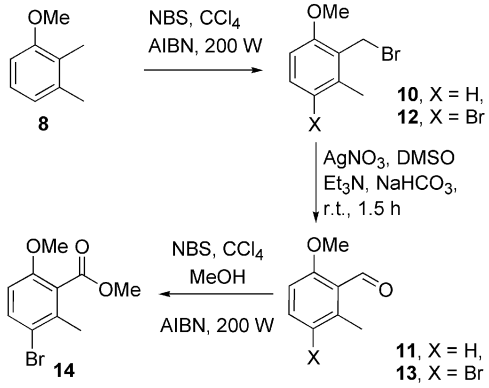
[a] Conditions A: K_2CO_3, DMF, 70 °C. [b] Conditions B: NaH, DMF, 0 °C. [c] Ratio calculated on the basis of the ^{1}H NMR spectra of each compound.

2,2,6,6-tetramethylpiperidine (LiTMP) or *s*BuLi/TMEDA (*N*,*N*,*N*′,*N*′-tetramethyl-1,2-ethylenediamine) for introduction of the methyl group was reported for synthesis of ester **7** under stringent reaction conditions and on a milligram scale.



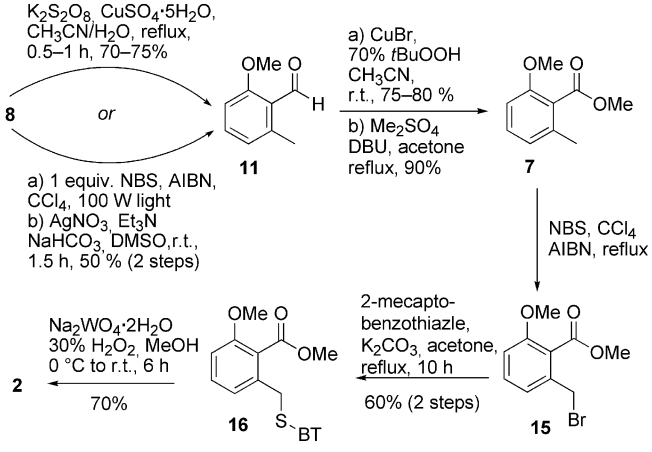
Scheme 3. Literature procedures for the synthesis of starting material **7**.

Due to the ready availability of 2,3-dimethylanisole (**8**), our initial efforts banked on its use. Unfortunately, in our hands, despite utmost care in replicating the reaction conditions,[11] compound **8** underwent ring bromination in addition to benzylic bromination (Scheme 4) during the implementation of the two-step procedure for the synthesis of compound **11** en route to the synthesis of desired starting material **7**. The new product was isolated in 30% yield, and besides recovery of starting material **8**, a 1:1 mixture of compounds **11** and **13** was obtained through the intermediacy of **10** and **12**, respectively. This was evident by analysis of the ^{1}H NMR spectra, which showed a set of peaks in the aldehyde region at δ = 10.53 and 10.63 ppm. As anticipated, there were two doublets centred at δ = 6.80 (J = 8.0 Hz) and 6.83 ppm (J = 8.4 Hz) and a triplet at δ = 7.37 ppm (J = 8.0 Hz) for the aromatic protons in desired compound **11**. In addition to these signals there were two doublets centred at δ = 6.74 (J = 8.8 Hz) and 7.66 ppm (J = 8.8 Hz) in the aromatic region, which were ascribed to ring brominated product **13**. Two sharp singlets at δ = 3.88 and 3.89 ppm and also at δ = 2.56 and 2.63 ppm correspond to the requisite –OCH_3 and –CH_3 groups in compounds **11** and **13**. Exploring the use of 2 equivalents of NBS to circumvent the incomplete consumption of starting material **8**, to our disappointment, led to the predominant formation of **13** in 50% yield over two steps. In another attempt to prevent the observed ring bromination, benzylic bromination with 1 equivalent of NBS was carried out under reduced intensity of light by using a 100 W bulb instead of a 200 W bulb. To our delight, under this slight variation, no ring bromination was observed and the two-step procedure of benzylic bromination at the C-2 methyl group followed by oxidation of the benzylic bromide afforded the exclusive formation of aldehyde **11**, however, in 50% yield. The attempted conversion of aldehyde **11** into desired ester **7** with the reported use of NBS was once again marred with undesired ring bromination and led to the exclusive formation of ring brominated ester **14**.



Scheme 4. Synthesis of intermediates **7** and **14**.

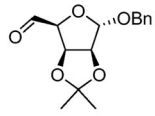
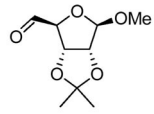
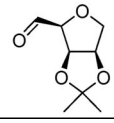
Because the use of NBS for the regioselective oxidation of the C-2 methyl group in compound **8** into an aldehyde group or its subsequent oxidation to an ester functionality was troublesome, we resorted to other available alternatives in the literature for the desired conversion. Besides the use of NBS, regioselective oxidation of the C-2 methyl group in 2,3-dimethylanisole (**11**) was achieved by using $K_2S_2O_8$ on a ca. 10-g scale.[14] To our satisfaction, the conversion of **8** into **11** could be easily effected in 70–75% yield by using this method with good consistency and reproducibility. Aldehyde **11** was subsequently converted into acid by CuBr-mediated oxidation[15] with *t*BuOOH, and the acid was converted into ester **7** by using Me_2SO_4 and 1,8-diazabicycloundec-7-ene (DBU) in acetone with good yields.[16] Ester **7** was then converted into building block **2** in three steps as described for compound **3** in Scheme 1. This includes (a) the benzylic bromination with NBS to furnish **15**, (b) reaction of the crude bromide with 2-mercaptobenzothiazole in the presence of K_2CO_3 as base in acetone to afford sulfide **16** in 60% yield (over 2 steps) and finally (c) the oxidation of sulfide **16** with 30% H_2O_2 in the presence of sodium tungstate in MeOH. Sulfone **2** was obtained in 70% yield as a crystalline solid (Scheme 5).



Scheme 5. Synthesis of building block **2**.

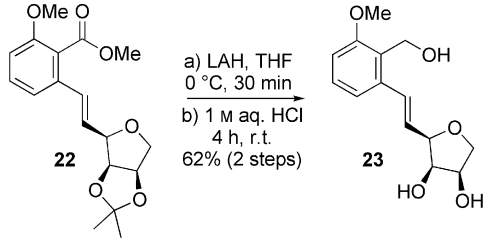
Building block **2** was then treated with aldehydes **5k**, **5m** and **5n** containing the furanoside ring to achieve the synthesis of closely related analogues of (+)-varitriol. The reaction was carried out by using conditions B, that is, NaH as a base in DMF at 0 °C, and the products were obtained after purification by silica-gel chromatography in good yields (Table 2).

Table 2. Julia olefination of aldehydes **5k**, **5m** and **5n** with sulfone **2**.

Entry	Aldehyde	Olefin (% yield)	*E*/*Z* ratio[b]
1	**5k**	 **20** (70)[a]	4:1
2	**5m**	 **21** (77)[a]	8.5:1.5
3	**5n**	 **22** (67)[a]	*E* only

[a] Conditions B: NaH, DMF, 0 °C. [b] Ratio calculated on the basis of the ^{1}H NMR spectra of each compound.

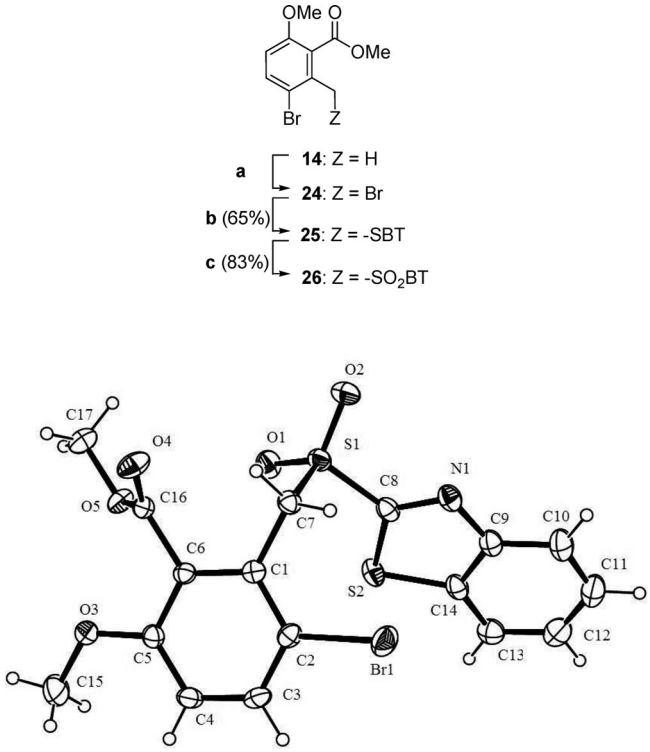
Finally, to establish the new strategy, Julia olefinated product **22** was taken further to the triol stage. Compound **22** was subjected to reduction of the ester functionality by lithium aluminium hydride (LAH) at 0 °C in dry THF. TLC analysis affirmed the complete consumption of the starting material and the appearance of a new polar spot. The crude product from LAH reduction was further subjected to deprotection by 1 M aqueous HCl at room temperature (Scheme 6). Triol **23** was successfully isolated in 62% yield (2 steps). The ^{1}H and ^{13}C NMR spectroscopic analysis confirmed the presence of benzylic ($-C_6H_3C\mathit{H}_2OH$) protons at δ = 4.76 ppm as a singlet in the ^{1}H NMR spectrum and at δ = 55.8 ppm in the ^{13}C NMR spectrum; also, the deprotection was confirmed by the disappearance of two singlets at δ = 1.31 and 1.50 ppm in ^{1}H NMR spectrum and at δ = 24.9 and 26.1 ppm in the ^{13}C NMR spectrum, corresponding to the acetonide methyl groups.



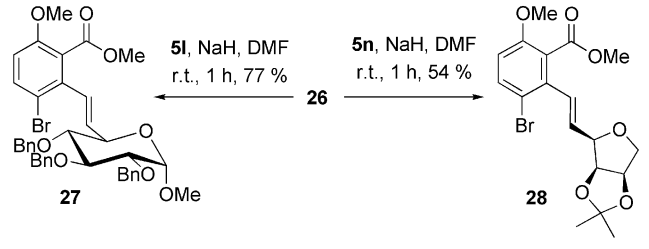
Scheme 6. Synthesis of triol **23**.

While our objective of synthesizing (+)-varitriol analogues focused on maintaining the aromatic part identical as required in the natural product and varying only the

furanoside part, the availability of aromatic ester **14** containing a bromine substituent tempted its use for demonstrating the versatility of the developed strategy. Besides this, the presence of an aryl bromide functionality in **14** provides a means for further derivatization in the aromatic part of the natural product. Ester **14** was converted into sulfone **26** via sulfide **25** (Scheme 7) by following the same sequence of reaction as that described for **2** and **3**. The crystalline nature of **26** allowed its X-ray diffraction analysis,[17] which fully confirmed the presence of bromine at the *para* position with respect to the methoxy group in the aromatic ring. Sulfone **26** reacted efficiently with carbohydrate-derived aldehydes **5l** and **5n** as representative examples under reaction conditions B to furnish **27** and **28** in 77 and 54% yield, respectively (Scheme 8), which are valuable precursors of (+)-varitriol analogues. With the synthesis of **27**, it has been demonstrated that the furanoside part can be replaced by a pyranoside ring system in search for more analogues.



Scheme 7. Synthesis and ORTEP structure of sulfone **26**. Reagents and conditions: (a) NBS, AIBN, CCl_4, reflux; (b) 2-mercaptobenzothiazole, K_2CO_3, acetone, reflux, 10 h, 65%; (c) 30% H_2O_2, $Na_2WO_4{\cdot}2H_2O$, MeOH, 0 °C to r.t., 6 h, 83%.



Scheme 8. Synthesis of analogues of (+)-varitriol from building block **26**.

Conclusions

In conclusion, convenient syntheses of three new building blocks **2**, **3** and **26** from simple aromatic substrates have been realized in good yields with convenient preparative procedures. These new building blocks have enabled highly efficient coupling with a variety of aldehydes towards the synthesis of various analogues of (+)-varitriol containing the furanoside and pyranoside ring systems with varying configurations at the stereocentres therein. Further use of these building blocks demonstrating their versatility and utility in other synthetic endeavours is currently underway.

Experimental Section

General Information: All reactions were carried out in oven-dried glassware. Dry DMF was prepared by stirring in calcium hydride and kept under 4 Å molecular sieves after downward distillation. Solvents used for chromatography were LR grade. Anhydrous K_2CO_3 was prepared by keeping it in a hot-air oven for 24 h at 100 °C. Thin-layer chromatography was performed on aluminium plates coated with silica gel 60. Visualization was observed by UV light irradiation or by dipping into a solution of cerium(IV) sulfate (2.5 g) and ammonium molybdate (6.25 g) in 10% sulfuric acid (250 mL) followed by charring on a hot plate. Melting points were determined in capillaries and are uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the reference. The proton numbering for the spectral assignment (^{1}H chemical shift) follows the numbering of the carbon atoms in the corresponding name of the compound. Mass spectra were recorded with a MICRO-Q TOF mass spectrometer by using the ESI technique at 10 eV. Optical rotations were measured with an Autopol IV polarimeter at room temperature.

General Procedure for the Preparation of Bromides 4a, 15 and 24 from 4, 7 and 14, Respectively: To a solution of the ester (1 mmol, 1 equiv.) in CCl_4 (15 mL) was added fresh NBS (1 equiv.) added. To this solution was added a catalytic amount of AIBN (5 wt.-%). The reaction mixture was heated at reflux for 2–4 h. After the disappearance of starting material (TLC), the reaction mixture was cooled and filtered. The resulting crude bromide was used as such for further reactions.

General Procedure for the Preparation of Ester Sulfides 4b, 16 and 25: To a solution of bromide (1 mmol, 1 equiv.) in dry acetone (10 mL) was added anhydrous K_2CO_3 (2 equiv.) and 2-mercaptobenzothiazole (1.1 equiv.), and the resulting suspension was heated at reflux for 8–12 h. After complete consumption of the starting material, the solvent was evaporated under reduced pressure. The resulting mass was added with water (50 mL) and extracted with ethyl acetate (3 × 15 mL). The collected organic layer was dried with anhydrous Na_2SO_4, filtered, concentrated and subjected to purification by silica gel column chromatography.

Methyl 2-{(Benzo[*d*]thiazol-2-ylthio)methyl}benzoate (4b): 72% yield; R_f = 0.43, (ethyl acetate/hexanes, 1:9); colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1077, 1263, 1426, 1456, 1712 cm^{-1}. ^{1}H NMR

(400 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, COOCH_3), 5.00 (s, 2 H, SCH_2Ar), 7.27 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5-H), 7.31–7.34 (td, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 4-H), 7.38–7.46 (m, 2 H, 5′, 6′-H), 7.67 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.71 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-H), 7.90 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 7′-H), 7.98–8.00 (m, 1 H, 4′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.0, 52.2, 120.9, 121.4, 124.1, 125.9, 127.8, 128.8, 131.2, 131.7, 132.4, 135.5, 139.3, 153.1, 167.0, 167.4 ppm. HRMS (EI): calcd. for $C_{16}H_{13}NO_2S_2$ [M + H]$^+$ 316.0466; found 316.0461.

Methyl 2-{(Benzo[*d*]thiazol-2-ylthio)methyl}-6-methoxybenzoate (16): 69% yield; R_f = 0.3, (CH_2Cl_2/hexanes, 1:1, 2× elusion), colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1070, 1113, 1260, 1427, 1465, 1585, 1727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, OCH_3), 3.82 (s, 3 H, COOCH_3), 4.54 (s, 2 H, ArCH_2S), 6.76 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 5-H), 7.05 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.16–7.22 (m, 2 H, 5′, 6′-H), 7.29–7.33 (m, 1 H, 4-H), 7.63 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4′-H), 7.80 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 7′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.1, 52.4, 56.1, 110.9, 121.0, 121.5, 122.4, 123.3, 124.3, 126.0, 131.0, 135.4, 135.6, 153.1, 157.0, 166.2, 167.7 ppm. HRMS (EI): calcd. for $C_{17}H_{15}NO_3S_2$ [M + H]$^+$ 346.0572; found 346.0577.

Methyl 2-{(Benzo[*d*]thiazol-2-ylthio)methyl}-3-bromo-6-methoxybenzoate (25): 65% yield; R_f = 0.3, (CH_2Cl_2/hexanes, 1:1); colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1071, 1091, 1271, 1292, 1426, 1456, 1575, 1731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 3.84 (s, 3 H, COOCH_3), 4.80 (s, 2 H, SCH_2Ar), 6.78 (d, $^3J_{H,H}$ = 9.2 Hz, 1 H, 5-H), 7.30 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H), 7.41–7.44 (m, 1 H, 6′-H), 7.58 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 5′-H), 7.75 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 7′-H), 7.92 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.0, 52.7, 56.2, 112.5, 116.2, 121.0, 121.5, 124.4, 125.8, 126.1, 133.7, 134.8, 135.3, 152.7, 156.0, 166.2, 166.7 ppm. HRMS (EI): calcd. for $C_{17}H_{14}BrNO_3S_2$ [M + Na]$^+$ 445.9496; found 445.9492.

General Procedure for the Oxidation of Sulfides 4b, 16 and 25 into Sulfones 3, 2 and 26, Respectively: To a solution of sulfide (1 mmol, 1 equiv.) in MeOH (2 mL) at 0 °C was added $Na_2WO_4{\cdot}2H_2O$ (0.5 equiv.). After 5 min of stirring, 30% H_2O_2 (4 equiv.) was added, and the reaction mixture was allowed to attain room temperature and stirred for 5–6 h. After complete consumption of the starting material, MeOH from the reaction mixture was evaporated under reduced pressure. The resulting mass was quenched with a saturated solution of sodium metabisulfite until the effervescence stopped. The resulting solution was then extracted with ethyl acetate (3 × 15 mL). The collected organic layer was dried with anhydrous Na_2SO_4, filtered, concentrated and subjected to purification by silica gel column chromatography.

Methyl 2-{(Benzo[*d*]thiazol-2-ylsulfonyl)methyl}benzoate (3): 86% yield; R_f = 0.3 (ethyl acetate/hexanes, 2:8); colourless crystals, m.p. 104–108 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1078, 1118, 1268, 1332, 1469, 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (s, 3 H, COOCH_3), 5.47 (s, 2 H, SCH_2Ar), 7.32–7.34 (m, 1 H, 5-H), 7.42–7.44 (m, 2 H, Ar-H, BT-H), 7.57 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H), 7.64 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, 4-H), 7.94–7.96 (m, 2 H, BT-H), 8.23 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 7′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.2, 58.1, 122.2, 125.5, 127.5, 127.6, 127.9, 129.3, 131.2, 131.3, 132.2, 133.5, 137.2, 152.6, 165.4, 167.2 ppm. HRMS (EI): calcd. for $C_{16}H_{13}NO_4S_2$ [M + Na]$^+$ 370.0184; found 370.0190.

Methyl 2-{(Benzo[*d*]thiazol-2-ylsulfonyl)methyl}-6-methoxybenzoate (2): 75% yield; R_f = 0.3, (ethyl acetate/hexanes, 2:8), colourless crystals. m.p. 134–137 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1070, 1154, 1273, 1334, 1470, 1589, 1718 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 3.81 (s, 3 H, COOCH_3), 4.96 (s, 2 H, ArCH_2S), 6.92 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5-H), 6.94 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 3-H), 7.30 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H), 7.56–7.60 (m, 1 H, 5′-H), 7.62–7.67 (td, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 8.4 Hz, 1 H, 6′-H), 7.95 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4′-H), 8.25 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 7′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.6, 56.2, 57.9, 109.9, 112.5, 122.3, 124.4, 125.5, 126.0, 127.6, 128.0, 131.2, 137.2, 152.6, 157.6, 164.9, 167.2 ppm. HRMS (EI): calcd. for $C_{17}H_{15}NO_5S_2$ [M + H]$^+$ 378.0470; found 378.0473.

Methyl 2-{(Benzo[*d*]thiazol-2-ylsulfonyl)methyl}-3-bromo-6-methoxybenzoate (26): 83% yield; R_f = 0.3, (ethyl acetate/hexanes, 3:7), colourless crystals; m.p. 156–160 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1072, 1153, 1288, 1337, 1435, 1465, 1578, 1717 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OCH_3), 3.80 (s, 3 H, COOCH_3), 5.24 (s, 2 H, SO_2CH_2Ar), 6.81 (d, $^3J_{H,H}$ = 9.2 Hz, 1 H, 5-H), 7.48 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 5′-H), 7.51–7.59 (m, 2 H, 4′-H, 6′-H), 7.90–7.92 (m, 1 H, 7′-H), 8.15–8.17 (m, 1 H, 4′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.8, 56.4, 57.9, 114.3, 117.9, 122.2, 125.6, 126.2, 126.7, 127.6, 128.0, 135.3, 137.5, 152.7, 156.9, 165.3, 166.8 ppm. HRMS (EI): calcd. for $C_{17}H_{14}BrNO_5S_2$ [M + Na]$^+$ 455.9575; found 455.9579.

General Procedure for the Julia Olefination of Sulfones with Aldehydes

Conditions A: To a suspension of sulfone **3** (0.2 g, 0.5757 mmol, 1 equiv.) and anhydrous K_2CO_3 (0.239 g, 1.73 mmol, 3 equiv.) in dry DMF (3 mL) was added a solution of aldehyde (1 equiv.) in dry DMF (2 mL), and the reaction mixture was heated at 70 °C for 10–12 h. After complete consumption of the starting material, the reaction mixture was quenched with water (10 mL) and extracted with ethyl acetate (3 × 15 mL). The collected organic layer was dried with anhydrous Na_2SO_4, filtered, concentrated and subjected to purification by silica gel column chromatography.

Conditions B: To a suspension of NaH (0.026 g, 0.6333 mmol, 1.1 equiv.) in dry DMF (2 mL) was added a solution of sulfone **3** (0.2 g, 0.5757 mmol, 1 equiv.) at 0 °C. The solution turned to a reddish orange colour, which indicated the formation of the carbanion. After 10 min, a solution of aldehyde (1 equiv.) in dry DMF (1 mL) was added to the reaction mixture. The disappearance of the reddish orange colour was observed. The reaction mixture was allowed to attain room temperature and maintained for further 30 min to 1 h. After complete consumption of the starting material, the reaction mixture was quenched with water (10 mL) and extracted with ethyl acetate (3 × 15 mL). The collected organic layer was dried with anhydrous Na_2SO_4, filtered, concentrated and subjected to purification by silica gel column chromatography.

(*E*)-Methyl 2-[2-(Pyridin-2-yl)vinyl]benzoate (6a): 87% yield, (*E* only); R_f = 0.32 (ethyl acetate/hexanes, 2:8), colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1076, 1248, 1431, 1583, 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.95 (s, 3 H, COOCH_3), 7.13–7.21 (m, 2 H, 1-H, 2′-H), 7.38 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, 4′-H), 7.53–7.58 (m, 2 H, 6-H, 8-H), 7.71 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, 7-H), 7.78 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3′-H), 7.96 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5-H), 8.41 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H, ArCHC*H*Py), 8.63 (d, $^3J_{H,H}$ = 4.4 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.2, 121.7, 122.3, 127.4, 127.9, 129.0, 130.2, 130.7, 132.3, 132.4, 137.0, 138.4, 148.9, 155.5, 167.6 ppm. HRMS (EI): calcd. for $C_{15}H_{13}NO_2$ [M + H]$^+$ 240.1025; found 240.1028.

***tert*-Butyl 3-[2-(Methoxycarbonyl)styryl]-1*H*-indole-1-carboxylate (6b):** 75% yield, (*E*:*Z* = 4:1); R_f = 0.5 (ethyl acetate/hexanes, 2:8); yellow oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1093, 1154, 1237, 1452, 1720 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.61 (s, 9 H, *t*Bu), 3.86 (s, 3 H, COOCH_3), 7.07 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H, ArCHC*H*In), 7.23–7.29

(m, 4 H, Ar-H), 7.42–7.47 (m, 1 H, Ar-H), 7.68 (t, $^3J_{H,H}$ = 3.2 Hz, 2 H, 4-H), 7.85–7.87 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 7′-H), 7.91–7.93 (m, 1 H, Ar-H), 8.05 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H, ArC*H*CHIn), 8.12 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-H) ppm. Non-overlapped peaks of *Z*-isomer: δ = 1.48 (s, 9 H, *t*Bu), 3.79 (s, 3 H, COOCH_3), 6.65 (d, $^3J_{H,H}$ = 12.4 Hz, 1 H, ArCHC*H*In) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.2, 55.1, 83.9, 115.3, 119.2, 120.2, 122.9, 123.0, 124.8, 126.4, 126.9, 127.4, 128.2, 128.6, 130.7, 132.1, 132.2, 136.0, 139.5, 149.5, 167.9 ppm. Non-overlapped peaks of *Z*-isomer: δ = 28.0, 52.0, 83.5, 114.9, 122.8, 124.6, 124.7, 130.6, 130.7, 149.6, 167.4 ppm. HRMS (EI): calcd. for $C_{23}H_{23}NO_4$ [M + Na]$^+$ 400.1525; found 400.1534.

Methyl 2-[2-(Furan-2-yl)vinyl]benzoate (6c): 79% yield, (*E*:*Z* = 4:1); R_f = 0.65 (ethyl acetate/hexanes, 2:8); brownish oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1076, 1167, 1245, 1433, 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, COOCH_3), 6.39–6.43 (m, 2 H, 3′, 4′-H), 6.84 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArCHC*H*furyl), 7.28–7.32 (td, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 7.8 Hz, 1 H, 3-H), 7.42 (d, $^3J_{H,H}$ = 1.2 Hz, 1 H, 5′-H), 7.46–7.51 (m, 1 H, 4-H), 7.66 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.87 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H ArC*H*CHfuryl), 7.90–7.92 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-H) ppm. Non-overlapped peaks of *Z*-isomer: δ = 3.86 (s, 3 H, COOCH_3), 5.93 (d, $^3J_{H,H}$ = 4.0 Hz, 1 H, 3′-H), 6.22–6.24 (m, 1 H, 4′, 5′-H), 6.91 (d, $^3J_{H,H}$ = 12.0 Hz, 1 H, ArCHC*H*furyl), 7.20 (d, $^3J_{H,H}$ = 1.2 Hz, 1 H, 3-H), 7.35–7.40 (m, 1 H, ArH), 8.02 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.2, 109.2, 111.6, 119.1, 125.5, 126.4, 127.1, 128.6, 130.7, 132.1, 138.6, 142.5, 153.3, 167.9 ppm. Non-overlapped peaks of *Z*-isomer: δ = 51.9, 109.6, 111.1, 117.6, 127.3, 128.1, 130.4, 130.8, 131.8, 141.5 ppm. HRMS (EI): calcd. for $C_{14}H_{12}O_3$ [M + Na]$^+$ 251.0684; found 251.0681.

(*E*)-Methyl 2-(2-nitrostyryl)benzoate (6d): 80% yield, (*E* only); R_f = 0.51 (ethyl acetate/hexanes, 1:9); yellow solid; m.p. 107–109 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1078, 1250, 1342, 1514, 1572, 1712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, COOCH_3), 7.36–7.44 (m, 2 H, Ar-H, olefin), 7.47 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArCHC*H*ArNO_2), 7.56 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, 5-H), 7.62 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.76 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H), 7.87 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3′-H), 7.97–8.01 (m, 2 H, NO_2ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.2, 124.7, 126.3, 127.8, 128.0, 128.1, 128.5, 128.9, 130.7, 132.6, 132.8, 133.2, 133.3, 138.8, 147.9, 167.6 ppm. HRMS (EI): calcd. for $C_{16}H_{13}NO_4$ [M + Na]$^+$ 306.0742; found 306.0748.

Methyl 2-(2,4,6-Trimethoxystyryl)benzoate (6e): 75% yield, (*E*:*Z* = 4:1); R_f = 0.5 (ethyl acetate/hexanes, 2:8); colourless sticky gum. IR (CH_2Cl_2): $\tilde{\nu}$ = 1120, 1191, 1492, 1603, 1718 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, COOCH_3), 3.79 (s, 6 H, 2 OCH_3), 3.81 (s, 3 H, OCH_3), 6.07 (s, 2 H, 3′, 5′-H), 7.12–7.16 (m, 1 H, 3-H), 7.24 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H, ArCHC*H*ArOMe), 7.37 (t, $^3J_{H,H}$ = 8.4 Hz, 1 H, 4-H), 7.67 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 3-H), 7.73–7.75 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-H), 8.13 (d, $^3J_{H,H}$ = 16.8 Hz, 1 H, ArC*H*CHArOMe) ppm. Non-overlapped peaks of *Z*-isomer: 3.38 (s, 6 H, 2 OCH_3), 3.67 (s, 3 H, OCH_3), 5.89 (s, 2 H, 3′, 5′-H), 6.42 (d, *J* = 12.0 Hz, 1 H, ArCHC*H*Ar-OMe), 6.96–7.00 (m, 1 H, 4-H), 7.05–7.09 (m, 2 H, ArH), 7.78–7.82 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.8, 55.3, 55.8, 90.7, 108.3, 122.6, 126.0, 126.5, 128.2, 130.2, 131.7, 141.1, 159.6, 160.4, 168.4 ppm. Non-overlapped peaks of *Z*-isomer: δ = 55.1, 90.4, 121.1, 126.1, 128.6, 129.1, 129.8, 130.8, 131.1, 141.6, 158.2, 160.7, 167.9 ppm. HRMS (EI): calcd. for $C_{19}H_{20}O_5$ [M + Na]$^+$ 351.1208; found 351.1212.

Methyl 2-(3-Chlorostyryl)benzoate (6f): 86% yield, (*E*:*Z* = 24:1); R_f = 0.7 (ethyl acetate/hexanes, 2:8); colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1077, 1246, 1262, 1432, 1593, 1718 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, COOCH_3), 6.84 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArCHC*H*ArCl), 7.15–7.23 (m, 2 H, 2′, 5′-H), 7.25–7.29 (m, 1 H, 5-H), 7.34 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6′-H), 7.43–7.47 (m, 1 H, 4-H), 7.61 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.86–7.88 (dd, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 4′-H), 7.92 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHArCl) ppm. Non-overlapped peaks of *Z*-isomer: δ = 3.82 (s, 3 H, COOCH_3), 6.55 (d, $^3J_{H,H}$ = 12 Hz, 1 H, ArCHC*H*ArCl) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.1, 124.9, 126.7, 127.1, 127.5, 127.7, 128.6, 129.0, 129.8, 129.9, 130.7, 132.2, 134.6, 138.8, 139.3, 167.7 ppm. Non-overlapped peaks of *Z*-isomer: δ = 127.9, 129.3, 130.3, 134.3 ppm. HRMS (EI): calcd. for $C_{16}H_{13}O_2Cl$ [M + Na]$^+$ 295.0502; found 295.0511.

Methyl 2-(But-1-enyl)benzoate (6g): 84% yield, (*E*:*Z* = 1:1); R_f = 0.5, (ethyl acetate/hexanes, 1:9); colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1074, 1284, 1435, 1721 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, CH_2CH_3), 2.23–2.31 (qd,$^{3,3}J_{H,H}$ = 1.6, 7.6 Hz, 2 H, CH_2CH_3), 3.89 (s, 3 H, COOCH_3), 6.14–6.21 (dt, $^{3,3}J_{H,H}$ = 6.4, 16.0 Hz, 1 H, ArCHC*H*Et), 7.13 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, 3-H), 7.23–7.31 (m, 3 H, 2-ArH, olefin), 7.54 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, 6-H), 7.91–7.94 (m, 1 H, 4-H) ppm. Non-overlapped peaks of *Z*-isomer: δ = 1.00 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, CH_2CH_3), 2.09–2.17 (qd, $^{3,3}J_{H,H}$ = 0.8, 7.2 Hz, 2 H, CH_2CH_3), 3.87 (s, 3 H, COOCH_3), 5.68–5.74 (dt, $^{3,3}J_{H,H}$ = 7.6, 11.2 Hz, 1 H, ArCHC*H*Et), 6.83 (d, $^3J_{H,H}$ = 11.6 Hz, 1 H, ArC*H*CHEt), 7.43–7.46 (m, 2 H, ArH), 7.82–7.84 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 8.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 14.3, 21.7, 26.2, 51.8, 51.9, 126.4, 126.5, 127.2, 127.5, 128.0, 128.2, 130.3, 130.7, 131.4, 131.8, 133.8, 135.5, 139.1, 139.7, 167.8, 168.1 ppm.

(*E*)-Methyl 2-{2-[5-(*tert*-Butoxycarbonylamino)-2,2-dimethyl-1,3-dioxan 5-yl]vinyl}benzoate (6h): 80% yield, (*E* only); R_f = 0.51 (ethyl acetate/hexanes, 2:8); viscous oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1076, 1166, 1246, 1367, 1481, 1716 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (s, 9 H, *t*Bu), 1.39 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 3.81 (s, 3 H, COOCH_3), 3.87–3.96 (m, 4 H, 2 CH_2), 5.24 (s, 1 H, N*H*), 6.09 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H, ArCHC*H*C), 7.19–7.23 (m, 1 H, 5-H), 7.29 (d, $^3J_{H,H}$ = 16.4 Hz, 1 H, ArC*H*CHC), 7.36–7.40 (m, 1 H, 4-H), 7.47 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.80–7.83 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.8, 18.0, 26.6, 27.1, 28.4, 30.6, 50.7, 51.7, 64.9, 78.3, 97.0, 126.0, 126.3, 126.9, 128.2, 129.2, 130.0, 130.9, 137.6, 153.6, 166.3 ppm. HRMS (EI): calcd. for $C_{21}H_{29}NO_6$ [M + Na]$^+$ 414.1893; found 414.1894.

(*S*)-Methyl 2-[2-(2,2-Dimethyl-1,3-dioxolan-4-yl)vinyl]benzoate (6i): 65% yield, (*E*:*Z* = 4.8:1); R_f = 0.51 (ethyl acetate/hexanes, 2:8); viscous oil. $[\alpha]_D^{37}$ = +2.625 (*c* = 3.5, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1059, 1262, 1370, 1720 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 3 H, CCH_3), 1.48 (s, 3 H, CCH_3), 3.71 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5′-Ha), 3.89 (s, 3 H, COOCH_3), 4.17–4.21 (dd, $^{3,3}J_{H,H}$ = 6.0, 8.0 Hz, 1 H, 5′-Hb), 4.73 (q, $^3J_{H,H}$ = 7.2 Hz, 1 H, 4′-H), 6.03–6.09 (dd, $^{3,3}J_{H,H}$ = 7.6, 16.0 Hz, 1 H, ArCHC*H*R), 7.30–7.34 (td, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5-H), 7.45–7.51 (m, 2 H, 4-H, ArC*H*CHR), 7.58 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.87–7.89 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-H) ppm. Non-overlapped peaks of *Z*-isomer: 1.39 (s, 3 H, CCH_3), 1.46 (s, 3 H, CCH_3), 3.65 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5′-Ha), 3.87 (s, 3 H, COOCH_3), 4.59–4.65 (m, 1 H, 5′-Hb), 5.71–5.76 (dd, $^{3,3}J_{H,H}$ = 8.0, 12.0 Hz, 1 H, ArCHC*H*R), 7.19 (d, $^3J_{H,H}$ = 12.0 Hz, 1 H, ArC*H*CHR), 7.35–7.39 (m, 1 H, 3-H), 7.97–7.99 (m, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 26.5, 52.1, 69.5, 77.2, 109.6, 128.3, 130.8, 31.9, 137.7, 167.6 ppm. Non-overlapped peaks of *Z*-isomer: δ = 25.3, 25.9, 52.0, 69.7, 76.4, 109.5, 128.3, 130.8, 131.9, 137.7, 167.2 ppm. HRMS (EI): calcd. for $C_{15}H_{18}O_4$ [M + Na]$^+$ 285.1103; found 285.1107.

Methyl 2-{2-[(4*S*,4′*R*,5*R*)-2,2,2′,2′-Tetramethyl-4,4′-bi(1,3-dioxolan)-5-yl]vinyl}benzoate (6j): 64% yield, (*E*:*Z* = 15.7:1); R_f = 0.25 (ethyl acetate/hexanes, 2:8); viscous oil. $[\alpha]_D^{37}$ = +15.495 (*c* = 7.0, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1077, 1263, 1434, 1719 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, 2′ CCH_3), 1.40 (s, 3 H, 2′ CCH_3), 1.45 (s, 3 H, 2 CCH_3), 1.47 (s, 3 H, 2 CCH_3), 3.84 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5′-H), 3.89 (s, 3 H, COOCH_3), 3.97–4.01 (dd, $^{3,3}J_{H,H}$ = 5.2, 8.4 Hz, 1 H, 5′-H), 4.10–4.14 (dd, $^{3,3}J_{H,H}$ = 6.0, 8.4 Hz, 1 H, 4′-H), 4.18–4.23 (m, 1 H, 4-H), 4.54–4.58 (td, $^{3,3}J_{H,H}$ = 0.8, 7.2 Hz, 1 H, 5-H), 6.08–6.14 (dd, $^{3,3}J_{H,H}$ = 6.8, 16.0 Hz, 1 H, ArCHC*H*R), 7.29–7.33 (td, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5-H), 7.44–7.55 (m, 3 H, ArH, ArC*H*CHR), 7.86–7.88 (dd, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.3, 26.7, 26.9, 27.0, 52.0, 66.9, 76.6, 80.2, 81.2, 109.6, 127.4, 127.5, 128.8, 129.8, 130.4, 131.4, 132.0, 138.4, 167.7 ppm. HRMS (EI): calcd. for $C_{20}H_{26}O_6$ [M + Na]$^+$ 385.1627; found 385.1629.

Methyl 2-{2-[(3α*S*,4*R*,6*S*,6α*S*)-6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl]vinyl}benzoate (6k): 65% yield, (*E*:*Z* = 5.6:1); R_f = 0.5, (ethyl acetate/hexanes, 2:8); viscous oil. $[\alpha]_D^{36}$ = –3.157 (*c* = 6.2, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1011, 1208, 1262, 1722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (s, 3 H, CCH_3), 1.42 (s, 3 H, CCH_3), 3.81 (s, 3 H, COOCH_3), 4.44 (d, $^3J_{H,H}$ = 12.0 Hz, 1 H, PhC*H*H), 4.59–4.70 (m, 5 H, PhC*H*H, 3′, 4′, 5′-H), 5.06 (s, 1 H, 2′-H), 6.18–6.24 (dd, $^{3,3}J_{H,H}$ = 8.0, 16.0 Hz, 1 H, ArCHC*H*R), 7.16–7.28 (m, 6 H, Bn, 5-H), 7.37–7.41 (td, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 9.6 Hz, 1 H, 4-H), 7.49 (d, $^3J_{H,H}$ = 15.6 Hz, 1 H, ArC*H*CHR), 7.58 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.79–7.81 (dd, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6-H) ppm. Non-overlapped peaks of *Z*-isomer: δ = 1.17 (s, 3 H, CCH_3), 1.44 (s, 3 H, CCH_3), 3.81 (s, 3 H, COOCH_3), 4.35 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H), 5.02 (s, 1 H), 5.92–5.97 (dd, $^{3,3}J_{H,H}$ = 9.2, 12.0 Hz, 1 H, ArCHC*H*R), 7.11–7.13 (m, 1 H, PhC*H*H), 7.33–7.35 (m, 3 H, ArH), 7.89–7.91 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.9, 26.2, 52.0, 68.9, 81.8, 85.5, 105.4, 112.5, 126.3, 127.5, 127.7, 127.8, 128.04, 128.07, 128.2, 128.5, 128.6, 130.4, 132.1, 132.9, 137.4, 138.3, 167.7 ppm. Non-overlapped peaks of *Z*-isomer: δ = 68.9, 75.9, 81.6, 85.6, 124.4, 125.8, 127.0, 127.6, 128.0, 128.4, 129.3, 130.6, 131.7, 134.9, 137.2, 138.0, 167.3 ppm. HRMS (EI): calcd. for $C_{24}H_{26}O_6$ [M + Na]$^+$ 433.1627; found 433.1632.

(*E*)-Methyl 2-{2-[3,4,5-Tris(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-yl]vinyl}benzoate (6l): 50% yield, (*E* only); R_f = 0.5 (ethyl acetate/hexanes, 2:8); viscous oil. $[\alpha]_D^{35}$ = +1.855 (*c* = 3.5, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1074, 1261, 1453, 1721 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.28 (t, $^3J_{H,H}$ = 9.6 Hz, 1 H, 4′-H), 3.34 (s, 3 H, OCH_3), 3.48–3.51 (dd, $^{3,3}J_{H,H}$ = 3.6, 9.6 Hz, 1 H, 3′-H), 3.75 (s, 3 H, OCH_3), 3.96 (t, $^3J_{H,H}$ = 9.2 Hz, 1 H, 5′-H), 4.19–4.23 (dd, $^{3,3}J_{H,H}$ = 7.2, 9.6 Hz, 1 H, 2′-H), 4.55–4.74 (m, 6 H, OBn, 6′-H), 4.77 (d, $^2J_{H,H}$ = 10.8 Hz, 1 H, OBn), 4.89 (d, $^2J_{H,H}$ = 10.8 Hz, 1 H, OBn), 5.96–6.01 (dd, $^{3,3}J_{H,H}$ = 6.8, 16.0 Hz, 1 H, ArCHC*H*R), 7.12–7.36 (m, 19 H, ArH, Bn), 7.42–7.46 (dd, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 7.79 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.0, 55.3, 71.2, 73.4, 75.1, 75.8, 79.9, 81.8, 82.3, 98.2, 127.3, 127.4, 127.5, 127.6, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 129.2, 130.5, 131.8, 132.0, 138.2, 138.3, 167.6 ppm. HRMS (EI): calcd. for $C_{37}H_{38}O_7$ [M + Na]$^+$ 617.2515; found 617.2527.

Methyl 2-[(*E*)-2-{(3α*R*,4*R*,6*R*,6α*R*)-6-Methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}vinyl]benzoate (6m): 56% yield, (*E* only); R_f = 0.5, (ethyl acetate/hexanes, 2:8); viscous oil. $[\alpha]_D^{35}$ = –4.648 (*c* = 3.5, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1076, 1102, 1255, 1372, 1720 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, 2′ CCH_3), 1.54 (s, 3 H, 2′ CCH_3), 3.40 (s, 3 H, OCH_3), 3.92 (s, 3 H, COOCH_3), 4.69 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, 4′-H), 4.76 (d, $^3J_{H,H}$ = 5.6 Hz, 1 H, 3′-H), 4.89 (d, $^3J_{H,H}$ = 5.6 Hz, 1 H, 2′-H), 5.05 (s, 1 H, 5′-H), 6.11–6.17 (dd, $^{3,3}J_{H,H}$ = 8.4, 16.0 Hz, 1 H, ArCHC*H*R), 7.31–7.35 (m, 1 H, 5-H), 7.40 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 7.45–7.50 (td, $^4J_{H,H}$ = 1.2 Hz, $^3J_{H,H}$ = 7.2 Hz, 1 H, 4-H), 7.53 (d, $^3J_{H,H}$ = 6.8 Hz, 1 H, 3-H), 7.88–7.90 (dd, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0, 26.5, 52.0, 54.6, 84.7, 85.6, 88.0, 109.3, 112.4, 127.3, 127.4, 128.8, 130.4, 131.3, 131.5, 132.0, 138.1, 167.6 ppm. HRMS (EI): calcd. for $C_{18}H_{22}O_6$ [M + Na]$^+$ 357.1314; found 357.1319.

Methyl 2-[(*E*)-2-{(3α*S*,4*R*,6α*R*)-2,2-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}vinyl]benzoate (6n): 75% yield, (*E* only); R_f = 0.25, (ethyl acetate/hexanes, 2:8); viscous oil. $[\alpha]_D^{35}$ = –5.268 (*c* = 4.0, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1076, 1095, 1258, 1371, 1718 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (s, 3 H, CCH_3), 1.45 (s, 3 H, CCH_3), 3.47–3.51 (dd, $^{3,3}J_{H,H}$ = 4.0, 10.8 Hz, 1 H, 4′-H), 3.81 (s, 3 H, OCH_3), 4.00–4.05 (m, 2 H, 5′-H), 4.62–4.65 (dd, $^{3,3}J_{H,H}$ = 4.0, 6.0 Hz, 1 H, 3′-H), 4.75–4.77 (dd, $^{3,3}J_{H,H}$ = 3.6, 6.0 Hz, 1 H, 2′-H), 6.18–6.24 (dd, $^{3,3}J_{H,H}$ = 8.0, 16.0 Hz, 1 H, ArCHC*H*R), 7.21–7.25 (td, $^4J_{H,H}$ = 0.8 Hz, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H), 7.40 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, 4-H), 7.48 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 7.58 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 3-H), 7.79–7.81 (m, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.8, 26.1, 52.0, 72.8, 81.4, 82.5, 83.5, 112.2, 126.4, 127.4, 127.7, 128.5, 130.3, 132.0, 132.9, 138.4, 167.7 ppm. HRMS (EI): calcd. for $C_{17}H_{20}O_5$ [M + Na]$^+$ 327.1208; found 327.1215.

2-Methoxy-6-methylbenzaldehyde and 3-Bromo-6-methoxy-2-methylbenzaldehyde (11 and 13): 30% yield; R_f = 0.25, (ethyl acetate/hexanes, 0.4:9.6); crystalline solid. IR (CH_2Cl_2): $\tilde{\nu}$ = 1080, 1256, 1284, 1433, 1462, 1576, 1728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, OCH_3), 2.63 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.74 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 3-H), 6.80 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5′-H), 6.83 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 5-H), 7.37 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H), 7.66 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 4′-H), 10.53 (s, 1 H, C*H*O), 10.63 (s, 1 H, C*H*O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.9, 21.3, 55.8, 55.9, 109.0, 110.5, 118.3, 123.3, 124.1, 125.1, 126.5, 134.3, 137.8, 140.4, 141.9, 162.0, 163.1, 191.8, 192.2 ppm.

Methyl 2-(2-{(3α*S*,4*R*,6*S*,6α*S*)-6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}vinyl)-6-methoxybenzoate (20): 70% yield, (*E*:*Z* = 4:1); R_f = 0.4, (ethyl acetate/hexanes, 2:8), colourless oil. $[\alpha]_D^{36}$ = –8.160 (*c* = 4.0, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1008, 1070, 1265, 1468, 1576, 1729 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CCH_3), 1.48 (s, 3 H, CCH_3), 3.82 (s, 3 H, OCH_3), 3.92 (s, 3 H, COOCH_3), 4.52 (d, $^3J_{H,H}$ = 11.6 Hz, 1 H, 3′-H), 4.55–4.58 (dd, $^{3,3}J_{H,H}$ = 4.0, 8.0 Hz, 1 H, 4′-H), 4.61–4.66 (m, 1 H, 2′-H), 4.67–4.76 (m, 3.5 H), 5.12 (s, 1 H, 5′-H), 6.32–6.37 (dd, $^{3,3}J_{H,H}$ = 7.6, 16.0 Hz, 1 H, ArCHC*H*R), 6.66 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 6.79–6.88 (m, 2 H, ArH), 7.21–7.35 (m, 10 H, ArH, Bn) ppm. Non-overlapped peaks of *Z*-isomer: δ = 1.31 (s, 3 H, CCH_3), 1.50 (s, 3 H, CCH_3), 3.84 (s, 3 H, OCH_3), 3.88 (s, 3 H, COOCH_3), 4.43 (d, $^3J_{H,H}$ = 12.0 Hz, 1 H, 3′-H), 5.09 (s, 1 H, 5′-H), 6.00–6.05 (dd, $^{3,3}J_{H,H}$ = 8.0, 12.0 Hz, 1 H, ArCHC*H*R), 6.97 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0, 26.1, 52.3, 56.0, 69.0, 80.9, 81.7, 85.5, 105.4, 110.2, 112.6, 118.4, 122.9, 126.9, 127.6, 127.8, 128.0, 128.1, 128.4, 128.5, 130.4, 135.3, 137.4, 156.5, 168.3 ppm. Non-overlapped peaks of *Z*-isomer: δ = 24.9, 68.8, 75.9, 85.6, 105.3, 110.4, 130.3 ppm. HRMS (EI): calcd. for $C_{25}H_{28}O_7$ [M + Na]$^+$ 463.1733; found 463.1731.

Methyl 2-Methoxy-6-(2-{(3α*R*,4*R*,6*R*,6α*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}vinyl)benzoate (21): 77%

yield, (*E*:*Z* = 8.5:1.5); R_f = 0.4, (ethyl acetate/hexanes, 2:8), colourless oil. $[\alpha]_D^{36}$ = –1.598 (*c* = 3.0, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1065, 1263, 1468, 1576, 1729 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, CCH_3), 1.51 (s, 3 H, CCH_3), 3.36 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.92 (s, 3 H, COOCH_3), 4.65–4.70 (m, 2 H, 3′, 4′-H), 4.77 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 2′-H), 5.02 (s, 1 H, 5′-H), 6.18–6.24 (dd, $^{3,3}J_{H,H}$ = 8.0, 16.0 Hz, 1 H, ArCHC*H*R), 6.53 (d, $^{3,3}J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 6.83 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H), 7.09 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 3-H), 7.31 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H) ppm. Non-overlapped peaks of *Z*-isomer: δ = 1.30 (s, 3 H, CCH_3), 1.45 (s, 3 H, CCH_3), 3.34 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.89 (s, 3 H, COOCH_3), 4.89 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 2′-H), 5.01 (s, 1 H, 5′-H), 5.76–5.71 (dd, $^{3,3}J_{H,H}$ = 8.0, 12.0 Hz, 1 H, ArCHC*H*R), 6.88 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H), 7.38 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0, 26.4, 52.4, 54.7, 56.0, 84.6, 85.5, 87.9, 109.4, 110.2, 112.4, 117.9, 122.8, 128.9, 130.4, 131.9, 135.1, 156.4, 168.2 ppm. Non-overlapped peaks of *Z*-isomer: δ = 24.6, 54.4, 82.8, 84.8, 85.8, 108.9, 110.3, 122.0, 132.3 ppm. HRMS (EI): calcd. for $C_{19}H_{24}O_7$ $[M + Na]^+$ 387.1420; found 387.1420.

Methyl 2-[(*E*)-2-{(3α*S*,4*R*,6α*R*)-2,2-Dimethyltetrahydrofuro[3,4-*d*]-[1,3]-dioxol-4-yl}vinyl]-6-methoxybenzoate (22): 67% yield, (*E* only); R_f = 0.3, (ethyl acetate/hexanes, 2:8, 2× elusion), colourless crystals; m.p. 105–110 °C. $[\alpha]_D^{35}$ = –46.291 (*c* = 4.0, $CHCl_3$). IR (CH_2Cl_2): $\tilde{\nu}$ = 1066, 1092, 1264, 1471, 1577, 1727 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, CCH_3), 1.50 (s, 3 H, CCH_3), 3.50–3.54 (dd, $^{3,3}J_{H,H}$ = 3.6, 10.8 Hz, 1 H, 3′-H), 3.80 (s, 3 H, OCH_3), 3.89 (s, 3 H, COOCH_3), 3.98–4.01 (dd, $^{3,3}J_{H,H}$ = 3.6, 7.6 Hz, 1 H, 4′-H), 4.05 (d, $^{3,3}J_{H,H}$ = 10.8 Hz, 1 H, 2′-H), 4.63–4.81 (m, 2 H, 5′-H), 6.31–6.37 (dd, $^{3,3}J_{H,H}$ = 7.2, 16.0 Hz, 1 H, ArCHC*H*R), 6.65 (d, $^{3,3}J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 6.81 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 5-H), 7.20 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 3-H), 7.29 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.9, 26.1, 52.3, 55.9, 72.8, 81.3, 82.3, 83.3, 110.2, 112.3, 118.3, 122.8, 127.0, 130.2, 130.3, 135.3, 156.4, 168.4 ppm. HRMS (EI): calcd for $C_{18}H_{22}O_6$ $[M + H]^+$ 335.1495; found 335.1493.

(2*R*,3*R*,4*R*)-2-[2-(Hydroxymethyl)-3-methoxystyryl]tetrahydrofuran-3,4-diol (23): 62% yield (2 steps); R_f = 0.3, ($MeOH/CH_2Cl_2$, 0.2:9.8); colourless needles, m.p. 137–140 °C. IR (CH_2Cl_2): $\tilde{\nu}$ = 1000, 1123, 1263, 1469, 1579, 3373 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.77–3.84 (m, 4 H, OCH_3, 5′-H), 3.87–3.91 (m, 1 H, 5′-H), 4.08–4.12 (m, 1 H, 4′-H), 4.23–4.28 (m, 1 H, 3′-H), 4.42 (t, $^3J_{H,H}$ = 4.4 Hz, 1 H, 2′-H), 4.76 (s, 2 H, ArCH_2O), 6.13–6.18 (dd, $^{3,3}J_{H,H}$ = 6.4, 16.0 Hz, 1 H, ArCHC*H*R), 6.78 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H), 6.94 (d, $^{3,3}J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 7.07 (d, $^3J_{H,H}$ = 7.6 Hz, 1 H, 6-H), 7.21 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.7, 55.8, 72.0, 72.1, 73.1, 81.5, 109.7, 119.4, 125.9, 129.0, 129.2, 129.9, 138.0, 157.8 ppm. HRMS (EI): calcd. for $C_{14}H_{18}O_5$ $[M + Na]^+$ 289.1052; found 289.1053.

Methyl 3-Bromo-6-methoxy-2-methylbenzoate (14): 50% yield; R_f = 0.4, (CH_2Cl_2/hexanes, 1:1), colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1263, 1435, 1462, 1731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, ArCH_3), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, COOCH_3), 6.65 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 5-H), 7.50 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1, 52.5, 56.1, 110.2, 116.1, 125.5, 133.8, 135.5, 155.4, 167.9 ppm. HRMS (EI): calcd. for $C_{10}H_{11}BrO_3$ $[M + Na]^+$ 280.9789; found 280.9782.

Methyl 3-Bromo-6-methoxy-2-{(*E*)-2-[(2*R*,3*R*,4*S*,5*R*,6*S*)-3,4,5-tris-(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-yl]vinyl}benzoate (27): 77% yield, (*E* only); R_f = 0.4, (ethyl acetate/hexanes, 2:8), colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1045, 1068, 1260, 1286, 1431, 1454, 1569, 1731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.22 (t, *J* = 9.2 Hz, 1 H, 4′-H), 3.32 (s, 3 H, OCH_3), 3.47–3.50 (dd, $^{3,3}J_{H,H}$ = 3.6, 9.6 Hz, 1 H, 3′-H), 3.70 (s, 3 H, OCH_3), 3.74 (s, 3 H, COOCH_3), 3.94 (t, $^3J_{H,H}$ = 9.6 Hz, 1 H, 5′-H), 4.12–4.16 (dd, $^{3,3}J_{H,H}$ = 6.4, 9.6 Hz, 1 H), 4.56–4.62 (m, 3 H, OCH_2Ph), 4.67 (m, 3 H, OCH_2Ph), 4.88 (d, $^2J_{H,H}$ = 10.8 Hz, 1 H, OCH_2Ph), 5.88–5.94 (dd, $^{3,3}J_{H,H}$ = 6.0, 16.0 Hz, 1 H, ArCHC*H*R), 6.66 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 5-H), 6.67–6.72 (m, 1 H, ArC*H*CHR), 7.13–7.31 (m, 17 H, 5-H, OBn), 7.45 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.4, 55.1, 56.2, 70.5, 73.4, 75.1, 75.9, 79.8, 81.8, 82.2, 98.0, 111.5, 114.4, 125.0, 127.6, 127.9, 128.01, 128.05, 128.1, 128.2, 128.3, 128.4, 128.5, 129.7, 133.2, 133.9, 136.0, 138.1, 138.2, 138.7, 155.7, 167.4 ppm. HRMS (EI): calcd. for $C_{38}H_{39}BrO_8$ $[M + Na]^+$ 725.1726; found 725.1728.

Methyl 3-Bromo-2-[(*E*)-2-{(3α*S*,4*R*,6α*R*)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}vinyl]-6-methoxybenzoate (28): 54% yield, (*E* only); R_f = 0.4, (ethyl acetate/hexanes, 2:8), colourless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 1066, 1264, 1471, 1577, 1727 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, CCH_3), 1.50 (s, 3 H, CCH_3), 3.52–3.55 (dd, $^{3,3}J_{H,H}$ = 3.6, 10.8 Hz, 1 H, 3′-H), 3.82 (s, 3 H, OCH_3), 3.87 (s, 1 H, COOCH_3), 3.99–4.02 (dd, $^{3,3}J_{H,H}$ = 3.6, 6.8 Hz, 1 H, 4′-H), 4.07 (d, $^3J_{H,H}$ = 10.8 Hz, 1 H, 2′-H), 4.66–4.68 (dd, $^{3,3}J_{H,H}$ = 4.0, 6.0 Hz, 1 H, 5′-H), 4.80–4.83 (dd, $^{3,3}J_{H,H}$ = 4.0, 6.0 Hz, 1 H, 5′-H), 6.05–6.11 (dd, $^{3,3}J_{H,H}$ = 7.2, 16.0 Hz, 1 H, ArCHC*H*R), 6.73 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 5-H), 6.77 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, ArC*H*CHR), 7.51 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2, 25.2, 51.6, 55.2, 71.9, 80.3, 81.2, 82.1, 110.6, 111.4, 113.6, 123.6, 129.3, 129.9, 132.8, 134.8, 154.7, 166.4 ppm. HRMS (EI): calcd. for $C_{18}H_{21}BrO_6$ $[M + H]^+$ 413.0600; found 413.0591.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra of **2**, **3**, **6i**–**6n**, **20**–**23**, **26**, **27** and **28**.

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[17] CCDC-746252 (for **26**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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