

# Supporting Information

## Enantioselective Synthesis, Stereochemical Correction and Biological Investigation of the Rodgersinine Family of 1,4-Benzodioxane Neolignans

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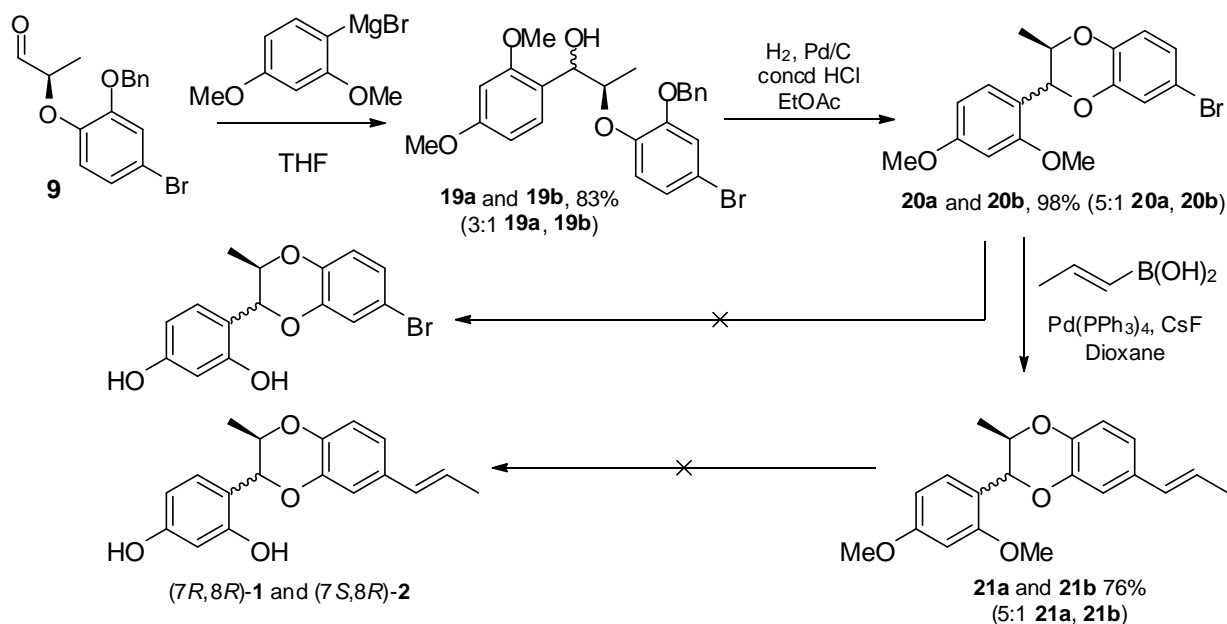
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## Methyl ether protected approach:

**Scheme 1. Synthesis of methyl ether protected analogues of *trans* and *cis* rogersinine A**



2,4-Dimethoxyphenylmagnesium bromide was added to aldehyde **9** to give a 3:1 mixture of diastereomers **19a** and **19b** which the underwent hydrogenolysis and concomitant cyclisation to give a mixture of *trans* **20a** and *cis* **20b** 1,4-benzodioxanes. A Suzuki reaction installed the (*E*)-propenyl sidechain, providing *trans* and *cis* 2,4-dimethoxy rogersinine A **21a** and **21b**. Unfortunately, all attempts at deprotection of **21a** and **21b** or **20a** and **20b** were unsuccessful.

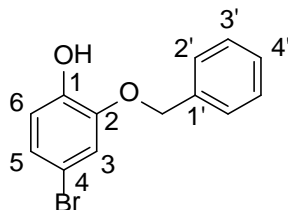
The details of the experimental procedures are detailed below.

## General experimental details:

All reactions were carried out under a nitrogen atmosphere in dry, freshly distilled solvents unless otherwise noted. All optical rotation measurements were determined at 20 °C on the sodium D line ( $\lambda = 589 \text{ nm}$ , 0.1 dm cell). Ultraviolet–visible and circular dichroism spectra were run as methanol solutions. NMR spectra were recorded on a 300 MHz, 400 MHz or 500 MHz spectrometer. Chemical shifts are reported relative to the solvent peak of chloroform ( $\delta$  7.26 for  $^1\text{H}$  and  $\delta$  77.0 for  $^{13}\text{C}$ ).  $^1\text{H}$  NMR data is reported as position ( $\delta$ ), relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak; qd, quartet of doublets), coupling constant (*J*, Hz), and the assignment of the atom.  $^{13}\text{C}$  NMR data are reported as position ( $\delta$ ) and assignment of the atom. NMR assignments were performed using HSQC and HMBC experiments. High-resolution mass spectroscopy (HRMS) was carried out by either chemical ionization (CI) or electrospray ionization (ESI) on a MicroTOF-Q mass spectrometer. Unless noted, chemical reagents were used as purchased.

## Experimental procedures and compound data:

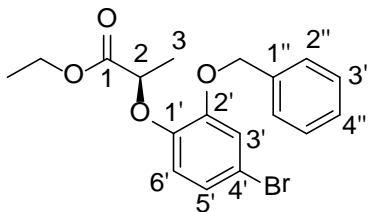
### 2-Benzyloxy-4-bromophenol **6**



To a stirred suspension of catechol **5** (15.0 g, 0.136 mol) and KOH (7.64 g, 0.136 mol) in MeOH (150 mL) under an atmosphere of nitrogen, was added BnCl (15.6 mL, 0.136 mol) over a period of 10 min. The resulting mixture was stirred at room temperature for 1 h and then heated at reflux for 4 h. After cooling to room temperature, the solution was acidified with 2 M HCl and extracted with diethyl ether (4 x 100 mL). The combined organic extracts were then washed with brine (50 mL), dried (MgSO<sub>4</sub>) and the solvent was removed *in vacuo*. The crude product was purified by distillation and then by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield 2-(benzyloxy)phenol (11.7 g, 43 %) as a colourless oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.56.  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 5.10 (2H, s, CH<sub>2</sub>Ar), 5.66 (1H, s, OH), 6.81–6.96 (4H, m, H-3, H-4, H-5 and H-6) and 7.34–7.43 (5H, m, Ar-H).  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>) 71.1 (OCH<sub>2</sub>Ar), 112.2 (C-3), 114.7 (C-6), 120.1 (C-4), 121.8 (C-5), 127.8 (C-2'), 128.4 (C-4'), 128.7 (C-3'), 136.4 (C-1'), 145.8 (C-1) and 145.9 (C-2). The <sup>1</sup>H and <sup>13</sup>C NMR data was in agreement with the literature values.<sup>1,2</sup>

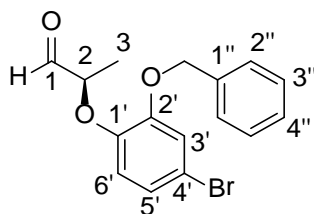
To a solution of 2-(benzyloxy)phenol (3.04 g, 15.2 mmol) in CH<sub>2</sub>Cl<sub>2</sub>/acetic acid (22.5 mL, 2:1, v/v), cooled to 0 °C was added a solution of Br<sub>2</sub> (0.78 mL, 15.2 mmol) in acetic acid (7.50 mL) dropwise over 10 min. The solution was stirred at 0 °C for 10 min, then water (20 mL) was added and the organic layer was separated. The aqueous mixture was further extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 50 mL) and the combined organic extracts were washed with sat. aq. Na<sub>2</sub>SO<sub>3</sub> (15 mL), water (15 mL) and brine (15 mL). The solution was then dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield the *title product* **6** (3.96 g, 93 %) as a yellow solid. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.51. **Melting Point:** 65.5–67 °C (Lit.<sup>3</sup> 66–68 °C).  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 5.08 (2H, s, OCH<sub>2</sub>Ar), 5.57 (1H, s, OH), 6.80 (1H, d, *J* = 9.0 Hz, H-6), 6.99 (1H, dd, *J* = 3.0 and 9.0 Hz, H-5), 7.06 (1H, d, *J* = 3.0 Hz, H-3) and 7.40–7.42 (5H, m, Ar-H).  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 71.4 (OCH<sub>2</sub>Ar), 111.5 (C-4), 115.5 (C-3), 116.0 (C-6), 124.6 (C-5), 128.0 (C-2'), 128.7 (C-4'), 128.8 (C-3'), 135.6 (C-1'), 145.1 (C-1) and 162.3 (C-2). The <sup>1</sup>H NMR data was in agreement with the literature values.<sup>3</sup>

**(2R)-Ethyl 2-(2'-(benzyloxy)-4'-bromophenoxy)propanoate 8**



To a solution of phenol **6** (3.00 g, 0.011 mol),  $\text{PPh}_3$  (4.93 g, 0.019 mol) and (*S*)-ethyl lactate **7** (2.22 g, 0.019 mol) in THF (90 mL) under an atmosphere of nitrogen, at 0 °C was added DIAD (3.70 mL, 0.019 mol) dropwise. The reaction mixture was then allowed to warm to room temperature. After stirring for 1 h, the mixture was then concentrated *in vacuo*. The crude product was purified by flash chromatography (19:1 *n*-hexanes, ethyl acetate) to yield the *title product 8* (3.62 g, 89 %) as a colourless oil.  **$R_f$  (4:1 *n*-hexanes, ethyl acetate)** 0.58.  **$[\alpha]_D + 47.7$**  (*c* 0.84,  $\text{CHCl}_3$ ). **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3035 (CH aromatic), 2987 and 2937 (CH alkane), 1748 (C=O ester), 1589 and 1490 (C=C aromatic), 1455, 1404 and 1378 (CH alkane), 1256, 1196, 1141, 1115 and 1096 (C-O ether, ester), 910, 877, 798, 733 and 697 (CH aromatic).  **$\delta_H$  (300 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ )** 1.21 (3H, t,  $J = 6.0$  Hz,  $\text{CH}_2\text{CH}_3$ ), 1.58 (3H, d,  $J = 6.0$  Hz, H-3), 4.15–4.20 (2H, m,  $\text{CH}_2\text{CH}_3$ ), 4.70 (1H, q,  $J = 9.0$  Hz, H-2), 5.09 (2H, s,  $\text{OCH}_2\text{Ar}$ ), 6.80 (1H, d,  $J = 9.0$  Hz, H-6'), 6.98 (1H, dd,  $J = 3.0$  and  $9.0$  Hz, H-5'), 7.07 (1H, d,  $J = 3.0$  Hz, H-3') and 7.32–7.45 (5H, m, Ar-H).  **$\delta_C$  (75 MHz;  $\text{CDCl}_3$ )** 14.1 ( $\text{CH}_2\text{CH}_3$ ), 18.5 (C-3), 61.1 ( $\text{CH}_2\text{CH}_3$ ), 71.4 ( $\text{OCH}_2\text{Ar}$ ), 74.9 (C-2), 114.9 (C-4'), 118.5 (C-3'), 119.3 (C-6'), 124.2 (C-5'), 127.4 (C-2''), 128.0 (C-4''), 128.5 (C-3''), 136.4 (C-1''), 147.0 (C-1'), 150.4 (C-2') and 171.9 (C-1).  **$m/z$  (ESI+):** 403 ( $^{81}\text{BrMNa}^+$ , 100 %), 401 ( $^{79}\text{BrMNa}^+$ , 100), 398 ( $^{81}\text{BrMH}^+$ , 5), 396 ( $^{79}\text{BrMH}^+$ , 5) and 323 (33). **HRMS (ESI+):** Found ( $\text{MNa}^+$ ): 403.0338  $\text{C}_{18}\text{H}_{19}^{81}\text{BrNaO}_4$  requires 403.0339. Found ( $\text{MNa}^+$ ): 401.0354  $\text{C}_{18}\text{H}_{19}^{79}\text{BrNaO}_4$  requires 401.0359.

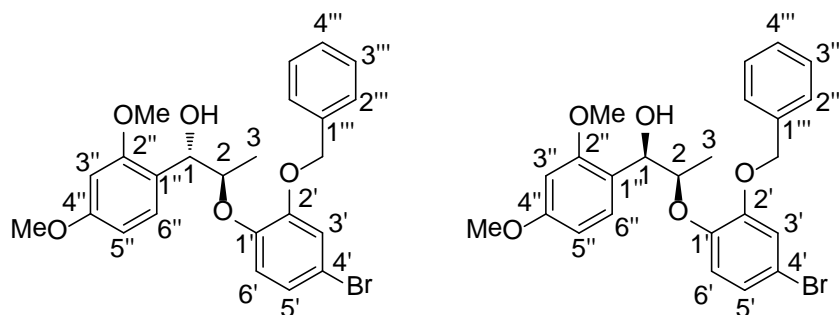
**(2R)-2-(2'-(Benzyloxy)-4'-bromophenoxy)propan-1-al 9**



To a solution of ester **8** (3.60 g, 9.50 mmol) in  $\text{CH}_2\text{Cl}_2$  (120 mL) under an atmosphere of nitrogen at -78 °C was added DIBAL (1 M in cyclohexane, 10.5 mL, 10.5 mmol). The mixture was stirred at -78 °C for 15 min. The reaction was quenched with 2 M HCl (50 mL) then extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 80 mL), dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield the *title product 9* (2.61 g, 82 %) as a white crystalline solid.  **$R_f$  (4:1 *n*-hexanes, ethyl acetate)** 0.38.  **$[\alpha]_D + 25.8$**  (*c* 0.64,  $\text{CHCl}_3$ ). **Melting Point:** 62–65 °C. **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3066 and 3034 (CH aromatic), 2984 and 2934 (CH alkane), 2874 and 2818 (CH aldehyde), 1734 (C=O aldehyde), 1588 and 1492 (C=C aromatic), 1455, 1403 and 1380 (CH alkane), 1254, 1207, 1137, 1074 and 1001 (C-O ether), 917, 880, 836, 815, 737 and 696 (CH aromatic).  **$\delta_H$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ )** 1.42 (3H, d,  $J = 6.8$  Hz, H-3), 4.50 (1H, q,  $J = 6.8$  Hz, H-2), 5.08 (2H, s,  $\text{OCH}_2\text{Ar}$ ), 6.80 (1H, d,  $J = 8.4$  Hz, H-6'), 7.01 (1H, dd,  $J = 2.0$  and  $8.4$  Hz, H-5'), 7.11 (1H, d,  $J = 6.8$  Hz, H-3').

= 2.0 Hz, H-3'), 7.33–7.40 (5H, m, Ar-H) and 9.74 (1H, d,  $J$  = 0.8 Hz, CHO).  $\delta_{\text{C}}$  (100 MHz;  $\text{CDCl}_3$ ) 15.6 (C-3), 71.2 ( $\text{OCH}_2\text{Ar}$ ), 80.6 (C-2), 115.4 (C-4'), 117.9 (C-3'), 119.8 (C-6'), 124.1 (C-5'), 127.4 (C-2''), 128.2 (C-4''), 128.6 (C-3''), 136.0 (C-1''), 146.5 (C-1'), 150.5 (C-2') and 202.1 (C-1).  $m/z$  (ESI+): 359 ( $^{81}\text{BrMNa}^+$ , 25), 357 ( $^{79}\text{BrMNa}^+$ , 25), 339 (100) and 91 (10). HRMS (ESI+): Found ( $\text{MNa}^+$ ): 359.0082  $\text{C}_{16}\text{H}_{15}^{81}\text{BrNaO}_3$  requires 359.0077. Found ( $\text{MNa}^+$ ): 357.0097  $\text{C}_{16}\text{H}_{15}^{79}\text{BrNaO}_3$  requires 357.0097.

**(1*S*,2*R*)-2-(2'-(Benzyloxy)-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol 19a and  
(1*R*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol 19b**

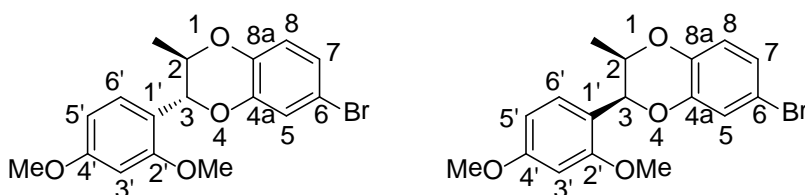


To a stirred solution of aldehyde **9** (0.300 g, 0.895 mmol) in THF (15 mL), under an atmosphere of nitrogen at room temperature, was added 2,4-dimethoxyphenylmagnesium bromide (0.5 M in THF, 5.37 mL, 2.69 mmol) dropwise. The mixture was stirred at room temperature for 24 h. The reaction was quenched with the addition of sat. aq.  $\text{NH}_4\text{Cl}$  (15 mL). The mixture was separated and the aqueous layers further extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (14:1, *n*-hexanes, ethyl acetate) to yield (1*S*,2*R*)-2-(2'-benzyloxy-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol **19a** (0.256 g, 61 %) as a pale yellow oil.  $R_f$  (4:1 *n*-hexanes, ethyl acetate) 0.31.  $[\alpha]_{\text{D}} -30.0$  ( $c$  0.60,  $\text{CHCl}_3$ ). IR:  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3510 (broad, OH), 3070 and 3031 (CH aromatic), 2990, 2935 and 2835 (CH alkane), 1612, 1587 and 1491 (C=C aromatic), 1454, 1403 and 1382 (CH alkane), 1288, 1248, 1205, 1156, 1131, 1034 and 992 (C-O ether, alcohol), 919, 880, 832, 797, 737, 697 and 675 (CH aromatic).  $\delta_{\text{H}}$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 1.15 (3H, d,  $J$  = 6.4 Hz, H-3), 3.03 (1H, s, OH), 3.71 (3H, s, OMe), 3.78 (3H, s, OMe), 4.56 (1H, dq,  $J$  = 3.2 and 6.4 Hz, H-2), 5.06 (2H, s,  $\text{OCH}_2\text{Ar}$ ), 5.16 (1H, d,  $J$  = 2.4 Hz, H-1), 6.38 (1H, d,  $J$  = 2.4 Hz, H-3''), 6.43 (1H, dd,  $J$  = 2.4 and 8.4 Hz, H-5''), 6.92 (1H, d,  $J$  = 8.4 Hz, H-6'), 7.03 (1H, dd,  $J$  = 2.0 and 8.4 Hz, H-5'), 7.08 (1H, d,  $J$  = 2.4 Hz, H-3') and 7.31–7.44 (6H, m, H-6'', H-2'', H-3''' and H-4''').  $\delta_{\text{C}}$  (100 MHz;  $\text{CDCl}_3$ ) 13.4 (C-3), 55.2 (OMe), 55.3 (OMe), 69.3 (C-1), 71.4 ( $\text{OCH}_2\text{Ar}$ ), 79.0 (C-2), 98.0 (C-3''), 104.2 (C-5''), 114.1 (C-4'), 117.8 (C-3'), 119.4 (C-6'), 120.4 (C-1''), 124.3 (C-5'), 127.5 (C-2'''), 128.1 (C-6''), 128.2 (C-4'''), 128.6 (C-3'''), 136.2 (C-1'''), 146.9 (C-1'), 150.9 (C-2'), 156.9 (C-2'') and 160.0 (C-4'').  $m/z$  (ESI+): 513 ( $^{81}\text{BrMK}^+$ , 63 %), 511 ( $^{79}\text{BrMK}^+$ , 60), 497 ( $^{81}\text{BrMNa}^+$ , 98 %), 495 ( $^{79}\text{BrMNa}^+$ , 100), 492 (42), 490 (40), 457 (61), 455 (58), 376 (10), 268 (16) and 178 (14). HRMS (ESI+): Found ( $^{81}\text{BrMNa}^+$ ): 497.0773  $\text{C}_{24}\text{H}_{25}^{81}\text{BrNaO}_5$  requires 497.0758. Found ( $^{79}\text{BrMNa}^+$ ): 495.0785  $\text{C}_{24}\text{H}_{25}^{79}\text{BrNaO}_5$  requires 495.0778.

In a separate fraction, (1*R*,2*R*)-2-(2'-benzyloxy-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol **19b** (0.094 g, 22 %) was isolated as a pale yellow oil.  $R_f$  (4:1 *n*-hexanes, ethyl acetate) 0.25.  $[\alpha]_{\text{D}} -97.1$  ( $c$  0.7,  $\text{CHCl}_3$ ). IR:  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3509 (broad, OH), 3066 and 3034 (CH aromatic), 2932, 2874 and 2839 (CH alkane), 1613, 1588 and 1492 (C=C aromatic), 1455, 1403 and 1380 (CH alkane), 1291, 1254, 1209, 1158, 1131 and 1036 (C-O ether, alcohol), 922, 873, 835, 801, 739 and 698 (CH aromatic).  $\delta_{\text{H}}$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 1.14 (3H, d,  $J$  = 6.4 Hz, H-3), 3.50 (1H, s, OH), 3.76 (3H, s, OMe), 3.78

(3H, d,  $J = 4.0$  Hz, OMe), 4.32–4.35 (1H, m, H-2), 5.04 (1H, d,  $J = 8.4$  Hz, H-1), 5.08 (2H, s,  $\text{OCH}_2\text{Ar}$ ), 6.42 (1H, d,  $J = 2.0$  Hz, H-3''), 6.43 (1H, dd,  $J = 2.0$  and  $8.4$  Hz, H-5''), 6.82 (1H, d,  $J = 8.4$  Hz, H-6'), 6.99 (1H, dd,  $J = 2.4$  and  $8.4$  Hz, H-5'), 7.07 (1H, d,  $J = 2.0$  Hz, H-3'), 7.24 (1H, d,  $J = 8.4$  Hz, H-6'') and 7.33–7.46 (5H, m, H-2''', H-3''' and H-4''').  $\delta_{\text{C}}$  (100 MHz;  $\text{CDCl}_3$ ) 16.4 (C-3), 55.3 (OMe), 55.3 (OMe), 71.2 (C-1), 72.0 ( $\text{OCH}_2\text{Ar}$ ), 82.7 (C-2), 98.4 (C-3''), 104.4 (C-5''), 114.3 (C-4'), 117.6 (C-3'), 119.9 (C-6'), 121.0 (C-1''), 124.2 (C-5'), 127.5 (C-2'''), 128.1 (C-6''), 128.2 (C-4'''), 128.6 (C-3'''), 136.1 (C-1'''), 147.4 (C-1'), 150.7 (C-2'), 157.9 (C-2'') and 160.3 (C-4'').  $m/z$  (ESI+): 513 ( $^{81}\text{BrMK}^+$ , 63 %), 511 ( $^{79}\text{BrMK}^+$ , 60), 497 ( $^{81}\text{BrMNa}^+$ , 98 %), 495 ( $^{79}\text{BrMNa}^+$ , 100), 492 (42), 490 (40), 457 (61), 455 (58), 376 (10), 268 (16) and 178 (14). HRMS (ESI+): Found ( $\text{MNa}^+$ ): 497.0773  $\text{C}_{24}\text{H}_{25}^{81}\text{BrNaO}_5$  requires 497.0758. Found ( $\text{MNa}^+$ ): 495.0785  $\text{C}_{24}\text{H}_{25}^{79}\text{BrNaO}_5$  requires 495.0778.

**(2R,3R)-2-Methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane 20a and  
(2R,3S)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane 20b**

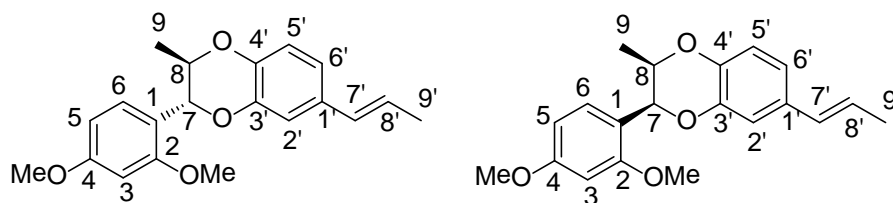


To a 3.5:1 mixture of benzyl ether **19a** and benzyl ether **19b** (70.0 mg, 0.15 mmol) and 10 % Pd/C (12.0 mg) in ethyl acetate (10 mL) was added 37 % HCl (1.0 mL) and the resultant suspension was stirred under an atmosphere of hydrogen for 30 min. The catalyst was then removed by filtration through Celite<sup>®</sup> and washed with ethyl acetate. The filtrate was washed with sat. aq.  $\text{NaHCO}_3$  (2 x 15 mL) and water (15 mL). The aqueous layers were back extracted with ethyl acetate (2 x 15 mL). The combined organic layers were dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The crude product was purified firstly by flash chromatography (14:1 *n*-hexanes, ethyl acetate) to yield the *title products* **20a** and **20b** (53.0 mg, 98 %) as a 5:1 inseparable mixture of *trans* **20a** to *cis* **20b** isomers as a white solid. Further purification with silver impregnated silica (2:1 *n*-hexanes,  $\text{CH}_2\text{Cl}_2$ ) was able to yield pure samples of **20a** and **20b** suitable for complete characterisation.  $R_f$  (4:1 *n*-hexanes, ethyl acetate) 0.81. **Melting Point:** 67.0–77.0 °C. **20a (trans):**  $[\alpha]_{\text{D}} +3.8$  (c 1.32, MeOH). **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3043 (CH aromatic), 2961, 2936 and 2840 (CH alkane), 1615, 1589, 1509 and 1492 (C=C aromatic), 1463, 1439, 1420 and 1381 (CH alkane), 1301, 1260, 1207, 1158, 1131, 1114, 1103, 1070, 1033 and 1009 (C-O ether), 936, 924, 898, 872, 835, 824, 798, 746, 636 and 608 (CH aromatic).  $\delta_{\text{H}}$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 1.18 (3H, d,  $J = 6.4$  Hz,  $\text{CH}_3$ ), 3.81 (3H, s, OMe), 3.82 (3H, s, OMe), 4.09–4.16 (1H, m, H-2), 5.11 (1H, d,  $J = 8.4$  Hz, H-3), 6.48 (1H, d,  $J = 2.4$  Hz, H-3'), 6.53 (1H, dd,  $J = 2.4$  and  $8.4$  Hz, H-5'), 6.77 (1H, d,  $J = 8.8$  Hz, H-8), 6.93 (1H, dd,  $J = 2.0$  and  $8.8$  Hz, H-7), 7.06 (1H, d,  $J = 2.0$  Hz, H-5) and 7.19 (1H, d,  $J = 8.4$  Hz, H-6').  $\delta_{\text{C}}$  (100 MHz;  $\text{CDCl}_3$ ) 16.5 ( $\text{CH}_3$ ), 55.4 (OMe), 55.5 (OMe), 74.1 (C-2), 74.4 (C-3), 98.5 (C-3'), 104.9 (C-5'), 112.4 (C-6), 117.6 (C-1'), 118.1 (C-8), 120.0 (C-5), 123.9 (C-7), 128.8 (C-6'), 142.9 (C-8a), 145.2 (C-4a), 158.2 (C-2') and 161.2 (C-4').  $m/z$  (ESI+): 389 ( $^{81}\text{BrMNa}^+$ , 25 %), 387 ( $^{79}\text{BrMNa}^+$ , 25), 367 ( $^{81}\text{BrMH}^+$ , 95), 365 ( $^{79}\text{BrMH}^+$ , 100), 287(20) and 178 (25). HRMS (ESI+): Found ( $\text{MH}^+$ ): 367.0372  $\text{C}_{17}\text{H}_{18}^{81}\text{BrO}_4$  requires 367.0363. Found ( $\text{MH}^+$ ): 365.0392  $\text{C}_{17}\text{H}_{18}^{79}\text{BrO}_4$  requires 365.0383.

**20b (cis):**  $[\alpha]_{\text{D}} +31.3$  (c 0.32, MeOH). **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 2996 (CH aromatic), 2957, 2921 and 2868 (CH alkane), 1615, 1590, 1509 and 1493 (C=C aromatic), 1463 and 1380 (CH alkane), 1258, 1209, 1158, 1131, 1105, 1070, 1034 and 992 (C-O ether), 923, 830, 799, 748, 700 and 618 (CH aromatic).  $\delta_{\text{H}}$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 1.05 (3H, d,  $J = 6.4$  Hz,  $\text{CH}_3$ ), 3.81 (3H, s, OMe), 3.81 (3H, s, OMe), 4.63 (1H, dq,  $J = 2.4$  and  $6.4$  Hz, H-2), 5.44 (1H, d,  $J = 2.4$  Hz, H-3), 6.46 (1H, d,  $J = 2.4$

Hz, H-3'), 6.51 (1H, dd,  $J = 2.4$  and  $8.4$  Hz, H-5'), 6.77 (1H, d,  $J = 8.4$  Hz, H-8), 6.95 (1H, dd,  $J = 2.4$  and  $8.4$  Hz, H-7), 7.10 (1H, d,  $J = 2.4$  Hz, H-5) and 7.35 (1H, d,  $J = 8.4$  Hz, H-6').  $\delta_c$  (100 MHz;  $CDCl_3$ ) 12.8 (CH<sub>3</sub>), 55.4 (OMe), 55.5 (OMe), 71.2 (C-3), 72.4 (C-2), 98.1 (C-3'), 104.4 (C-5'), 112.4 (C-6), 117.2 (C-1'), 118.7 (C-8), 120.1 (C-5), 124.3 (C-7), 127.5 (C-6'), 141.4 (C-8a), 144.4 (C-4a), 157.0 (C-2') and 160.7 (C-4').  $m/z$  (ESI+): 389 ( $^{81}BrMNa^+$ , 25 %), 387 ( $^{79}BrMNa^+$ , 25), 367 ( $^{81}BrMH^+$ , 95), 365 ( $^{79}BrMH^+$ , 100), 287 (20) and 178 (25). HRMS (ESI+): Found (MH<sup>+</sup>): 367.0372 C<sub>17</sub>H<sub>18</sub><sup>81</sup>BrO<sub>4</sub> requires 367.0363. Found (MH<sup>+</sup>): 365.0392 C<sub>17</sub>H<sub>18</sub><sup>79</sup>BrO<sub>4</sub> requires 365.0383.

**(7R,8R)-7-(2,4-Dimethoxyphenyl)-8-methyl-3',7-epoxy-8,4'-oxyneolign-7'-ene 21a**  
**((7R,8R)-*trans*-dimethyl rogersinine A (21a)) and**  
**(7S,8R)-7-(2,4-dimethoxyphenyl)-8-methyl-3',7-epoxy-8,4'-oxyneolign-7'-ene 21b**  
**((7S,8R)-*cis*-2,4-dimethyl rogersinine A (21b))**

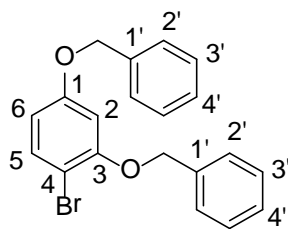


To a stirred solution of a 5:1 mixture of bromide **20a** and bromide **20b** (47.0 mg, 0.129 mmol) in dioxane (3 mL) was added *trans*-prop-1-enylboronic acid (33.0 mg, 0.384 mmol) and CsF (78.0 mg, 0.512 mmol) and the mixture was heated under an atmosphere of nitrogen. After the mixture reached reflux, Pd(PPh<sub>3</sub>)<sub>4</sub> (100 mg, 0.109 mmol) was added and the mixture heated at reflux for 3 days. The mixture was then left to cool to room temperature. Ethyl acetate (5 mL) was added, followed by brine (5 mL), the mixture was separated and the aqueous layer further extracted with ethyl acetate (2 x 20 mL). The organic layers were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified using flash chromatography (2:1, *n*-hexanes, CH<sub>2</sub>Cl<sub>2</sub>) to yield unreacted starting material (2*R*,3*R*)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane **20a** and (2*R*,3*S*)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane **20b** (12.0 mg, 0.033 mmol) and the *title products* **21a** and **21b** (32.0 mg, 76 %, 100 % brsm.) as a 5:1 inseparable mixture of *trans* **21a** to *cis* **21b** isomers as an orange oil. Further purification with silver impregnated silica (2:1 *n*-hexanes, CH<sub>2</sub>Cl<sub>2</sub>) was able to separate starting materials **20a** and **20b** from products **21a** and **21b**.  $R_f$  (4:1 *n*-hexanes, ethyl acetate) 0.78. IR:  $\nu_{max}$ (film)/cm<sup>-1</sup>; 3087, 3060 and 3000 (CH aromatic), 2958, 2936 and 2838 (CH alkane), 1677 (C=C alkene), 1615, 1584 and 1506 (C=C aromatic), 1465, 1455, 1438, 1420 and 1381 (CH alkane), 1266, 1208, 1158, 1134, 1119, 1107, 1070 and 1032 (C-O ether), 965, 938, 926, 910, 871, 824, 785 and 731 (CH aromatic). **21a** (*trans*):  $\delta_H$  (400 MHz;  $CDCl_3$ ; Me<sub>4</sub>Si) 1.18 (3H, d,  $J = 6.4$  Hz, H-9), 1.82 (3H, d,  $J = 6.8$  Hz, H-9'), 3.81 (3H, s, OMe), 3.82 (3H, s, OMe), 4.12–4.18 (1H, m, H-8), 5.13 (1H, d,  $J = 7.6$  Hz, H-7), 6.01–6.09 (1H, m, H-8'), 6.26 (1H, dd,  $J = 1.6$  and  $15.6$  Hz, H-7'), 6.48 (1H, d,  $J = 2.4$  Hz, H-3), 6.53 (1H, dd,  $J = 2.4$  and  $8.4$  Hz, H-5), 6.83 (2H, s, H-5' and H-6'), 6.93 (1H, s, H-2') and 7.23 (1H, d,  $J = 8.4$  Hz, H-6).  $\delta_c$  (100 MHz;  $CDCl_3$ ) 16.6 (C-9), 18.4 (C-9'), 55.4 (OMe), 55.5 (OMe), 74.0 (C-7), 74.6 (C-8), 98.6 (C-3), 104.9 (C-5), 114.1 (C-2'), 116.7 (C-5'), 118.2 (C-1), 119.1 (C-6'), 123.8 (C-8'), 128.9 (C-6), 130.4 (C-7'), 131.5 (C-1'), 142.7 (C-4'), 144.3 (C-3'), 158.2 (C-2) and 161.1 (C-4). **21b** (*cis*):  $\delta_H$  (400 MHz;  $CDCl_3$ ; Me<sub>4</sub>Si) 1.06 (3H, d,  $J = 6.4$  Hz, H-9), 1.82 (3H, d,  $J = 6.8$  Hz, H-9'), 3.81 (3H, s, OMe), 3.82 (3H, s, OMe), 4.62 (1H, dq,  $J = 2.4$  and  $6.4$  Hz, H-8), 5.45 (1H, d,  $J = 2.4$  Hz, H-7), 6.05–6.11 (1H, m, H-8'), 6.28 (1H, dd,  $J = 1.6$  and  $15.0$  Hz, H-7'), 6.46 (1H, d,  $J = 2.4$  Hz, H-3), 6.51 (1H, dd,  $J = 2.4$  and  $8.4$  Hz,

H-5), 6.83 (2H, s, H-5' and H-6'), 6.95 (1H, d,  $J = 2.0$  Hz, H-2') and 7.40 (1H, d,  $J = 8.4$  Hz, H-6).  $\delta_C$  (100 MHz;  $CDCl_3$ ) 12.9 (C-9), 18.4 (C-9'), 55.4 (OMe), 55.5 (OMe), 71.3 (C-8), 72.4 (C-7), 98.1 (C-3), 104.4 (C-5), 114.1 (C-2'), 117.4 (C-5'), 117.8 (C-1), 119.4 (C-6'), 123.8 (C-8'), 127.6 (C-6), 130.4 (C-7'), 131.5 (C-1'), 141.1 (C-4'), 143.5 (C-3'), 157.0 (C-2) and 160.6 (C-4).  $m/z$  (ESI+): 349 ( $MNa^+$ , 30 %), 327 ( $MH^+$ , 100) and 178 (55). HRMS (ESI+): Found ( $MNa^+$ ): 349.1406  $C_{20}H_{22}NaO_4$  requires 349.1410. Found ( $MH^+$ ): 327.1587  $C_{20}H_{23}O_4$  requires 327.1591.

Methods involving the use of both Lewis acids ( $BBr_3$  and TMSI) for varying lengths of time and at various temperatures on mixtures of **20a** and **20b**, and **21a** and **21b** did not yield any of the desired demethylated material, giving either degraded material or returned starting material, depending on the conditions. Strong nucleophilic reagents LiSEt and NaSEt also did not provide the desired demethylated products, under a range of conditions.

### 1,3-Bis(benzyloxy)-4-bromobenzene

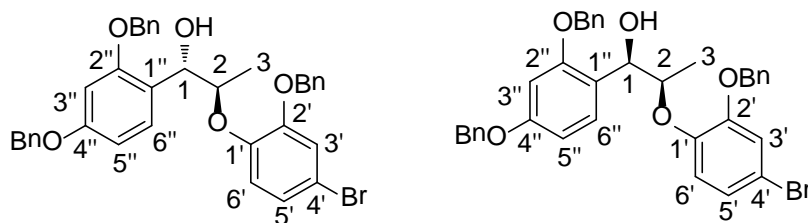


To a solution of resorcinol (2.20 g, 0.020 mol) in MeOH (100 mL) was added  $NH_4Br$  (2.15 g, 0.022 mol) and Oxone® (13.5 g, 0.022 mol) and the mixture was stirred at room temperature under an atmosphere of nitrogen for 30 min. The reaction mixture was then filtered and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (3:1 *n*-hexanes, ethyl acetate) to yield 4-bromoresorcinol (2.46 g, 65 %) as a white solid.  $R_f$  (3:1 *n*-hexanes, ethyl acetate) 0.68. **Melting Point:** 101–103 °C (lit.<sup>4</sup> 100–102 °C).  $\delta_H$  (400 MHz;  $CDCl_3$ ;  $Me_4Si$ ) 5.91 (2H, s, OH), 6.35 (1H, dd,  $J = 2.4$  and 8.4 Hz, H-6), 6.56 (1H, d,  $J = 2.4$  Hz, H-2) and 7.25 (1H, d,  $J = 8.4$  Hz, H-5).  $\delta_C$  (100 MHz;  $CDCl_3$ ) 100.6 (C-4), 103.5 (C-2), 109.5 (C-6), 132.2 (C-5), 153.1 (C-3) and 156.9 (C-1). The  $^1H$  NMR and  $^{13}C$  NMR data was in agreement with the literature values.<sup>5</sup>

To a solution of 4-bromoresorcinol (3.43 g, 0.018 mol) in acetone (40 mL) at room temperature, under an atmosphere of nitrogen, was added  $K_2CO_3$  (7.54 g, 0.055 mol). The mixture was cooled to 0 °C and BnBr (5.30 mL, 0.045 mol) was added dropwise. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed *in vacuo* and the residue taken up in a water/ethyl acetate mixture (1:1, 50 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried ( $MgSO_4$ ) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate). Only the pure fractions were collected to yield the 1,3-bis(benzyloxy)-4-bromobenzene (4.48 g, 67%) as a pale yellow solid.  $R_f$  (3:1 *n*-hexanes, ethyl acetate) 0.72. **Melting Point:** 36–38 °C. (lit.<sup>6</sup> 38–39 °C).  $\delta_H$  (400 MHz;  $CDCl_3$ ;  $Me_4Si$ ) 5.00 (2H, s,  $OCH_2Ar$ ), 5.10 (2H, s,  $OCH_2Ar$ ), 6.46 (1H, dd,  $J = 2.8$  and 8.8 Hz, H-6), 6.60 (1H, d,  $J = 2.8$  Hz, H-2) and 7.31–7.40 (11H, m, H-5 and Ar-H).  $\delta_C$  (100 MHz;  $CDCl_3$ ) 70.4 ( $OCH_2Ar$ ), 70.8 ( $OCH_2Ar$ ), 102.5 (C-2), 103.5 (C-4), 107.6 (C-6), 127.0 (C-2'), 127.5 (C-2'), 127.9 (C-4'), 128.1 (C-4'), 128.6 (C-3'), 128.6 (C-3'), 133.2 (C-5), 136.4 (C-1'), 136.5 (C-1'), 155.7 (C-3) and 159.2 (C-1). The  $^1H$  NMR data was in agreement with the literature values.<sup>7</sup>



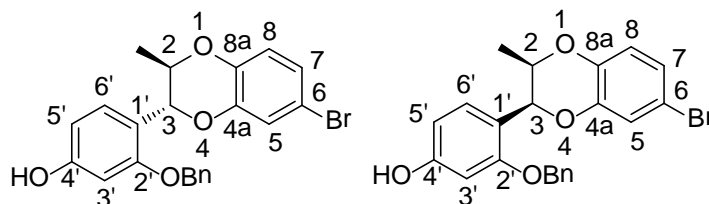
**(1*S*,2*R*)-2-(2'-(Benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol 11a and  
(1*R*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol 11b**



To a stirred solution of 1,3-bis(benzyloxy)-4-bromobenzene (0.661 g, 1.79 mmol) in dry THF (30 mL), under an atmosphere of nitrogen at  $-78^{\circ}\text{C}$ , was added  $t\text{BuLi}$  (1.4 M in THF, 2.56 mL, 3.58 mmol). After 3 min, a solution of aldehyde **9** (0.500 g, 1.49 mmol) in dry THF (15 mL) was added slowly and the mixture was left to warm to room temperature and stirred for a further 20 h. Sat. aq.  $\text{NH}_4\text{Cl}$  (25 mL) was added and the aqueous mixture extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield the (1*S*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol **11a** (0.305 g, 33 %) as a colourless oil. **11a** (*anti*):  $R_f$  (4:1 *n*-hexanes, ethyl acetate) 0.42.  $[\alpha]_D -22.7$  ( $c$  1.37,  $\text{CHCl}_3$ ). **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3511 (broad, OH), 3033 (CH aromatic), 2931 and 2867 (CH alkane), 1611, 1586 and 1495 (C=C aromatic), 1454 and 1380 (CH alkane), 1250, 1125 and 1024 (C-O ether, alcohol), 729 and 695 (CH aromatic).  $\delta_H$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 1.14 (3H, d,  $J = 6.4$  Hz, H-3), 3.09 (1H, s, OH), 4.55 (1H, qd,  $J = 2.8$  and  $6.4$  Hz, H-2), 4.85 (1H, d,  $J = 11.2$  Hz,  $\text{OCH}_2\text{Ph}$ ), 4.92 (1H, d,  $J = 11.2$  Hz,  $\text{OCH}_2\text{Ph}$ ), 4.96 (2H, s,  $\text{OCH}_2\text{Ph}$ ), 5.01 (2H, s,  $\text{OCH}_2\text{Ph}$ ), 5.20 (1H, d,  $J = 2.8$  Hz, H-1), 6.55 (1H, dd,  $J = 1.6$  and  $8.4$  Hz, H-5''), 6.57 (1H, d,  $J = 1.6$  Hz, H-3''), 6.65 (2H, d,  $J = 1.2$  Hz, H-5' and H-6'), 7.00–7.01 (1H, m, H-3'), and 7.23–7.46 (16H, m, H-6'' and Ar-H).  $\delta_C$  (100 MHz;  $\text{CDCl}_3$ ) 13.4 (C-3), 68.6 (C-1), 70.1 ( $\text{OCH}_2\text{Ar}$ ), 70.2 ( $\text{OCH}_2\text{Ar}$ ), 71.3 ( $\text{OCH}_2\text{Ar}$ ), 79.1 (C-2), 99.9 (C-3''), 105.6 (C-5''), 114.1 (C-4'), 117.6 (C-3'), 119.8 (C-6'), 120.8 (C-1''), 124.4 (C-5'), 127.5 (Ar-CH), 127.7 (Ar-CH), 128.0 (C-6''), 128.1 (Ar-CH), 128.5 (Ar-CH), 128.6 (Ar-CH), 128.6 (Ar-CH), 136.1 (Ar-C), 136.3 (Ar-C), 136.9 (Ar-C), 146.5 (C-1'), 150.8 (C-2'), 155.9 (C-2'') and 159.2 (C-4').  $m/z$  (**ESI** $^{+}$ ): 649 ( $^{81}\text{BrMNa}^{+}$ , 100 %), 647 ( $^{79}\text{MNa}^{+}$ , 90), 569 (10), 360 (15) and 290 (8). **HRMS** (**ESI** $^{+}$ ): Found ( $\text{MNa}^{+}$ ): 649.1369  $\text{C}_{36}\text{H}_{33}^{81}\text{BrNaO}_5$  requires 649.1386. Found ( $\text{MNa}^{+}$ ): 647.1386  $\text{C}_{36}\text{H}_{33}^{79}\text{BrNaO}_5$  requires 647.1404.

In a separate fraction, (1*R*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol **11b** (0.071 g, 8 %) was collected as a colourless oil. **11b** (*syn*):  $R_f$  (4:1 *n*-hexanes, ethyl acetate) 0.36.  $[\alpha]_D -89.3$  ( $c$  1.086,  $\text{CHCl}_3$ ). **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3507 (broad, OH), 3032 (CH aromatic), 2927 and 2874 (CH alkane), 1611, 1587 and 1495 (C=C aromatic), 1454 and 1380 (CH alkane), 1253, 1170, 1128 and 1027 (C-O ether, alcohol), 736 and 697 (CH aromatic).  $\delta_H$  (400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 1.16 (3H, d,  $J = 6.4$  Hz, H-3), 4.32–4.38 (1H, m, H-2), 5.01 (2H, s,  $\text{OCH}_2\text{Ph}$ ), 5.01 (1H, s,  $\text{OCH}_2\text{Ph}$ ), 5.05 (2H, s,  $\text{OCH}_2\text{Ph}$ ), 5.09 (1H, d,  $J = 7.6$  Hz, H-1), 6.53 (1H, dd,  $J = 2.4$  and  $8.4$  Hz, H-5''), 6.58 (1H, d,  $J = 2.4$  Hz, H-3''), 6.75 (1H, d,  $J = 8.4$  Hz, H-6'), 6.94 (1H, dd,  $J = 2.0$  and  $8.4$  Hz, H-5'), 7.05 (1H, d,  $J = 2.0$  Hz, H-3') and 7.23–7.43 (16H, m, H-6'' and Ar-H).  $\delta_C$  (100 MHz;  $\text{CDCl}_3$ ) 16.6 (C-3), 70.1 ( $\text{OCH}_2\text{Ar}$ ), 70.2 ( $\text{OCH}_2\text{Ar}$ ), 71.3 ( $\text{OCH}_2\text{Ar}$ ), 72.1 (C-1), 82.9 (C-2), 100.5 (C-3''), 106.0 (C-5''), 114.4 (C-4'), 117.6 (C-3'), 120.0 (C-6'), 121.7 (C-1''), 124.2 (C-5'), 127.3 (Ar-CH), 127.5 (Ar-CH), 127.5 (Ar-CH), 127.9 (Ar-CH), 128.0 (Ar-CH), 128.2 (Ar-CH), 128.6 (Ar-CH), 128.6 (Ar-CH), 128.9 (C-6''), 136.1 (Ar-C), 136.7 (Ar-C), 136.8 (Ar-C), 147.5 (C-1'), 150.7 (C-2'), 157.0 (C-2'') and 159.5 (C-4').  $m/z$  (**ESI** $^{+}$ ): 665 ( $^{81}\text{BrMK}^{+}$ , 100 %), 663 ( $^{79}\text{MK}^{+}$ , 95), 569 (70) and 360 (80). **HRMS** (**ESI** $^{+}$ ): Found ( $\text{MK}^{+}$ ): 665.1103  $\text{C}_{36}\text{H}_{33}^{81}\text{BrKO}_5$  requires 665.1125. Found ( $\text{MK}^{+}$ ): 663.1123  $\text{C}_{36}\text{H}_{33}^{79}\text{BrKO}_5$  requires 663.1143.

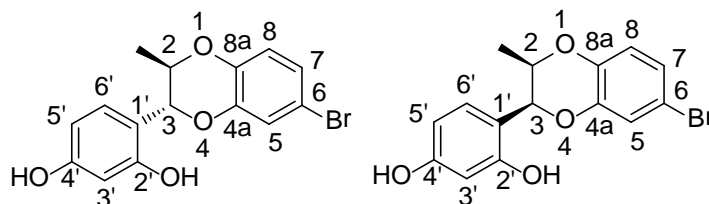
**(2*R*,3*R*)-2-Methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane**  
**and**  
**(2*R*,3*S*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane**



To a mixture of alcohols **11a** and **11b** (0.650 g, 1.04 mmol) in ethyl acetate (60 mL) was added 37 % HCl (4.5 mL) and 10 % Pd/C (0.098 g) and the mixture stirred under an atmosphere of hydrogen for 2 h. The mixture was filtered through Celite® and the filtrate washed with sat. aq. NaHCO<sub>3</sub> (2 x 50 mL) and water (50 mL). The aqueous washings were further extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield (2*R*,3*R*)-2-Methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane in a 10:1 ratio as an inseparable mixture of *trans* to *cis* isomers (0.066 g, 15 %) as an orange oil. **R<sub>f</sub>** (1:1 *n*-hexanes, ethyl acetate) 0.81. **IR:**  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup>; 3384 (broad, OH), 2961 (CH aromatic), 2929 (CH alkane), 1602 and 1487 (C=C aromatic), 1454 (CH alkane), 1269, 1167 and 1015 (C-O ether, alcohol), 737 and 697 (CH aromatic). **214a (trans):**  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.20 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 4.08–4.15 (1H, m, H-2), 5.04 (2H, d, *J* = 5.6 Hz, OCH<sub>2</sub>Ph), 5.16 (1H, d, *J* = 8.0 Hz, H-3), 6.47 (1H, dd, *J* = 2.4 and 8.4 Hz, H-5'), 6.51 (1H, d, *J* = 2.4 Hz, H-3'), 6.76 (1H, d, *J* = 8.4 Hz, H-8), 6.93 (1H, dd, *J* = 2.4 and 8.4 Hz, H-7), 7.06 (1H, d, *J* = 2.4 Hz, H-5), 7.16 (1H, d, *J* = 8.4 Hz, H-6') and 7.30–7.39 (5H, m, Ar-H).  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>) 16.6 (CH<sub>3</sub>), 70.4 (OCH<sub>2</sub>Ph), 74.2 (C-2), 74.5 (C-3), 100.2 (C-3'), 108.0 (C-5'), 112.6 (C-6), 117.9 (C-1'), 118.1 (C-8), 120.0 (C-5), 124.0 (C-7), 127.3 (Ar-CH), 128.1 (Ar-CH), 128.7 (Ar-CH), 129.1 (C-6'), 136.3 (Ar-C), 142.9 (C-8a), 145.2 (C-4a), 157.1 (C-4') and 157.5 (C-2'). **214b (cis):**  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.06 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 4.63 (1H, qd, *J* = 2.4 and 6.4 Hz, H-2), 5.07 (2H, d, *J* = 8.0 Hz, OCH<sub>2</sub>Ph), 5.51 (1H, d, *J* = 2.4 Hz, H-3), 6.47 (1H, dd, *J* = 2.4 and 8.4 Hz, H-5'), 6.51 (1H, d, *J* = 2.4 Hz, H-3'), 6.75 (1H, d, *J* = 8.4 Hz, H-8), 6.94 (1H, dd, *J* = 2.4 and 8.4 Hz, H-7), 7.10 (1H, d, *J* = 2.4 Hz, H-5), 7.21 (1H, d, *J* = 8.4 Hz, H-6') and 7.30–7.39 (5H, m, Ar-H).  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>) 12.9 (CH<sub>3</sub>), 70.0 (OCH<sub>2</sub>Ph), 71.2 (C-2), 72.4 (C-3), 99.8 (C-3'), 107.6 (C-5'), 112.6 (C-6), 117.0 (C-8), 118.7 (C-1'), 120.1 (C-5), 124.3 (C-7), 127.0 (Ar-CH), 127.9 (Ar-CH), 128.7 (Ar-CH), 129.0 (C-6'), 136.3 (Ar-C), 143.3 (C-8a), 144.1 (C-4a), 157.1 (C-4') and 157.5 (C-2'). **m/z (APCI+):** 429 (<sup>81</sup>BrMH<sup>+</sup>, 24 %), 427 (<sup>79</sup>MH<sup>+</sup>, 25), 338 (100) and 149 (20). **HRMS (APCI+):** Found (MH<sup>+</sup>): 429.0529 C<sub>22</sub>H<sub>20</sub><sup>81</sup>BrO<sub>4</sub> requires 429.0520. Found (MH<sup>+</sup>): 427.0539 C<sub>22</sub>H<sub>20</sub><sup>79</sup>BrO<sub>4</sub> requires 427.0539.

In a separate fraction, a 5:1 mixture of (2*R*,3*R*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane **12a** and (2*R*,3*S*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane **12b** (0.260 g, 74 %) isomers were collected as a pale orange oil (see below).

**(2*R*,3*R*)-2-Methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12a**  
**and**  
**(2*R*,3*S*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12b**



**Method A; Hydrogenation of diols 11a and 11b:** To a mixture of alcohols **11a** and **11b** (0.650 g, 1.04 mmol) in ethyl acetate (60 mL) was added 37 % HCl (4.5 mL) and 10 % Pd/C (0.098 g) and the mixture stirred under an atmosphere of hydrogen for 2 h. The mixture was filtered through Celite® and the filtrate washed with sat. aq. NaHCO<sub>3</sub> (2 x 50 mL) and water (50 mL). The aqueous washings were further extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield the *title products* **12a** and **12b** in a 5:1 ratio as a mostly inseparable mixture of *trans* **12a** to *cis* **12b** isomers (0.260 g, 74 %) as an orange oil. With repeated purification by flash chromatography (1:1 diethyl ether, *n*-hexanes) a pure sample of the *trans* isomer **12a** was able to be obtained as a white powder: **12a (trans):** *R<sub>f</sub>* (3:1 diethyl ether, *n*-hexanes) 0.39. **Melting Point:** 98–100 °C. [ $\alpha$ ]<sub>D</sub> +16.43 (*c* 0.70, MeOH). **IR:**  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup>; 3391 (broad, OH), 2982 (CH aromatic), 2930 (CH alkane), 1611 (C=C aromatic), 1487 (CH alkane), 1269, 1204, 1097, 1011 and 976 (C-O ether, alcohol), 847 and 734 (CH aromatic).  **$\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si)** 1.21 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 4.28–4.34 (1H, m, H-2), 4.86 (1H, d, *J* = 8.0 Hz, H-3), 4.91 (1H, br s, OH), 6.07 (1H, br s, OH), 6.39 (1H, d, *J* = 2.4 Hz, H-3'), 6.40 (1H, dd, *J* = 2.4 and 8.0 Hz, H-5'), 6.79 (1H, d, *J* = 8.0 Hz, H-8), 7.00 (1H, dd, *J* = 2.4 and 8.0 Hz, H-7), 7.03 (1H, d, *J* = 8.0 Hz, H-6') and 7.10 (1H, d, *J* = 2.4 Hz, H-5).  **$\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>)** 17.2 (CH<sub>3</sub>), 72.8 (C-2), 79.5 (C-3), 104.3 (C-3'), 108.2 (C-5'), 112.6 (C-6), 114.0 (C-1'), 118.4 (C-8), 120.3 (C-5), 125.2 (C-7), 130.2 (C-6'), 142.9 (C-8a), 143.6 (C-4a), 155.8 (C-2') and 157.4 (C-4'). ***m/z* (ESI+):** 361 (<sup>81</sup>BrMNa<sup>+</sup>, 100 %), 359 (<sup>79</sup>MNa<sup>+</sup>, 95), 281 (60), 150 (35) and 114 (80). **HRMS (ESI+):** Found (MNa<sup>+</sup>): 360.9869 C<sub>15</sub>H<sub>13</sub><sup>81</sup>BrNaO<sub>4</sub> requires 360.9870. Found (MNa<sup>+</sup>): 358.9886 C<sub>15</sub>H<sub>13</sub><sup>79</sup>BrNaO<sub>4</sub> requires 358.9889.

The *cis* isomer **12b** was not able to be separated, so was characterised as a mixture with the *trans* isomer **12a**. **12b (cis):** *R<sub>f</sub>* (3:1 diethyl ether, *n*-hexanes) 0.39. **IR:**  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup>; 3361 (broad, OH), 2961 (CH aromatic), 2933 (CH alkane), 1607 (C=C aromatic), 1487 (CH alkane), 1268, 1206, 1148, 1097, 1011 and 976 (C-O ether, alcohol), 803 and 683 (CH aromatic).  **$\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si)** 1.14 (3H, d, *J* = 6.8 Hz, CH<sub>3</sub>), 4.59 (1H, dq, *J* = 2.0 and 6.8 Hz, H-2), 5.27 (1H, br s, OH), 5.39 (1H, d, *J* = 2.0 Hz, H-3), 6.16 (1H, br s, OH), 6.38 (1H, d, *J* = 2.4 Hz, H-3'), 6.41 (1H, dd, *J* = 2.4 and 8.0 Hz, H-5'), 6.78 (1H, d, *J* = 8.0 Hz, H-8), 7.00 (1H, dd, *J* = 2.4 and 8.0 Hz, H-7), 7.01 (1H, d, *J* = 8.0 Hz, H-6') and 7.12 (1H, d, *J* = 2.4 Hz, H-5).  **$\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>)** 12.6 (CH<sub>3</sub>), 75.8 (C-2), 80.2 (C-3), 102.9 (C-3'), 107.9 (C-5'), 112.6 (C-6), 114.1 (C-1'), 118.4 (C-8), 120.2 (C-5), 125.2 (C-7), 130.4 (C-6'), 142.9 (C-8a), 143.7 (C-4a), 155.8 (C-2') and 156.8 (C-4'). ***m/z* (APCI+):** 339 (<sup>81</sup>BrMH<sup>+</sup>, 95 %), 337 (<sup>79</sup>MNa<sup>+</sup>, 100), 259 (40) and 149 (90). **HRMS (APCI+):** Found (MH<sup>+</sup>): 339.0050 C<sub>15</sub>H<sub>14</sub><sup>81</sup>BrO<sub>4</sub> requires 339.0050. Found (MH<sup>+</sup>): 337.0078 C<sub>15</sub>H<sub>14</sub><sup>79</sup>BrO<sub>4</sub> requires 337.0070.

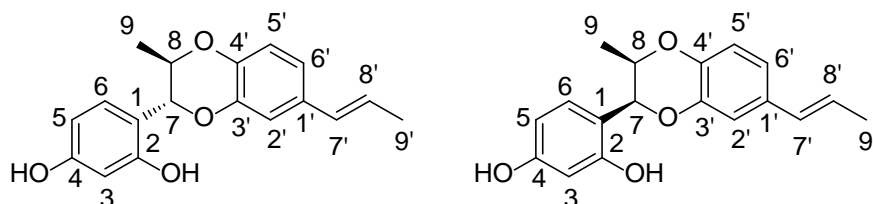
In a separate fraction, a 10:1 mixture of (2*R*,3*R*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane (0.066 g, 15 %) was collected as a pale orange oil (see above).

**Method B; Hydrogenation of (2*R*,3*R*)-2-Methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane:** To a 10:1 mixture of alcohols (0.188 g, 0.44 mmol) in ethyl acetate (20 mL) was added 37 % HCl (1.5 mL) and 10 % Pd/C (0.028 g,) and the mixture stirred under an atmosphere of hydrogen for 2 h. The mixture was filtered through Celite® and the filtrate washed with sat. aq. NaHCO<sub>3</sub> (2 x 20 mL) and water (20 mL). The aqueous washings were further extracted with ethyl acetate (2 x 20 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield the *title products* **12a** and **12b** as a mostly inseparable mixture of *trans* **12a** to *cis* **12b** isomers (0.088 g, 59 %) as an orange oil.

In a separate fraction, the starting material (2*R*,3*R*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane (0.075 g, 40 %) was collected as a pale orange oil.

Various methods were attempted, in the hope of obtaining rogersinine B directly from **12a** and **12b**, including a Sonogashira-type reaction, and a Stille reaction. Unfortunately, attempts at using these transition metal-based methods to install the alkyne sidechain were unsuccessful.

**(7*R*,8*R*)-*trans*-Rodgersinine A (1) and (7*S*,8*R*)-*cis*-rogersinine A (2)**  
**(*trans*-rogersinine A (1) and *cis*-rogersinine A (2))**



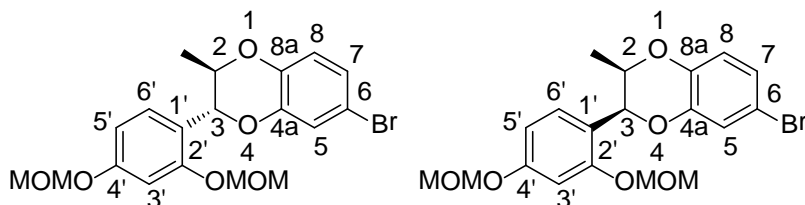
To a solution of bromide (2*R*,3*R*)-**12a** (51.0 mg, 0.151 mmol) in dry THF (8 mL), under an atmosphere of nitrogen, was added *trans*-propenylboronic acid (39.0 mg, 0.454 mmol), CsF (92.0 mg, 0.605 mmol) and the reaction mixture was heated. Once the reaction mixture was at reflux, Pd(PPh<sub>3</sub>)<sub>4</sub> (8.7 mg, 0.008 mmol) was added and the reaction heated at reflux for 18 h. The reaction mixture was then cooled and ethyl acetate (5 mL) and brine (5 mL) added. The layers were separated and the aqueous layer washed with ethyl acetate (2 x 5 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (3:1 diethyl ether, *n*-hexanes) to yield the *title products* (7*R*,8*R*)-**1** and (7*S*,8*R*)-**2** in a 5:1 ratio as mostly inseparable mixture of *trans* (7*R*,8*R*)-**1** to *cis* (7*S*,8*R*)-**2** isomers (40.0 mg, 89 %) as a white solid.

With repeated purification by flash chromatography (1:1 diethyl ether, *n*-hexanes) a pure sample of the *trans* isomer (7*R*,8*R*)-**1** was able to be obtained as a white powder. **R<sub>f</sub>** (3:1 diethyl ether, *n*-hexanes) 0.49. **Melting Point:** 54–56 °C. [ $\alpha$ ]<sub>D</sub> + 20.00 (*c* 0.16, MeOH), 95:5 mixture of *trans* (7*R*,8*R*)-**1** to *cis* (7*S*,8*R*)-**2** isomers. (lit.<sup>8</sup> [ $\alpha$ ]<sub>D</sub> +24.8 (*c* 0.075, MeOH)). **ECD** (MeOH; *c* 0.15 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 220 (+2.1), 236 (0), 252 (-0.3), 270 (0), 286 (+0.2) nm. **UV** (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 269 (4.02) nm. **IR:**  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup>; 3394 (broad, OH), 2959 (CH aromatic), 2930 and 2853 (CH alkane), 1629 (C=C alkene), 1610 and 1506 (C=C aromatic), 1272, 1216, 1160, 1097 and 973 (C-O ether, alcohol), 846 and 800 (CH aromatic, CH alkene).  **$\delta_{\text{H}}$**  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.20 (3H, d, *J* = 6.4 Hz, H-9), 1.84 (3H, dd, *J* = 1.6 and 6.4 Hz, H-9'), 4.32–4.39 (1H, m, H-8), 4.81 (1H, d, *J* = 8.4 Hz, H-7), 4.91 (1H, br s, OH), 6.04 (1H, dq, *J* = 6.4 and 15.2 Hz H-8'), 6.27 (1H, dd, *J* = 1.6

and 15.2 Hz, H-7'), 6.41 (1H, br s, H-3), 6.41 (1H, d,  $J = 8.0$  Hz, H-5), 6.49 (1H, br s, OH), 6.84 (1H, d,  $J = 8.4$  Hz, H-5'), 6.89 (1H, dd,  $J = 1.6$  and  $8.4$  Hz, H-6'), 6.95 (1H, d,  $J = 1.6$  Hz, H-2') and 6.99 (1H, d,  $J = 8.0$  Hz, H-6).  $\delta_C$  (100 MHz;  $CDCl_3$ ) 17.4 (C-9), 18.4 (C-9'), 72.5 (C-8), 80.7 (C-7), 104.5 (C-3), 107.9 (C-5), 114.0 (C-1), 114.3 (C-2'), 117.1 (C-5'), 120.3 (C-6'), 124.4 (C-8'), 130.1 (C-6), 130.4 (C-7'), 131.8 (C-1'), 142.4 (C-4'), 142.5 (C-3'), 156.2 (C-2) and 157.3 (C-4).  $m/z$  (ESI+): 321 ( $MNa^+$ , 5 %) and 127 (100). HRMS (ESI+): Found ( $MNa^+$ ): 321.1099  $C_{18}H_{18}NaO_4$  requires 321.1097. All  $^1H$  NMR and  $^{13}C$  NMR data was in agreement with literature values.<sup>8</sup> The  $[\alpha]_D$  and ECD data matched the literature values for what had been reported to be for the enantiomer of this compound.<sup>8</sup> Thus, the structure of the natural product has been reassigned to that of this compound, (7*R*,8*R*)-*trans*-rodgersinine A (**1**).

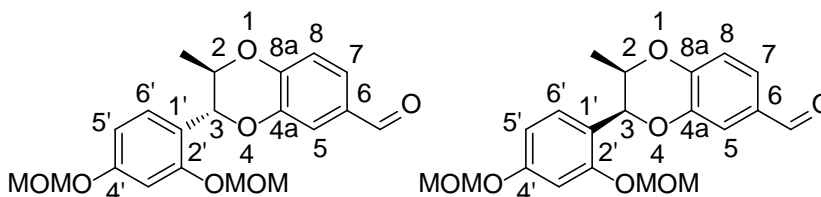
With repeated purification by flash chromatography (1:1 diethyl ether, *n*-hexanes) a pure sample of the *cis* isomer (7*S*,8*R*)-**2** was unable to be obtained, however when repeated separation was performed with HPLC (5 %  $i$ PrOH in *n*-hexanes, 0.4 mL/min, 15  $\mu$ L of 10 mg/0.5 mL solution, 28.5–30.5 min) giving a pure sample of *cis*-rodgersinine A (7*S*,8*R*)-**2** as a colourless film.  $R_f$  (3:1 diethyl ether, *n*-hexanes) 0.49.  $[\alpha]_D +67.78$  ( $c$  0.090, MeOH), 85:15 mixture of *cis* (7*S*,8*R*)-**2** to *trans* (7*R*,8*R*)-**1** isomers. (lit.<sup>8</sup>  $[\alpha]_D +79.9$  ( $c$  0.18, MeOH)). ECD (MeOH;  $c$  0.30 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 239 (-0.3), 245 (0), 259 (+0.5) nm. UV (MeOH)  $\lambda_{max}$  (log  $\epsilon$ ) 269 (3.81) nm. IR:  $\nu_{max}$ (film)/ $cm^{-1}$ : 3372 (broad, OH), 2959 (CH aromatic), 2927 and 2870 (CH alkane), 1606 (C=C alkene), 1505 and 1491 (C=C aromatic), 1263, 1207, 1155, 1095 and 974 (C-O ether, alcohol), 833, 800 and 736 (CH aromatic, CH alkene).  $\delta_H$  (400 MHz;  $CDCl_3$ ;  $Me_4Si$ ) 1.20 (3H, d,  $J = 6.4$  Hz, H-9), 1.84 (3H, dd,  $J = 1.2$  and  $6.4$  Hz, H-9'), 4.55 (1H, dq,  $J = 2.4$  and  $6.4$  Hz, H-8), 5.15 (1H, br s, OH), 5.38 (1H, d,  $J = 2.4$  Hz, H-7), 6.05 (1H, dq,  $J = 6.4$  and  $16.0$  Hz, H-8'), 6.28 (1H, dd,  $J = 1.6$  and  $16.0$  Hz, H-7'), 6.41 (1H, br s, H-3), 6.41 (1H, dd,  $J = 1.2$  and  $8.0$  Hz, H-5), 6.81 (1H, d,  $J = 8.0$  Hz, H-5'), 6.89 (1H, dd,  $J = 2.0$  and  $8.0$  Hz, H-6'), 6.95 (1H, d,  $J = 2.0$  Hz, H-2') and 7.04 (1H, d,  $J = 8.0$  Hz, H-6).  $\delta_C$  (100 MHz;  $CDCl_3$ ) 12.5 (C-9), 18.4 (C-9'), 72.8 (C-8), 77.2 (C-7), 103.9 (C-3), 107.8 (C-5), 113.8 (C-1), 114.2 (C-2'), 117.8 (C-5'), 120.4 (C-6'), 124.3 (C-8'), 128.6 (C-6), 130.1 (C-7'), 131.7 (C-1'), 140.8 (C-4'), 142.2 (C-3'), 155.6 (C-2) and 156.7 (C-4).  $m/z$  (ESI+): 321 ( $MNa^+$ , 25 %), 223 (30), 145 (60) and 101 (100). HRMS (ESI+): Found ( $MNa^+$ ): 321.1095  $C_{18}H_{18}NaO_4$  requires 321.1097. All  $^1H$  NMR and  $^{13}C$  NMR data was in agreement with literature values.<sup>8</sup> The  $[\alpha]_D$  and ECD data matched the literature values for what had been reported for the natural product.<sup>8</sup> Thus, the structure of the natural product was confirmed to be (7*S*,8*R*)-*cis*-rodgersinine A (**2**).

**(2*R*,3*R*)-2-Methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane**  
**and**  
**(2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane**



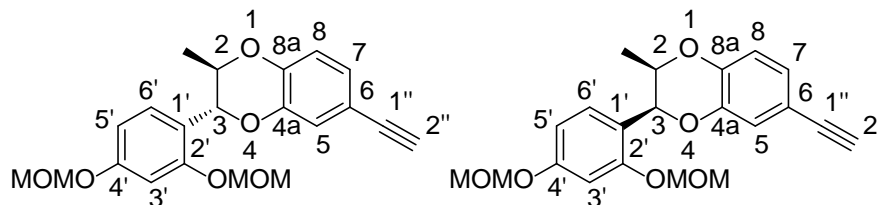
To a mixture of diols (2*R*,3*R*)-**12a** and (2*R*,3*S*)-**12b** (0.109 g, 0.320 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at room temperature, under an atmosphere of nitrogen, was added DIPEA (0.17 mL, 0.970 mmol) followed by MOMCl (0.15 mL, 1.29 mmol) and the mixture was stirred at room temperature for 7 h. Sat. aq. NH<sub>4</sub>Cl (8 mL) was added and the organic layer separated. The aqueous layer was further extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 10 mL) and the combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield the (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane as an inseparable 5:1 mixture of *trans* to *cis* isomers (0.093 g, 68 %) as a colourless oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.55. **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 2953 and 2931 (CH aromatic), 2826 (CH alkane), 1612, 1587, 1507 and 1486 (C=C aromatic), 1448 (CH alkane), 1266, 1208, 1152, 1074, 1004 and 925 (C-O ether), 898, 803 and 682 (CH aromatic). (*trans*):  **$\delta_{\text{H}}$**  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.21 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.11–4.18 (1H, m, H-2), 5.13 (1H, d, *J* = 8.0 Hz, H-3), 5.17 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 6.76 (1H, dd, *J* = 2.4 and 8.4 Hz, H-5'), 6.78 (1H, d, *J* = 8.4 Hz, H-8), 6.85 (1H, d, *J* = 2.4 Hz, H-3'), 6.94 (1H, dd, *J* = 2.4 and 8.4 Hz, H-7), 7.06 (1H, d, *J* = 2.4 Hz, H-5) and 7.21 (1H, d, *J* = 8.4 Hz, H-6').  **$\delta_{\text{C}}$**  (100 MHz; CDCl<sub>3</sub>) 16.6 (CH<sub>3</sub>), 56.1 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 74.3 (C-2), 74.4 (C-3), 94.5 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.7 (OCH<sub>2</sub>OCH<sub>3</sub>), 103.2 (C-3'), 109.3 (C-5'), 112.5 (C-6), 118.1 (C-8), 119.2 (C-1'), 120.0 (C-5), 124.1 (C-7), 128.8 (C-6'), 142.9 (C-8a), 145.2 (C-4a), 155.8 (C-2') and 158.7 (C-4'). (*cis*):  **$\delta_{\text{H}}$**  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.08 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.63 (1H, qd, *J* = 2.4 and 6.4 Hz, H-2), 5.17 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.46 (1H, d, *J* = 2.4 Hz, H-3), 6.74 (1H, dd, *J* = 2.4 and 8.4 Hz, H-5'), 6.76 (1H, d, *J* = 8.4 Hz, H-8), 6.82 (1H, d, *J* = 2.4 Hz, H-3'), 6.92 (1H, dd, *J* = 2.4 and 8.4 Hz, H-7), 7.11 (1H, d, *J* = 2.4 Hz, H-5) and 7.36 (1H, d, *J* = 8.4 Hz, H-6').  **$\delta_{\text{C}}$**  (100 MHz; CDCl<sub>3</sub>) 12.8 (CH<sub>3</sub>), 56.1 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 71.3 (C-2), 72.5 (C-3), 94.5 (OCH<sub>2</sub>OCH<sub>3</sub>), 95.0 (OCH<sub>2</sub>OCH<sub>3</sub>), 102.7 (C-3'), 109.0 (C-5'), 112.5 (C-6), 118.7 (C-8), 119.2 (C-1'), 120.1 (C-5), 124.5 (C-7), 127.7 (C-6'), 142.9 (C-8a), 144.4 (C-4a), 154.5 (C-2') and 158.2 (C-4'). ***m/z*** (ESI<sup>+</sup>): 449 (<sup>81</sup>BrMNa<sup>+</sup>, 20), 447 (<sup>79</sup>BrMNa<sup>+</sup>, 20), 393 (95), 381 (100) and 353 (15). **HRMS** (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 449.0396 C<sub>19</sub>H<sub>21</sub><sup>81</sup>BrNaO<sub>6</sub> requires 449.0394. Found (MNa<sup>+</sup>): 447.0414 C<sub>19</sub>H<sub>21</sub><sup>79</sup>BrNaO<sub>6</sub> requires 447.0414.

**(2*R*,3*R*)-2-Methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane (2*R*,3*R*)-13a**  
**and**  
**(2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane (2*R*,3*S*)-13b**



To a stirred solution of (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane (74.0 mg, 174  $\mu$ mol) in dry THF (8 mL), under an atmosphere of nitrogen at -78 °C, was added *t*BuLi (1.4 M in THF, 0.25 mL, 0.348 mmol). After 30 sec, dry DMF (0.22 mL, 2.78 mmol) was added and the mixture stirred at -78 °C for 45 min and then allowed to warm to room temperature and left for a further 30 min. Sat. aq. NH<sub>4</sub>Cl (5 mL) was added and the aqueous mixture extracted with ethyl acetate (3 x 6 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane (2*R*,3*R*)-13a and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane (2*R*,3*S*)-13b as an inseparable 5:1 mixture of *trans* (2*R*,3*R*)-13a to *cis* (2*R*,3*S*)-13b isomers (39.0 mg, 60 %) as a pale yellow oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.29. **IR:**  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup>; 2928 (CH aromatic), 2825 (CH alkane), 1690 (C=O, aldehyde), 1608, 1585 and 1505 (C=C aromatic), 1444 (CH alkane), 1280, 1218, 1154, 1130, 1112, 1074, 1007 and 926 (C-O ether), 896, 816 and 787 (CH aromatic). (2*S*,3*S*)-13a (*trans*):  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.26 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.23–4.30 (1H, m, H-2), 5.16 (1H, d, *J* = 8.0 Hz, H-3), 5.18 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 6.76 (1H, dd, *J* = 2.4 and 8.4 Hz, H-5'), 6.87 (1H, d, *J* = 2.4 Hz, H-3'), 7.03 (1H, d, *J* = 8.0 Hz, H-8), 7.24 (1H, d, *J* = 8.4 Hz, H-6'), 7.43 (1H, dd, *J* = 2.4 and 8.0 Hz, H-7), 7.45 (1H, d, *J* = 2.4 Hz, H-5) and 9.83 (1H, s, CHO).  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>) 16.6 (CH<sub>3</sub>), 56.2 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 74.1 (C-3), 75.2 (C-2), 94.4 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.7 (OCH<sub>2</sub>OCH<sub>3</sub>), 103.2 (C-3'), 109.3 (C-5'), 117.4 (C-8), 118.4 (C-5), 118.9 (C-1'), 124.0 (C-7), 128.8 (C-6'), 130.5 (C-6), 144.7 (C-4a), 149.3 (C-8a), 155.8 (C-2'), 158.8 (C-4') and 190.8 (CHO). (2*S*,3*R*)-13b (*cis*):  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.12 (3H, d, *J* = 6.4 Hz, CH<sub>3</sub>), 3.48 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.75 (1H, qd, *J* = 2.4 and 6.4 Hz, H-2), 5.18 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.20 (2H, d, *J* = 1.6 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.49 (1H, d, *J* = 2.4 Hz, H-3), 6.76 (1H, dd, *J* = 2.4 and 8.4 Hz, H-5'), 6.84 (1H, d, *J* = 2.4 Hz, H-3'), 7.02 (1H, d, *J* = 8.0 Hz, H-8), 7.24 (1H, d, *J* = 8.4 Hz, H-6'), 7.45 (1H, dd, *J* = 2.4 and 8.0 Hz, H-7), 7.50 (1H, d, *J* = 2.4 Hz, H-5) and 9.85 (1H, s, CHO).  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>) 12.9 (CH<sub>3</sub>), 56.2 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 72.1 (C-2), 72.5 (C-3), 94.4 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.7 (OCH<sub>2</sub>OCH<sub>3</sub>), 102.7 (C-3'), 109.0 (C-5'), 118.0 (C-8), 118.5 (C-5), 118.9 (C-1'), 124.5 (C-7), 127.6 (C-6'), 130.5 (C-6), 143.9 (C-4a), 148.0 (C-8a), 154.5 (C-2'), 158.3 (C-4') and 190.8 (CHO). ***m/z*** (ESI<sup>+</sup>): 397 (MNa<sup>+</sup>, 100 %), 381 (20) and 227 (20). **HRMS** (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 397.1253 C<sub>20</sub>H<sub>22</sub>NaO<sub>7</sub> requires 397.1258.

**(2*R*,3*R*)-2-Methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*R*,3*R*)-14a**  
**and**  
**(2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*R*,3*S*)-14b**



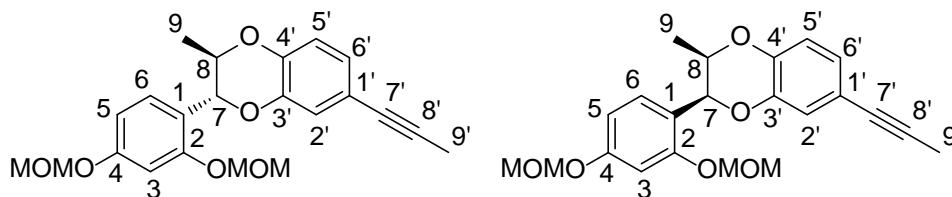
To a solution of trimethylsilyl diazomethane (0.051 mL, 0.103 mmol) in THF (3 mL) under an atmosphere of nitrogen at -78 °C was added <sup>n</sup>BuLi (1.4 M in *n*-hexanes, 0.073 mL, 0.103 mmol) dropwise. The mixture was then stirred at -78 °C for 25 min before a solution of aldehydes (2*R*,3*R*)-**13a** and (2*R*,3*S*)-**13b** (0.032 g, 0.086 mmol) in THF (1.5 mL) was added dropwise and the solution stirred at -78 °C for an hour before warming to room temperature and stirring for 1 h. Sat. aq. NH<sub>4</sub>Cl (4 mL) was added and the organic layer separated. The aqueous layer was further extracted with ethyl acetate (3 x 5 mL) and the combined organic extracts were washed with water (5 mL) and brine (5 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield the *title products* (2*R*,3*R*)-**14a** and (2*R*,3*S*)-**14b** (0.023 g, 73 %) as an inseparable 5:1 mixture of *trans* (2*R*,3*R*)-**14a** to *cis* (2*R*,3*S*)-**14b** isomers as a pale yellow oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.44. **IR:** ν<sub>max</sub>(film)/cm<sup>-1</sup>; 3300 (C≡CH, terminal alkyne), 2959 and 2926 (CH aromatic), 2847 (CH alkane), 1737, 1614, 1580 and 1505 (C=C aromatic), 1448 (CH alkane), 1280, 1218, 1154, 1074, 1008 and 923 (C-O ether), 847, 817 and 729 (CH aromatic), 613 (C≡CH, terminal alkyne). (2*S*,3*S*)-**14a** (*trans*): δ<sub>H</sub> (500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.22 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>), 2.95 (1H, s, H-2''), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.15–4.22 (1H, m, H-2), 5.13 (1H, d, *J* = 8.0 Hz, H-3), 5.17 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 6.76 (1H, dd, *J* = 2.0 and 8.0 Hz, H-5'), 6.84 (1H, d, *J* = 8.0 Hz, H-8), 6.85 (1H, d, *J* = 2.0 Hz, H-3'), 7.01 (1H, dd, *J* = 2.0 and 8.0 Hz, H-7), 7.06 (1H, d, *J* = 2.0 Hz, H-5) and 7.23 (1H, d, *J* = 8.0 Hz, H-6'). δ<sub>C</sub> (125 MHz; CDCl<sub>3</sub>) 16.6 (CH<sub>3</sub>), 56.1 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 74.2 (C-3), 74.7 (C-2), 75.4 (C-2''), 83.6 (C-1''), 94.5 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.7 (OCH<sub>2</sub>OCH<sub>3</sub>), 103.2 (C-3'), 109.0 (C-5'), 114.1 (C-6), 116.9 (C-8), 119.3 (C-1'), 120.8 (C-5), 125.6 (C-7), 128.8 (C-6'), 144.0 (C-8a), 144.6 (C-4a), 155.8 (C-2') and 158.7 (C-4'). (2*S*,3*R*)-**14b** (*cis*): δ<sub>H</sub> (500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.02 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>), 2.97 (1H, s, H-2''), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.66 (1H, qd, *J* = 2.0 and 6.5 Hz, H-2), 5.17 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.46 (1H, d, *J* = 2.0 Hz, H-3), 6.74 (1H, dd, *J* = 2.0 and 8.0 Hz, H-5'), 6.84 (1H, d, *J* = 8.0 Hz, H-8), 6.85 (1H, d, *J* = 2.0 Hz, H-3'), 7.02 (1H, dd, *J* = 2.0 and 8.0 Hz, H-7), 7.11 (1H, d, *J* = 2.0 Hz, H-5) and 7.38 (1H, d, *J* = 8.0 Hz, H-6'). δ<sub>C</sub> (125 MHz; CDCl<sub>3</sub>) 12.8 (CH<sub>3</sub>), 56.1 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 71.6 (C-2), 72.5 (C-3), 75.4 (C-2''), 83.6 (C-1''), 94.5 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.7 (OCH<sub>2</sub>OCH<sub>3</sub>), 102.7 (C-3'), 109.0 (C-5'), 114.1 (C-6), 117.5 (C-8), 119.3 (C-1'), 121.0 (C-5), 126.0 (C-7), 127.7 (C-6'), 143.6 (C-8a), 144.7 (C-4a), 155.0 (C-2') and 158.2 (C-4'). **m/z** (ESI<sup>+</sup>): 393 (MNa<sup>+</sup>, 25), 381 (100), 337 (30), 301 (20), 227 (60) and 159 (30). **HRMS** (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 393.1308 C<sub>21</sub>H<sub>22</sub>NaO<sub>6</sub> requires 393.1309.



**(7*R*,8*R*)-trans-(2,4-Bis(methoxymethoxy))-rodgersinine B**

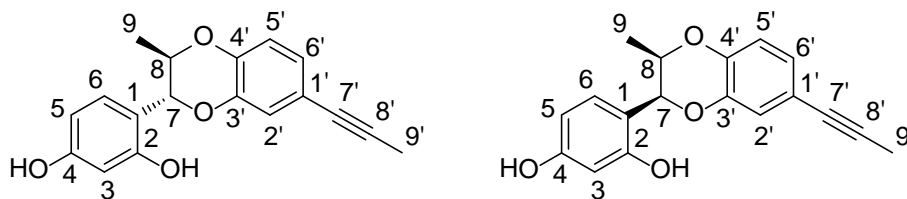
**and**

**(7*S*,8*R*)-cis-(2,4-bis(methoxymethoxy))-rodgersinine B**



To a solution of alkynes (2*R*,3*R*)-**14a** and (2*R*,3*S*)-**14b** (8.1 mg, 0.022 mmol) in THF (1.5 mL) under an atmosphere of nitrogen at -78 °C was added <sup>t</sup>BuLi (1.4 M in *n*-hexanes, 0.028 mL, 0.039 mmol) dropwise and the solution was stirred at this temperature for 5.5 min before iodomethane (0.100 mL, 1.61 mmol) was added dropwise. The mixture was stirred at this temperature for 45 min, then slowly warmed to room temperature, where it was stirred for a further 20 min. Sat. aq. NH<sub>4</sub>Cl (3 mL) was added and the organic layer separated. The aqueous layer was further extracted with ethyl acetate (3 x 5 mL) and the combined organic extracts were washed with water (5 mL) and brine (5 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield (7*R*,8*R*)-*trans*-(2,4-bis(methoxymethoxy))-rodgersinine B and (7*S*,8*R*)-*cis*-(2,4-bis(methoxymethoxy))-rodgersinine B (5.9 mg, 70 %) as an inseparable 5:1 mixture of *trans* to *cis* isomers as a pale yellow oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.46. **IR:** ν<sub>max</sub>(film)/cm<sup>-1</sup>; 2933 (CH aromatic), 2857 and 2824 (CH alkane), 1613, 1584 and 1505 (C=C aromatic), 1305, 1264, 1155, 1119, 1075, 1005 and 911 (C-O ether), 810 and 732 (CH aromatic). (7*S*,8*S*)-(*trans*): δ<sub>H</sub> (500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.21 (3H, d, *J* = 6.5 Hz, H-9), 2.01 (3H, s, H-9'), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.14–4.19 (1H, m, H-8), 5.13 (1H, d, *J* = 8.0 Hz, H-7), 5.17 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 6.76 (1H, dd, *J* = 2.0 and 8.5 Hz, H-5), 6.81 (1H, d, *J* = 8.5 Hz, H-5'), 6.85 (1H, d, *J* = 2.0 Hz, H-3), 6.90 (1H, dd, *J* = 2.0 and 8.5 Hz, H-6'), 6.95 (1H, d, *J* = 2.0 Hz, H-2') and 7.23 (1H, d, *J* = 8.5 Hz, H-6). δ<sub>C</sub> (125 MHz; CDCl<sub>3</sub>) 4.3 (C-9'), 16.6 (C-9), 56.1 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 74.1 (C-7), 74.5 (C-8), 79.4 (C-7'), 83.7 (C-8'), 94.5 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.7 (OCH<sub>2</sub>OCH<sub>3</sub>), 103.2 (C-3), 109.3 (C-5), 116.6 (C-1), 116.7 (C-5'), 119.5 (C-1'), 120.1 (C-2'), 124.9 (C-6'), 128.9 (C-6), 143.5 (C-4'), 143.9 (C-3'), 155.8 (C-2) and 158.6 (C-4). (7*R*,8*S*)-(*cis*): δ<sub>H</sub> (500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.08 (3H, d, *J* = 6.5 Hz, H-9), 2.02 (3H, s, H-9'), 3.47 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 3.49 (3H, s, -OCH<sub>2</sub>OCH<sub>3</sub>), 4.65 (1H, qd, *J* = 2.0 and 6.5 Hz, H-8), 5.17 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.19 (2H, d, *J* = 1.5 Hz, -OCH<sub>2</sub>OCH<sub>3</sub>), 5.45 (1H, d, *J* = 2.0 Hz, H-7), 6.74 (1H, dd, *J* = 2.0 and 8.5 Hz, H-5), 6.81 (1H, d, *J* = 8.5 Hz, H-5'), 6.85 (1H, d, *J* = 2.0 Hz, H-3), 6.90 (1H, dd, *J* = 2.0 and 8.5 Hz, H-6'), 6.98 (1H, d, *J* = 2.0 Hz, H-2') and 7.38 (1H, d, *J* = 8.5 Hz, H-6). δ<sub>C</sub> (125 MHz; CDCl<sub>3</sub>) 4.3 (C-9'), 12.8 (C-9), 56.1 (OCH<sub>2</sub>OCH<sub>3</sub>), 56.3 (OCH<sub>2</sub>OCH<sub>3</sub>), 71.5 (C-8), 72.4 (C-7), 79.4 (C-7'), 83.8 (C-8'), 94.4 (OCH<sub>2</sub>OCH<sub>3</sub>), 94.5 (OCH<sub>2</sub>OCH<sub>3</sub>), 102.7 (C-3), 109.0 (C-5), 116.6 (C-1), 117.1 (C-5'), 119.1 (C-1'), 120.2 (C-2'), 125.2 (C-6'), 127.7 (C-6), 142.0 (C-4'), 143.2 (C-3'), 154.5 (C-2) and 158.1 (C-4). **m/z** (ESI<sup>+</sup>): 407 (MNa<sup>+</sup>, 20), 381 (100), 353 (18) and 239 (25). **HRMS** (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 407.1471 C<sub>22</sub>H<sub>24</sub>NaO<sub>6</sub> requires 407.1465.

**(7*R*,8*R*)-trans-Rodgersinine B (3) and (7*S*,8*R*)-cis-rodgersinine B (4)**  
**(trans-rodgersinine B (3) and cis-rodgersinine B (4))**



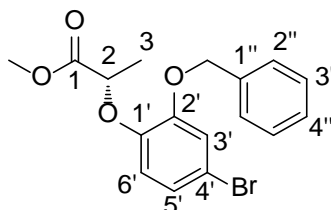
To a solution of a 5:1 mixture ethers (7*R*,8*R*)-*trans*-(2,4-bis(methoxymethoxy))-rodgersinine B and (7*S*,8*R*)-*cis*-(2,4-bis(methoxymethoxy))-rodgersinine B (5.4 mg, 0.014 mmol) in MeOH (2 mL) was added 2 M HCl (0.5 mL) and the resultant mixture stirred at room temperature for 20 h. Following this, the reaction was gently heated at 40 °C for a further 2 h until complete by TLC. 1 M NaOH was added until the solution was pH 5 and then the solution was extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (1:1 *n*-hexanes, ethyl acetate) to give the *title products* (7*R*,8*R*)-**3** and (7*S*,8*R*)-**4** (4.10 mg, quant.) in a 5:1 ratio as an inseparable mixture of *trans* (7*R*,8*R*)-**3** to (7*S*,8*R*)-**4** isomers as a pale yellow semi-solid. **R<sub>f</sub>** (1:1 *n*-hexanes, ethyl acetate) 0.43. **IR:**  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup>; 3374 (broad, OH), 2954 (CH aromatic), 2922 and 2852 (CH alkane), 1607, 1579, 1504 and 1459 (C=C aromatic), 1262, 1226, 1172, 1095, 1023 and 975 (C-O ether, alcohol), 840, 811 and 780 (CH aromatic). ***m/z*** (ESI<sup>+</sup>): 319 (MNa<sup>+</sup>, 60 %), 227 (100) and 158 (50). **HRMS (ESI<sup>+</sup>):** Found (M<sup>+</sup>): 319.0931 C<sub>18</sub>H<sub>16</sub>NaO<sub>4</sub> requires 319.0941.

The mixture of isomers was able to be separated by HPLC (5 % <sup>i</sup>PrOH in *n*-hexanes, 0.4 mL/min, 15  $\mu$ L of 5 mg/0.25 mL solution, 40.5–43 min) to give a pure sample of (7*R*,8*R*)-*trans*-rodgersinine B (**3**) as a colourless film. (7*R*,8*R*)-**3** (*trans*): [ $\alpha$ ]<sub>D</sub> +18.0 (*c* 0.20, MeOH); (lit.<sup>8</sup> [ $\alpha$ ]<sub>D</sub> +18.7 (*c* 0.270, MeOH)). **ECD** (MeOH; *c* 0.375 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 229 (+0.5), 234 (0), 247 (-0.5), 274 (0), 303 (+0.2) nm. **UV** (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 258 (4.11) and 287 (3.73) nm.  **$\delta_{\text{H}}$**  (500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.21 (3H, d, *J* = 6.0 Hz, H-9), 2.02 (3H, s, H-9'), 4.32–4.37 (1H, m, H-8), 4.81 (1H, d, *J* = 8.5 Hz, H-7), 5.00 (1H, br s, OH), 6.36 (1H, br s, OH), 6.40 (1H, d, *J* = 2.5 Hz, H-3), 6.41 (1H, dd, *J* = 2.5 and 8.5 Hz, H-5), 6.82 (1H, d, *J* = 8.5 Hz, H-5'), 6.95 (1H, dd, *J* = 2.0 and 8.5 Hz, H-6'), 7.00 (1H, d, *J* = 2.0 Hz, H-2') and 7.00 (1H, d, *J* = 8.5 Hz, H-6).  **$\delta_{\text{C}}$**  (125 MHz; CDCl<sub>3</sub>) 4.3 (C-9'), 17.3 (C-9), 72.8 (C-8), 79.1 (C-7'), 80.1 (C-7), 84.3 (C-8'), 104.4 (C-3), 108.0 (C-5), 113.9 (C-1), 116.9 (C-1'), 117.0 (C-5'), 120.3 (C-2'), 126.0 (C-6'), 130.3 (C-6), 142.2 (C-4'), 143.5 (C-3'), 156.0 (C-2) and 157.4 (C-4). All <sup>1</sup>H NMR and <sup>13</sup>C NMR data was in agreement with literature values.<sup>8</sup> The [ $\alpha$ ]<sub>D</sub> and ECD data matched the literature values for what had been reported to be for the enantiomer of this compound.<sup>8</sup> Thus, the structure of the natural product has been reassigned to that of this compound, (7*R*,8*R*)-*trans*-rodgersinine B (**3**).

In a separate fraction of the HPLC separation (5 % <sup>i</sup>PrOH in *n*-hexanes, 0.4 mL/min, 15  $\mu$ L of 5 mg/0.25 mL solution, 43.5–46 min) (7*S*,8*R*)-*cis*-rodgersinine B (**4**) was isolated as a colourless film. (7*S*,8*R*)-**4** (*cis*): [ $\alpha$ ]<sub>D</sub> +66.67 (*c* 0.030, MeOH); (lit.<sup>8</sup> [ $\alpha$ ]<sub>D</sub> +62.0 (*c* 0.030, MeOH)). **ECD** (MeOH; *c* 0.35 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 236 (+0.5), 258 (+0.8), 286 (+0.3) nm. **UV** (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 258 (4.05) and 286 (3.66) nm.  **$\delta_{\text{H}}$**  (500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.21 (3H, d, *J* = 6.5 Hz, H-9), 2.02 (3H, s, HH-9'), 4.57 (1H, qd, *J* = 2.5 and 6.5 Hz, H-8), 4.78 (1H, br s, OH), 5.37 (1H, d, *J* = 2.5 Hz, H-7), 6.36 (1H, d, *J* = 2.5 Hz, H-3), 6.41 (1H, dd, *J* = 2.5 and 8.5 Hz, H-5), 6.50 (1H, br s, OH), 6.81 (1H, d, *J* = 8.5 Hz, H-5'), 6.94 (1H, dd, *J* = 1.5 and 8.5 Hz, H-6'), 7.01 (1H, d, *J* = 1.5 Hz, H-2') and 7.03 (1H, d, *J* = 8.5 Hz, H-6).  **$\delta_{\text{C}}$**  (125 MHz; CDCl<sub>3</sub>) 4.3 (C-9'), 12.6 (C-9), 72.9 (C-8), 77.0 (C-7), 79.1 (C-7'), 84.3 (C-8'), 103.8 (C-3), 107.9 (C-5), 113.7 (C-1), 116.7 (C-1'), 117.7 (C-5'), 120.2 (C-2'), 126.1 (C-6'), 128.5 (C-6), 141.8 (C-4'), 141.8 (C-3'), 155.3 (C-2) and 156.7 (C-4). All <sup>1</sup>H NMR and <sup>13</sup>C NMR data was

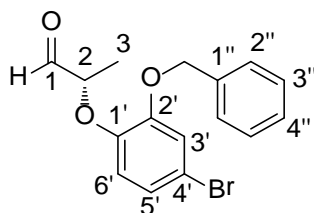
in agreement with literature values.<sup>8</sup> The  $[\alpha]_D$  and ECD data was identical to that of the literature values for what had been reported for the natural product.<sup>8</sup> Thus, the structure of the natural product was confirmed to be this product, (7*S*,8*R*)-*cis*-rodgersinine B (**4**).

**(2*S*)-Methyl 2-(2'-(benzyloxy)-4'-bromophenoxy)propanoate **16****



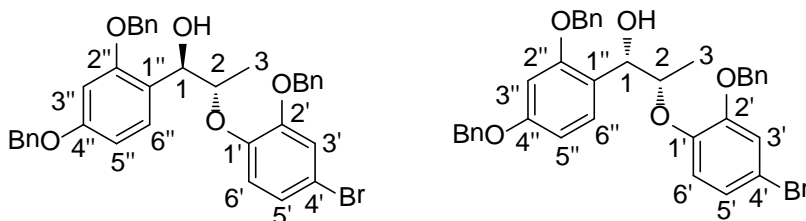
To a solution of phenol **6** (0.200 g, 0.717 mmol),  $\text{PPh}_3$  (0.329 g, 1.25 mmol) and (*R*)-methyl lactate **15** (0.131 g, 1.25 mmol) in THF (10 mL) under an atmosphere of nitrogen, at 0 °C was added DIAD (0.25 mL, 1.25 mmol) dropwise. The reaction mixture was allowed to warm to room temperature. After stirring for 4 h, the mixture was then concentrated *in vacuo*. The crude product was purified by flash chromatography (14:1 *n*-hexanes, ethyl acetate to 9:1 *n*-hexanes, ethyl acetate) to yield the *title product* **16** (0.223 g, 85 %) as a colourless oil.  $R_f$  (**4:1 *n*-hexanes, ethyl acetate**) 0.55.  $[\alpha]_D$  -47.7 (*c* 0.502,  $\text{CHCl}_3$ ). **IR:**  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ ; 3066 and 3033 (CH aromatic), 2992 and 2949 (CH alkane), 1754 (C=O ester), 1587 and 1492 (C=C aromatic), 1454, 1403 and 1378 (CH alkane), 1251, 1200, 1139, 1115, 1096 and 1003 (C-O ether), 978, 880, 836, 740, 696 and 641 (CH aromatic).  $\delta_H$  (**400 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$** ) 1.56 (3H, d,  $J$  = 6.8 Hz, H-3), 3.66 (3H, s, OMe), 4.69 (1H, q,  $J$  = 6.8 Hz  $\text{CH}_2\text{CH}_3$ ), 5.04 (2H, d,  $J$  = 4.0 Hz,  $\text{OCH}_2\text{Ar}$ ), 6.79 (1H, d,  $J$  = 8.4 Hz, H-6'), 6.97 (1H, dd,  $J$  = 2.0 and 8.4 Hz, H-5'), 7.06 (1H, d,  $J$  = 2.0 Hz, H-3') and 7.28–7.44 (5H, m, Ar-H).  $\delta_C$  (**100 MHz;  $\text{CDCl}_3$** ) 18.4 (C-3), 52.0 (OMe), 71.2 ( $\text{OCH}_2\text{Ar}$ ), 74.7 (C-2), 114.9 (C-4'), 118.2 (C-3'), 119.3 (C-6'), 124.1 (C-5'), 127.3 (C-2''), 127.9 (C-4''), 128.4 (C-3''), 136.3 (C-1''), 146.8 (C-1'), 150.3 (C-2') and 172.2 (C-1).  $m/z$  (**ESI+**): 405 ( $^{81}\text{BrMK}^+$ , 40 %), 403 ( $^{79}\text{MK}^+$ , 40), 389 ( $^{81}\text{BrMNa}^+$ , 100) and 387 ( $^{79}\text{BrMNa}^+$ , 100). **HRMS (ESI+):** Found ( $\text{MNa}^+$ ): 389.0171  $\text{C}_{17}\text{H}_{17}^{81}\text{BrNaO}_4$  requires 389.0183. Found ( $\text{MNa}^+$ ): 387.0191  $\text{C}_{17}\text{H}_{17}^{79}\text{BrNaO}_4$  requires 387.0202.

**(2S)-2-(2'-(Benzyloxy)-4'-bromophenoxy)propan-1-al, (2S)-9**



To a solution of ester **16** (7.80 g, 21.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (160 mL) under an atmosphere of nitrogen at -78 °C was added DIBAL (1 M in cyclohexane, 23.5 mL, 23.5 mmol). The mixture was stirred at -78 °C for 3 h. The reaction was quenched with 2 M HCl (80 mL) then extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 80 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (14:1 *n*-hexanes, ethyl acetate to 9:1 *n*-hexanes, ethyl acetate) to yield the *title product* (2S)-**9** (4.79 g, 67 %) as a white crystalline solid. *R<sub>f</sub>* (4:1 *n*-hexanes, ethyl acetate) 0.38. [ $\alpha$ ]<sub>D</sub> -27.7 (*c* 0.68, CHCl<sub>3</sub>). **Melting Point:** 61–64 °C. The IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were identical to that of the enantiomer **9**. *m/z* (ESI<sup>+</sup>): 359 (<sup>81</sup>BrMNa<sup>+</sup>, 20), 357 (<sup>79</sup>BrMNa<sup>+</sup>, 20) and 107 (100). **HRMS (ESI<sup>+</sup>):** Found (MNa<sup>+</sup>): 359.0090 C<sub>16</sub>H<sub>15</sub><sup>81</sup>BrNaO<sub>3</sub> requires 359.0077. Found (MNa<sup>+</sup>): 357.0098 C<sub>16</sub>H<sub>15</sub><sup>79</sup>BrNaO<sub>3</sub> requires 357.0097.

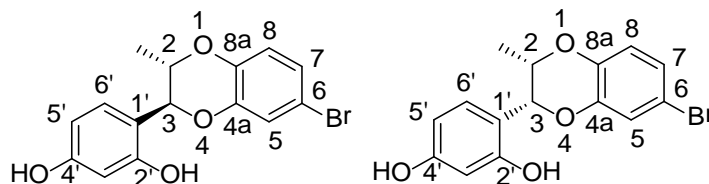
**(1R,2S)-2-(2'-(Benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol (1R,2S)-11a and (1S,2S)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol (1S,2S)-11b**



To a stirred solution of bromide 1,3-bis(benzyloxy)-4-bromobenzene (1.98 g, 5.37 mmol) in dry THF (90 mL), under an atmosphere of nitrogen at -78 °C, was added <sup>t</sup>BuLi (1.4 M in THF, 7.67 mL, 10.7 mmol). After 5 min, a solution of aldehyde (2S)-**9** (1.50 g, 4.48 mmol) in dry THF (45 mL) was added slowly and the mixture was left to warm to room temperature and stirred for a further 20 h. Sat. aq. NH<sub>4</sub>Cl (60 mL) was added and the aqueous mixture extracted with ethyl acetate (3 x 60 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield (1R,2S)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol (1R,2S)-**11a** (1.18 g, 42 %) as a colourless oil. (1R,2S)-**11a** (*anti*): [ $\alpha$ ]<sub>D</sub> +26.7 (*c* 1.10, CHCl<sub>3</sub>). The IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were identical to that of the enantiomer (1S,2R)-**11a**. *m/z* (ESI<sup>+</sup>): 665 (<sup>81</sup>BrMK<sup>+</sup>, 40 %), 647 (<sup>79</sup>MK<sup>+</sup>, 35), 649 (<sup>81</sup>BrMNa<sup>+</sup>, 100), 647 (<sup>79</sup>MNa<sup>+</sup>, 90), 360 (30) and 114 (33). **HRMS (ESI<sup>+</sup>):** Found (MNa<sup>+</sup>): 649.1400 C<sub>36</sub>H<sub>33</sub><sup>81</sup>BrNaO<sub>5</sub> requires 649.1386. Found (MNa<sup>+</sup>): 647.1418 C<sub>36</sub>H<sub>33</sub><sup>79</sup>BrNaO<sub>5</sub> requires 647.1404.

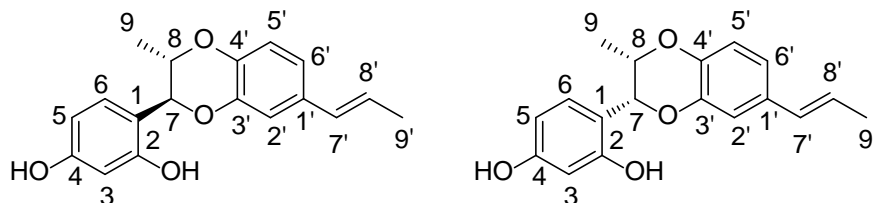
In a separate fraction, (1S,2S)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol (1S,2S)-**11b** (0.284 g, 10 %) was collected as a colourless oil. (1S,2S)-**11b** (*syn*): [ $\alpha$ ]<sub>D</sub> +87.7 (*c* 0.554, CHCl<sub>3</sub>). The IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were identical to that of the enantiomer (1R,2R)-**11b**. *m/z* (ESI<sup>+</sup>): 665 (<sup>81</sup>BrMK<sup>+</sup>, 50 %), 647 (<sup>79</sup>MK<sup>+</sup>, 45), 649 (<sup>81</sup>BrMNa<sup>+</sup>, 100), 647 (<sup>79</sup>MNa<sup>+</sup>, 85), 360 (15) and 114 (30). **HRMS (ESI<sup>+</sup>):** Found (MNa<sup>+</sup>): 649.1389 C<sub>36</sub>H<sub>33</sub><sup>81</sup>BrNaO<sub>5</sub> requires 649.1386. Found (MNa<sup>+</sup>): 647.1404 C<sub>36</sub>H<sub>33</sub><sup>79</sup>BrNaO<sub>5</sub> requires 647.1404.

**(2*S*,3*S*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane (2*S*,3*S*)-12a and  
(2*S*,3*R*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane (2*S*,3*R*)-12b**



To a mixture of alcohols (1*R*,2*S*)-**11a** and (1*S*,2*S*)-**11b** (1.20 g, 1.91 mmol) in ethyl acetate (60 mL) was added 37 % HCl (4.5 mL) and 10 % Pd/C (0.180 g) and the mixture stirred under an atmosphere of hydrogen for 70 min. The mixture was filtered through Celite® and the filtrate washed with sat. aq. NaHCO<sub>3</sub> (2 x 50 mL) and water (50 mL). The aqueous washings were further extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield the *title products* (2*S*,3*S*)-**12a** and (2*S*,3*R*)-**12b** (0.396 g, 61 %) as a 5:1 ratio as an inseparable mixture of *trans* (2*S*,3*S*)-**12a** to *cis* (2*S*,3*R*)-**12b** isomers an orange oil. *R<sub>f</sub>* (3:1 diethyl ether, *n*-hexanes) 0.39. The IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR data are identical to that of the enantiomers (2*R*,3*R*)-**12a** and (2*R*,3*S*)-**12b**. *m/z* (ESI<sup>+</sup>): 361 (<sup>81</sup>BrMNa<sup>+</sup>, 60 %), 359 (<sup>79</sup>MNa<sup>+</sup>, 58), 301 (75), 203 (100), 150 (85) and 114 (95). HRMS (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 360.9862 C<sub>15</sub>H<sub>13</sub><sup>81</sup>BrNaO<sub>4</sub> requires 360.9870. Found (MNa<sup>+</sup>): 358.9874 C<sub>15</sub>H<sub>13</sub><sup>79</sup>BrNaO<sub>4</sub> requires 358.9889.

**(7*S*,8*S*)-*trans*-Rodgersinine A (1) and (7*R*,8*S*)-*cis*-roddersinine A (2)  
(*ent-trans*-roddersinine A (1) and *ent-cis*-roddersinine A (2))**



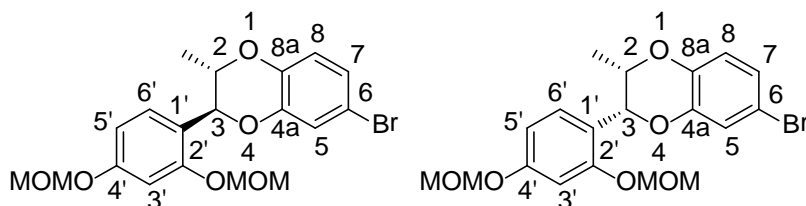
To a solution of a 5:1 mixture bromides (2*S*,3*S*)-**12a** and (2*S*,3*R*)-**12b** (50.0 mg, 0.148 mmol) in dry THF (8 mL), under an atmosphere of nitrogen, was added *trans*-propenylboronic acid (38.0 mg, 0.445 mmol), CsF (90.0 mg, 0.590 mmol) and the resultant mixture was heated. Once the reaction was at reflux, Pd(PPh<sub>3</sub>)<sub>4</sub> (8.6 mg, 0.007 mmol) was added and the reaction heated at reflux for 18 h. The reaction was then cooled and ethyl acetate (5 mL) and brine (5 mL) added. The layers were separated and the aqueous layer washed with ethyl acetate (2 x 5 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (3:1 diethyl ether, *n*-hexanes) to yield the *title products* (7*S*,8*S*)-**1** and (7*R*,8*S*)-**2** (44.0 mg, quant.) in a 5:1 ratio as mostly inseparable mixture of *trans* (7*S*,8*S*)-**1** to *cis* (7*R*,8*S*)-**2** isomers as a yellow oil. *R<sub>f</sub>* (3:1 diethyl ether, *n*-hexanes) 0.49. *m/z* (ESI<sup>+</sup>): 321 (MNa<sup>+</sup>, 20 %) and 303 (100). HRMS (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 321.1092 C<sub>18</sub>H<sub>18</sub>NaO<sub>4</sub> requires 321.1097.

A small sample of the mixture of isomers was able to be separated by HPLC (5 % *i*PrOH in *n*-hexanes, 0.4 mL/min, 15 µL of 10 mg/0.5 mL solution, 25.5–28 min) to give a pure sample of (7*S*,8*S*)-*trans*-roddersinine A (**1**) as a pale orange film. (7*S*,8*S*)-**1** (*trans*): [*α*]<sub>D</sub> -19.67 (*c* 0.30, MeOH); (lit.<sup>8</sup> of enantiomer [*α*]<sub>D</sub> +24.8 (*c* 0.075, MeOH)). ECD (MeOH; *c* 0.375 mg/10 mL) λ (Δε) 239 (0), 256 (+0.5), 274 (0), 287 (-0.2) nm. UV (MeOH) λ<sub>max</sub> (log ε) 268 (4.11) nm. The IR, <sup>1</sup>H NMR and

$^{13}\text{C}$  NMR data are identical to that of (7*R*,8*R*)-**1** and matched the literature values.<sup>8</sup> The  $[\alpha]_{\text{D}}$  and ECD data was opposite to that of the literature values for what had been reported for this compound.<sup>8</sup> Thus, the structure of the natural product has been reassigned to that of (7*R*,8*R*)-*trans*-rodersinine A (**1**), the enantiomer of this product, (7*S*,8*S*)-**1**.

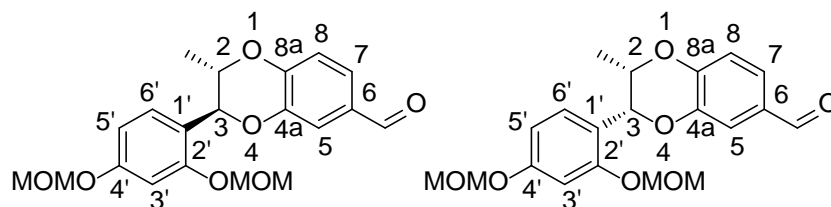
In a separate fraction of the HPLC separation (5 %  $i$ PrOH in *n*-hexanes, 0.4 mL/min, 15  $\mu\text{L}$  of 10 mg/0.5 mL solution, 28.5–30.5 min) (7*R*,8*S*)-*cis*-rodersinine A (**2**) was isolated as a pale orange film. (7*R*,8*S*)-**2** (*cis*):  $[\alpha]_{\text{D}}$  -79.00 (*c* 0.10, MeOH); (lit.<sup>8</sup> of enantiomer  $[\alpha]_{\text{D}}$  +79.9 (*c* 0.18, MeOH)). ECD (MeOH; *c* 0.35 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 240 (+0.1), 244 (0), 261 (-0.6) nm. UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 268 (3.88) nm. The IR,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR data are identical to that of (7*S*,8*R*)-**2** and match the literature values.<sup>8</sup> The  $[\alpha]_{\text{D}}$  and ECD data was opposite to that of the literature values for what had been reported for the natural product.<sup>8</sup> Thus, the structure of the natural product was confirmed to be (7*S*,8*R*)-*cis*-rodersinine A (**2**), the enantiomer of this product.

**(2*S*,3*S*)-2-Methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane**  
**and**  
**(2*S*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane**



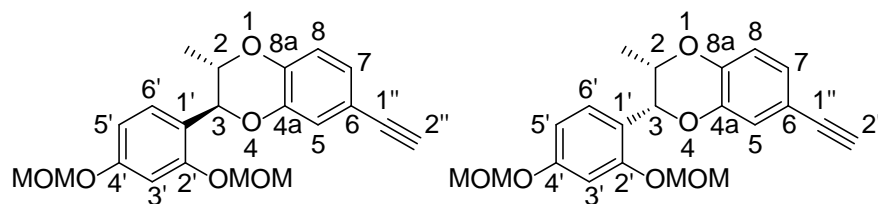
To a mixture of diols (2*S*,3*S*)-**12a** and (2*S*,3*R*)-**12b** (0.080 g, 0.237 mmol) in  $\text{CH}_2\text{Cl}_2$  (8 mL) at room temperature, under an atmosphere of nitrogen, was added DIPEA (0.11 mL, 0.593 mmol) followed by MOMCl (0.11 mL, 0.949 mmol) and the mixture was stirred at room temperature for 20 h. Sat. aq.  $\text{NH}_4\text{Cl}$  (8 mL) was added and the organic layer separated. The aqueous layer was further extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 mL) and the combined organic extracts were dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (9:1 *n*-hexanes, ethyl acetate) to yield (2*S*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*S*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane as an inseparable 5:1 mixture of *trans* to *cis* isomers (0.071 g, 71 %) as a colourless oil.  $R_{\text{f}}$  (4:1 *n*-hexanes, ethyl acetate) 0.55. The IR,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were identical to that of the enantiomers (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane.  $m/z$  (ESI+): 465 ( $^{81}\text{BrMK}^+$ , 22 %), 463 ( $^{79}\text{BrMK}^+$ , 20), 449 ( $^{81}\text{BrMNa}^+$ , 100), 447 ( $^{79}\text{BrMNa}^+$ , 95), 368 (40), 347 (60) and 114 (55). HRMS (ESI+): Found ( $\text{MNa}^+$ ): 449.0382  $\text{C}_{19}\text{H}_{21}^{81}\text{BrNaO}_6$  requires 449.0394. Found ( $\text{MNa}^+$ ): 447.0405  $\text{C}_{19}\text{H}_{21}^{79}\text{BrNaO}_6$  requires 447.0414.

**(2*S*,3*S*)-2-Methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane (2*S*,3*S*)-13a**  
**and**  
**(2*S*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane (2*S*,3*R*)-13b**



To a stirred solution of (2*S*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*S*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane (39.0 mg, 0.092 mmol) in dry THF (6 mL), under an atmosphere of nitrogen at -78 °C, was added <sup>t</sup>BuLi (1.4 M in THF, 0.13 mL, 0.183 mmol). After 30 sec, dry DMF (0.11 mL, 1.47 mmol) was added and the mixture stirred at -78 °C for 45 min and then allowed to warm to room temperature and left for a further 30 min. Sat. aq. NH<sub>4</sub>Cl (4 mL) was added and the aqueous mixture extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield *title products* (2*S*,3*S*)-**13a** and (2*S*,3*R*)-**13b** as an inseparable 5:1 mixture of *trans* (2*S*,3*S*)-**13a** to *cis* (2*S*,3*R*)-**13b** isomers (23.3 mg, 69 %) as a colourless oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.29. The **IR**, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were identical to that of the enantiomers (2*S*,3*S*)-**13a** and (2*S*,3*R*)-**13b**. **m/z** (ESI<sup>+</sup>): 397 (MNa<sup>+</sup>, 100 %), 360 (MH<sup>+</sup>, 40 %), 250 (5) and 114 (5). **HRMS** (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 397.1256 C<sub>20</sub>H<sub>22</sub>NaO<sub>7</sub> requires 397.1258.

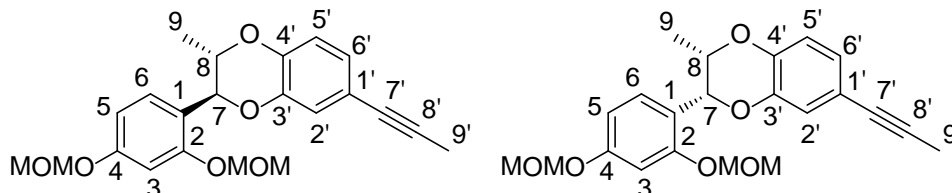
**(2*S*,3*S*)-2-Methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*S*,3*S*)-14a**  
**and**  
**(2*S*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*S*,3*R*)-14b**



To a solution of trimethylsilyl diazomethane (0.039 mL, 0.077 mmol) in THF (2 mL) under an atmosphere of nitrogen at -78 °C was added <sup>n</sup>BuLi (1.4 M in *n*-hexanes, 0.055 mL, 0.077 mmol) dropwise. The mixture was then stirred at -78 °C for 25 min before a solution of aldehydes (2*S*,3*S*)-**13a** and (2*S*,3*R*)-**13b** (0.024 g, 0.064 mmol) in THF (1 mL) was added dropwise and the solution stirred at -78 °C for an hour before warming to room temperature and stirring for 1 h. Sat. aq. NH<sub>4</sub>Cl (3 mL) was added and the organic layer separated. The aqueous layer was further extracted with ethyl acetate (3 x 5 mL) and the combined organic extracts were washed with water (5 mL) and brine (5 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield the *title products* (2*S*,3*S*)-**14a** and (2*S*,3*R*)-**14b** (0.021 g, 92 %) as an inseparable 5:1 mixture of *trans* (2*S*,3*S*)-**14a** to *cis* (2*S*,3*R*)-**14b** isomers as a pale yellow oil. **R<sub>f</sub>** (4:1 *n*-hexanes, ethyl acetate) 0.44. The **IR**, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were identical to that of

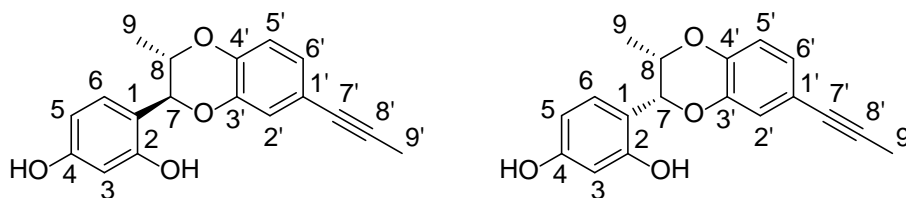
the enantiomers (2*S*,3*S*)-**14a** and (2*S*,3*R*)-**14b**. *m/z* (ESI<sup>+</sup>): 393 (MNa<sup>+</sup>, 70), 381(100), 227 (60) and 159 (20). HRMS (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 393.1308 C<sub>21</sub>H<sub>22</sub>NaO<sub>6</sub> requires 393.1309.

**(7*S*,8*S*)-*trans*-(2,4-Bis(methoxymethoxy))-rodgersinine B and  
(7*R*,8*S*)-*cis*-(2,4-bis(methoxymethoxy))-rodgersinine B**



To a solution of alkyne (2*S*,3*S*)-**14a** and (2*S*,3*R*)-**14b** (8.0 mg, 0.022 mmol) in THF (1.5 mL) under an atmosphere of nitrogen at -78 °C was added <sup>t</sup>BuLi (1.4 M in *n*-hexanes, 0.028 mL, 0.039 mmol) dropwise and the solution was stirred at this temperature for 5.5 min before iodomethane (0.100 mL, 1.61 mmol) was added dropwise. The mixture was stirred at this temperature for 45 min, then slowly warmed to room temperature, where it was stirred for a further 20 min. Sat. aq. NH<sub>4</sub>Cl (3 mL) was added and the organic layer separated. The aqueous layer was further extracted with ethyl acetate (3 x 5 mL) and the combined organic extracts were washed with water (5 mL) and brine (5 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (4:1 *n*-hexanes, ethyl acetate) to yield the *title products* (7.6 mg, 92 %) as an inseparable 5:1 mixture of *trans* to *cis* isomers as a pale yellow oil. *R<sub>f</sub>* (4:1 *n*-hexanes, ethyl acetate) 0.46. The IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were identical to that of their enantiomers. *m/z* (ESI<sup>+</sup>): 407 (MNa<sup>+</sup>, 20 %), 381 (100), 239 (25) and 114 (15). HRMS (ESI<sup>+</sup>): Found (MNa<sup>+</sup>): 407.1465 C<sub>22</sub>H<sub>24</sub>NaO<sub>6</sub> requires 407.1465.

**(7*S*,8*S*)-*trans*-Rodgersinine B (3) and (7*R*,8*S*)-*cis*-rodgersinine B (4)  
(*ent*)-*trans*-rodgersinine B (3) and (*ent*)-*cis*-rodgersinine B (4))**



To a 5:1 mixture of ethers (7*S*,8*S*)-*trans*-(2,4-bis(methoxymethoxy))-rodgersinine B and (7*R*,8*S*)-*cis*-(2,4-bis(methoxymethoxy))-rodgersinine B (7.6 mg, 0.020 mmol) in MeOH (2 mL) was added 2 M HCl (0.5 mL) and the resultant mixture stirred at room temperature for 20 h. Following this, the reaction was gently heated at 40 °C for a further 3.5 h. 1 M NaOH was added until the solution was pH 5 and then the solution was extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (1:1 *n*-hexanes, ethyl acetate) to give the *title products* (7*S*,8*S*)-**3** and (7*R*,8*S*)-**4** (5.06 mg, 86 %) in a 5:1 ratio as an inseparable mixture of *trans* (7*S*,8*S*)-**3** to *cis* (7*R*,8*S*)-**4** isomers as a pale yellow semi-solid. *R<sub>f</sub>* (1:1 *n*-hexanes, ethyl acetate) 0.43. IR: *v*<sub>max</sub>(film)/cm<sup>-1</sup>; 3365 (broad, OH), 2954 (CH aromatic), 2922 and 2852 (CH alkane), 1608, 1579, 1504 and



1459 (C=C aromatic), 1263, 1226, 1172, 1095, 1023 and 975 (C-O ether, alcohol), 840, 811, 781 and 732 (CH aromatic). **m/z (ESI+)**: 319 (MNa<sup>+</sup>, 10 %) and 239 (100). **HRMS (ESI+)** Found (M<sup>+</sup>): 319.0939 C<sub>18</sub>H<sub>16</sub>NaO<sub>4</sub> requires 319.0941.

The mixture of isomers was able to be separated by HPLC (5 % *i*PrOH in *n*-hexanes, 0.4 mL/min, 15  $\mu$ L of 5 mg/0.25 mL solution, 40.5–43 min) to give a pure sample of (7*S*,8*S*)-*trans*-rodgersinine B (**3**) as a colourless film. (7*R*,8*S*)-**3** (*trans*): [ $\alpha$ ]<sub>D</sub> -16.0 (*c* 0.30, MeOH); (lit.<sup>8</sup> of enantiomer [ $\alpha$ ]<sub>D</sub> +18.7 (*c* 0.270, MeOH)). **ECD** (MeOH; *c* 0.325 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 229 (-1.7), 234 (0), 247 (+0.4), 271 (0), 303 (-0.1) nm. **UV** (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 258 (3.89) and 287 (3.55) nm.  $\delta_{\text{H}}$  (**500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si**) 1.21 (3H, d, *J* = 6.0 Hz, H-9), 2.02 (3H, s, H-9'), 4.32–4.37 (1H, m, H-8), 4.81 (1H, d, *J* = 8.5 Hz, H-7), 5.00 (1H, br s, OH), 6.36 (1H, br s, OH), 6.40 (1H, d, *J* = 2.5 Hz, H-3), 6.41 (1H, dd, *J* = 2.5 and 8.5 Hz, H-5), 6.82 (1H, d, *J* = 8.5 Hz, H-5'), 6.95 (1H, dd, *J* = 2.0 and 8.5 Hz, H-6'), 7.00 (1H, d, *J* = 2.0 Hz, H-2') and 7.00 (1H, d, *J* = 8.5 Hz, H-6).  $\delta_{\text{C}}$  (**125 MHz; CDCl<sub>3</sub>**) 4.3 (C-9'), 17.3 (C-9), 72.8 (C-8), 79.1 (C-7'), 80.1 (C-7), 84.3 (C-8'), 104.4 (C-3), 108.0 (C-5), 113.9 (C-1), 116.9 (C-1'), 117.0 (C-5'), 120.3 (C-2'), 126.0 (C-6'), 130.3 (C-6), 142.2 (C-4'), 143.5 (C-3'), 156.0 (C-2) and 157.4 (C-4). The <sup>1</sup>H NMR and <sup>13</sup>C NMR data matched the literature values of the natural product.<sup>8</sup> The [ $\alpha$ ]<sub>D</sub> and ECD data was opposite to that of the literature values for what had been reported for this compound.<sup>8</sup> Thus, the structure of the natural product has been reassigned to that of (7*R*,8*R*)-*trans*-rodgersinine B (**3**), the enantiomer of this product.

In a separate fraction of the HPLC separation (5 % *i*PrOH in *n*-hexanes, 0.4 mL/min, 15  $\mu$ L of 5 mg/0.25 mL solution, 43.5–46 min) (7*R*,8*S*)-*cis*-rodgersinine B (**4**) was isolated as a colourless film. (7*R*,8*S*)-**4** (*cis*): [ $\alpha$ ]<sub>D</sub> -50.00 (*c* 0.030, MeOH); (lit.<sup>8</sup> [ $\alpha$ ]<sub>D</sub> + 62.0 (*c* 0.030, MeOH) of enantiomer). **ECD** (MeOH; *c* 0.30 mg/10 mL)  $\lambda$  ( $\Delta\epsilon$ ) 225 (0), 236 (-0.4), 259 (-0.7), 287 (-0.3) nm. **UV** (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 259 (4.01) and 286 (3.62) nm.  $\delta_{\text{H}}$  (**500 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si**) 1.21 (3H, d, *J* = 6.5 Hz, H-9), 2.02 (3H, s, H-9'), 4.57 (1H, qd, *J* = 2.5 and 6.5 Hz, H-8), 4.78 (1H, br s, OH), 5.37 (1H, d, *J* = 2.5 Hz, H-7), 6.36 (1H, d, *J* = 2.5 Hz, H-3), 6.41 (1H, dd, *J* = 2.5 and 8.5 Hz, H-5), 6.50 (1H, br s, OH), 6.81 (1H, d, *J* = 8.5 Hz, H-5'), 6.94 (1H, dd, *J* = 1.5 and 8.5 Hz, H-6'), 7.01 (1H, d, *J* = 1.5 Hz, H-2') and 7.03 (1H, d, *J* = 8.5 Hz, H-6).  $\delta_{\text{C}}$  (**125 MHz; CDCl<sub>3</sub>**) 4.3 (C-9'), 12.6 (C-9), 72.9 (C-8), 77.0 (C-7), 79.1 (C-7'), 84.3 (C-8'), 103.8 (C-3), 107.9 (C-5), 113.7 (C-1), 116.7 (C-1'), 117.7 (C-5'), 120.2 (C-2'), 126.1 (C-6'), 128.5 (C-6), 141.8 (C-4'), 141.8 (C-3'), 155.3 (C-2) and 156.7 (C-4). The <sup>1</sup>H NMR and <sup>13</sup>C NMR data matched the literature values of the natural product.<sup>8</sup> The [ $\alpha$ ]<sub>D</sub> and ECD data was opposite to that of the literature values which had been reported for the natural product.<sup>8</sup> Thus, the structure of the natural product was confirmed to be (7*S*,8*R*)-*cis*-rodgersinine B (**4**), the enantiomer of this product.

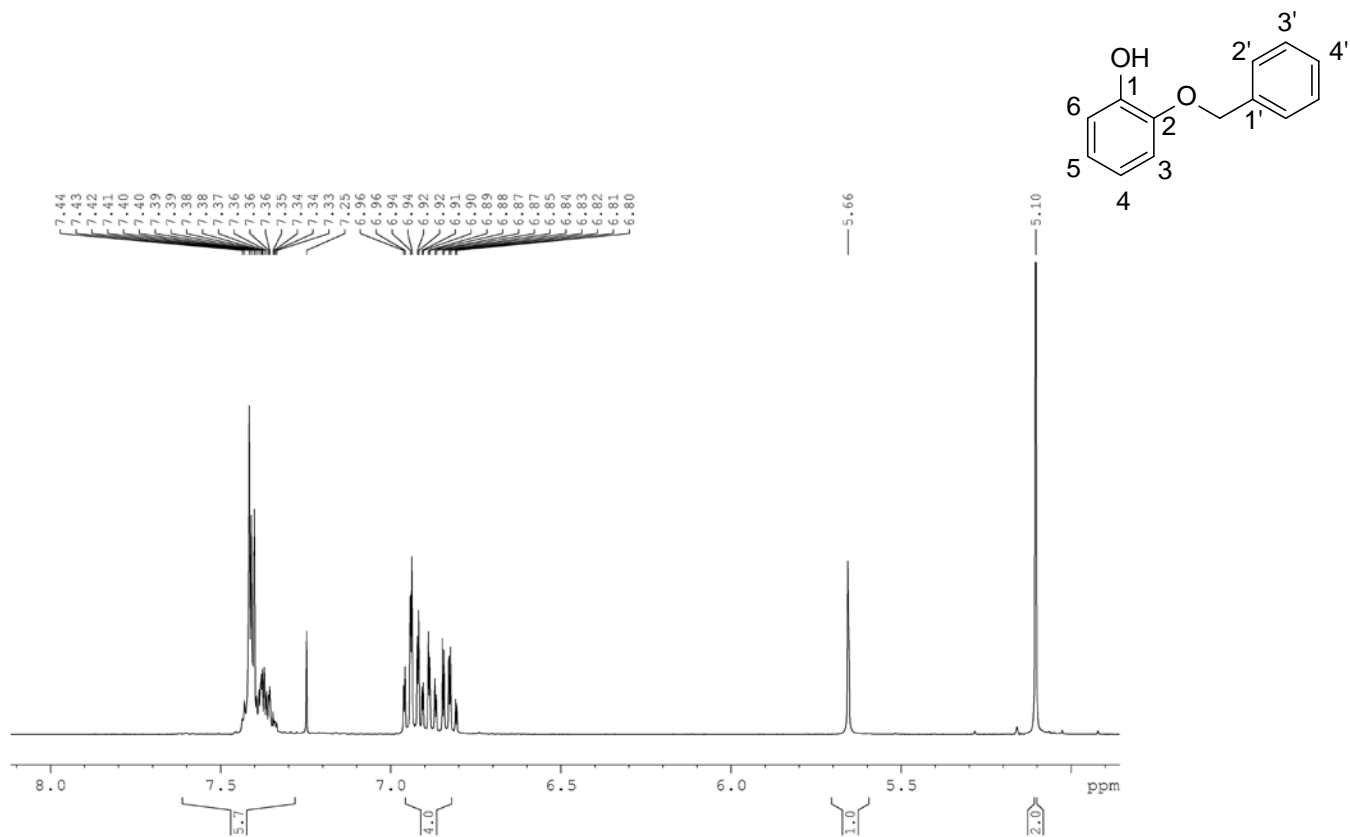


Figure 1. <sup>1</sup>H NMR spectrum of 2-(benzyloxy)phenol (400 MHz, CDCl<sub>3</sub>).

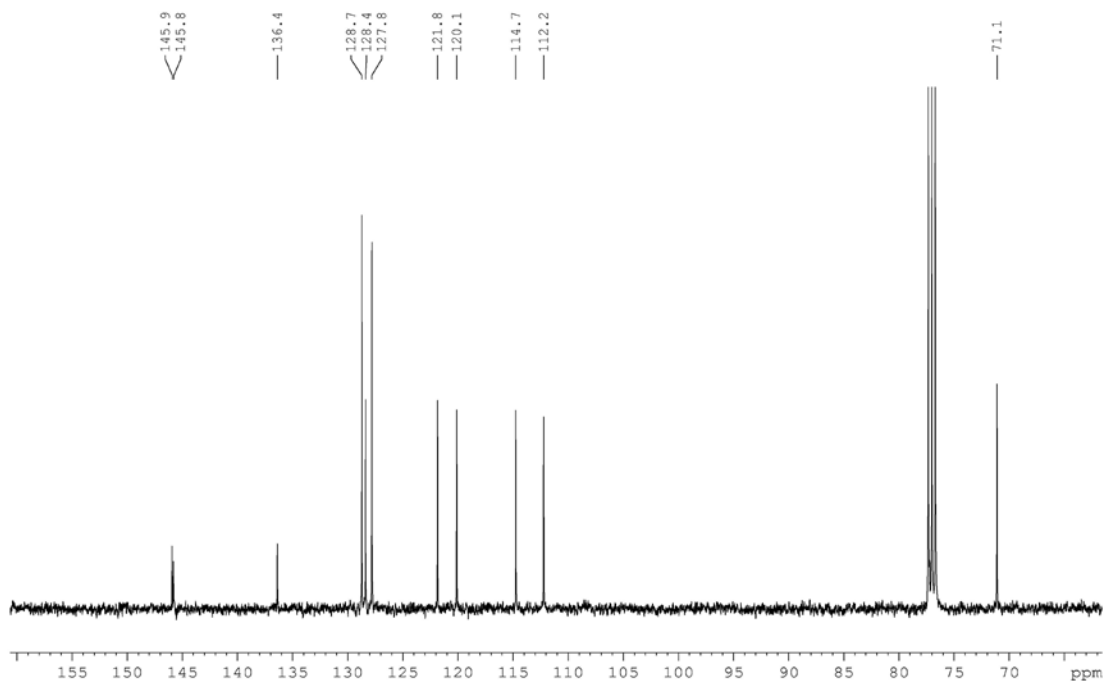


Figure 2. <sup>13</sup>C NMR spectrum of 2-(benzyloxy)phenol (100 MHz, CDCl<sub>3</sub>).

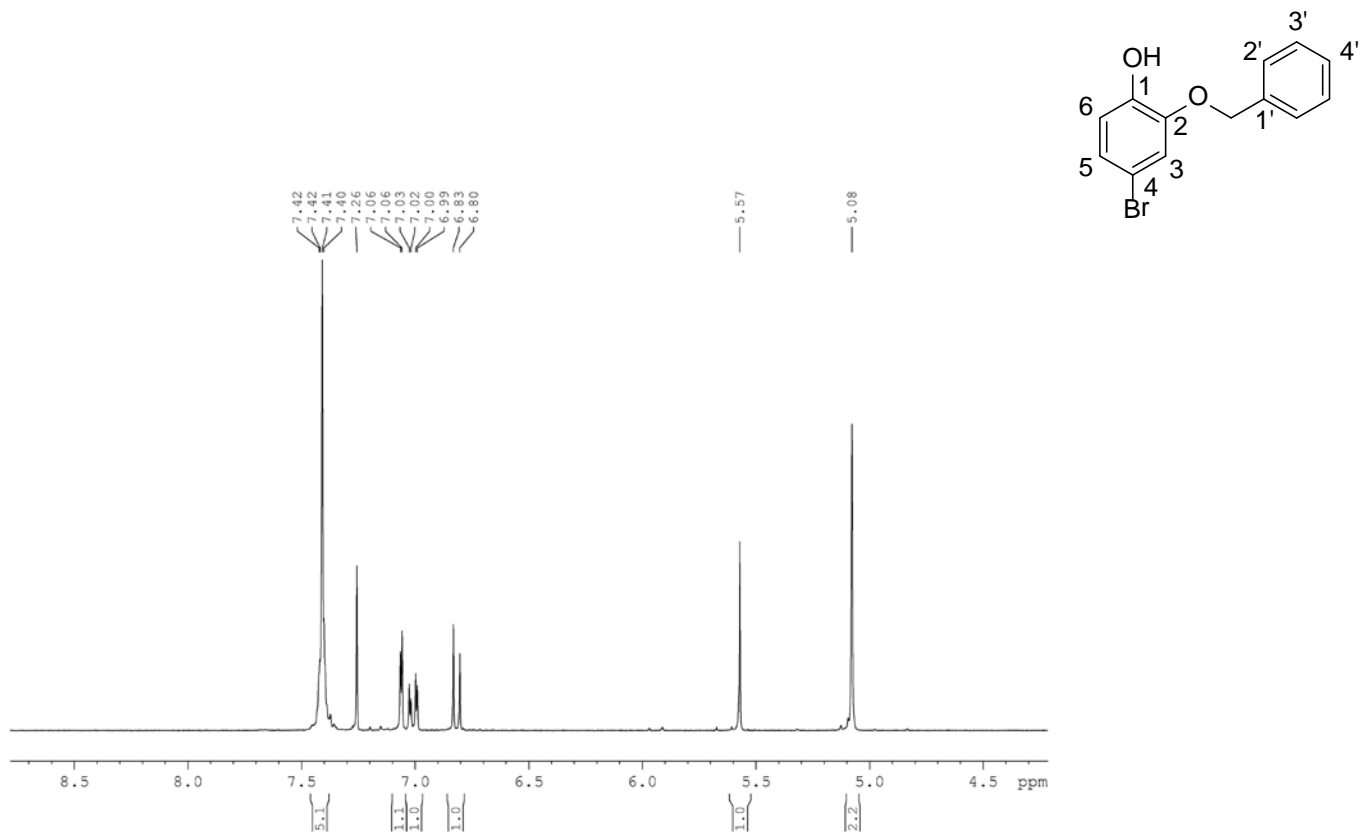


Figure 3. <sup>1</sup>H NMR spectrum of 2-benzyloxy-4-bromophenol 6 (300 MHz, CDCl<sub>3</sub>).

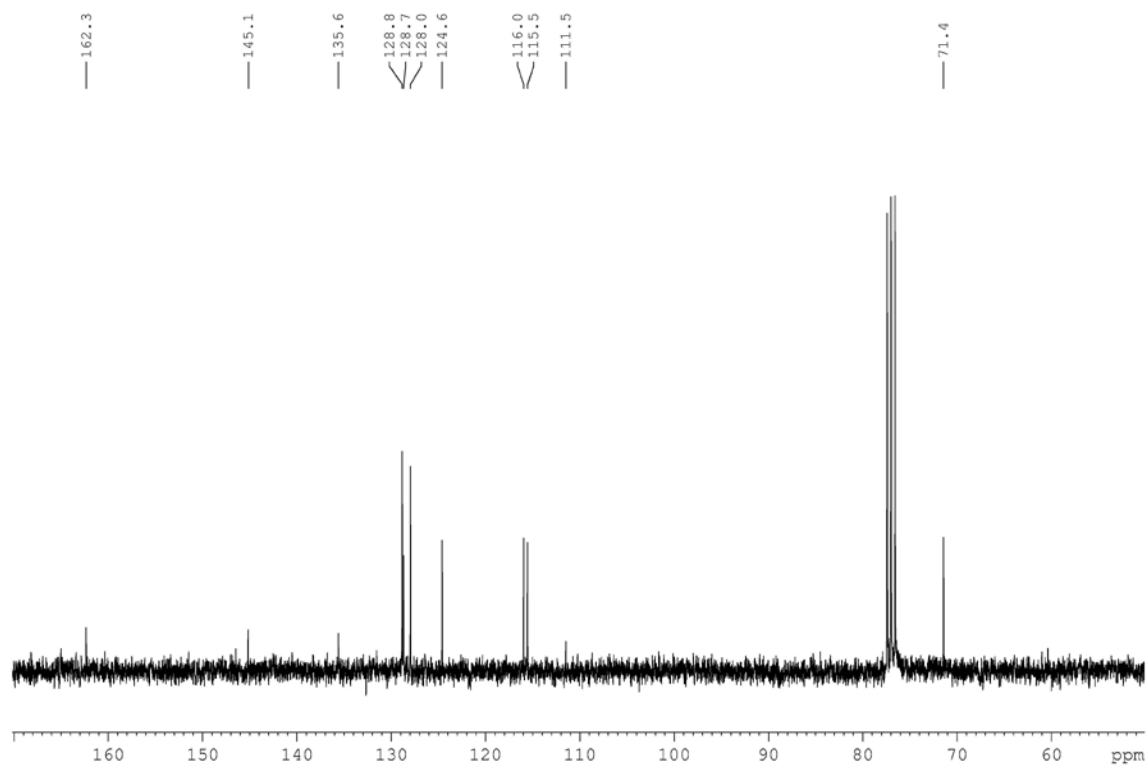


Figure 4. <sup>13</sup>C NMR spectrum of 2-benzyloxy-4-bromophenol 6 (75 MHz, CDCl<sub>3</sub>).

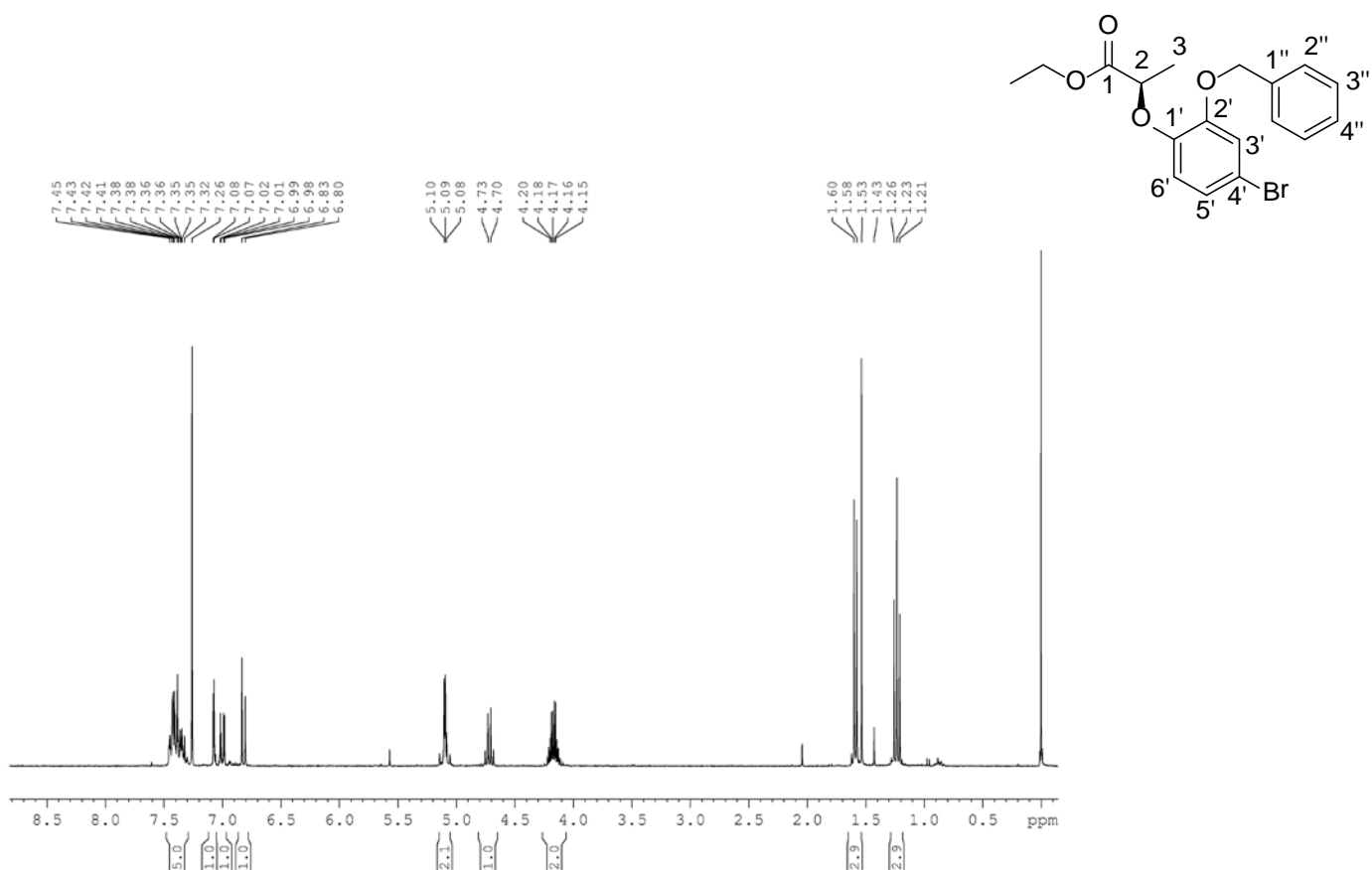


Figure 5. <sup>1</sup>H NMR spectrum of (2*R*)-ethyl 2-(2'-(benzyloxy)-4'-bromophenoxy)propanoate 8 (300 MHz, CDCl<sub>3</sub>).

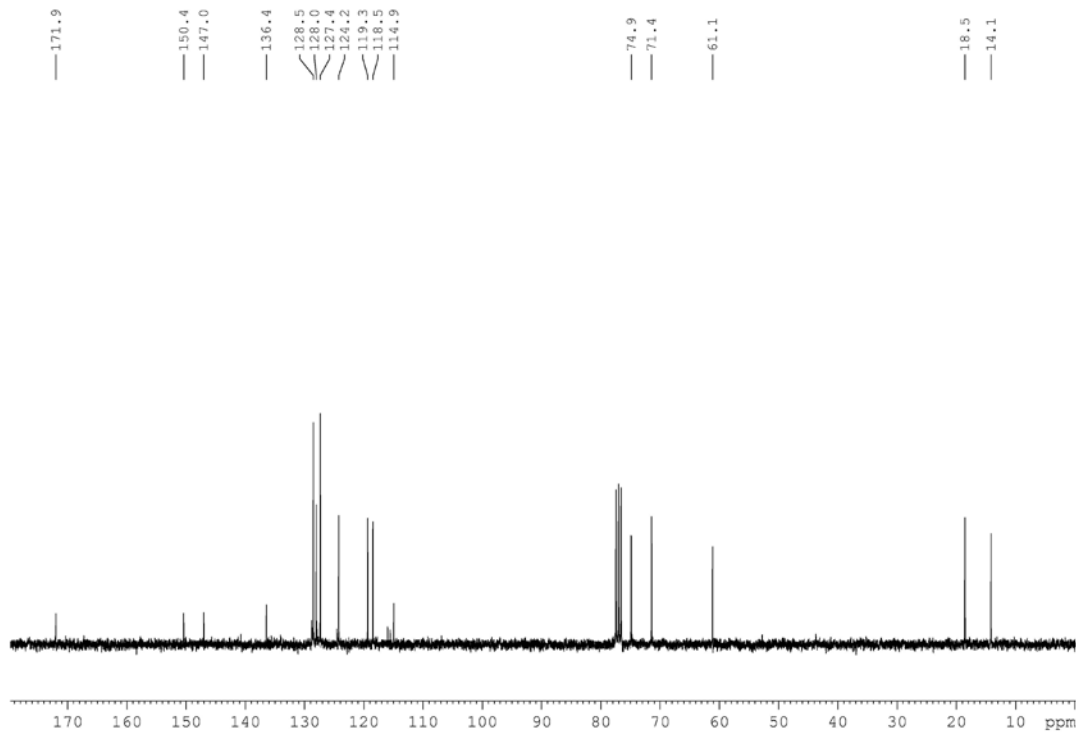


Figure 6. <sup>13</sup>C NMR spectrum of (2*R*)-ethyl 2-(2'-(benzyloxy)-4'-bromophenoxy)propanoate 8 (75 MHz, CDCl<sub>3</sub>).

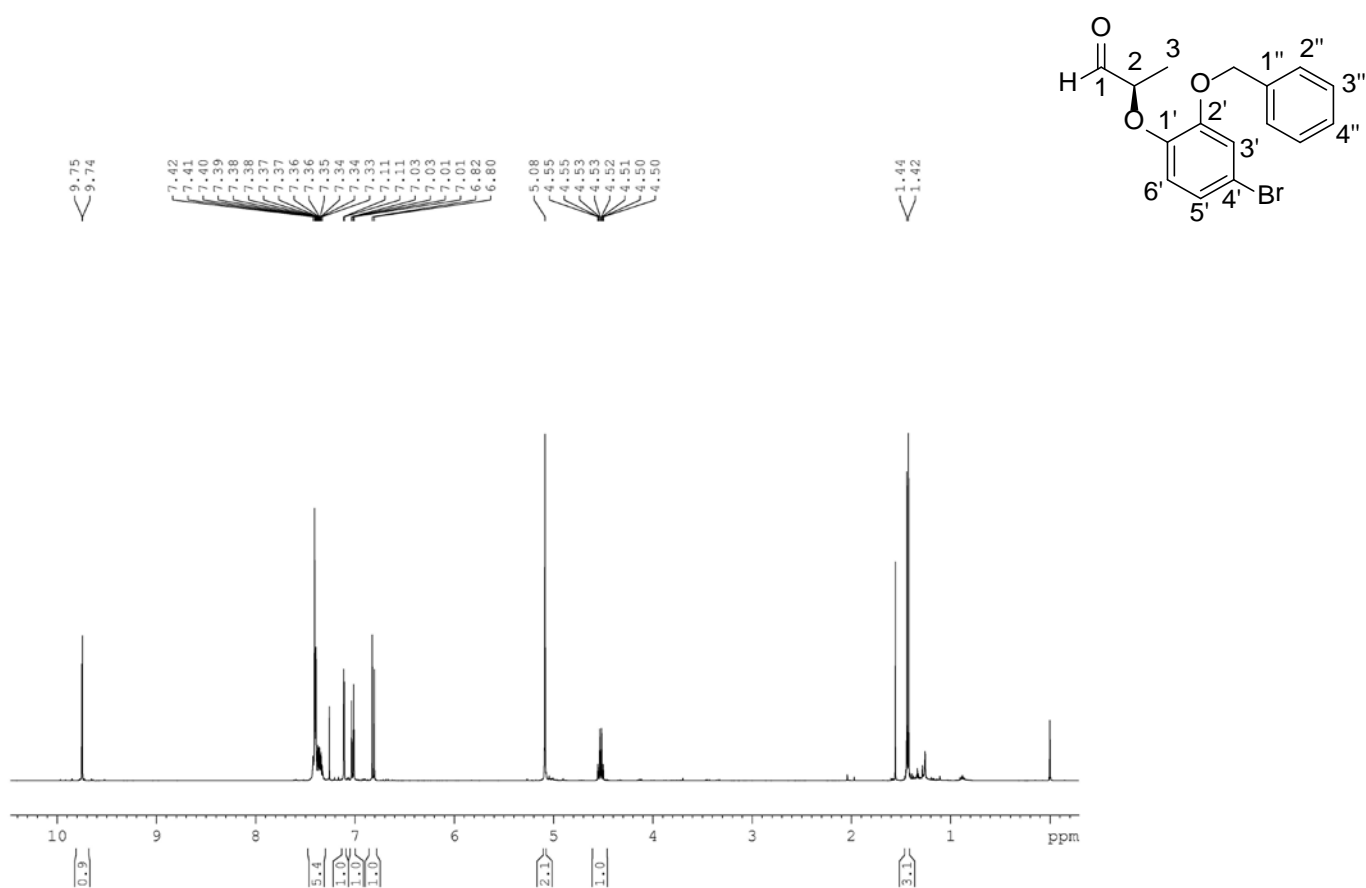


Figure 7. <sup>1</sup>H NMR spectrum of (2R)-2-(2'-(benzyloxy)-4'-bromophenoxy)propan-1-al 9 (400 MHz, CDCl<sub>3</sub>).

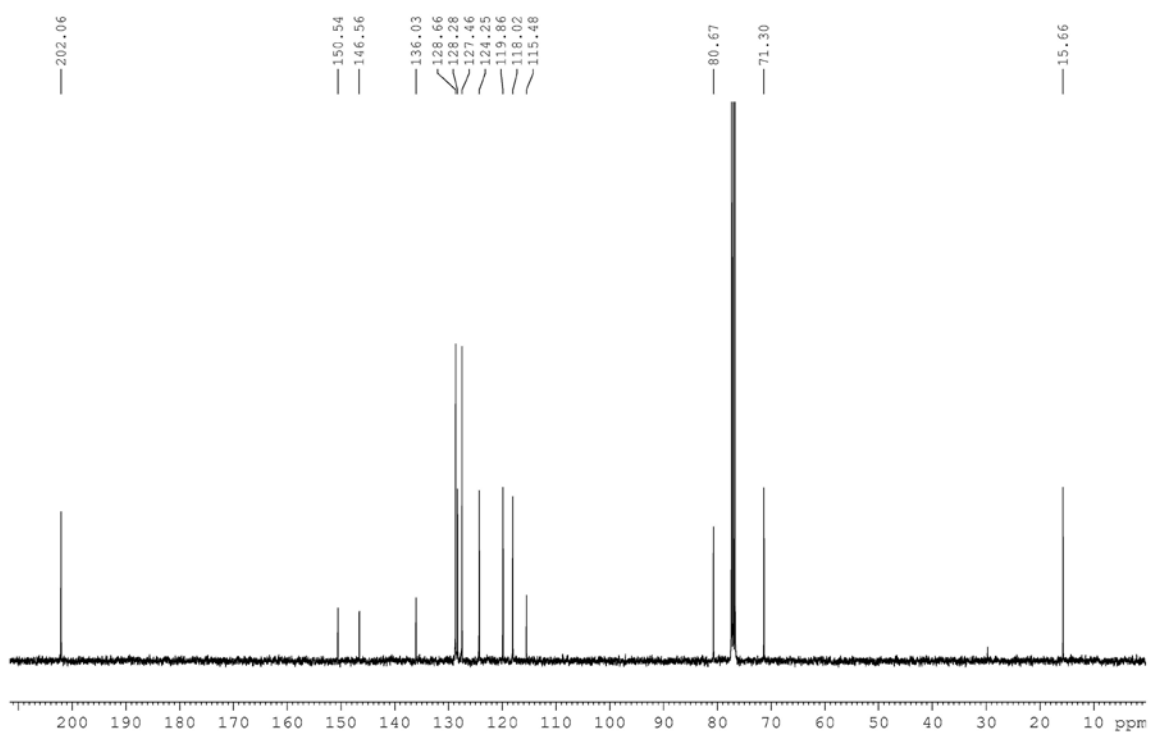


Figure 8. <sup>13</sup>C NMR spectrum of (2R)-2-(2'-(benzyloxy)-4'-bromophenoxy)propan-1-al 9 (100 MHz, CDCl<sub>3</sub>).

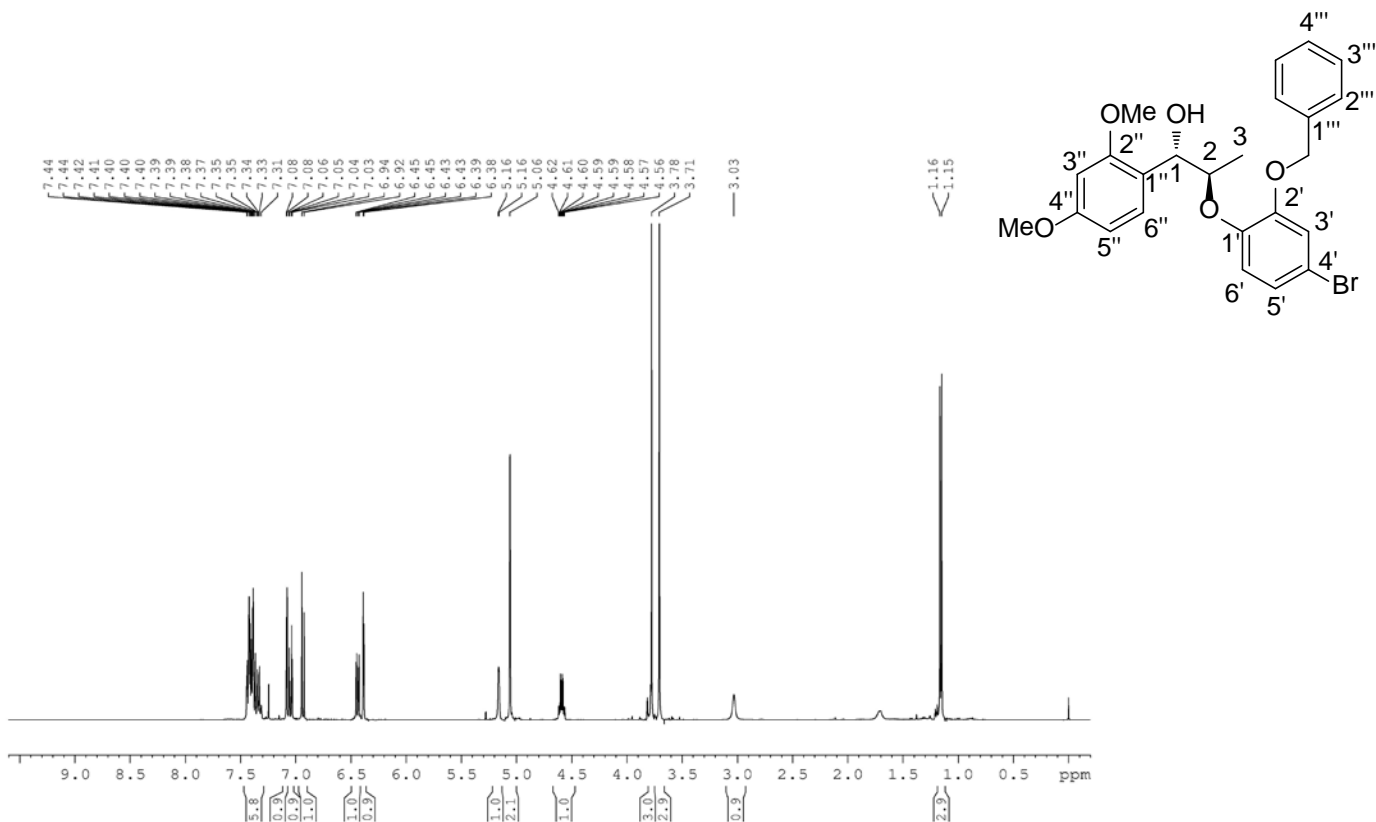


Figure 9. <sup>1</sup>H NMR spectrum of (1*S*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol 19a (400 MHz, CDCl<sub>3</sub>).

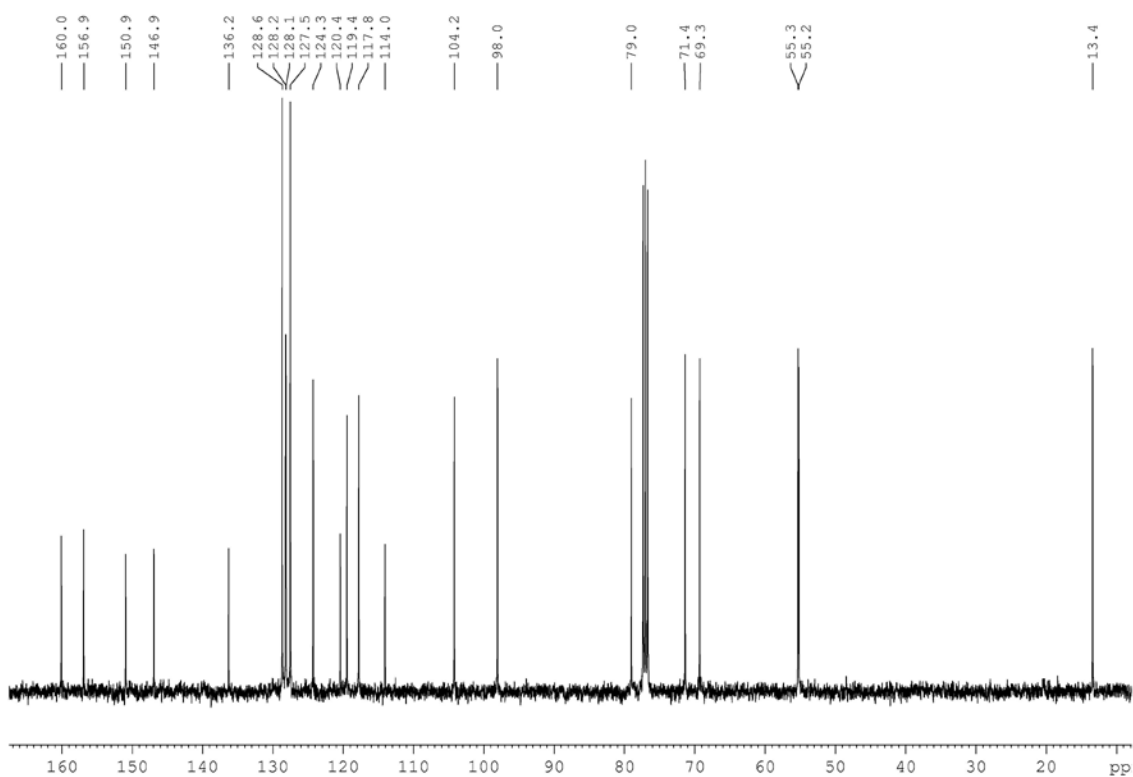


Figure 10. <sup>13</sup>C NMR spectrum of (1*S*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol 19a (100 MHz, CDCl<sub>3</sub>).

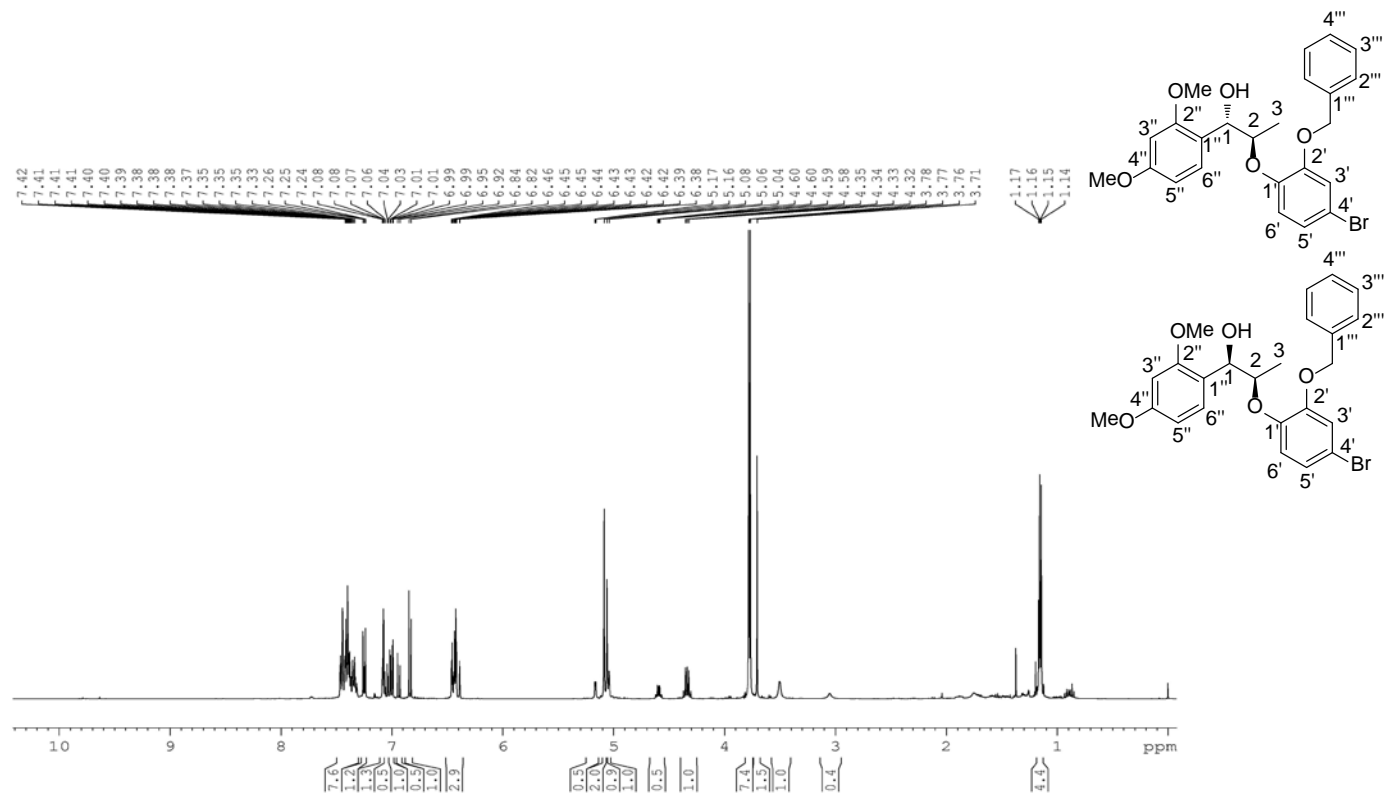


Figure 11.  $^1\text{H}$  NMR spectrum of (1*R*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol 19b and 19a (400 MHz,  $\text{CDCl}_3$ ).

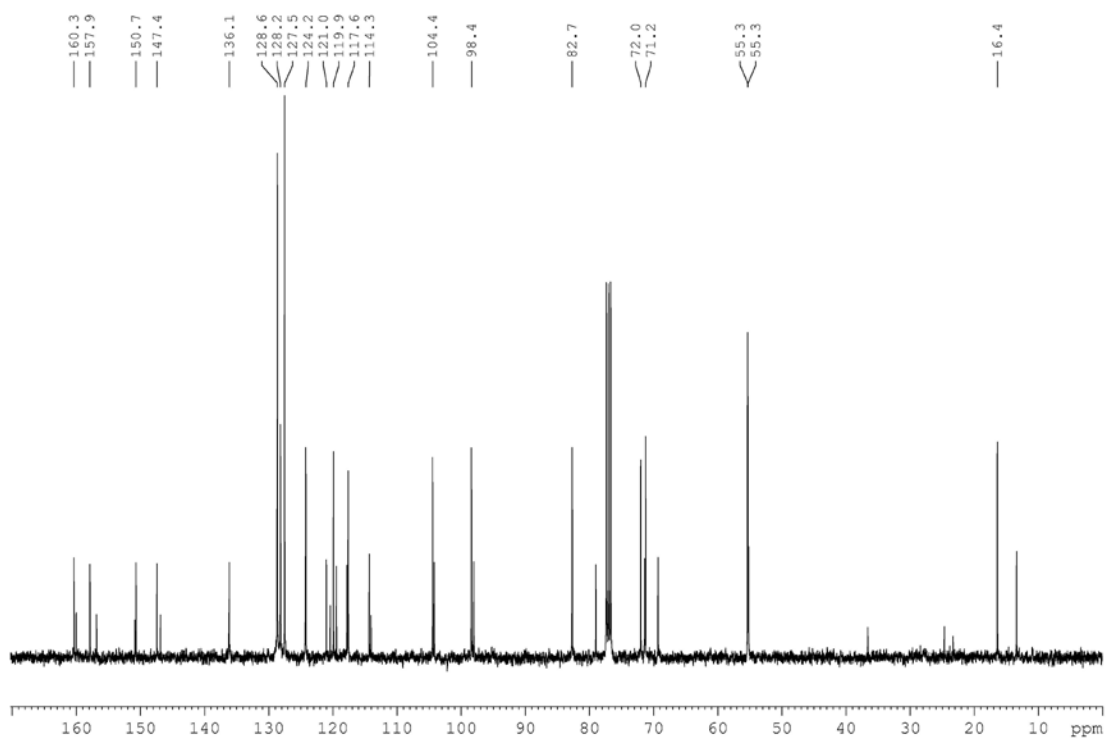


Figure 12.  $^{13}\text{C}$  NMR spectrum of (1*R*,2*R*)-2-(2'-(benzyloxy)-4'-bromophenoxy)-1-(2'',4''-dimethoxyphenyl)propan-1-ol 19b and 19a (100 MHz,  $\text{CDCl}_3$ ).

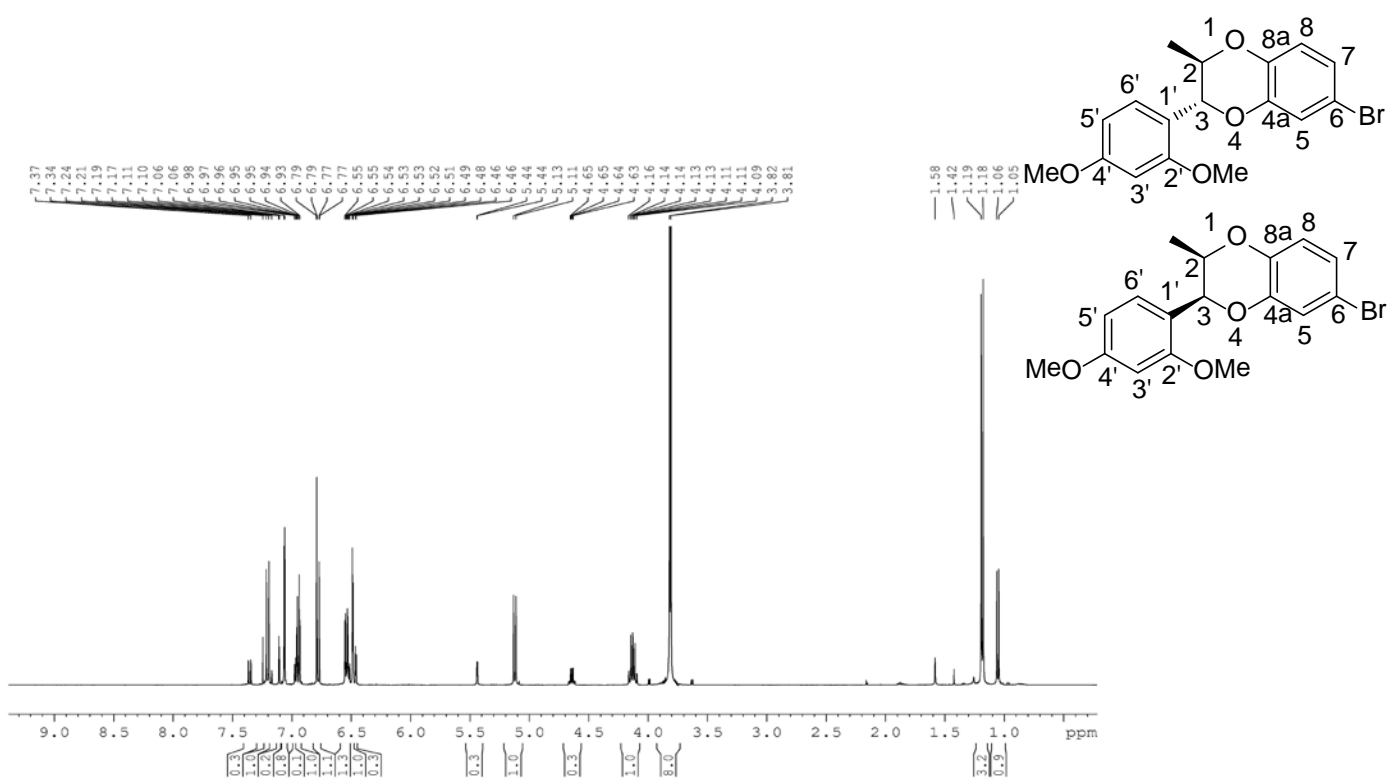


Figure 13. <sup>1</sup>H NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane 20a and (2*R*,3*S*)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane 20b (400 MHz, CDCl<sub>3</sub>).

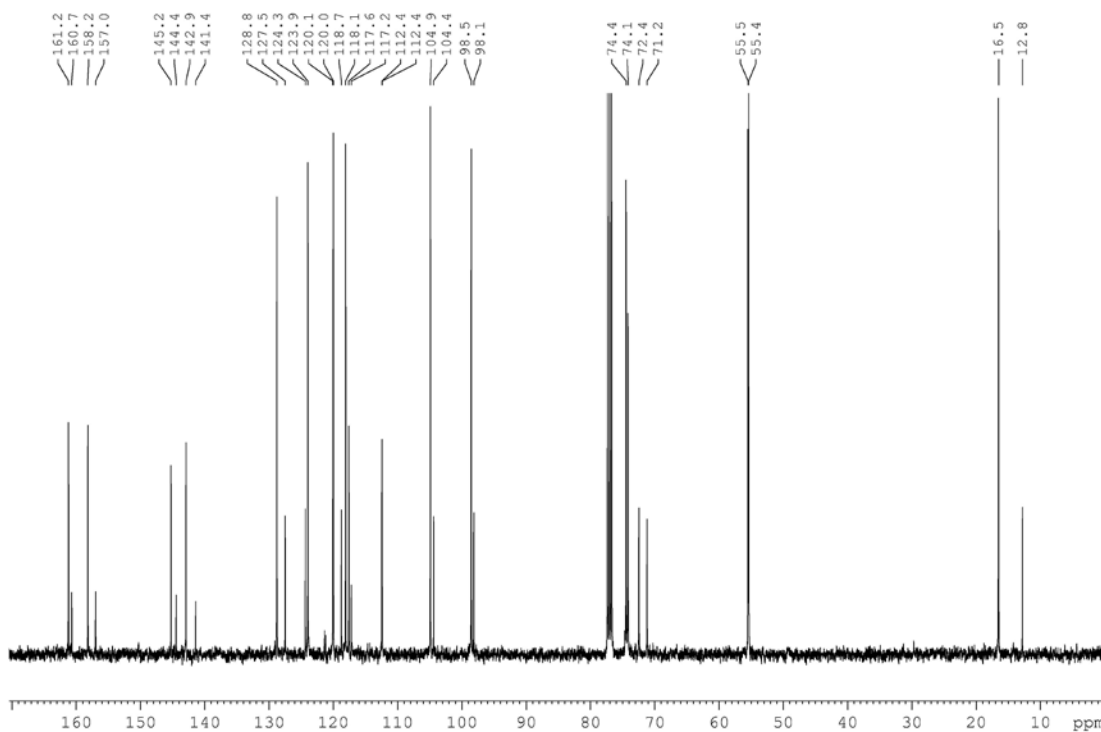
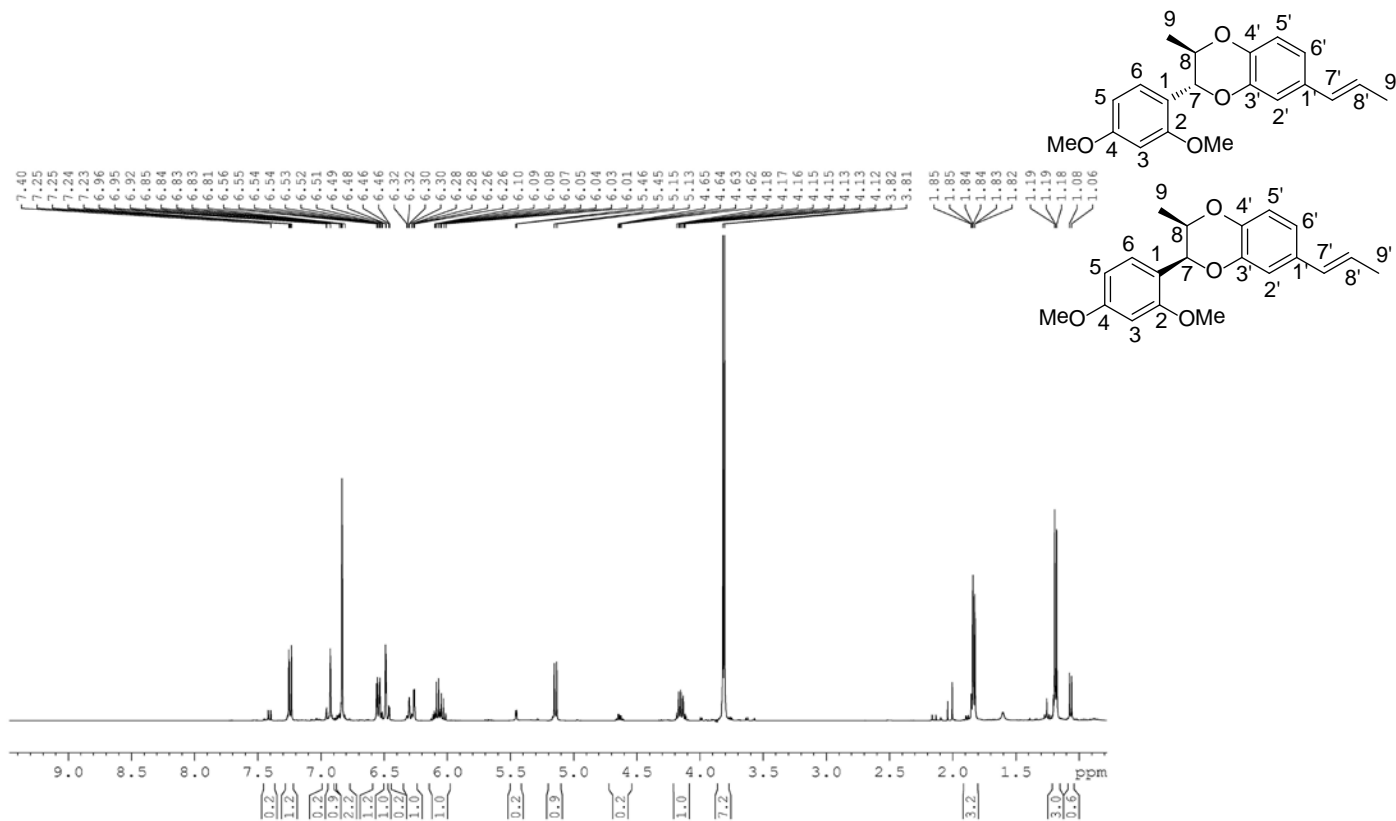
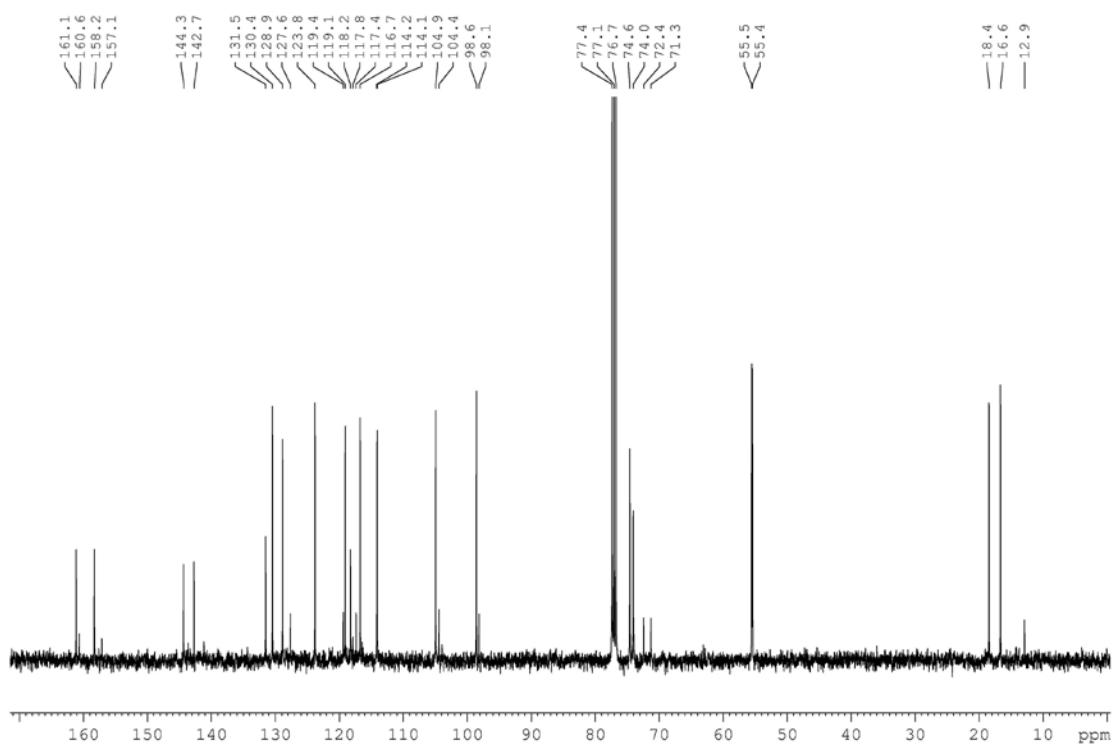


Figure 14. <sup>13</sup>C NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane 20a and (2*R*,3*S*)-2-methyl-3-(2',4'-dimethoxyphenyl)-6-bromo-1,4-benzodioxane 20b (100 MHz, CDCl<sub>3</sub>).





**Figure 15.** <sup>1</sup>H NMR spectrum of (7*R*,8*R*)-7-(2,4-dimethoxyphenyl)-8-methyl-3',7'-epoxy-8,4'-oxyneolign-7'-ene 21a and (7*S*,8*R*)-7-(2,4-dimethoxyphenyl)-8-methyl-3',7'-epoxy-8,4'-oxyneolign-7'-ene 21b (400 MHz, CDCl<sub>3</sub>).



**Figure 16.** <sup>13</sup>C NMR spectrum of (7*R*,8*R*)-7-(2,4-dimethoxyphenyl)-8-methyl-3',7'-epoxy-8,4'-oxyneolign-7'-ene 21a and (7*S*,8*R*)-7-(2,4-dimethoxyphenyl)-8-methyl-3',7'-epoxy-8,4'-oxyneolign-7'-ene 21b (100 MHz, CDCl<sub>3</sub>).

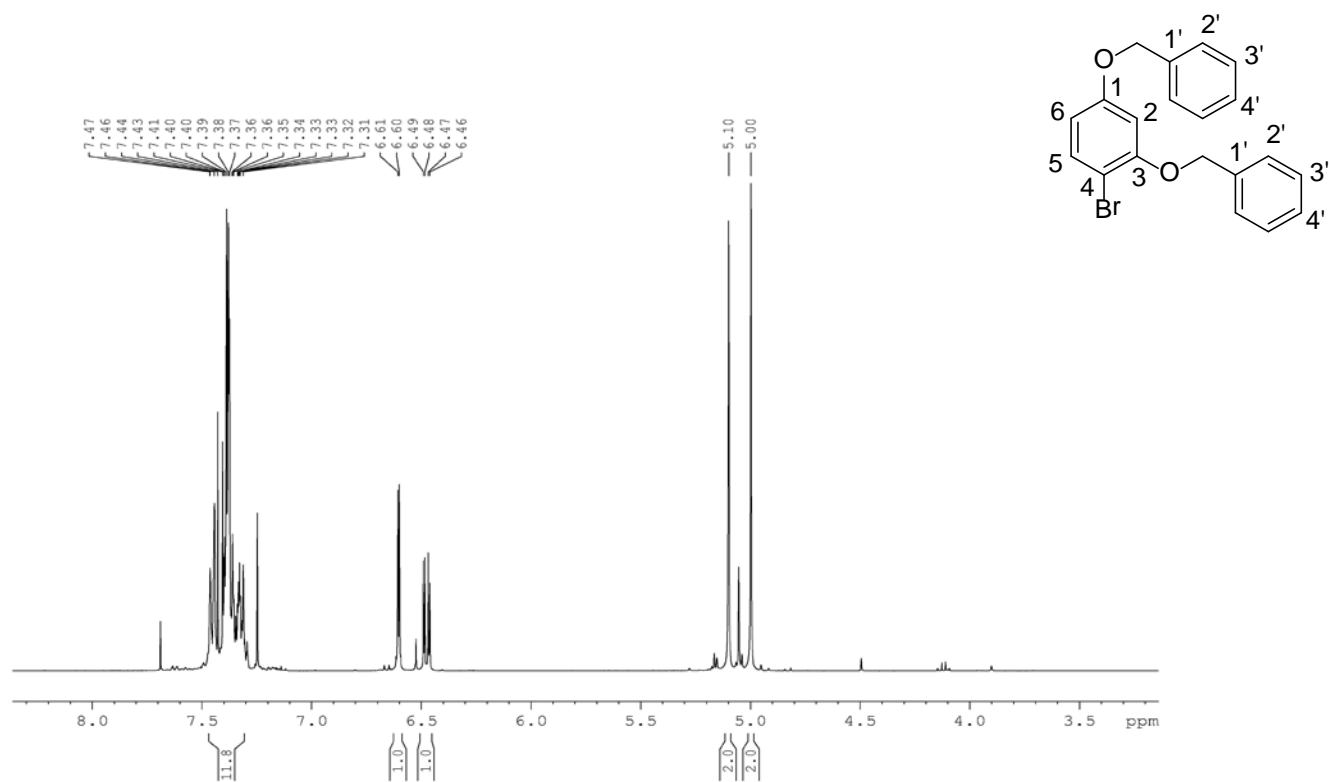


Figure 17.  $^1\text{H}$  NMR spectrum of 1,3-bis(benzyloxy)-4-bromobenzene (400 MHz,  $\text{CDCl}_3$ ).

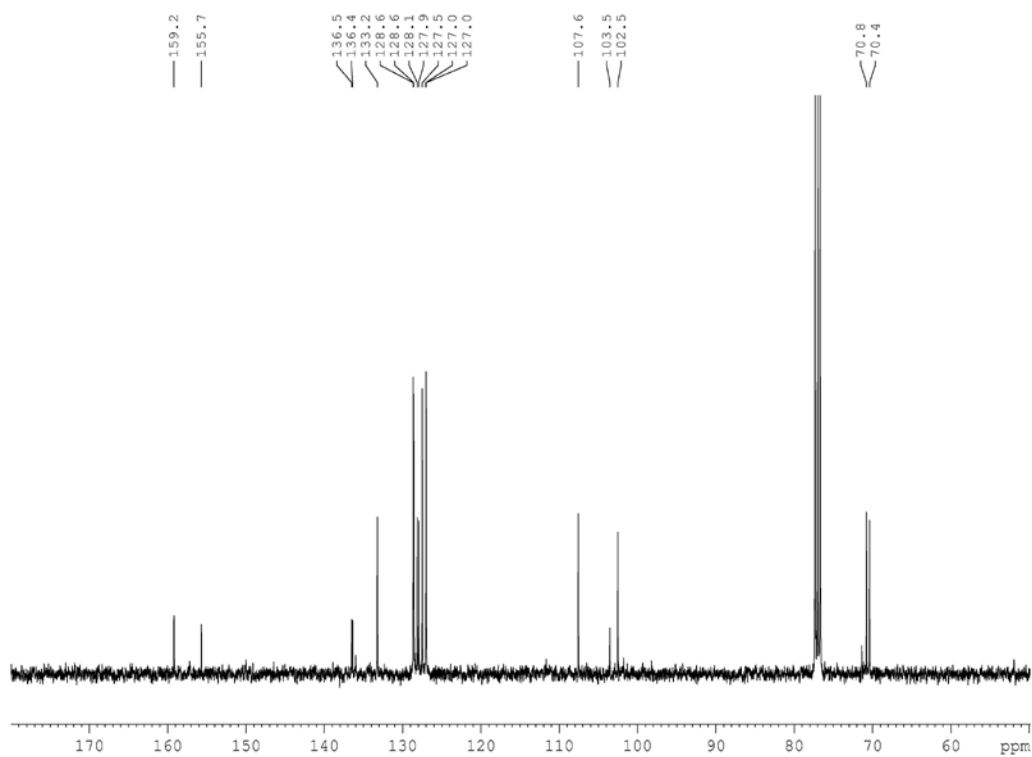


Figure 18.  $^{13}\text{C}$  NMR spectrum of 1,3-bis(benzyloxy)-4-bromobenzene (100 MHz,  $\text{CDCl}_3$ ).

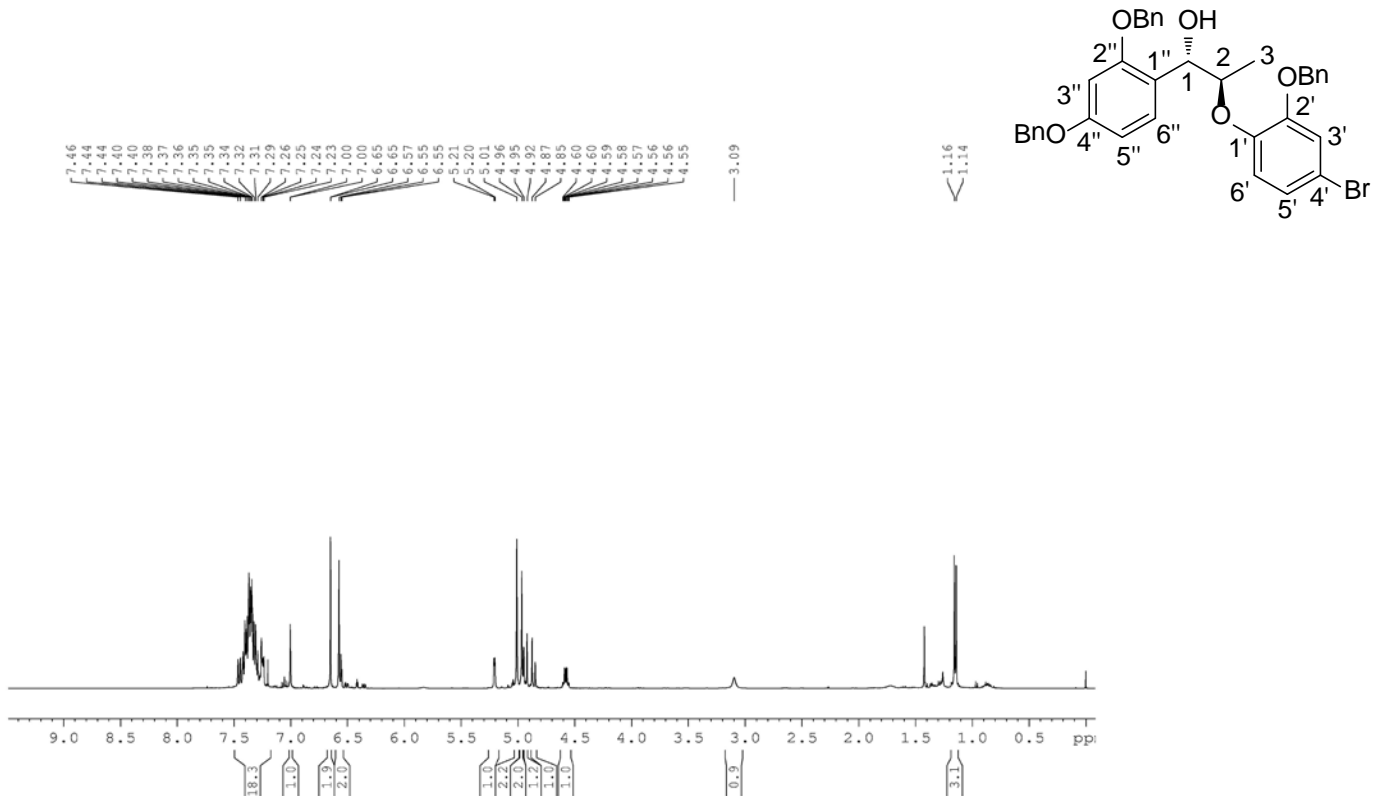


Figure 19. <sup>1</sup>H NMR spectrum of (1*S*,2*R*)-2-(2'-(Benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol 11a (400 MHz, CDCl<sub>3</sub>).

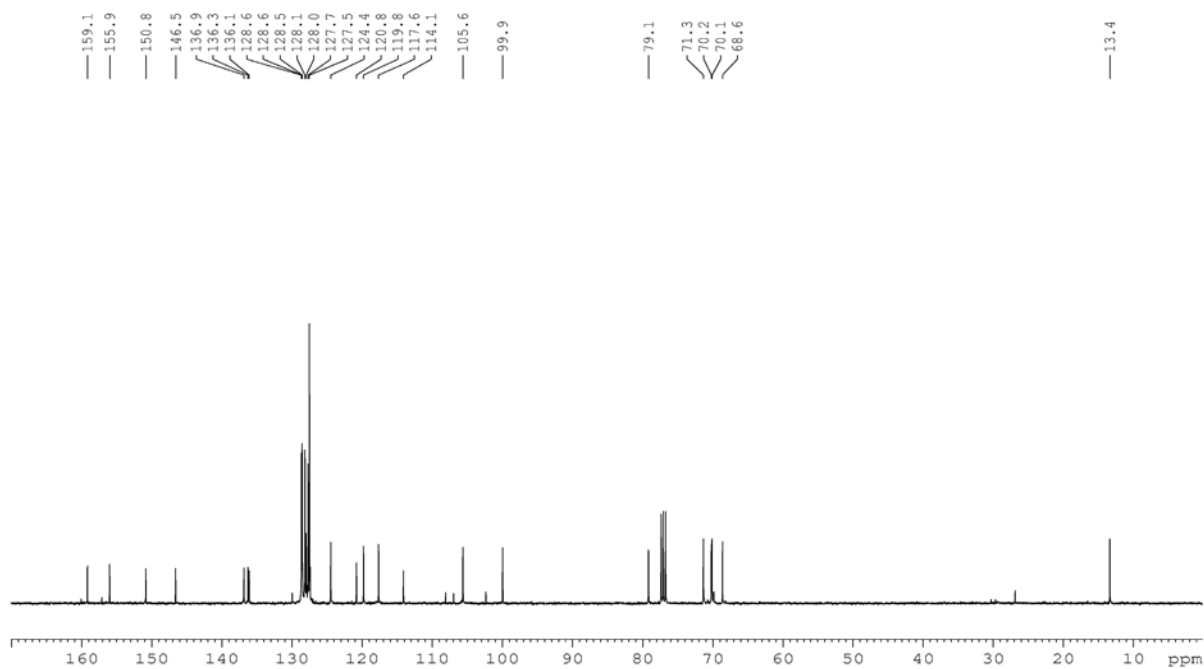


Figure 20. <sup>13</sup>C NMR spectrum of (1*S*,2*R*)-2-(2'-(Benzyloxy)-4'-bromophenoxy)-1-(2'',4''-bis(benzyloxy)phenyl)propan-1-ol 11a (100 MHz, CDCl<sub>3</sub>).



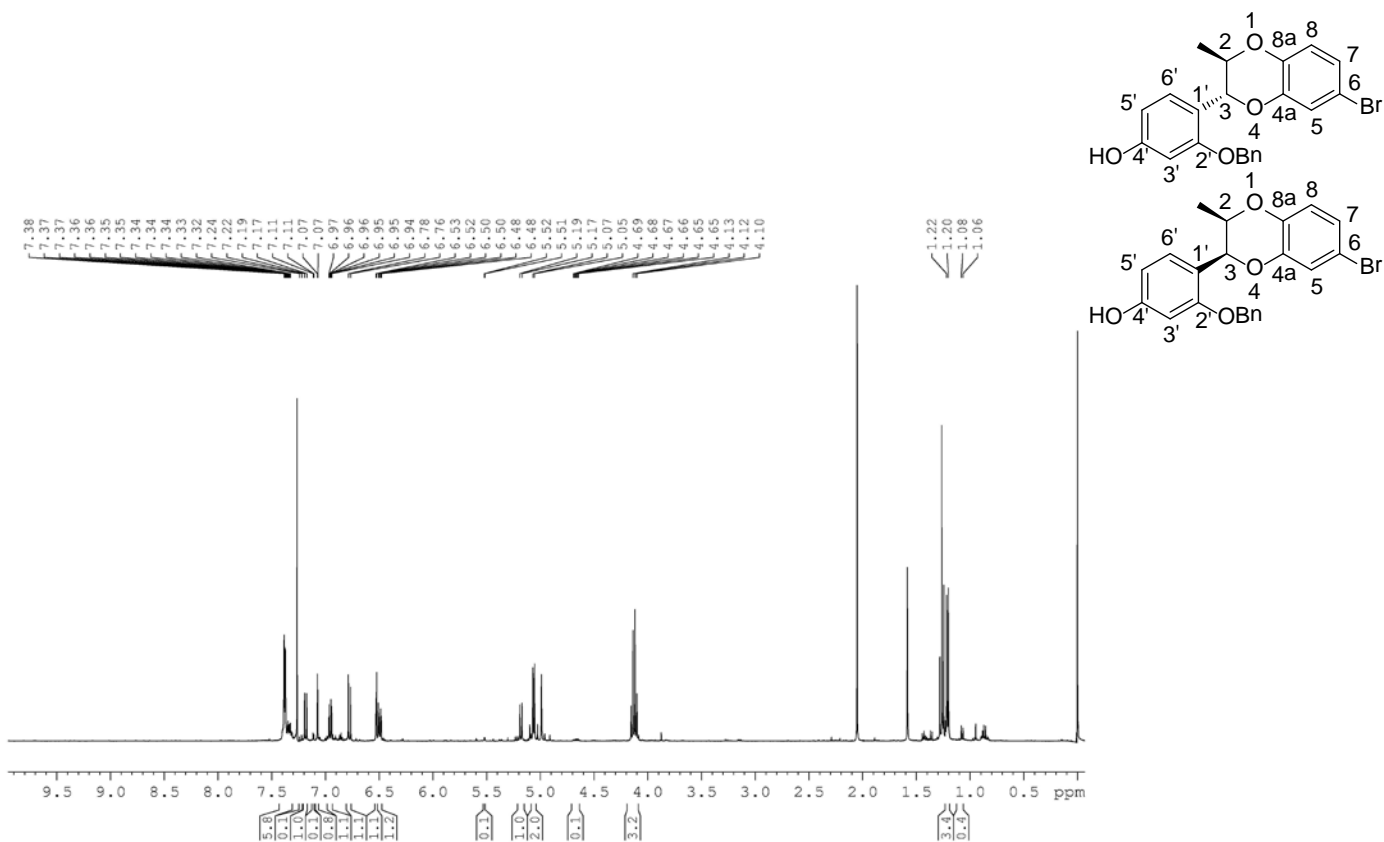


Figure 23.  $^1\text{H}$  NMR spectrum of  $(2R,3R)$ -2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane and  $(2R,3S)$ -2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane (400 MHz,  $\text{CDCl}_3$ ).

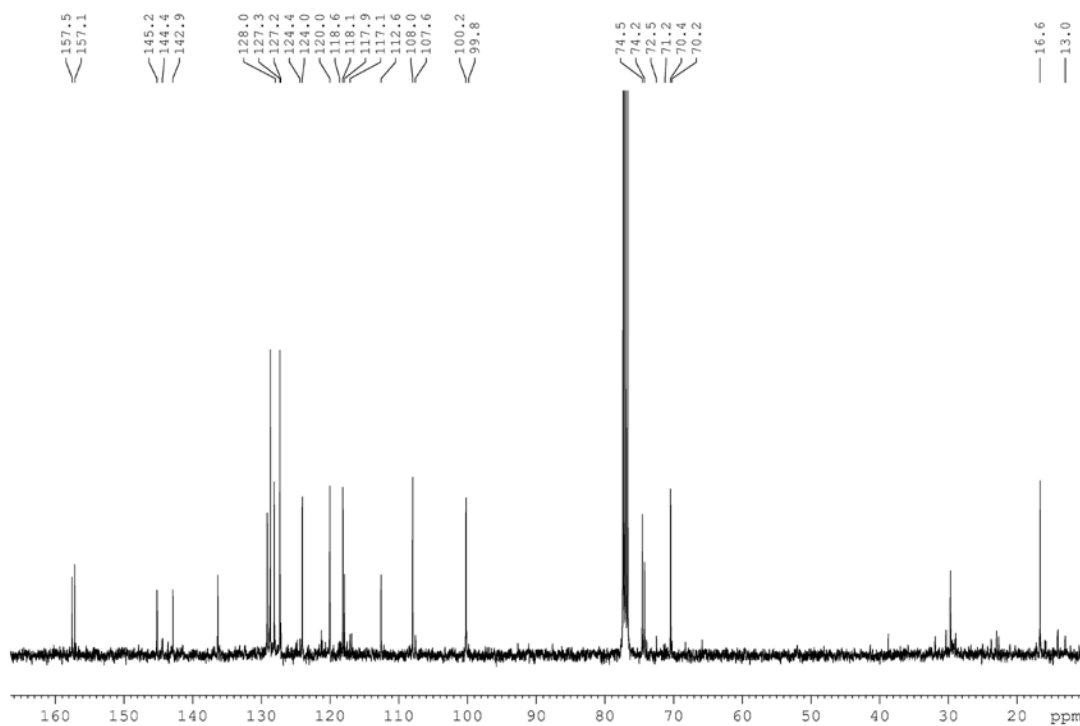


Figure 24.  $^{13}\text{C}$  NMR spectrum of  $(2R,3R)$ -2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane and  $(2R,3S)$ -2-methyl-3-(2'-benzyloxy-4'-hydroxyphenyl)-6-bromo-1,4-benzodioxane (100 MHz,  $\text{CDCl}_3$ ).

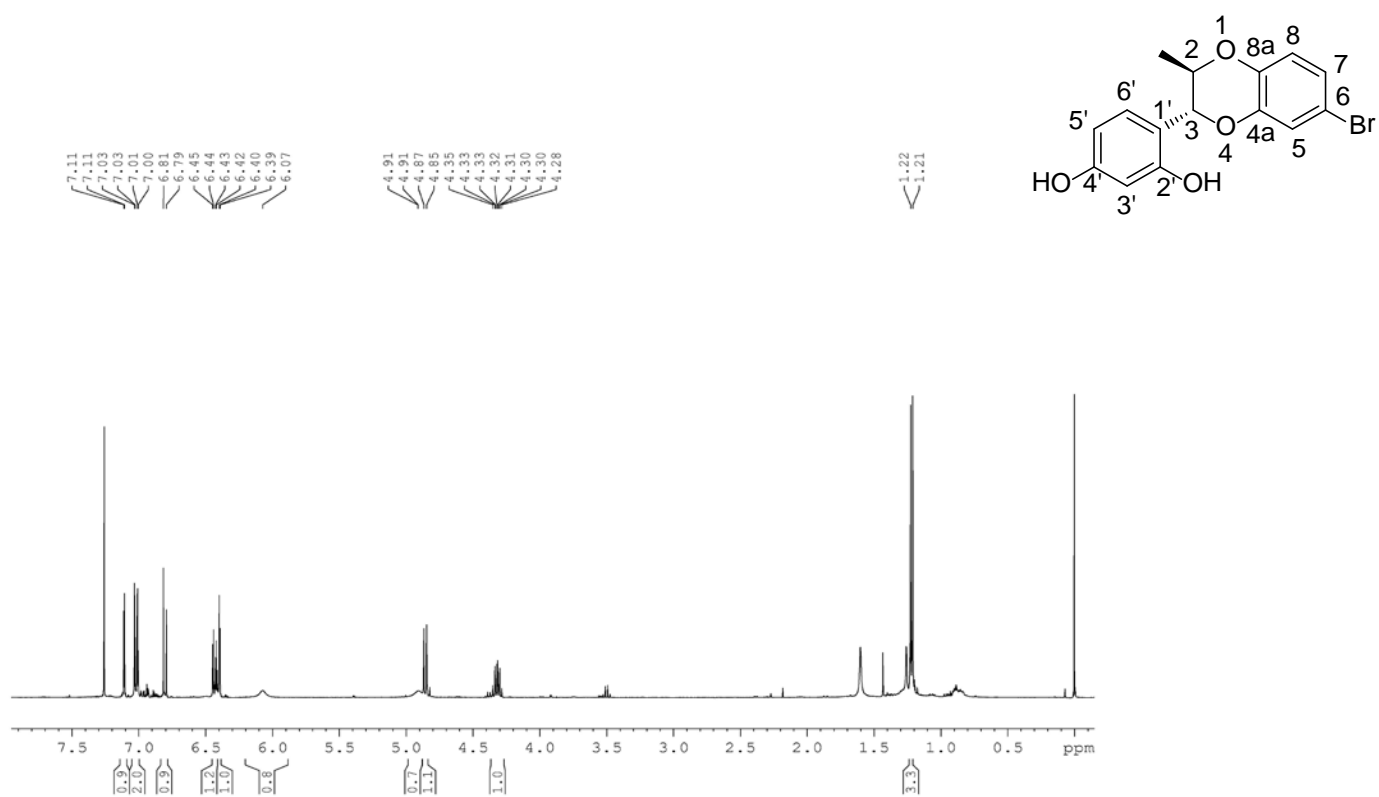


Figure 25. <sup>1</sup>H NMR spectrum of (2R,3R)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12a (400 MHz, CDCl<sub>3</sub>).

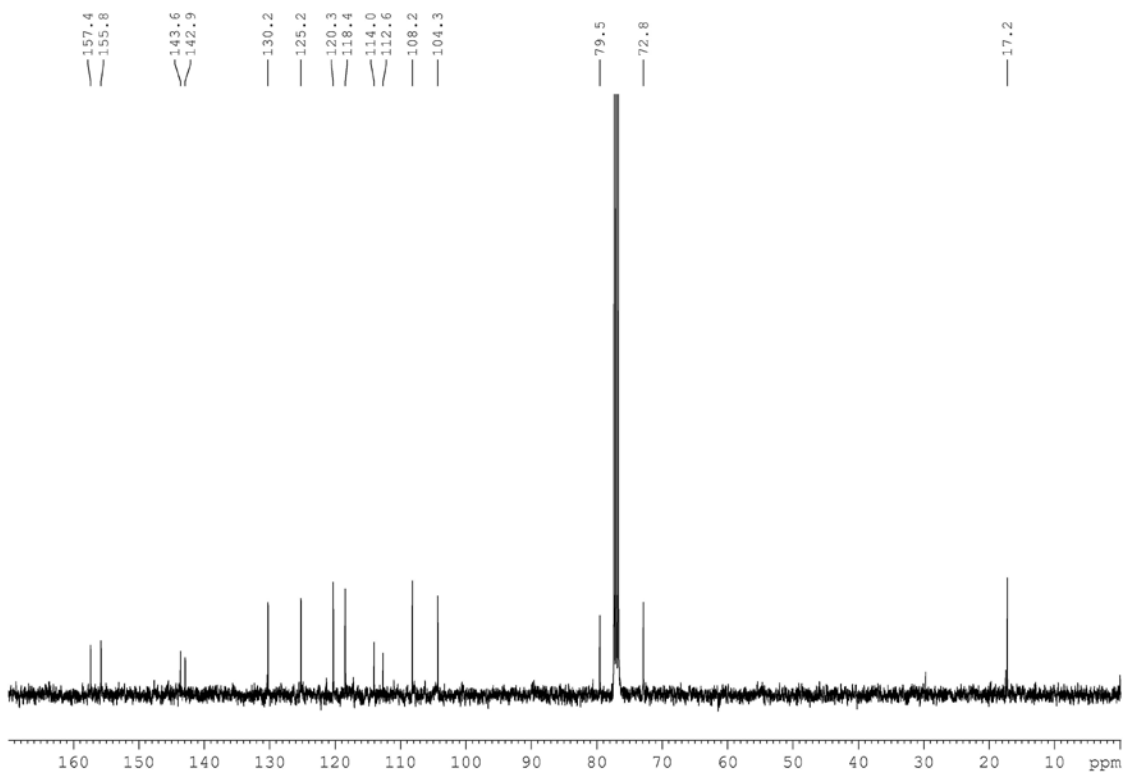


Figure 26. <sup>13</sup>C NMR spectrum of (2R,3R)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12a (100 MHz, CDCl<sub>3</sub>).

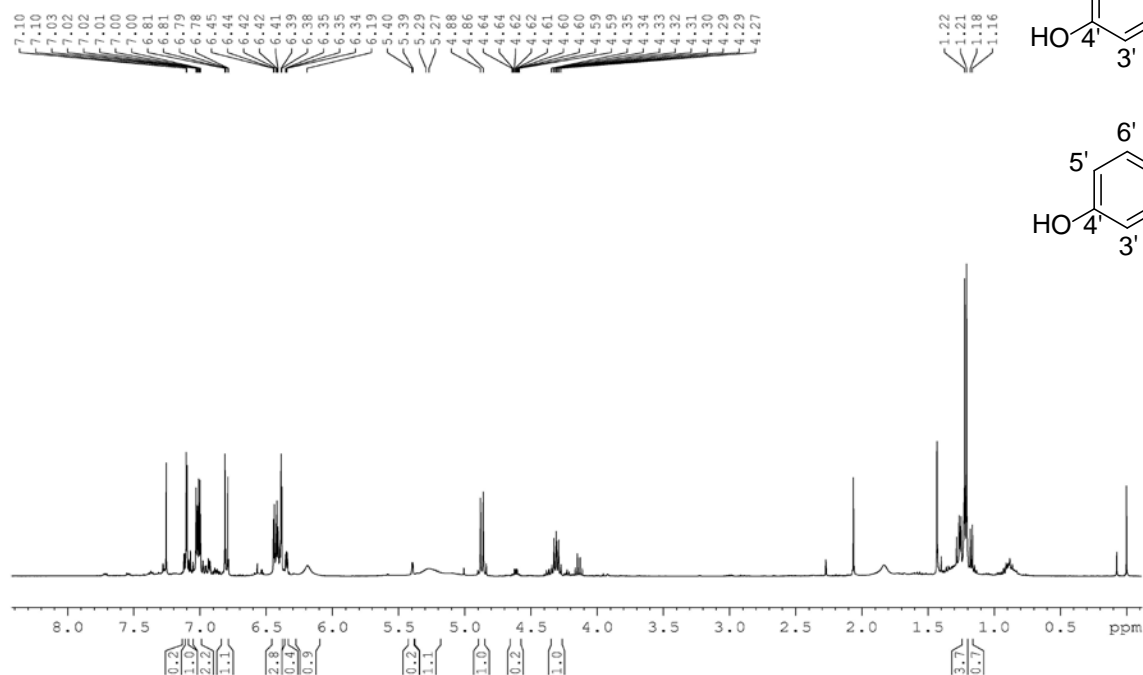


Figure 27. <sup>1</sup>H NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12a and (2*R*,3*S*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12b (400 MHz, CDCl<sub>3</sub>).

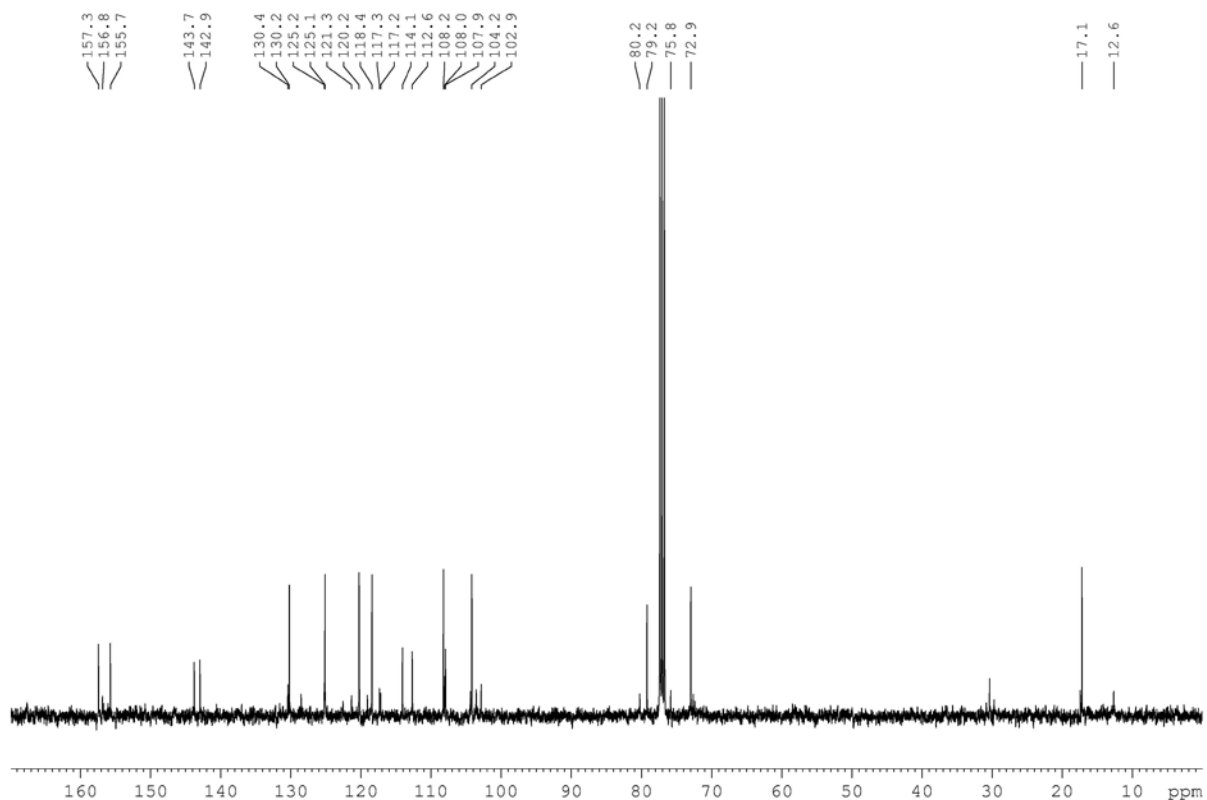


Figure 28. <sup>13</sup>C NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12a and (2*R*,3*S*)-2-methyl-3-(2',4'-dihydroxyphenyl)-6-bromo-1,4-benzodioxane 12b (100 MHz, CDCl<sub>3</sub>).

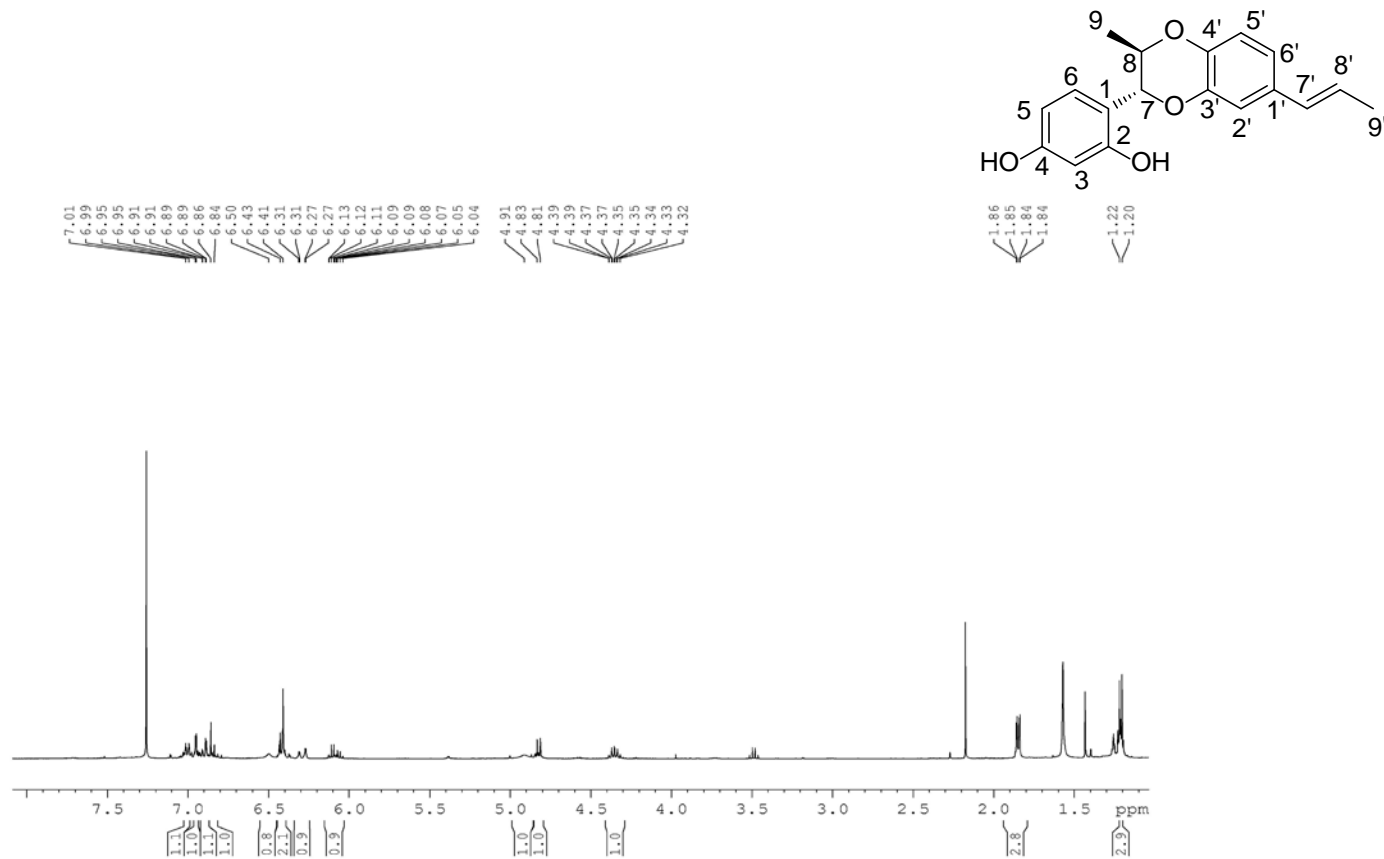


Figure 29.  $^1\text{H}$  NMR spectrum of *trans*-rodgersinine A (1) (400 MHz,  $\text{CDCl}_3$ ).

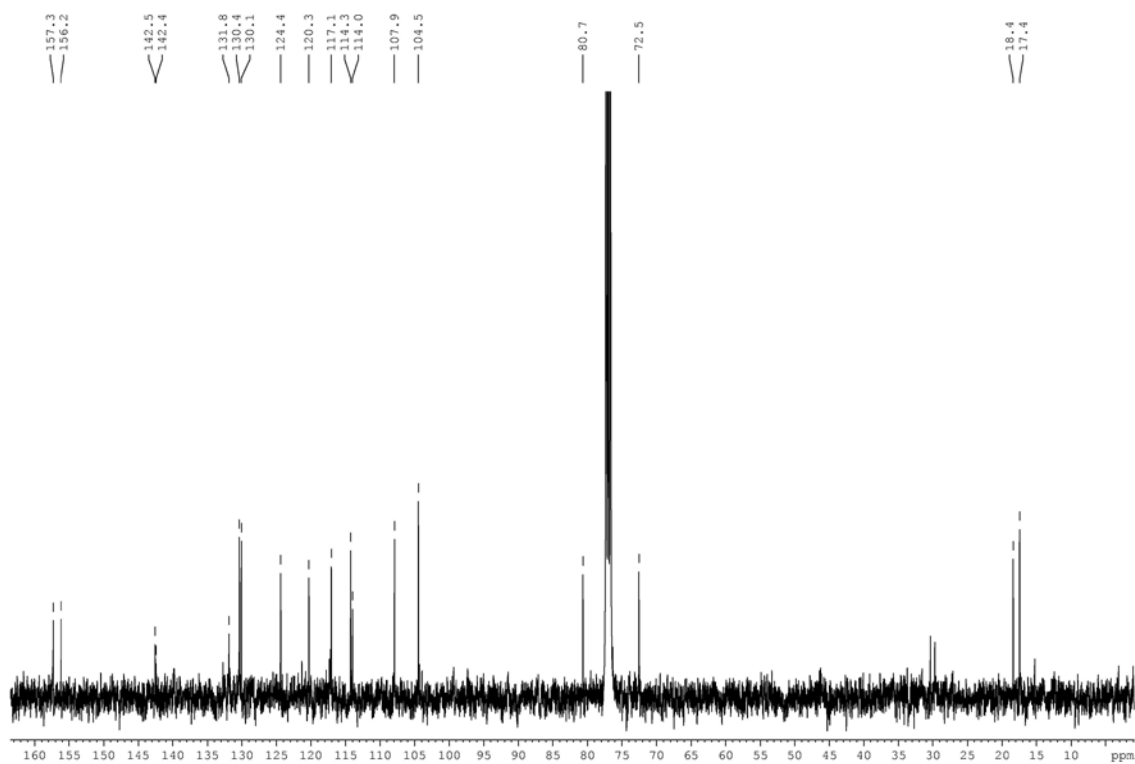
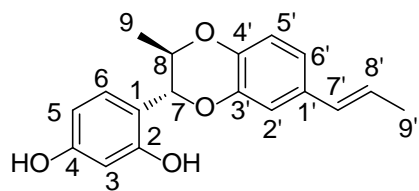


Figure 30.  $^{13}\text{C}$  NMR spectrum of *trans*-rodgersinine A (1) (100 MHz,  $\text{CDCl}_3$ ).





| Atom Number | Synthetic (+)- <i>trans</i> -roddersinine A (1)  |   | Natural (+)- <i>trans</i> -roddersinine A (1)                 |  |
|-------------|--|---|---|--|
|             | <sup>1</sup> H (δ) (400 MHz, CDCl <sub>3</sub> ) | <sup>13</sup> C (δ) (100 MHz, CDCl <sub>3</sub> ) | <sup>1</sup> H (δ) (400 MHz, CDCl <sub>3</sub> ) <sup>8</sup> | <sup>13</sup> C (δ) (100 MHz, CDCl <sub>3</sub> ) <sup>8</sup> |
| 1           |  | 114.0   |   | 113.9  |
| 2           |  | 156.2   |   | 156.1  |
| 3           | 6.41 (1H, br s)                                  | 104.5   | 6.35 (1H, br s)   | 104.4  |
| 4           |  | 157.3   |   | 157.4  |
| 5           | 6.41 (1H, d, <i>J</i> 8.0 Hz)                    | 107.9   | 6.40 (1H, d, <i>J</i> 7.9 Hz)                                 | 107.9  |
| 6           | 6.99 (1H, d, <i>J</i> 8.0 Hz)                    | 130.1   | 6.98 (1H, d, <i>J</i> 7.9 Hz)                                 | 130.0  |
| 7           | 4.81 (1H, d, <i>J</i> 8.4 Hz)                    | 80.7  | 4.80 (1H, d, <i>J</i> 8.0 Hz)                                 | 80.5   |
| 8           | 4.32-4.39 (1H, m)                                | 72.5  | 4.33 (1H, dq <i>J</i> 6.4, 8.0 Hz)                            | 72.6   |
| 9           | 1.20 (3H, d, <i>J</i> 6.4 Hz)                    | 17.4  | 1.19 (3H, d, <i>J</i> 6.6 Hz)                                 | 17.4   |
| 1'          |  | 131.8   |   | 131.8  |
| 2'          | 6.95 (1H, d, <i>J</i> 1.6 Hz)                    | 114.3   | 6.93 (1H, d, <i>J</i> 1.7 Hz)                                 | 114.2  |
| 3'          |  | 142.5   |   | 142.5  |
| 4'          |  | 142.4   |   | 142.4  |
| 5'          | 6.84 (1H, d, <i>J</i> 8.4 Hz)                    | 117.1   | 6.82 (1H, d, <i>J</i> 8.3 Hz)                                 | 117.0  |
| 6'          | 6.89 (1H, dd, <i>J</i> 1.6, 8.4 Hz)              | 120.3   | 6.88 (1H, dd, <i>J</i> 1.7, 8.3 Hz)                           | 120.2  |
| 7'          | 6.27 (1H, dd, <i>J</i> 1.6, 15.2 Hz)             | 130.4   | 6.27 (1H, d, <i>J</i> 15.3 Hz)                                | 130.3  |
| 8'          | 6.04 (1H, dq, <i>J</i> 6.4, 15.2 Hz)             | 124.4   | 6.06 (1H, dq, <i>J</i> 6.6, 15.3 Hz)                          | 124.4  |
| 9'          | 1.84 (3H, dd, <i>J</i> 1.6, 6.4 Hz)              | 18.4  | 1.83 (3H, d, <i>J</i> 6.6 Hz)                                 | 18.4   |

**Table 1.** NMR data comparison table for natural and synthetic (+)-*trans* roddersinine A (1).

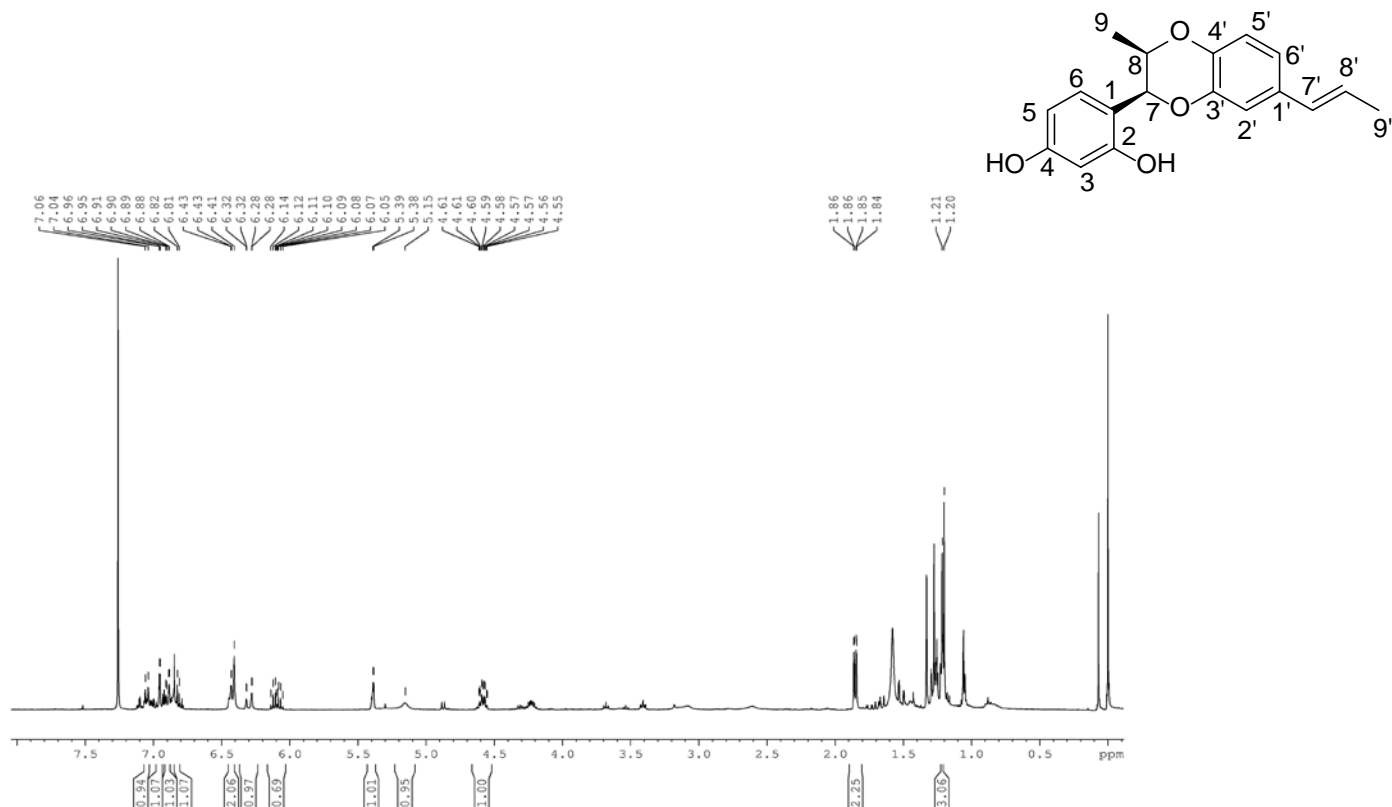


Figure 31. <sup>1</sup>H NMR spectrum of *cis*-rodgersinine A (2) (400 MHz, CDCl<sub>3</sub>).

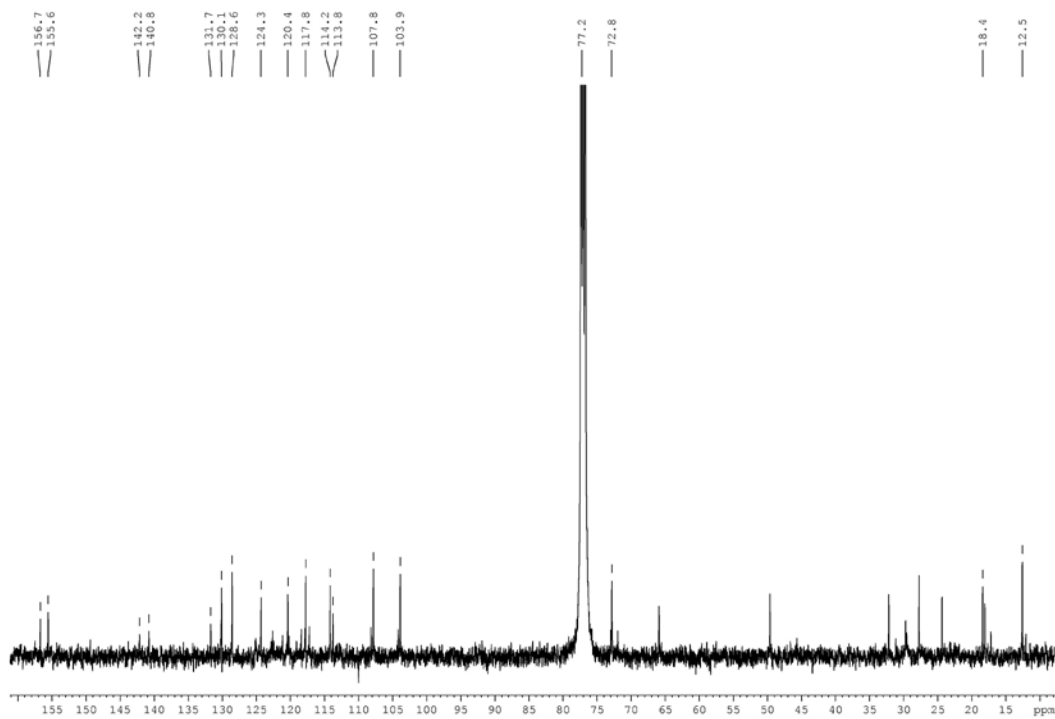
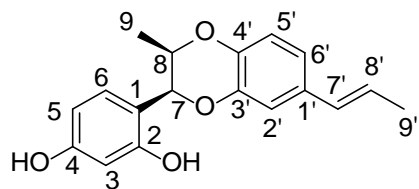


Figure 32. <sup>13</sup>C NMR spectrum of *cis*-rodgersinine A (2) (100 MHz, CDCl<sub>3</sub>).



| Atom Number | Synthetic (+)- <i>cis</i> -rodersinine A (2)     |   | Natural (+)- <i>cis</i> -rodersinine A (2)                    |  |
|-------------|--|---|---|--|
|             | <sup>1</sup> H (δ) (400 MHz, CDCl <sub>3</sub> ) | <sup>13</sup> C (δ) (100 MHz, CDCl <sub>3</sub> ) | <sup>1</sup> H (δ) (400 MHz, CDCl <sub>3</sub> ) <sup>8</sup> | <sup>13</sup> C (δ) (100 MHz, CDCl <sub>3</sub> ) <sup>8</sup> |
| 1           |  | 113.8   |   | 113.7  |
| 2           |  | 155.6   |   | 155.6  |
| 3           | 6.41 (1H, br s)                                  | 103.9   | 6.35 (1H, d, <i>J</i> 2.4 Hz)                                 | 103.9  |
| 4           |  | 156.7   |   | 156.6  |
| 5           | 6.41 (1H, dd, <i>J</i> 1.2, 8.0 Hz)              | 107.8   | 6.40 (1H, dd, <i>J</i> 2.4, 8.3 Hz)                           | 107.8  |
| 6           | 7.04 (1H, d, <i>J</i> 8.0 Hz)                    | 128.6   | 7.02 (1H, d, <i>J</i> 8.3 Hz)                                 | 128.6  |
| 7           | 5.38 (1H, d, <i>J</i> 2.4 Hz)                    | 77.2  | 5.37 (1H, d, <i>J</i> 2.4 Hz)                                 | 77.0   |
| 8           | 4.55 (1H, dq, <i>J</i> 2.4, 6.4 Hz)              | 72.8  | 4.56 (1H, qd, <i>J</i> 2.4, 6.5 Hz)                           | 72.9   |
| 9           | 1.20 (3H, d, <i>J</i> 6.4 Hz)                    | 12.5  | 1.20 (3H, d, <i>J</i> 6.5 Hz)                                 | 12.5   |
| 1'          |  | 131.7   |   | 131.7  |
| 2'          | 6.95 (1H, d, <i>J</i> 2.0 Hz)                    | 114.2   | 6.94 (1H, d, <i>J</i> 2.0 Hz)                                 | 114.2  |
| 3'          |  | 142.2   |   | 142.1  |
| 4'          |  | 140.8   |   | 140.7  |
| 5'          | 6.81 (1H, d, <i>J</i> 8.0 Hz)                    | 117.8   | 6.81 (1H, d, <i>J</i> 8.4 Hz)                                 | 117.8  |
| 6'          | 6.88 (1H, dd, <i>J</i> 2.0, 8.0 Hz)              | 120.4   | 6.88 (1H, dd, <i>J</i> 2.0, 8.4 Hz)                           | 120.4  |
| 7'          | 6.28 (1H, dd, <i>J</i> 1.6, 16.0 Hz)             | 130.1   | 6.28 (1H, d, <i>J</i> 14.0 Hz)                                | 130.1  |
| 8'          | 6.05 (1H, qd, <i>J</i> 6.4, 16.0 Hz)             | 124.3   | 6.10 (1H, qd, <i>J</i> 6.5, 14.0 Hz)                          | 124.4  |
| 9'          | 1.84 (3H, dd, <i>J</i> 1.2, 6.4 Hz)              | 18.4  | 1.83 (3H, d, <i>J</i> 6.5 Hz)                                 | 18.4   |

**Table 2.** NMR data comparison table for natural and synthetic (+)-*cis* rodersinine A (2).

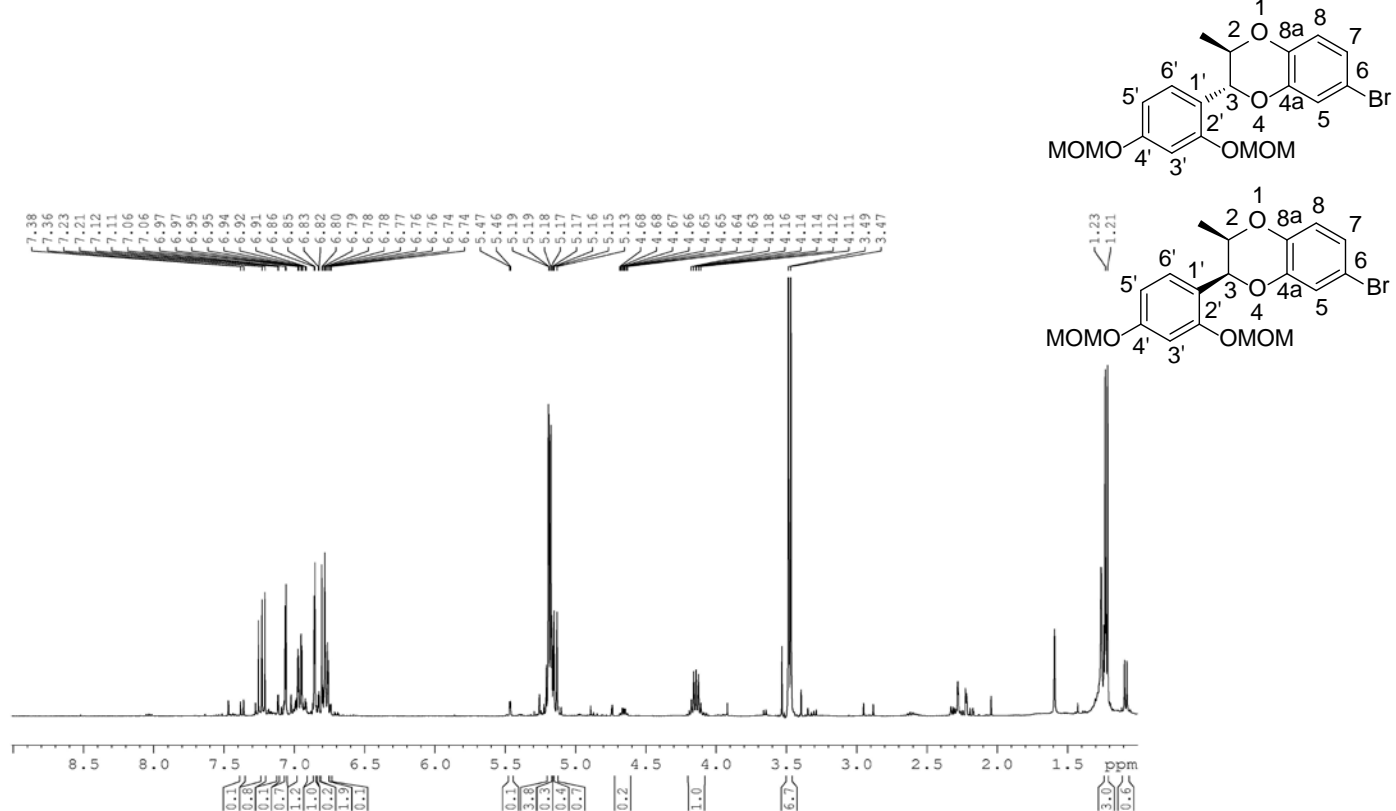


Figure 33.  $^1\text{H}$  NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane (400 MHz,  $\text{CDCl}_3$ ).

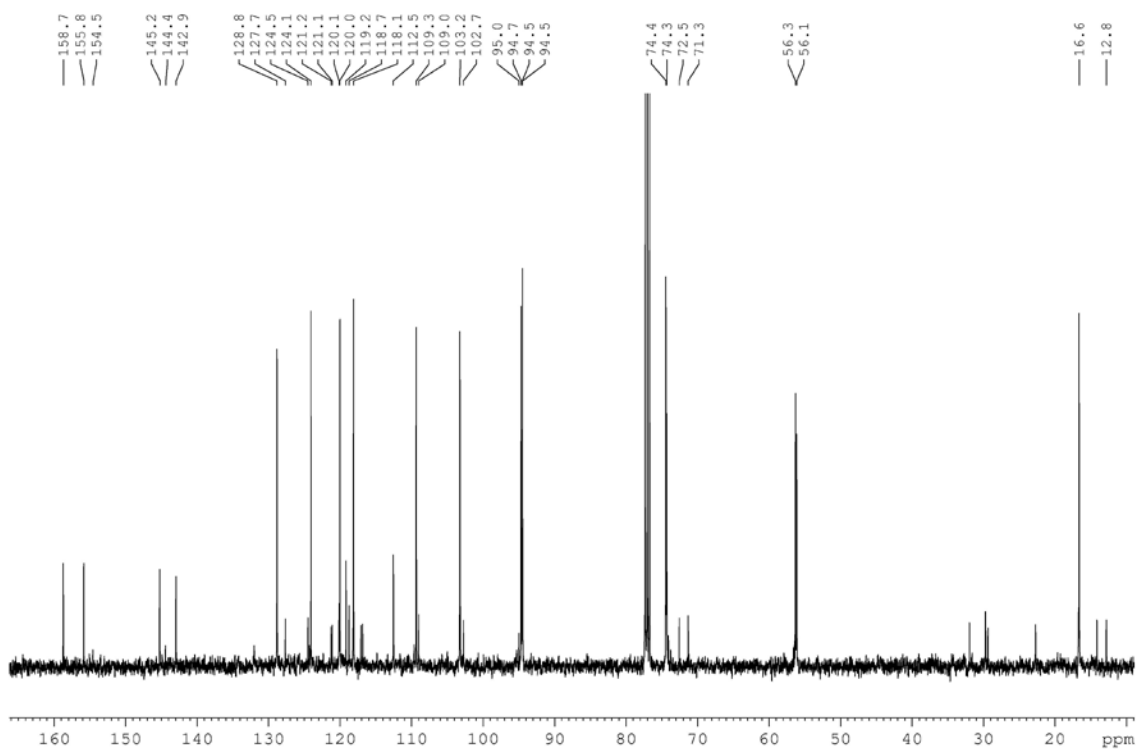


Figure 34.  $^{13}\text{C}$  NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-bromo-1,4-benzodioxane (100 MHz,  $\text{CDCl}_3$ ).

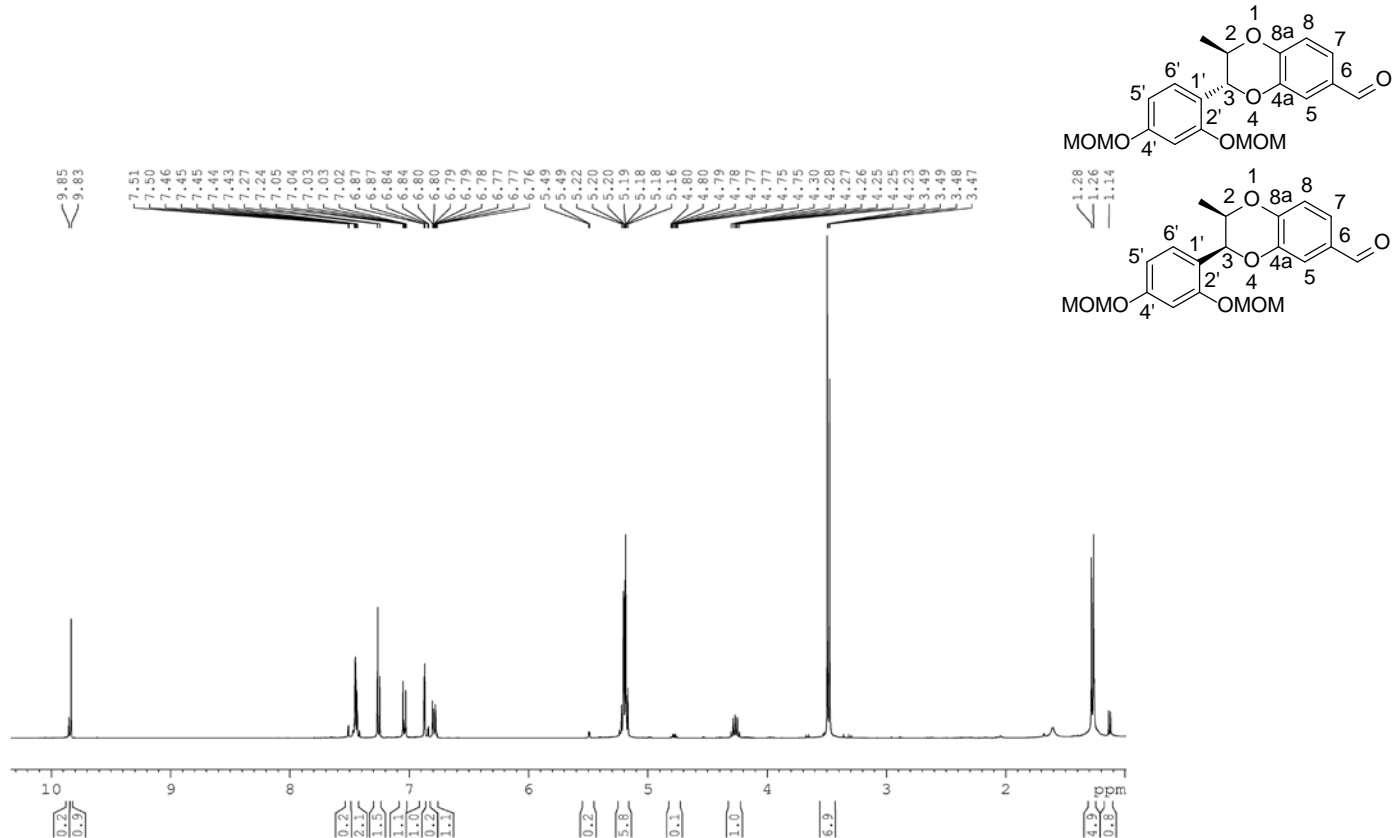


Figure 35.  $^1\text{H}$  NMR spectrum of  $(2R,3R)$ -2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane ( $(2R,3R)$ -13a) and  $(2R,3S)$ -2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane ( $(2R,3S)$ -13b) (400 MHz,  $\text{CDCl}_3$ ).

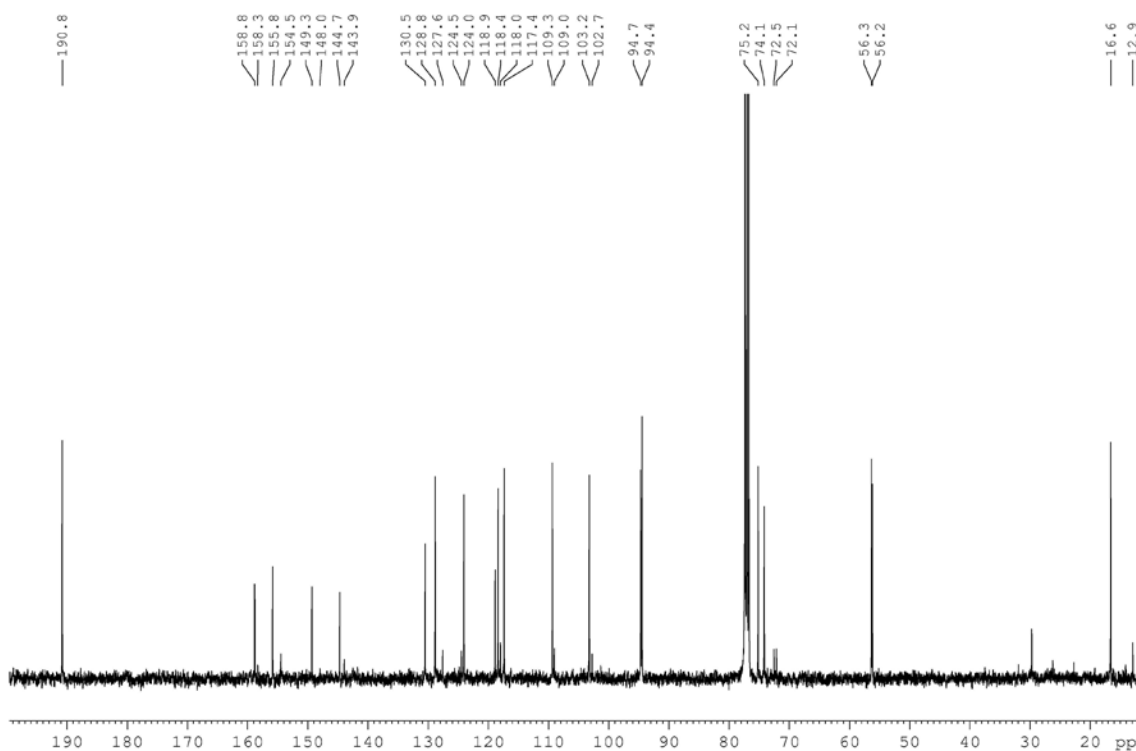


Figure 36.  $^{13}\text{C}$  NMR spectrum of  $(2R,3R)$ -2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane ( $(2R,3R)$ -13a) and  $(2R,3S)$ -2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-formyl-1,4-benzodioxane ( $(2R,3S)$ -13b) (100 MHz,  $\text{CDCl}_3$ ).

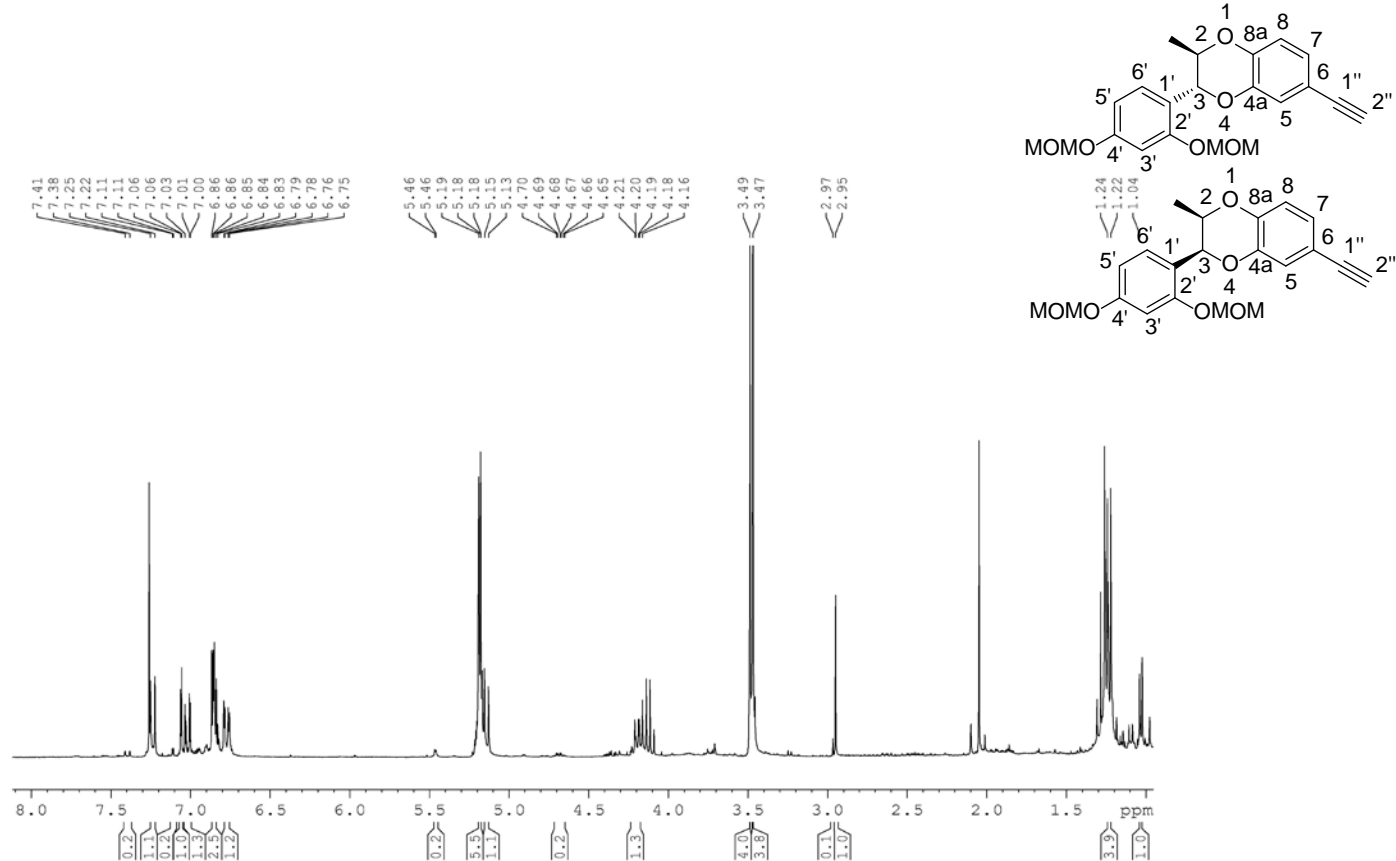


Figure 37.  $^1\text{H}$  NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*R*,3*R*)-14a and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*R*,3*S*)-14b (500 MHz,  $\text{CDCl}_3$ ).

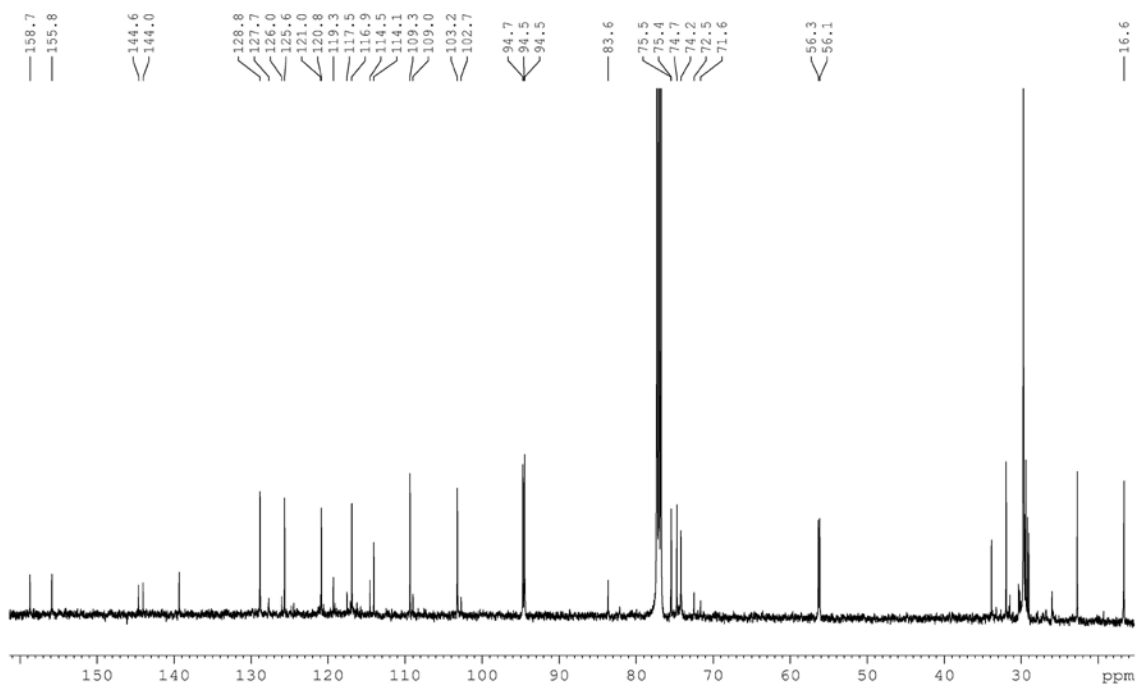


Figure 38.  $^{13}\text{C}$  NMR spectrum of (2*R*,3*R*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*R*,3*R*)-14a and (2*R*,3*S*)-2-methyl-3-(2',4'-bis(methoxymethoxy)phenyl)-6-ethynyl-1,4-benzodioxane (2*R*,3*S*)-14b (125 MHz,  $\text{CDCl}_3$ ).

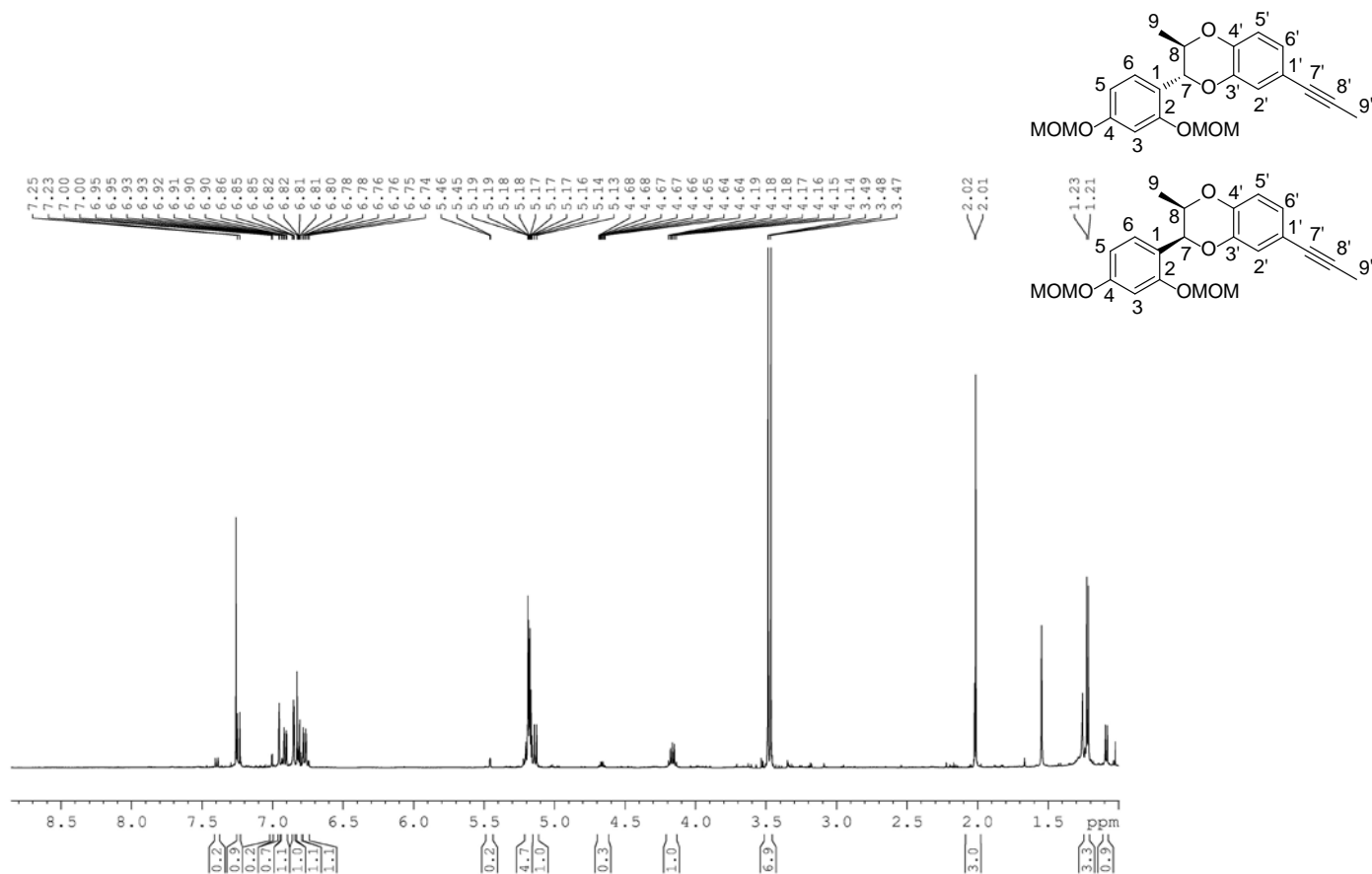


Figure 39. <sup>1</sup>H NMR spectrum of *(7R,8R)*-*trans*-(2,4-bis(methoxymethoxy))-rogersinine B and *(7S,8R)*-*cis*-(2,4-bis(methoxymethoxy))-rogersinine B (500 MHz, CDCl<sub>3</sub>).

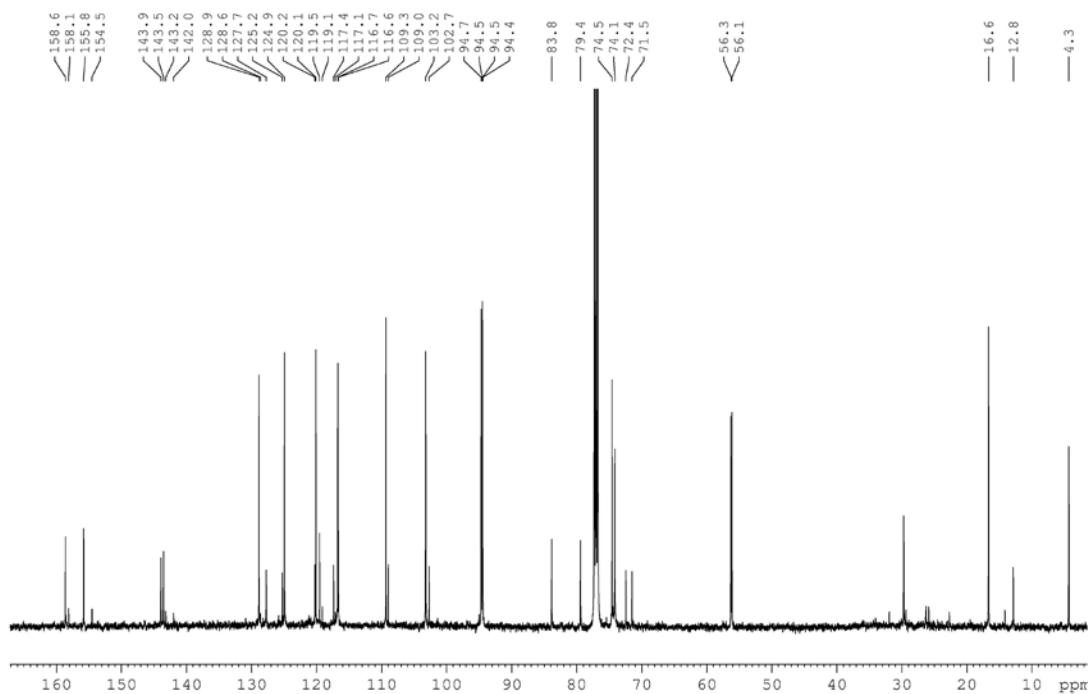


Figure 40. <sup>13</sup>C NMR spectrum of *(7R,8R)*-*trans*-(2,4-bis(methoxymethoxy))-rogersinine B and *(7S,8R)*-*cis*-(2,4-bis(methoxymethoxy))-rogersinine B (125 MHz, CDCl<sub>3</sub>).

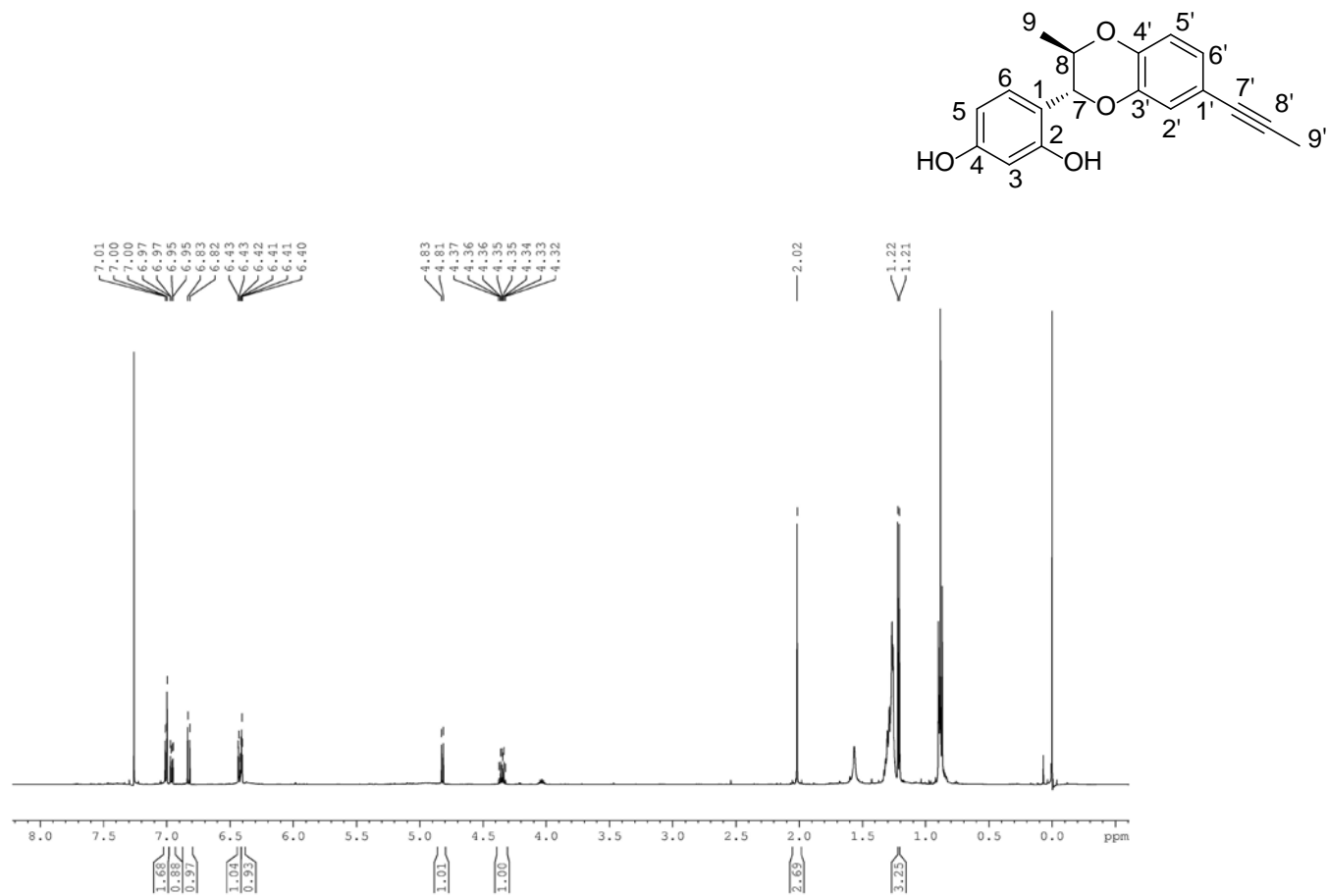


Figure 41. <sup>1</sup>H NMR spectrum of *trans*-rodgersinine B (3) (500 MHz, CDCl<sub>3</sub>).

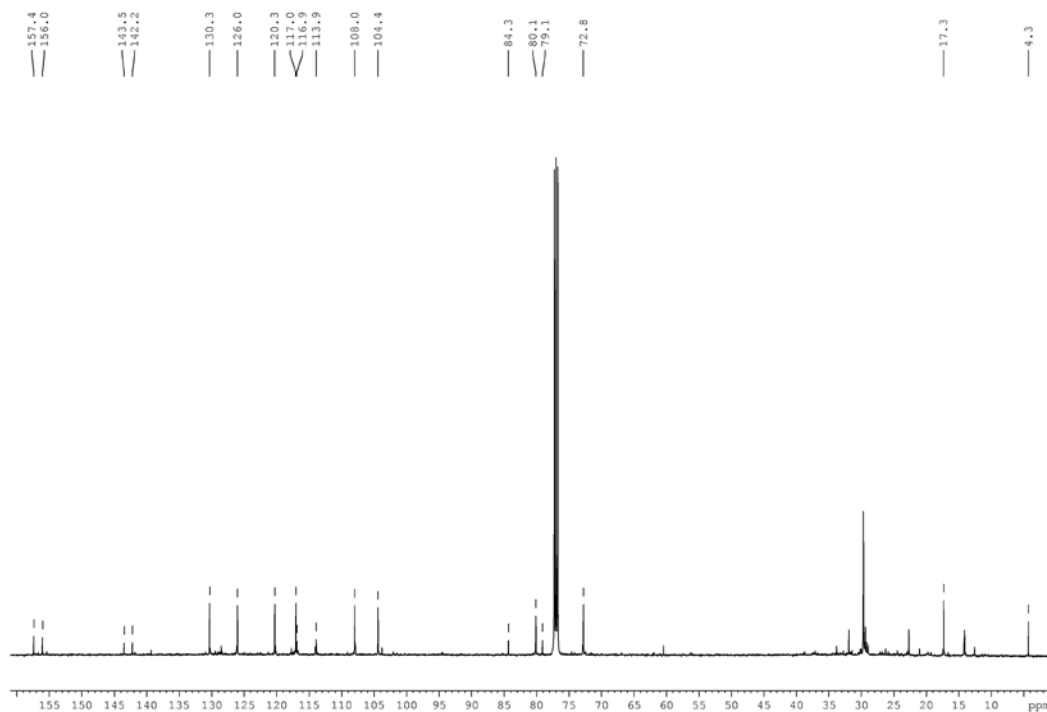
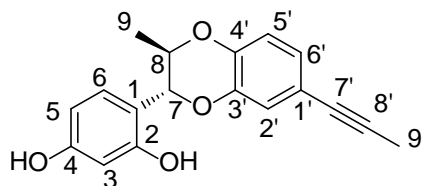


Figure 42. <sup>13</sup>C NMR spectrum of *trans*-rodgersinine B (3) (125 MHz, CDCl<sub>3</sub>).





| Atom Number | Synthetic (+)- <i>trans</i> -rogersinine B (3)   |   | Natural (+)- <i>trans</i> -rogersinine B (3)                  |  |
|-------------|--|---|---|--|
|             | <sup>1</sup> H (δ) (500 MHz, CDCl <sub>3</sub> ) | <sup>13</sup> C (δ) (125 MHz, CDCl <sub>3</sub> ) | <sup>1</sup> H (δ) (400 MHz, CDCl <sub>3</sub> ) <sup>8</sup> | <sup>13</sup> C (δ) (100 MHz, CDCl <sub>3</sub> ) <sup>8</sup> |
| 1           |  | 113.9   |   | 113.9  |
| 2           |  | 156.0   |   | 156.0  |
| 3           | 6.40 (1H, d, <i>J</i> 2.5 Hz)                    | 104.4   | 6.38 (1H, br s)   | 104.4  |
| 4           |  | 157.4   |   | 157.4  |
| 5           | 6.41 (1H, d, <i>J</i> 2.5, 8.5 Hz)               | 108.0   | 6.40 (1H, d, <i>J</i> 8.4 Hz)                                 | 108.0  |
| 6           | 7.00 (1H, d, <i>J</i> 8.5 Hz)                    | 130.3   | 6.99 (1H, d, <i>J</i> 8.4 Hz)                                 | 130.5  |
| 7           | 4.81 (1H, d, <i>J</i> 8.5 Hz)                    | 80.1  | 4.81 (1H, d, <i>J</i> 8.0 Hz)                                 | 80.1   |
| 8           | 4.32–4.37 (1H, m)                                | 72.8  | 4.32 (1H, qd, <i>J</i> 6.4, 8.0 Hz)                           | 72.8   |
| 9           | 1.21 (3H, d, <i>J</i> 6.0 Hz)                    | 17.3  | 1.21 (3H, d, <i>J</i> 6.4 Hz)*                                | 17.3   |
| 1'          |  | 116.9   |   | 116.9  |
| 2'          | 7.00 (1H, d, <i>J</i> 2.0 Hz)                    | 120.3   | 6.97 (1H, br s)   | 120.3  |
| 3'          |  | 143.5   |   | 143.5  |
| 4'          |  | 142.2   |   | 142.2  |
| 5'          | 6.82 (1H, d, <i>J</i> 8.5 Hz)                    | 117.0   | 6.80 (1H, d, <i>J</i> 8.3 Hz)                                 | 117.0  |
| 6'          | 6.95 (1H, dd, <i>J</i> 2.0, 8.5 Hz)              | 126.0   | 6.94 (1H, d, <i>J</i> 8.3 Hz)                                 | 126.0  |
| 7'          |  | 79.1  |   | 79.1   |
| 8'          |  | 84.3  |   | 84.3   |
| 9'          | 2.02 (3H, s)                                     | 4.3   | 2.00 (3H, s)  | 4.3  |

\* Signal misprinted in original isolation paper.

**Table 3.** NMR data comparison table for natural and synthetic (+)-*trans* rogersinine B (3).

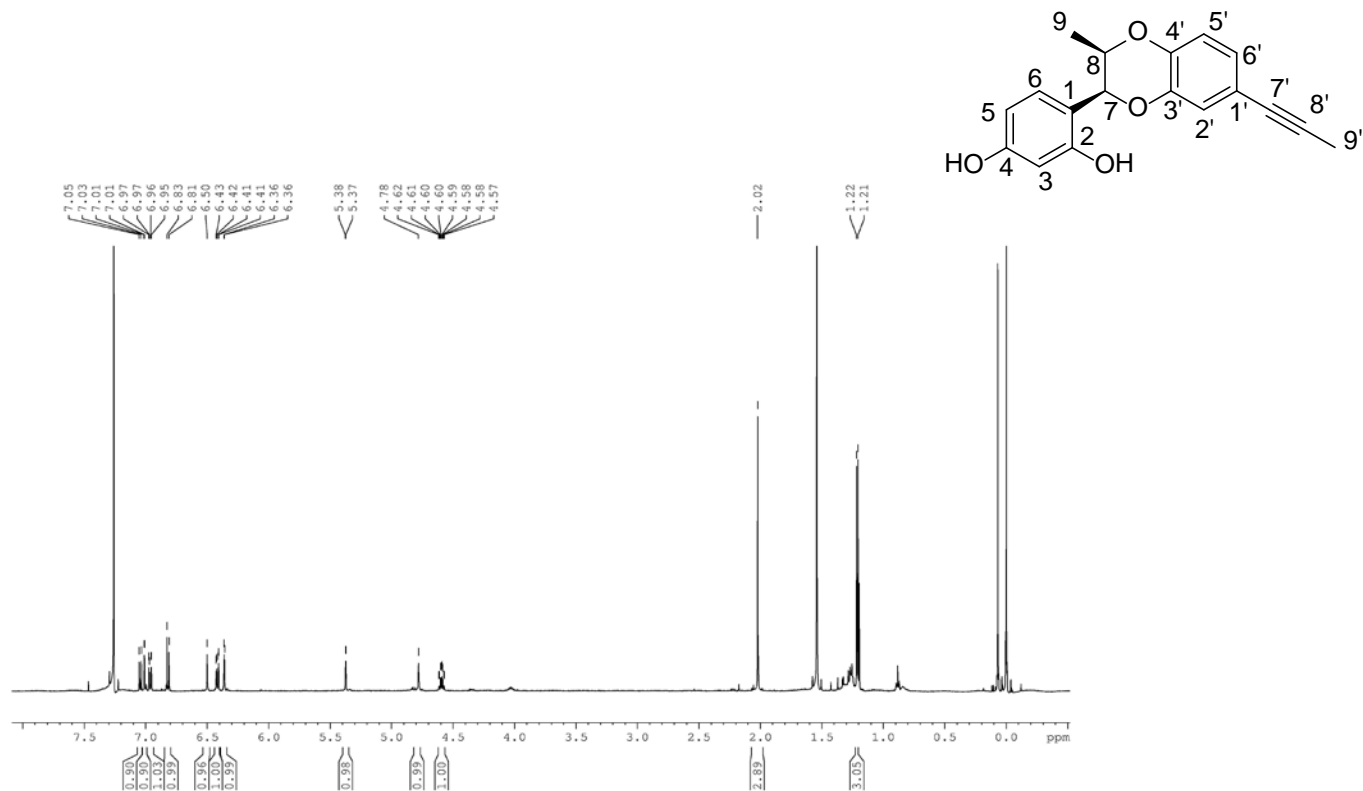


Figure 43.  $^1\text{H}$  NMR spectrum of *cis*-rodgersinine B (4) (500 MHz,  $\text{CDCl}_3$ ).

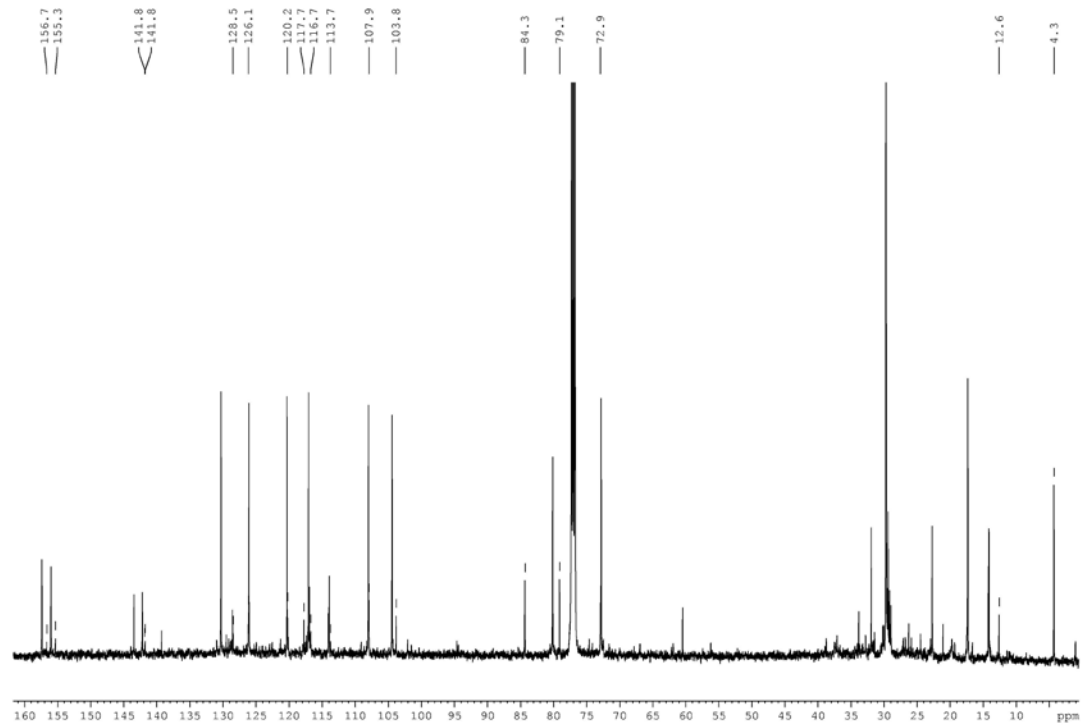
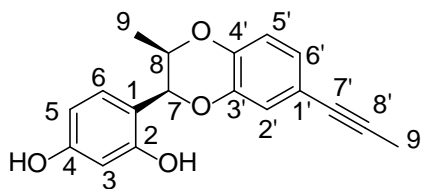


Figure 44.  $^{13}\text{C}$  NMR spectrum of *cis*-rodgersinine B (4) (125 MHz,  $\text{CDCl}_3$ ).



| Atom Number | Synthetic (+)- <i>cis</i> -rodersinine B (4)     |   | Natural (+)- <i>cis</i> -rodersinine B (4)                    |  |
|-------------|--|---|---|--|
|             | <sup>1</sup> H (δ) (500 MHz, CDCl <sub>3</sub> ) | <sup>13</sup> C (δ) (125 MHz, CDCl <sub>3</sub> ) | <sup>1</sup> H (δ) (400 MHz, CDCl <sub>3</sub> ) <sup>8</sup> | <sup>13</sup> C (δ) (100 MHz, CDCl <sub>3</sub> ) <sup>8</sup> |
| 1           |  | 113.7   |   | 113.7  |
| 2           |  | 155.3   |   | 155.3  |
| 3           | 6.36 (1H, <i>J</i> 2.5 Hz)                       | 103.8   | 6.43 (1H, br s)   | 103.8  |
| 4           |  | 156.7   |   | 156.7  |
| 5           | 6.41 (1H, dd, <i>J</i> 2.5, 8.5 Hz)              | 107.9   | 6.39 (1H, d, <i>J</i> 8.3 Hz)                                 | 107.9  |
| 6           | 7.03 (1H, d, <i>J</i> 8.5 Hz)                    | 128.5   | 7.03 (1H, d, <i>J</i> 8.3 Hz)                                 | 128.5  |
| 7           | 5.37 (1H, d, <i>J</i> 2.5 Hz)                    | 77.0  | 5.36 (1H, d, <i>J</i> 2.2 Hz)                                 | 77.0   |
| 8           | 4.57 (1H, qd, <i>J</i> 2.5, 6.5 Hz)              | 72.9  | 4.58 (1H, qd, <i>J</i> 2.2, 6.6 Hz)                           | 72.9   |
| 9           | 1.21 (3H, d, <i>J</i> 6.5 Hz)                    | 12.6  | 1.18 (3H, d, <i>J</i> 6.6 Hz)*                                | 12.6   |
| 1'          |  | 116.7   |   | 116.7  |
| 2'          | 7.01 (1H, d, <i>J</i> 1.5 Hz)                    | 120.2   | 6.99 (1H, d, <i>J</i> 1.7 Hz)                                 | 120.2  |
| 3'          |  | 141.8   |   | 141.8  |
| 4'          |  | 141.8   |   | 141.7  |
| 5'          | 6.81 (1H, d, <i>J</i> 8.5 Hz)                    | 117.7   | 6.80 (1H, d, <i>J</i> 8.3 Hz)                                 | 117.7  |
| 6'          | 6.95 (1H, dd, <i>J</i> 1.5, 8.5 Hz)              | 126.1   | 6.91 (1H, dd, <i>J</i> 1.7, 8.3 Hz)                           | 126.2  |
| 7'          |  | 79.1  |   | 79.0   |
| 8'          |  | 84.3  |   | 84.3   |
| 9'          | 2.02 (3H, s)                                     | 4.3   | 2.00 (3H, s)  | 4.3  |

Table 4. NMR data comparison table for natural and synthetic (+)-*cis* rodersinine B (4).

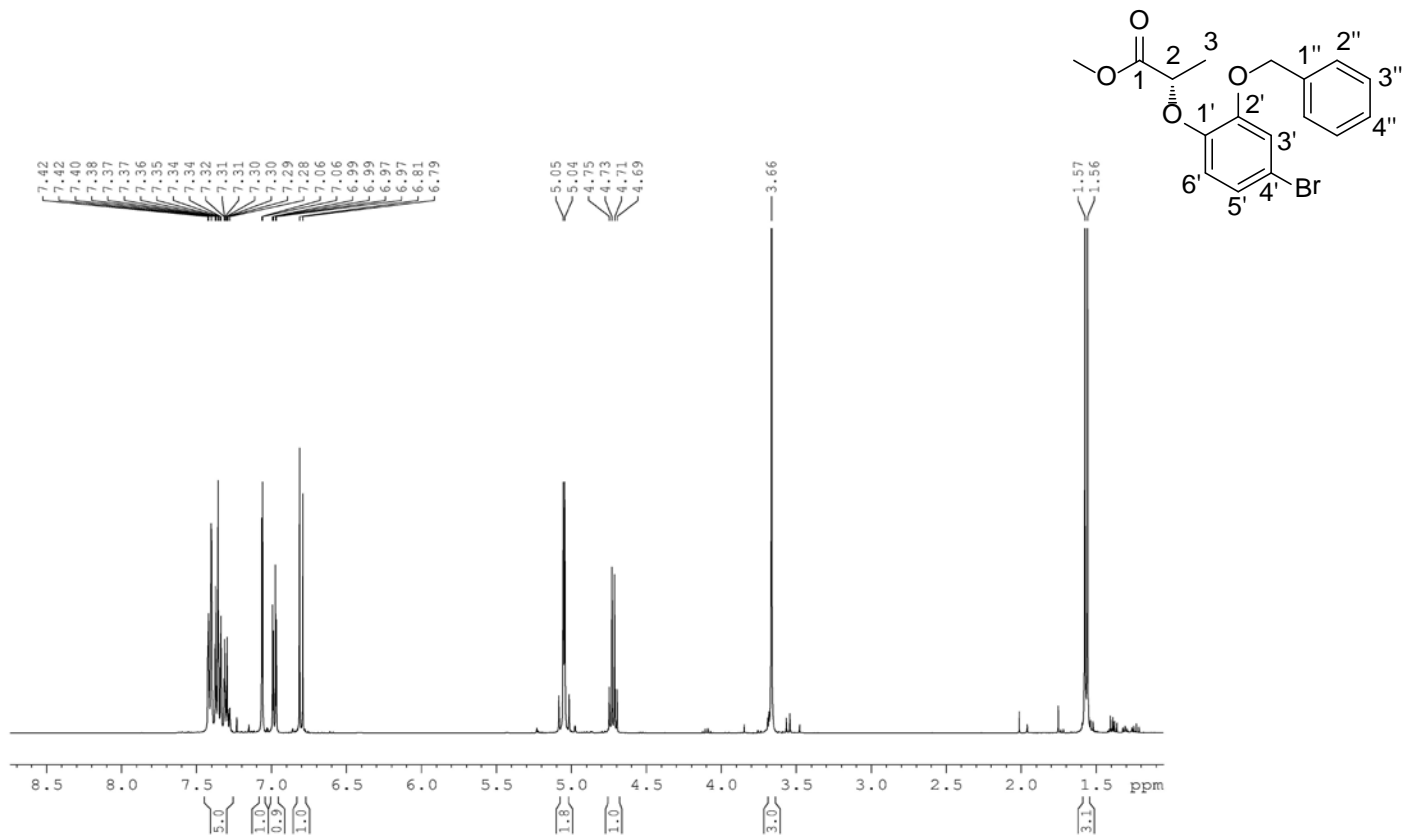


Figure 45. <sup>1</sup>H NMR spectrum of (2S)-methyl 2-(2'-(benzyloxy)-4'-bromophenoxy)propanoate 16 (400 MHz, CDCl<sub>3</sub>).

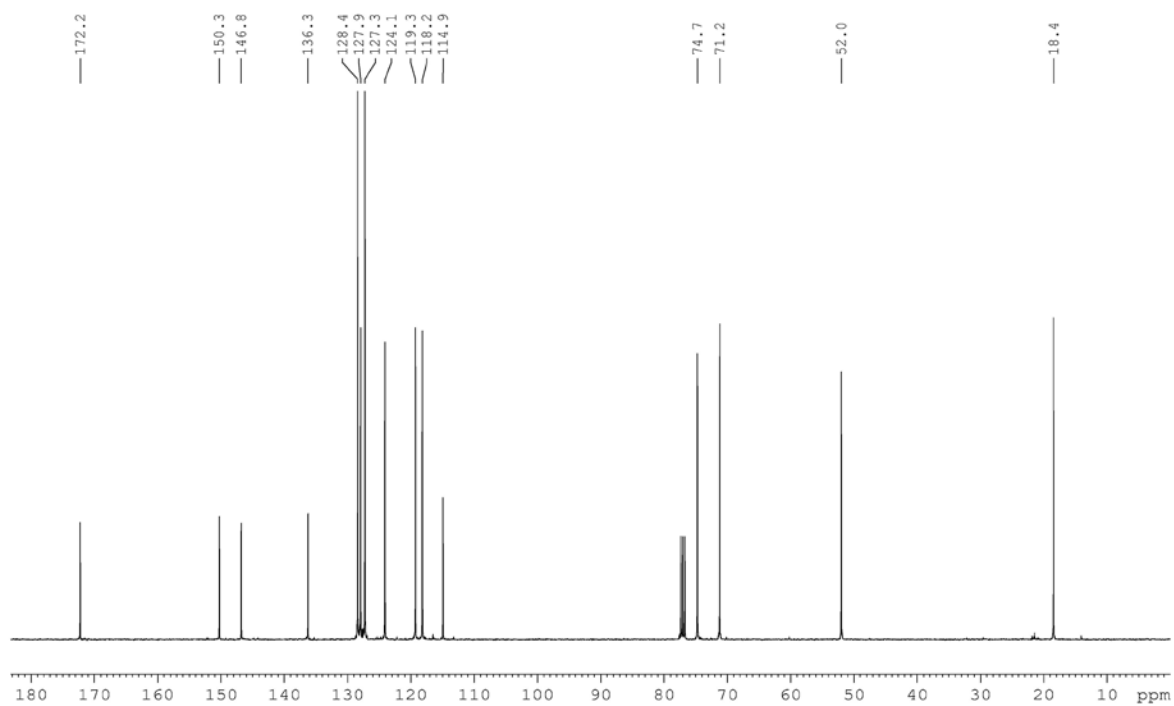


Figure 46. <sup>13</sup>C NMR spectrum of (2S)-methyl 2-(2'-(benzyloxy)-4'-bromophenoxy)propanoate 16 (100 MHz, CDCl<sub>3</sub>).

*(7R,8R)*-trans-Rodgersinine A

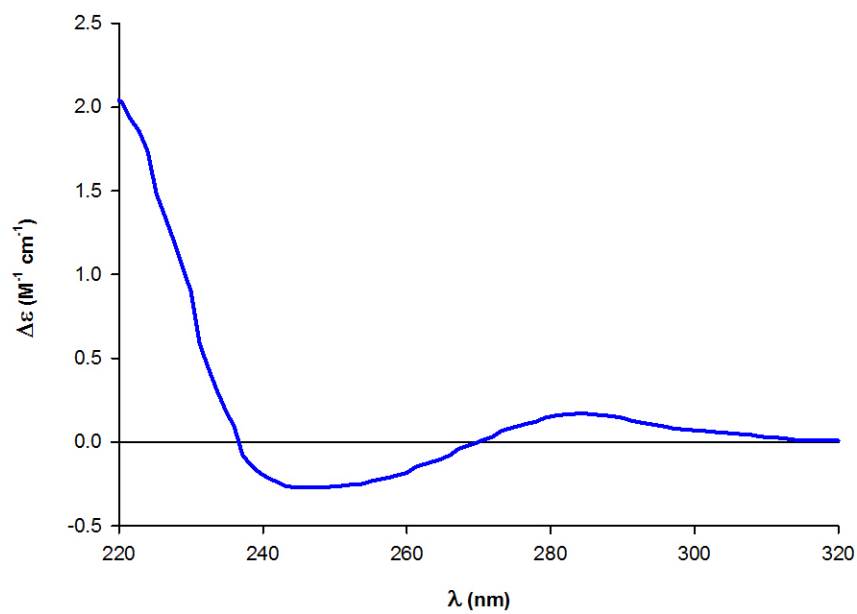


Figure 47. ECD spectrum of *(7R,8R)*-trans rodgersinine A (1).

*(7S,8S)*-trans-Rodgersinine A

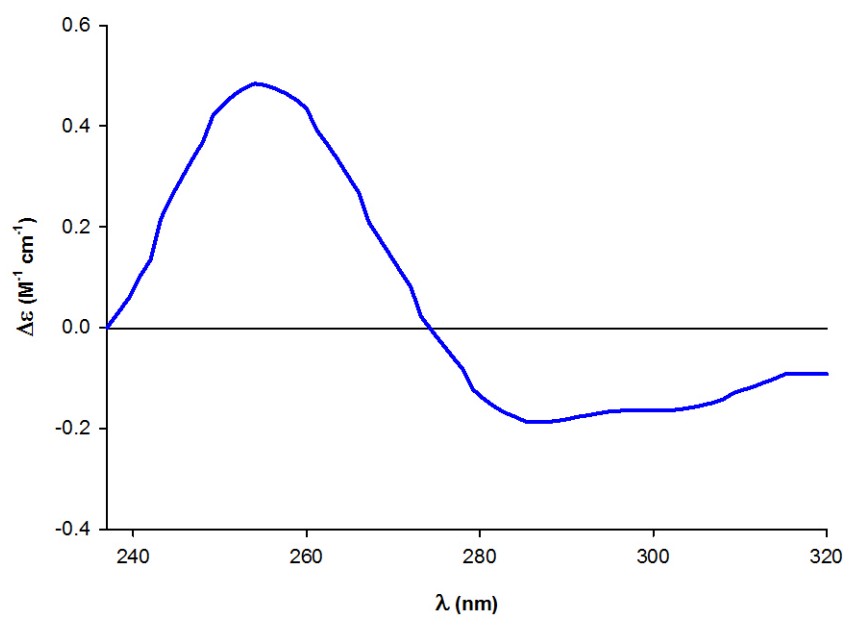


Figure 48. ECD spectrum of *(7S,8S)*-trans rodgersinine A (1).

(7*S*,8*R*)-*cis*-Rodgersinine A

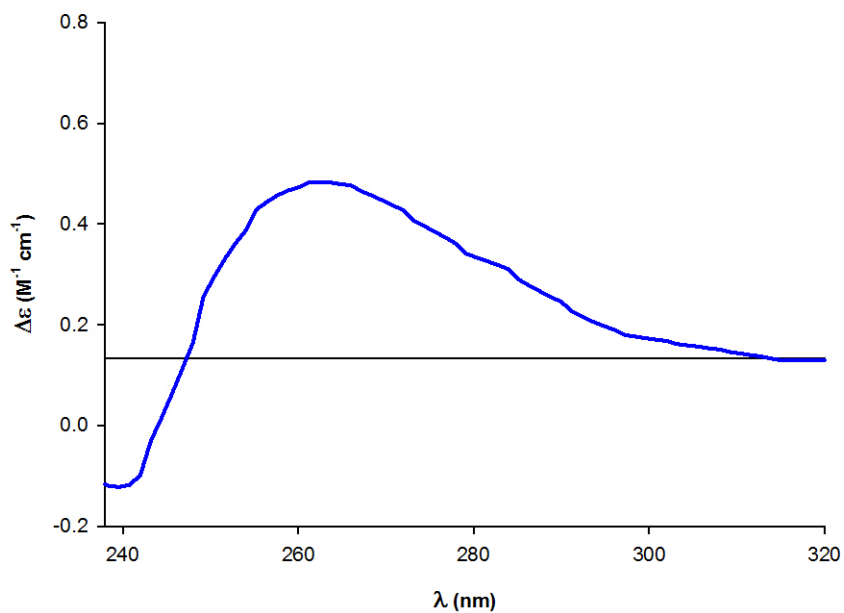


Figure 49. ECD spectrum of (7*S*,8*R*)-*cis* roddersinine A (2).

(7*R*,8*S*)-*cis*-Rodgersinine A

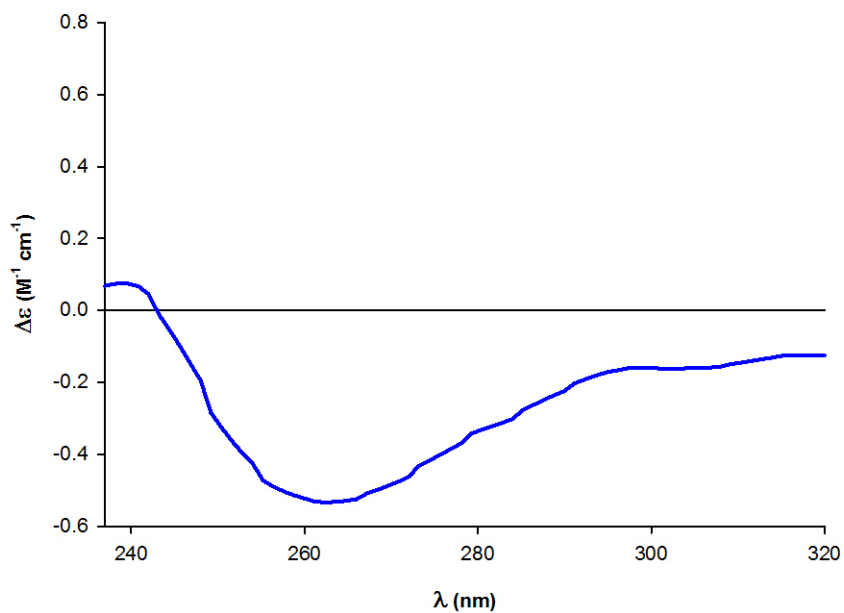


Figure 50. ECD spectrum of (7*R*,8*S*)-*cis* roddersinine A (2).

(7*S*,8*S*)-*trans*-Rodgersinine B

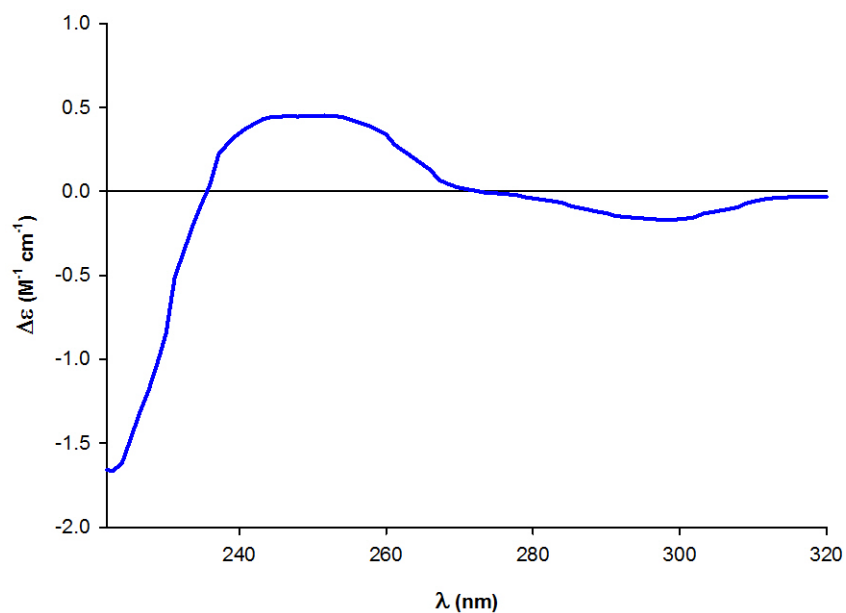


Figure 51. ECD spectrum of (7*S*,8*S*)-*trans* roddersinine B (3).

(7*R*,8*R*)-*trans*-Rodgersinine B

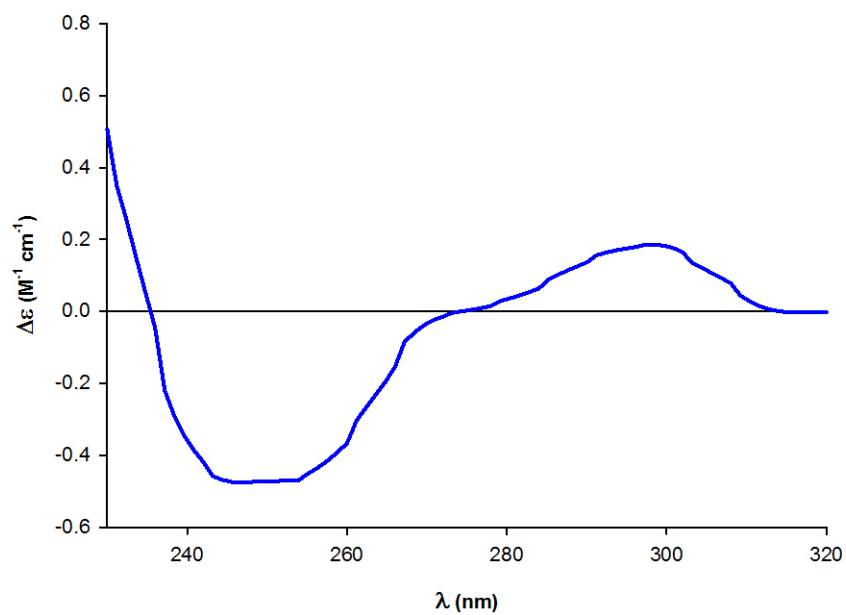


Figure 52. ECD spectrum of (7*R*,8*R*)-*trans* roddersinine B (3).

(7*R*,8*S*)-*cis*-Rodgersinine B

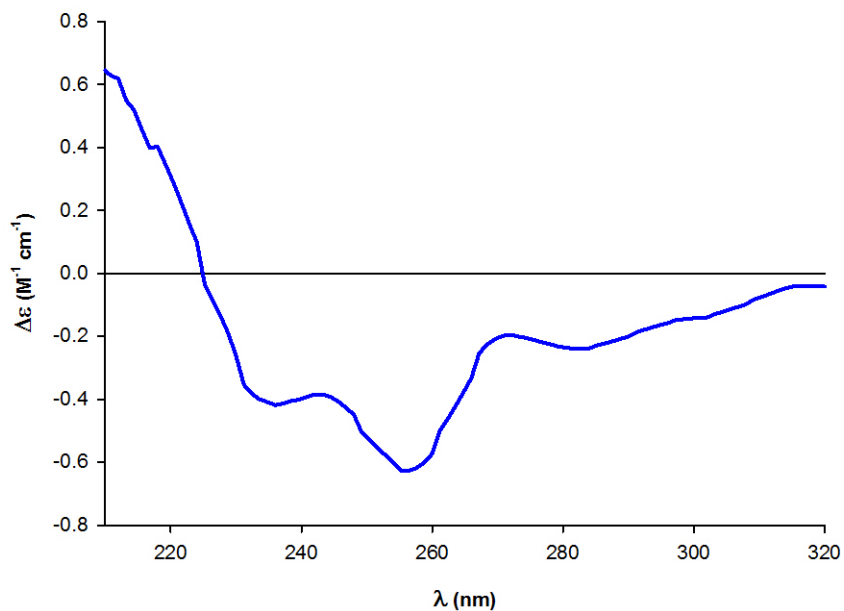


Figure 53. ECD spectrum of (7*R*,8*S*)-*cis* rodgersinine B (4).

(7*S*,8*R*)-*cis*-Rodgersinine B

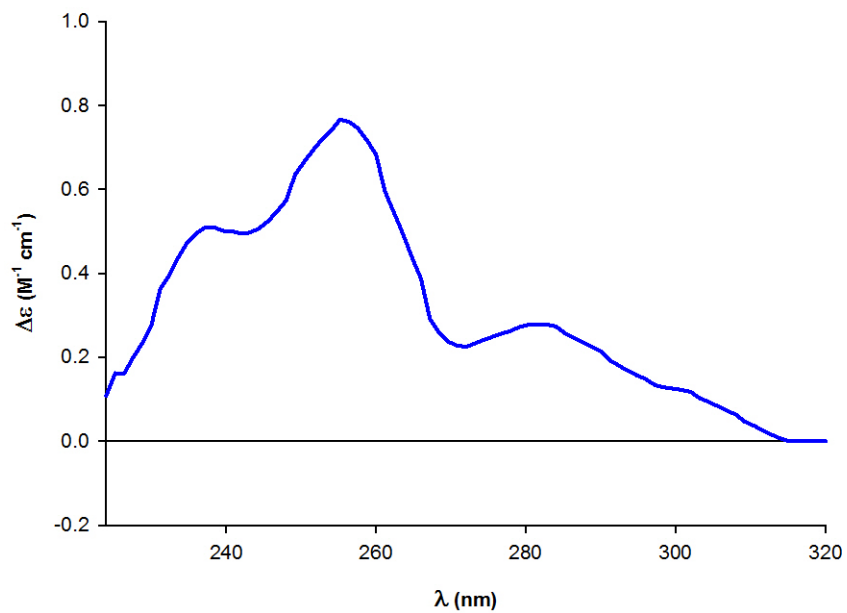


Figure 54. ECD spectrum of (7*S*,8*R*)-*cis* rodgersinine B (4).



### Enantiomers of *trans*-Rodgersinine A and B

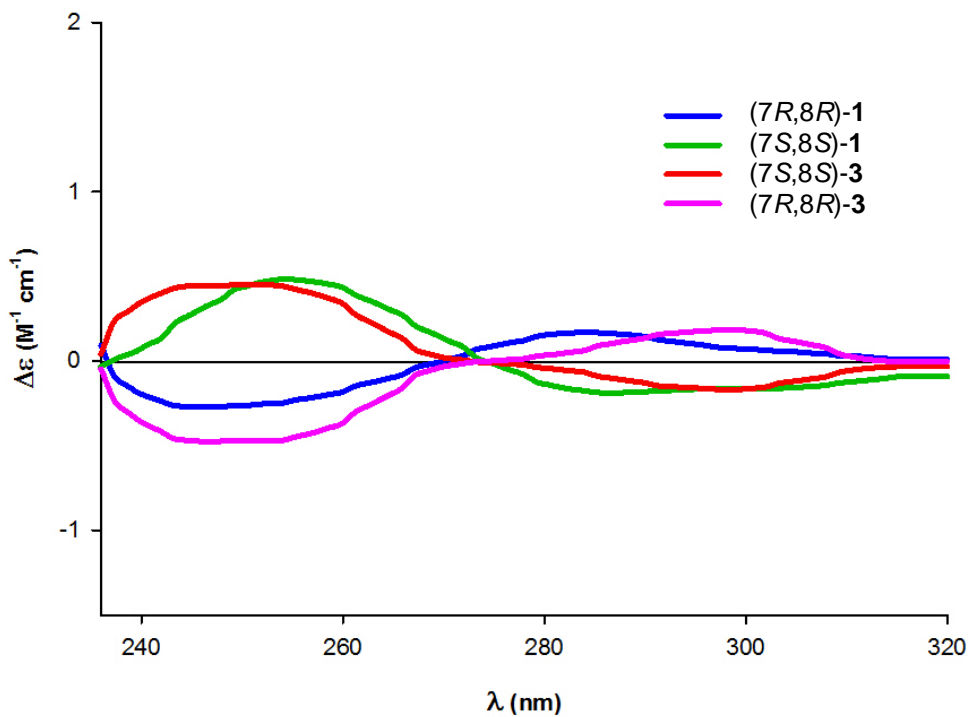


Figure 55. ECD spectra of *trans* rodgersinine A (1) and B (3) and enantiomers.

### Enantiomers of *cis*-Rodgersinine A and B

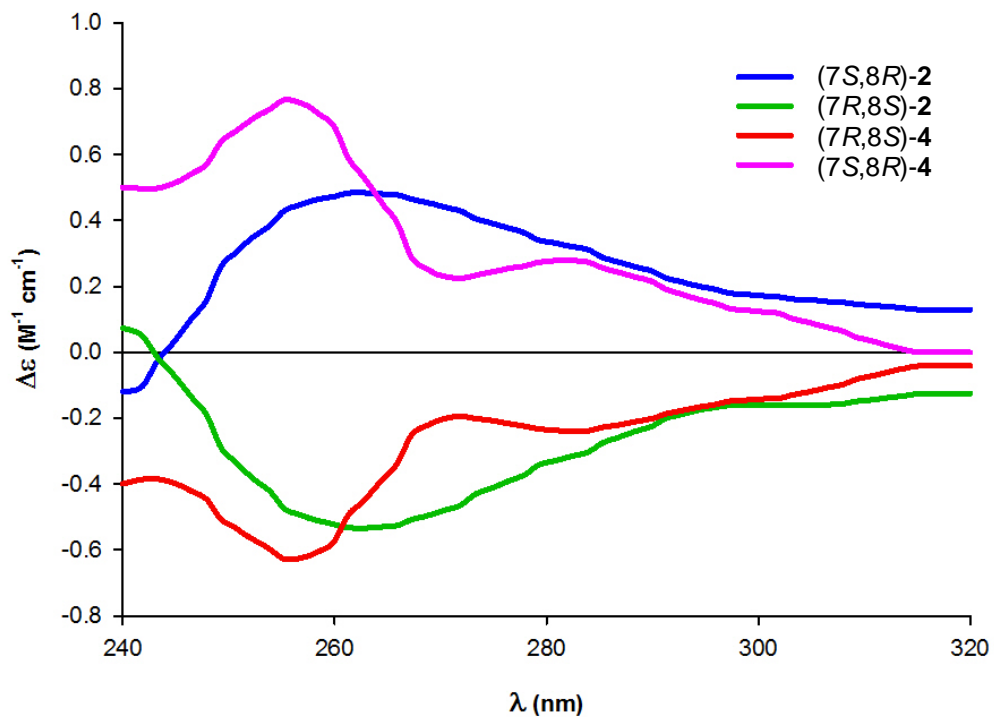


Figure 56. ECD spectra of *cis* rodgersinine A (2) and B (4) and enantiomers.

## Biological testing:

### Experimental Details:

Methods similar to previously described<sup>9</sup> were used with the following modifications. Human hepatoma Huh7.5.1 cells were cultured in DMEM containing 9% fetal bovine serum, 1× penicillin/streptomycin/fungizone, 4mM L-glutamine, and 1× non-essential amino acids. For cytotoxicity testing, cells were plated at 15,000 cells/well in 96-well plates, and compounds were added 24 hours after plating to existing medium. Addition of DMSO to cells served as the negative control. Seventy-two hours later, an equal volume of ATPlite reagent to medium was added directly to each well and mixed by pipetting up and down. The plate was read immediately on PerkinElmer Victor X2 plate reader. The concentration of compound that resulted in a 50% reduction of cellular ATP levels ( $CC_{50}$ ) was determined performing in Prism 6 (GraphPad Software) a 4-parameter regression of ATP levels using log-transformed concentration data. For antiviral testing, cells were plated in 12-well plates and infected with HCV at a multiplicity of infection of 0.05 for 5 hours. Virus inoculum was removed and replaced with fresh media containing three different doses approaching the  $CC_{50}$  (in  $\mu$ M) of each compound. Cytoplasmic protein lysates were harvested 72 hours post-infection and HCV proteins were detected by western blot using HCV positive patient serum. The cellular protein Actin was detected to verify equal loading of protein in each sample. For western blotting, luminescent based-film detection was employed as previously described.<sup>9</sup> For some compounds, western blotting using infrared-based detection was performed using an Odyssey CLx Imaging System (LiCor). For this, after separation of proteins by electrophoresis, proteins were transferred to nitrocellulose membranes, and membranes were allowed to dry for 1hr or overnight. Membranes were then wetted for 2 minutes in PBS and incubated for a maximum of 1 hour in Odyssey Blocking Buffer (part #927-40003). Primary antibodies for western blotting (human anti-HCV serum or goat anti-actin) were diluted in Odyssey Blocking Buffer containing 0.2% Tween (Fisher). Following one hour at room temperature or overnight incubation at 4°C, blots were washed and infrared-coupled secondary antibodies (donkey anti-human IgG (H+L) DyLight 800 (Part #SA510132; Thermo Fisher Pierce) or donkey anti-goat IgG (H+L) DyLight 680 (Part #PISA510090; Thermo Fisher Pierce), were diluted 1:15,000 and incubated for 1 hour at room temperature in the dark. Blots were washed and infrared images collected by imaging the membrane on the CLx instrument.

### Analysis:

(*7R,8R*)-*trans*-Rodgersinine A (**1**) has an approximate anti-HCV  $IC_{50}$  of ~125  $\mu$ M, well below that of its cytotoxicity  $CC_{50}$  (Figures 57 and 58). (*7S,8S*)-*trans*-Rodgersinine A (**1**), (*7R,8R*)-*trans*-rodgersinine B (**3**) and (*7S,8S*)-*trans*-rodgersinine B (**3**) all had similar cytotoxicity and anti-HCV profiles. The  $CC_{50}$  of (*7S,8S*)-*trans*-rodgersinine A (**1**) was approximately 33  $\mu$ M, while for both enantiomers of **3**, (*7R,8R*)-**3** and (*7S,8S*)-**3**, the  $CC_{50}$  is ~40-45  $\mu$ M. Once again, these cytotoxicity values are well above the anti-HCV  $IC_{50}$  values; for (*7R,8R*)-**3** and (*7S,8S*)-**3** this figure is approximately 15  $\mu$ M, while (*7R,8R*)-**1** is slightly more potent with an  $IC_{50}$  ~ 10  $\mu$ M.

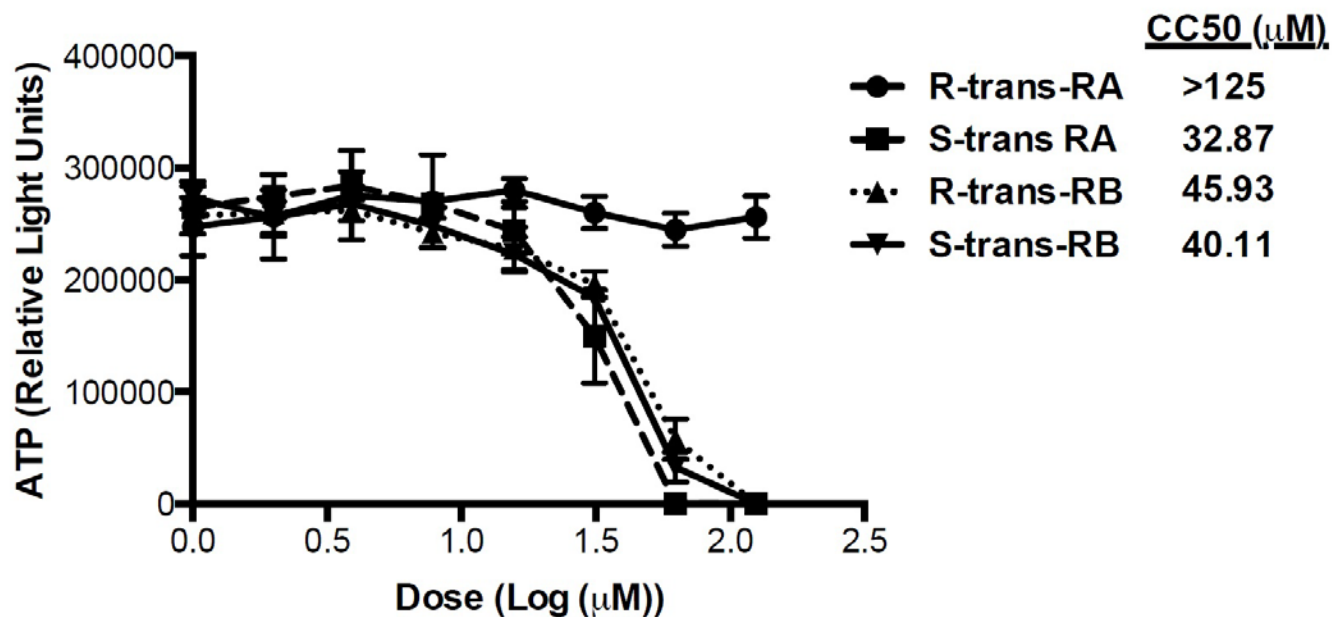


Figure 57. Cytotoxicity profile in human hepatoma Huh7.5.1 cells of (7*R*,8*R*)-*trans*-rodgersinine A (1), (7*S*,8*S*)-*trans*-rodgersinine A (1), (7*R*,8*R*)-*trans*-rodgersinine B (3) and (7*S*,8*S*)-*trans*-rodgersinine B (3). Compounds were added to cells at the indicated concentrations and 72 hours later, ATP levels were measured using the ATPlite assay.

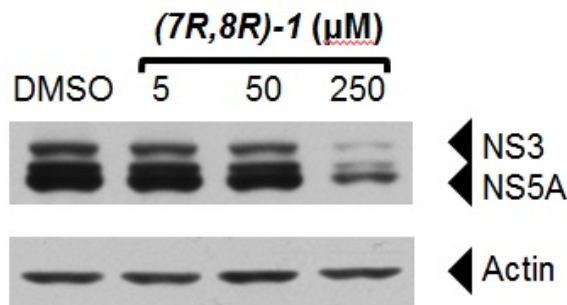
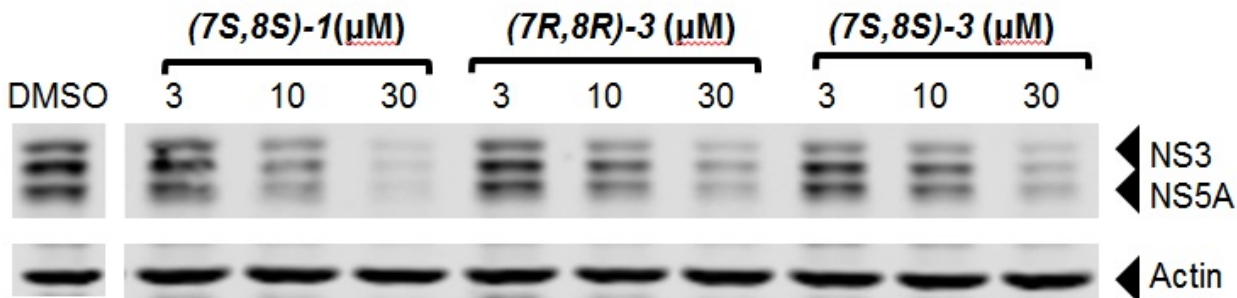


Figure 58. Anti-HCV profile of (7*R*,8*R*)-*trans*-rodgersinine A (1). Huh7.5.1 cells were infected with HCV at a multiplicity of infection of 0.05 for 5 hours. Virus inoculum was removed and replaced with fresh media containing the indicated concentrations (in μM) of each compound. Cytoplasmic protein lysates were harvested 72 hours post-infection and HCV proteins were detected by western blot using HCV positive patient serum. NS3 and NS5A refer to the HCV nonstructural 3 and 5A proteins. Actin was detected to verify equal loading of protein in each sample.

| Compound  | Cytotoxicity<br>CC <sub>50</sub> (μM) <sup>a</sup> | Antiviral<br>IC <sub>50</sub> (μM) <sup>b</sup> |
|---|--|---|
| (7 <i>R</i> ,8 <i>R</i> )- <i>trans</i> -<br>rodgersinine A (1) | >250   | 125   |
| (7 <i>S</i> ,8 <i>S</i> )- <i>trans</i> -<br>rodgersinine A (1) | 32.87  | 15  |
| (7 <i>R</i> ,8 <i>R</i> )- <i>trans</i> -<br>rodgersinine B (3) | 45.93  | 10  |
| (7 <i>S</i> ,8 <i>S</i> )- <i>trans</i> -<br>rodgersinine B (3) | 40.11  | 15  |

**Table 5.** <sup>a</sup> Cytotoxicity CC<sub>50</sub> data are derived from regression fitting of data in Fig. 57. <sup>b</sup> Antiviral IC<sub>50</sub> data are approximations based on visual inspection of the western blots shown in Fig. 58.

## References:

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