Supporting Information

Synthetic Urushiols from Biorenewable Carbon Resources: Chemical conversion of enzymatic degradation products of wood lignin to an ancient *yet* future coating material

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Contents

Experimental Section

General

All reactions dealing with air- or moisture-sensitive compounds were carried out in well-dried reaction vessels under a positive pressure of dry argon. Air- and moisture-sensitive liquids and solutions were transferred via a syringe or a PTFE cannula. Flash column chromatography was performed on Wakogel 60N, 38–100 μm, as described by Still et al [34]. or on a Biotage SP1 Flash Purification System (Biotage Corp., Sweden), or YFLC-AI-580 (Yamazen Corp., Osaka, Japan) with prepacked silica cartridges. Preparative recycling gel permeation chromatography (GPC) was performed with a Japan Analytical Industry LC-9204 instrument equipped with JAIGEL-1H-40/JAIGEL-2H-40 columns using toluene as an eluent.

Instruments

^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECS-400NR NMR spectrometer (391.8 and 98.5 MHz, respectively). The ^{1}H chemical shift values are reported in parts per million (ppm, δ scale) and referenced to the ^{1}H resonance of $CDCl_3$ (δ 7.26). The ^{13}C chemical shift values are reported in parts per million, and referenced to the ^{13}C resonance of $CDCl_3$ (δ 77.7). Data are presented as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, td = tripletdublet, m = multiplet, br = broad), coupling constant in Hertz (Hz) and signal area integration in natural numbers. IR spectra were recorded on PerkinElmer Spectrum One FT-IR spectrometers or Nicolet FT-IR 5700 spectrophotometer, and reported in cm^{-1}. GC analysis was conducted with Shimadzu GC-2010 and GC-2010 Plus instruments equipped with an FID detector and a capillary column, ZB-1MS (Phenomenex Inc., 10 m × 0.10 mm i.d., 0.10 μm film thickness). Melting points were recorded on a Yanaco MP-500D. High-resolution mass spectra (HRMS) were recorded using electron ionization with a JEOL JMS-700 mass spectrometer or electron spray ionization (ESI) with a Bruker Daltonics GmbH SolariX Fourier transformation-ion cyclotron resonance-mass spectrometry (FT-ICR-MS) or timsTOF spectrometer. Elemental analyses were carried out at the Microanalytical Laboratory of the Institute for Chemical Research, Kyoto University.

Materials

Unless otherwise noted, commercially available materials were used without purification. Anhydrous THF was purchased from Wako Pure Chemical Industries, Ltd. and distilled from benzophenone ketyl under argon (at atmospheric pressure) immediately before use. Water content of the solvents was determined with a Karl Fischer Moisture Titrator (MKC-610, Kyoto Electronics Company). Metal salts were purchased, and purities, commercial suppliers and production numbers are as follows: $FeCl_3$ (99.99%, Aldrich Inc., 140304). Lignin-derived aromatic compounds, guaiacylhydroxy-propanone **GHP** and syringylhydroxypropanone **SHP** were produced from enzymatic

degradation of APA-lignin, as reported in our recent report.[1] The APA-lignin was extracted from extractive-free wood flour (*Eucalyptus globulus*) by ball-milling followed by microwave heating extraction in an acetic acid-peracetic acid (APA) solvent, according to the reported method.[2] Due to the limited amount of **GHP** and **SHP** obtained from lignin in lab-scale, **GHP** and **SHP** were separately synthesized for this work (Scheme S1). Linolenyl bromide was synthesized according to the reported procedure (Scheme S1).[3] Corresponding Grignard reagent **1** was prepared according to the standard procedure.[4] TBS-protected G-enone **G-2** and S-enone **S-2** were synthesized from **GHP** and **SHP** according to the reported procedures.[5] Raw Urushi was purchased from Sato Kiyomatsu Shoten (Kyoto, Japan). Chinese urushiol and Cambodian thitsiol were obtained by acetone extraction from raw Urushi and Cambodian raw Thitsi.

[1] Kumagawa, E.; Katsumura, M.; Nishimura, H.; Watanabe, T.; Ishii, S.; Ohta, Y. *Environ. Microbiol. Rep.* **2024,** *16,* e13210.

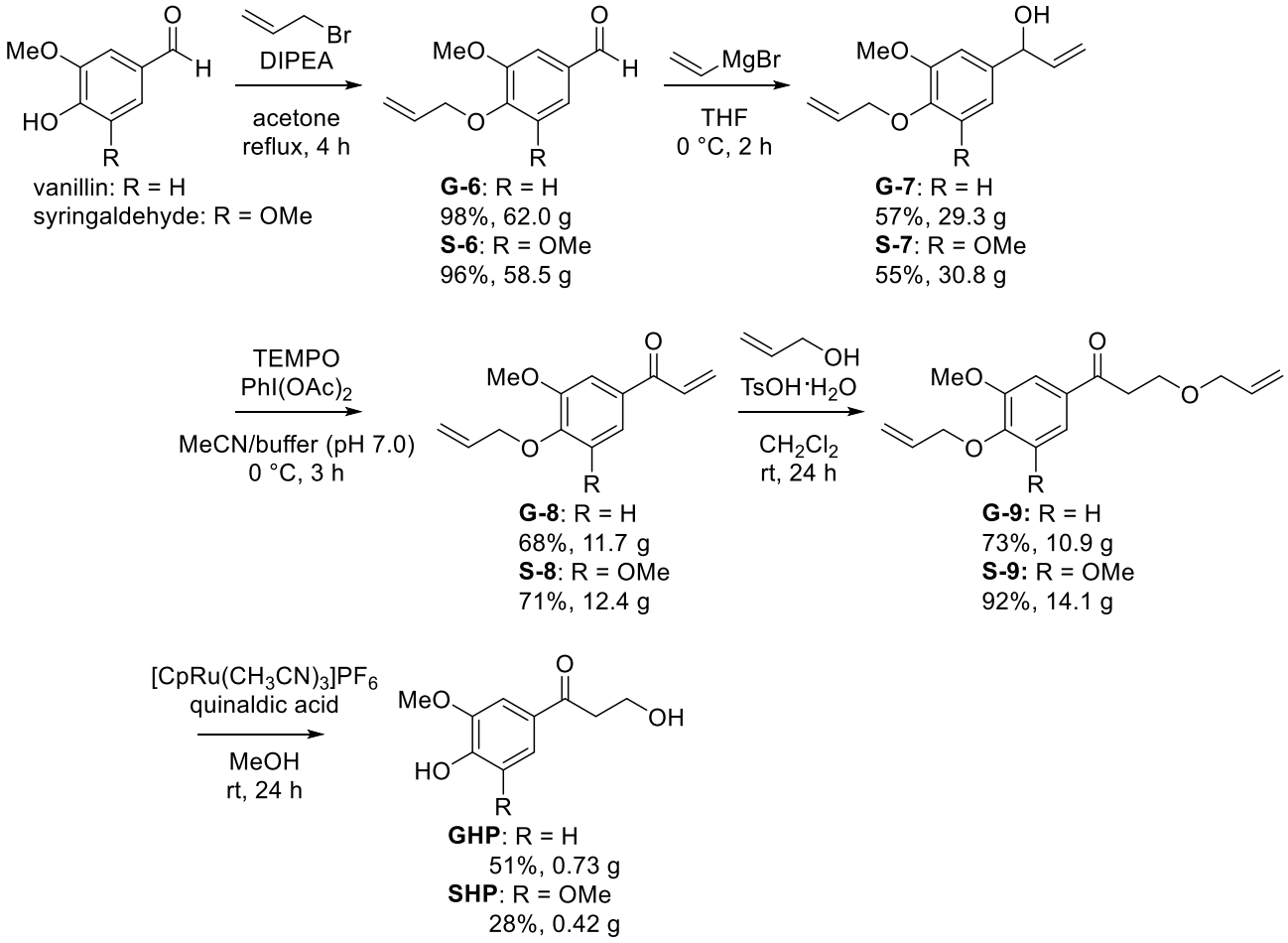
[2] Nishimura, H.; Yamada, M.; Watanabe, T. PCT/JP2021/040159.

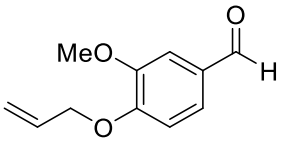
[3] Goel, O. P. US 2015/0344402, 2015.

[4] (a) Silverman, G. S., Rakita, P. E. *Handbook of Grignard Reagents*; Marcel Dekker, Inc.: New York, USA, 1996. (b) am Ende, D. J.; Clifford, P. J.; DeAntonis, D. M.; SantaMaria, C.; Brenek, S. J. Preparation of Grignard Reagents: FTIR and Calorimetric Investigation for Safe Scale-Up. *Organic Process Research & Development* **1999,** *3,* 319.

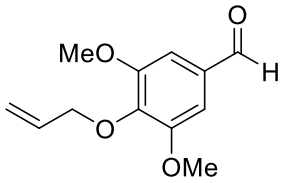
[5] (a) Ojo, O. S.; Nardone, B.; Musolino, S. F.; Neal, A. R.; Wilson, L.; Lebl, T.; Slawin, A. N. Z.; Cordes, D. B.; Taylor, J. E.; Naismith, J. H.; Smith, A. D.; Westwood, N. J. Synthesis of the natural product descurainolide and cyclic peptides from lignin-derived aromatics. *Org. Biomol. Chem.* **2018,** *16,* 266–273. (b) Hasegawa, R.; Ohta, Y.; Hatada, Y. WO 2015/133525, 2015.

Scheme S1. Synthesis of GHP/SHP

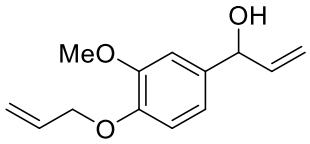




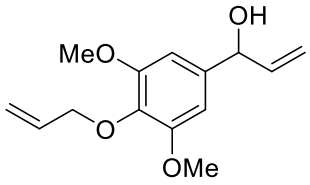
4-Allyloxy-3-methoxybenzaldehyde (G-6). To a solution of vanillin (50.0 g, 328.6 mmol), diisopropylethylamine (101 mL, 591.5 mmol) in acetone (100 mL) was added allyl bromide (47.3 mL, 558.6 mmol) at room temperature (rt) under argon atmosphere. The mixture solution was refluxed for 5 h. After cooling to rt, the precipitate was removed by filtration. The precipitate was washed with EtOAc. The combined solution was washed with water, brine, and dried over $MgSO_4$. After the removal of solvent by evaporation, the residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a light yellow liquid of **G-6** (62.0 g, 98%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 3.94 (s, 3H, -OC*H*$_3$), 4.71 (dt, *J* = 5.4, 1.5 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.35 (ddd, *J* = 10.5, 2.6, 1.3 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.44 (ddd, *J* = 17.3, 2.9, 1.6 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 6.09 (ddt, *J* = 17.3, 10.5, 5.4 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 6.98 (d, *J* = 8.7 Hz, 1H, Ar-^{5}*H*), 7.41–7.45 (m, 2H, Ar-^{2,6}*H*), 9.85 (s, 1H, -C*H*O).



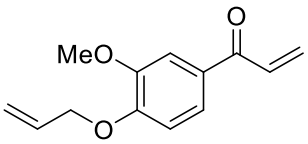
4-Allyloxy-3,5-dimethoxybenzaldehyde (S-6). This compound was synthesized by the same procedure to **G-6**. The product was isolated as a light yellow solid of **S-6** (58.5 g, 96%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 3.93 (s, 6H, -OC*H*$_3$), 4.63 (dt, *J* = 6.1, 1.2 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.21 (dtd, *J* = 10.3, 1.6, 1.0 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.33 (ddd, *J* = 17.1, 3.0, 1.5 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 6.08 (ddt, *J* = 17.1, 10.3, 6.1 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 7.13 (s, 2H, Ar-^{2,6}*H*), 9.87 (s, 1H, -C*H*O).



1-(4-allyloxy-3-methoxyphenyl)-2-propen-1-ol (G-7). To a solution of **G-6** (45.0 g, 234 mmol) in THF (225 mL) was added dropwise vinylmagnesium bromide (1.0 M, 258 mL, 257 mmol) solution in THF in ice bath for 90 min. After the addition, the mixture solution was stirred in ice bath for 2 h. After the confirmation of complete conversion of **G-6**, the reaction mixture was quenched with sat. NH_4Cl aq (405 mL) in ice bath. The solution was extracted with EtOAc (450 + 180 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a yellow oil of **G-7** (29.3 g, 57%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 1.95 (d, *J* = 3.8 Hz, 1H, -ArC*H*(OH)CH=CH$_2$), 3.88 (s, 3H, -OC*H*$_3$), 4.61 (dt, *J* = 5.4, 1.5 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.12–5.17 (m, 1H, -CH(O*H*)-), 5.20 (ddd, *J* = 10.3, 1.4, 1.4 Hz, 1H, -CH(OH)CH=C*H*$_2$), 5.28 (ddd, *J* = 10.5, 2.7, 1.3 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.25–5.43 (m, 2H, -CH(OH)CH=C*H*$_2$, -OCH$_2$CH=C*H*$_2$), 6.00–6.13 (m, 2H, -CH(OH)C*H*=CH$_2$, -OCH$_2$C*H*=CH$_2$), 6.83–6.89 (m, 2H, Ar–^{2,6}*H*), 6.93 (d, *J* = 1.4 Hz, 1H, Ar-^{5}*H*).

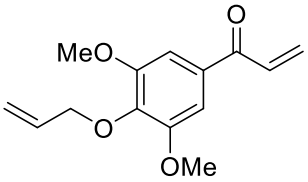


1-(4-allyloxy-3,5-dimethoxyphenyl)-2-propen-1-ol (S-7). This compound was synthesized by the same procedure to **G-7**. The product was isolated as a yellow oil of **S-7** (30.8 g, 55%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 1.96 (d, *J* = 3.8 Hz, 1H, -ArC*H*(OH)CH=CH$_2$), 3.85 (s, 6H, -OC*H*$_3$), 4.46 (dt, *J* = 6.1, 1.2 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.11–5.20 (m, 2H, -CH(O*H*)-, -OCH$_2$CH=C*H*$_2$), 5.22 (dt, *J* = 10.3, 1.3 Hz, 1H, -CH(OH)CH=C*H*$_2$), 5.30 (ddt, *J* = 17.2, 3.2, 1.6 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.37 (ddd, *J* = 17.1, 1.4, 1.4 Hz, 1H, -CH(OH)CH=C*H*$_2$), 5.99–6.16 (m, 2H, -CH(OH)C*H*=CH$_2$, -OCH$_2$C*H*=CH$_2$), 6.60 (m, 2H, Ar-^{2,6}*H*).

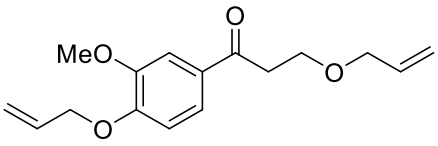


1-(4-Allyloxy-3-methoxyphenyl)propen-1-one (G-8). Caution: this compound spontaneously polymerizes when stored in dried liquid state under aerobic atmosphere. To avoid polymerization, this compound should be stored as solution under Ar atmosphere.

To a solution of **G-7** (17.5 g, 79.4 mmol) in MeCN (87.5 mL) and standard buffer solution (pH 6.86, 23.5 mL, Nacalai Tesque Inc.) was added 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO, 1.24 g, 7.94 mmol) and iodobenzene diacetate (28.1 g, 87.4 mmol) in ice bath under Ar atmosphere. The mixture solution was stirred in ice bath for 3 h. After warming to rt, the solution was diluted with EtOAc (87.5 mL) and washed with sat. $Na_2S_2O_3$ aq (87.5 mL × 2), sat $NaHCO_3$ aq (87.5 mL), water (87.5 mL), brine (87.5 mL), and dried over Na_2SO_4. After the removal of solvent by evaporation, the residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a yellow oil of **G-8** (11.7 g, 68%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 3.95 (s, 3H, -OC*H*$_3$), 4.70 (dt, *J* = 5.4, 1.4 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.33 (ddt, *J* = 10.6, 2.6, 1.4 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.44 (ddt, *J* = 17.3, 3.0, 1.5 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.87 (dd, *J* = 10.6, 1.8 Hz, 1H, -COCH=C*H*$_2$), 6.09 (ddt, *J* = 17.3, 10.5, 5.4 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 6.43 (dd, *J* = 17.0, 1.8 Hz, 1H, -COCH=C*H*$_2$), 6.91 (d, *J* = 8.8 Hz, 1H, Ar-^{5}*H*), 7.19 (dd, *J* = 17.0, 10.5 Hz, 1H, -COC*H*=CH$_2$), 7.54-7.59 (m, 2H, Ar-^{2,6}*H*).

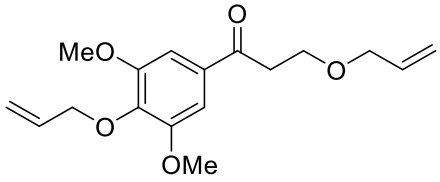


1-(4-Allyloxy-3,5-dimethoxyphenyl)propen-1-one (S-8). This compound was synthesized by the same procedure to **G-8**. The product was obtained as a light yellow oil (12.4 g, 71%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 3.92 (s, 6H, -OC*H*$_3$), 4.62 (d, *J* = 6.1 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.20 (ddt, *J* = 10.3, 1.7, 1.1 Hz, 2H, -OCH$_2$CH=C*H*$_2$), 5.32 (ddt, *J* = 17.2, 3.0, 1.5 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.91 (dd, *J* = 10.6, 1.7 Hz, 1H, -COCH=C*H*$_2$), 6.09 (ddt, *J* = 17.2, 10.4, 6.1 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 6.44 (dd, *J* = 17.1, 1.7 Hz, 1H, -COCH=C*H*$_2$), 7.15 (dd, *J* = 17.1, 10.6 Hz, 1H, -COC*H*=CH$_2$), 7.22 (m, 2H, Ar–^{2,6}*H*).

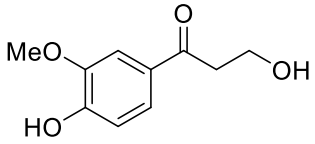


3-Allyloxy-1-(4-allyloxy-3-methoxyphenyl)-1-propanone (G-9). To a solution of **G-8** (11.7 g, 53.9 mmol) and *p*-toluenesulfonic acid monohydrate (0.51 g, 2.69 mmol) in CH_2Cl_2 (176 mL) was added

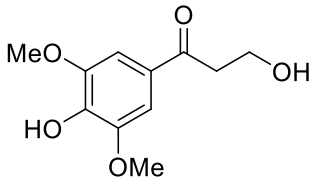
allyl alcohol (6.26 mL, 91.6 mmol) under Ar atmosphere at rt. The mixture solution was stirred at rt for 24 h. After confirming the complete consumption of **G-8** by TLC, the organic layer was washed with sat. $NaHCO_3$ aq (176 mL), brine (88 mL), and dried over $MgSO_4$. After the removal of solvent by evaporation, the residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a yellow oil of **G-9** (10.9 g, 73%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 3.23 (t, *J* = 6.6 Hz, 2H, -COC*H*$_2$CH$_2$O-), 3.87 (t, *J* = 6.6 Hz, 2H, -COCH$_2$C*H*$_2$O-), 3.93 (s, 3H, -OC*H*$_3$), 4.02 (dt, *J* = 5.7, 1.4 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 4.69 (dt, *J* = 5.4, 1.5 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.18 (ddt, *J* = 10.4, 1.8, 1.2 Hz, 2H, -OCH$_2$CH=C*H*$_2$), 5.28 (ddt, *J* = 17.2, 3.3, 1.6 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.33 (ddt, *J* = 10.5, 2.6, 1.4 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.43 (ddt, *J* = 17.3, 3.0, 1.6 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.91 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 6.08 (ddt, *J* = 17.2, 10.5, 5.4 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 6.89 (d, *J* = 8.3 Hz, 1H, Ar-^{5}*H*), 7.52–7.59 (m, 2H, Ar-^{2,6}*H*).



3-Allyloxy-1-(4-allyloxy-3,5-dimethoxyphenyl)-1-propanone (S-9). This compound was synthesized by the same procedure to **G-9**. The product was obtained as a light yellow oil (14.1 g, 92%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 3.25 (t, *J* = 6.6 Hz, 2H, -COC*H*$_2$CH$_2$O-), 3.88 (t, *J* = 6.6 Hz, 2H, -COCH$_2$C*H*$_2$O-), 3.90 (s, 6H, -OC*H*$_3$), 4.03 (dt, *J* = 5.7, 1.4 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 4.60 (dt, *J* = 6.1, 1.3 Hz, 2H, -OC*H*$_2$CH=CH$_2$), 5.16-5.22 (m, 2H, -OCH$_2$CH=C*H*$_2$), 5.28 (ddt, *J* = 11.7, 3.3, 1.6 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.32 (ddt, *J* = 11.6, 3.1, 1.5 Hz, 1H, -OCH$_2$CH=C*H*$_2$), 5.92 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 6.08 (ddt, *J* = 17.2, 10.3, 6.1 Hz, 1H, -OCH$_2$C*H*=CH$_2$), 7.23 (s, 2H, Ar-^{2,6}*H*).

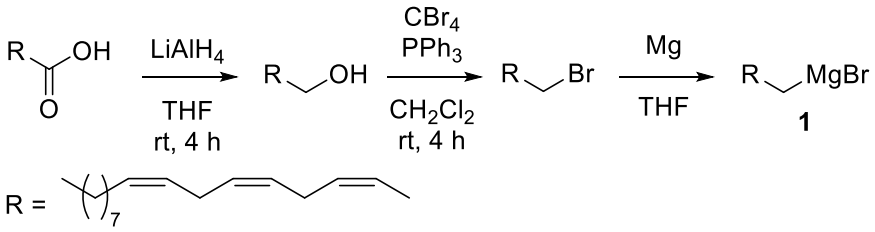


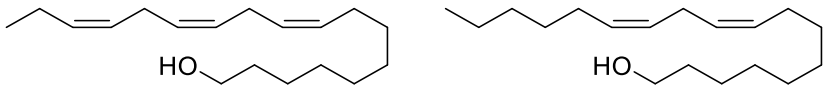
3-Allyloxy-1-(4-allyloxy-3-methoxyphenyl)-1-propanone (GHP). To a solution of **G-9** (2.0 g, 7.24 mmol) and quinaldic acid (12.5 mg, 0.072 mmol) in MeOH (10 mL) was added [CpRu(CH$_3$CN)$_3$]PF$_6$ (31.4 mg, 0.072 mmol) under Ar atmosphere. The mixture solution was stirred at rt for 24 h. After the removal of solvent by evaporation, the residue was dissolved in EtOAc and washed with water. The separated aqueous layer was extracted by EtOAc. The combined organic layer was washed with brine and dried over $MgSO_4$. After the removal of solvent by evaporation, the residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a brown solid of **GHP** (0.73 g, 51%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 2.72 (t, *J* = 6.6 Hz, 1H, -CH$_2$O*H*), 3.19 (t, *J* = 5.4 Hz, 2H, -COC*H*$_2$CH$_2$OH), 3.96 (s, 3H, -OC*H*$_3$), 4.02 (dt, *J* = 6.5, 5.4 Hz, 2H, -CH$_2$C*H*$_2$OH), 6.12 (s, 1H, Ar-O*H*), 6.96 (d, *J* = 8.4 Hz, 1H, Ar-^{5}*H*), 7.52–7.57 (m, 2H, Ar-^{2,6}*H*).



3-Allyloxy-1-(4-allyloxy-3,5-dimethoxyphenyl)-1-propanone (SHP). This compound was synthesized by the same procedure to **GHP**. The product was obtained as a light gray solid (0.42 g, 28%); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 2.67 (t, *J* = 6.6 Hz, 1H, -CH_2O*H*), 3.20 (t, *J* = 5.3 Hz, 2H, -$COCH_2CH_2OH$), 3.96 (s, 6H, -OCH_3), 4.03 (dt, *J* = 6.6, 5.3 Hz, 2H, -CH_2CH_2OH), 5.99 (s, 1H, Ar-O*H*), 7.26 (s, 2H, Ar-^{2,6}*H*).

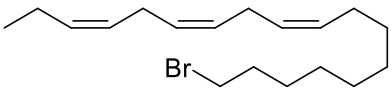
Scheme S2. Synthesis of Linolenyl Bromide and Grignard Reagent 1





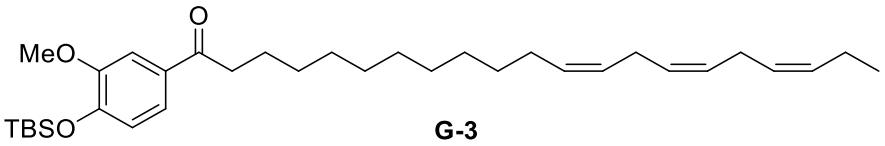
(9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trien-1-ol and (9*Z*,12*Z*)-octadeca-9,12-dien-1-ol.

A solution of α-linolenic acid (22.9 g, 82.4 mmol, ca 70% purity) in THF (92 mL) was added to a suspension of lithium aluminum hydride (9.38 g, 247 mmol) at 0 ºC. After stirring the reaction mixture at room temperature for 4 h, aqueous Na_2SO_4 was added at 0 ºC. The mixture was stirred for 30 min at room temperature and filtered. The filtrates were combined and concentrated under reduced pressure to give the 70:30 mixture of the title compound (21.65 g, 99%) as a colorless oil; ^{1}H NMR (392 MHz, $CDCl_3$) δ 0.89, 0.98 (t, *J* = 6.6, 7.8 Hz 3H, -C*H*$_3$), 1.20 (s, -O*H*), 1.30–1.37 (m, 10H, 16H -C*H*$_2$-), 1.57 (quint, *J* = 7.5 Hz, 2H, HO-CH_2-C*H*$_2$-), 2.03–2.12 (m, 4H, CH_3-C*H*$_2$-CH=CH-, -CH=CH-C*H*$_2$-CH_2-), 2.81, 2.77 (t, *J* = 6.3, 6.3 Hz, 4H, 2H, -CH=CH-C*H*$_2$-CH=CH-C*H*$_2$-CH=CH-, -CH=CH-C*H*$_2$-CH=CH-), 3.64 (t, *J* = 6.3 Hz, 2H, HO-C*H*$_2$-CH_2-), 5.28–5.43 (m, 6H, 4H, -C*H*=C*H*-CH_2-C*H*=C*H*-CH_2-C*H*=C*H*-, -C*H*=C*H*-CH_2-C*H*=C*H*-); ^{13}C NMR (99 MHz, $CDCl_3$) δ 14.20, 14.40, 20.69, 22.71, 25.67, 25.76 (2C) 25.87 (2C), 27.37 (3C), 29.37 (2C), 29.49, 29.53 (2C), 29.63 (2C), 29.77 (2C), 31.67, 32.94 (2C), 63.21 (2C), 127.82, 128.06, 128.14, 128.41 (2C), 130.25, 130.34, 130.47, 132.10; IR (neat, cm^{-1}) 3386, 2927, 2854, 1725, 1460, 1054, 975; HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{18}H_{32}O$ 264.4530, found 264.2455; $C_{18}H_{34}O$ 266.2610, found 266.2608.



(3*Z*,6*Z*,9*Z*)-18-bromooctadeca-3,6,9-triene.

The mixture of (9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trien-1-ol, (9*Z*,12*Z*)-octadeca-9,12-dien-1-ol (29.6 g) and CBr_4 (29.6 g, 89.3 mmol) was dissolved in dichloromethane (129 mL) at room temperature and then PPh_3 (23.4 g, 89.3 mmol) was added to the reaction mixture at 0 ºC. After stirring at 0 ºC for 4 h, the reaction mixture was concentrated under reduced pressure. To remove the phosphine oxide, hexane was added to the residue at 0 ºC and filtered. The filtrates were concentrated under reduced pressure to give the crude product. The crude product was purified by silica gel column chromatography with step gradient of 0–50 % ethyl acetate in hexane (R_f = 0.90) to give the title compound (15.2 g, 57%) as a colorless oil; ^{1}H NMR (392 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.7 Hz, 3H, -C*H*$_3$), 1.31–1.46 (m, 10H, -C*H*$_2$-), 1.86 (quint, *J* = 7.8 Hz, 2H, Br-CH$_2$-C*H*$_2$-), 2.03–2.12 (m, 4H, CH$_3$-C*H*$_2$-CH=CH-, -CH=CH-C*H*$_2$-CH$_2$-), 2.81 (t, *J* = 5.9 Hz, 4H, -CH=CH-C*H*$_2$-CH=CH-C*H*$_2$-CH=CH-), 3.41 (t, *J* = 6.7 Hz, 2H, Br-C*H*$_2$-), 5.28–5.44 (m, 6H, -C*H*=C*H*-CH$_2$-C*H*=C*H*-CH$_2$-C*H*=C*H*-); ^{13}C NMR (99 MHz, $CDCl_3$) δ 14.42, 20.71, 25.69, 25.77, 27.36, 28.31, 28.88, 29.32, 29.47, 29.74, 32.97, 34.15, 127.26, 127.88, 128.41, 128.43, 130.43, 132.12; IR (neat, cm^{-1}) 2929, 2856, 1712, 1458, 1177, 11056, 975, 721, 642, 561; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{18}H_{31}Br$ 326.1609 found, 326.1606.

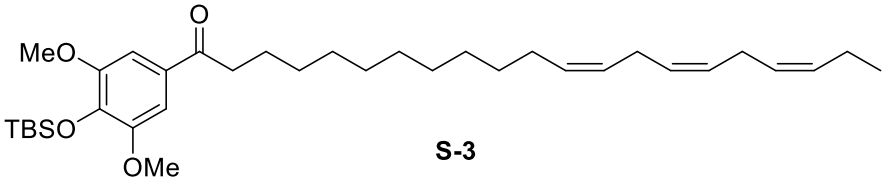


G-3

(12*Z*,15*Z*,18*Z*)-1-[4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl]henicosa-12,15,18-trien-1-one (G-3)

Dried LiCl (0.51 g, 12.0 mmol) and cuprous bromide dimethyl sulfide complex (2.46 g, 12.0 mmol) were stirred as a suspension in THF (30 mL) at ambient temperature for 20 min and the mixture was then cooled to −78 °C. A ((9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trien-1-yl)magnesium bromide (**1**) solution in THF [prepared from (3*Z*,6*Z*,9*Z*)-18-bromooctadeca-3,6,9-triene (3.92 g, 12.0 mmol) with magnesium turnings (0.33 g, 13.7 mmol) in THF (25 mL)] was added by a syringe. After 30 min at −78 °C, a solution of 1-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl)prop-2-en-1-one (1.0 g, 3.4 mmol) and trimethylsilyl chloride (1.5 mL, 12.0 mmol) in THF (5 mL) was added by a syringe. After 3 h at −78 °C, the reaction was quenched with sat. NH_4Claq (34 mL), then 0.5 M HCl (16 mL). After hydrolysis of the TMS enol ether (1 h), the reaction mixture was extracted with EtOAc (60 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and evaporated to give a dark brown oil. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a pale yellow oil of **G-3** (1.04 g, 56 %); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 0.18 (s, 6H, -SiC*H*$_3$), 0.97 (t, *J* = 7.0 Hz, 3H, -CH$_2$C*H*$_3$), 1.00 (s, 9H, -CC*H*$_3$), 1.24–1.37 (m, 14H, -CH$_2$(C*H*$_2$)$_7$CH$_2$CH=), 1.72 (tt, *J* = 7.4, 7.4 Hz, 2H, -COCH$_2$C*H*$_2$-), 1.98–2.12 (m, 4H, -CH$_2$C*H*$_2$CH=,

=CHCH_2CH$_3$), 2.81 (t, J = 5.8 Hz, 4H, =CHCH_2CH=), 2.90 (t, J = 7.4 Hz, 2H, -COCH_2CH$_2$-), 3.86 (s, 3H, -OCH_3), 5.28–5.43 (m, 6H, -CH=CH-), 6.86 (d, J = 8.1 Hz, 1H, Ar-^5H), 7.47 (dd, J = 8.1, 1.8 Hz, 1H, Ar-^6H), 7.52 (d, J = 1.8 Hz, 1H, Ar-^2H); ^{13}C NMR (CDCl$_3$, 98.5 MHz) δ −4.2 (2C, -SiCH$_3$), 14.6 (1C, -CH$_2C$H$_3$), 18.9 (1C, -SiC(CH$_3$)$_3$), 20.9 (1C, =CHCH$_2$CH$_3$), 25.1 (1C, =CHCH$_2$CH=), 25.9 (1C, =CHCH$_2$CH=), 26.0 (3C, -SiC(CH$_3$)$_3$), 27.6 (1C, -CH$_2C$H$_2$CH=CH-), 29.7 (1C, -CH$_2C$H$_2$CH$_2$-), 29.81 (1C, -CH$_2C$H$_2$CH$_2$-), 29.87 (4C, -CH$_2C$H$_2$CH$_2$-), 29.94 (1C, -CH$_2C$H$_2$CH$_2$-), 30.01 (1C, -CH$_2C$H$_2$CH$_2$-), 38.6 (1C, ArCOCH$_2$-), 55.8 (1C, -OCH$_3$), 111.5 (1C, ^{2}Ar), 120.6 (1C, ^{5}Ar), 122.8 (1C, ^{6}Ar), 127.5 (1C, -CH=CH-), 128.0 (1C, -CH=CH-), 128.6 (1C, -CH=CH-), 128.7 (1C, -CH=CH-), 130.8 (1C, -CH$_2C$H$_2$CH=CH-), 131.6 (1C, ^{1}Ar), 132.3 (1C, -CH=CHCH$_2$CH$_3$), 150.2 (1C, ^{4}Ar), 151.4 (1C, ^{3}Ar), 199.8 (1C, ArCO-); HRMS (ESI): *m/z* [M+H]$^+$ calcd for $C_{34}H_{57}O_3Si$ 541.4071, found 541.4064; Anal. Calcd for $C_{34}H_{56}O_3Si$ 0.1AcOEt C, 75.11; H, 10.39; N, 0.00. Found C, 75.00; H, 10.55; N, 0.00.

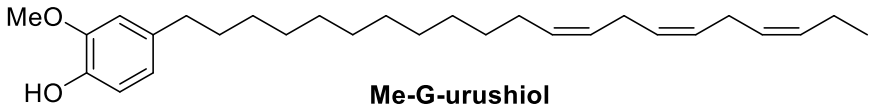


S-3

(12*Z*,15*Z*,18*Z*)-1-[4-(*tert*-Butyldimethylsilyloxy)-3,5-dimethoxyphenyl]henicosa-12,15,18-trien-1-one (S-3)

Dried LiCl (1.96 g, 46.1 mmol) and cuprous bromide dimethyl sulfide complex (9.48 g, 46.1 mmol) were stirred as a suspension in THF (126 mL) at ambient temperature for 20 min and the mixture was then cooled to −78 °C. A ((9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trien-1-yl)magnesium bromide (**1**) solution in THF [prepared from (3*Z*,6*Z*,9*Z*)-18-bromooctadeca-3,6,9-triene (15.1 g, 46.1 mmol) with magnesium turnings (1.28 g, 52.7 mmol) in THF (150 mL)] was added by a syringe. After 30 min at −78 °C, a solution of 1-(4-((tert-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)prop-2-en-1-one (4.25 g, 13.2 mmol) and trimethylsilyl chloride (5.83 mL, 46.1 mmol) in THF (21 mL) was added by a syringe. After 3 h at −78 °C, the reaction was quenched with sat. aqueous NH_4Cl (145 mL), then 0.5 M HCl (66 mL). After hydrolysis of the TMS enol ether (30 min), the reaction mixture was extracted with EtOAc (297 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and evaporated to give a dark brown oil. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a pale yellow oil of **S-3** (5.37 g, 71 %); ^{1}H NMR (CDCl$_3$, 392 MHz) δ 0.14 (s, 6H, -SiCH_3), 0.96 (t, J = 7.4 Hz, 3H, -CH$_2$CH_3), 1.01 (s, 9H, -CCH_3), 1.24–1.38 (m, 14H, -CH$_2$(CH_2)$_7$CH$_2$CH=), 1.72 (tt, J = 7.4 Hz, 2H, -COCH$_2$CH_2-), 2.01–2.12 (m, 4H, -CH$_2$CH_2CH=, =CHCH_2CH$_3$), 2.81 (t, J = 5.8 Hz, 4H, =CHCH_2CH=), 2.91 (t, J = 7.4 Hz, 2H, -COCH_2CH$_2$-), 3.85 (s, 6H, -OCH_3), 5.28–5.42 (m, 6H, -CH=CH-), 7.20 (s, 2H, Ar-$^{2,6}H$); ^{13}C NMR (CDCl$_3$, 98.5 MHz) δ -4.2 (2C, -SiCH$_3$), 14.6 (1C, -CH$_2C$H$_3$), 19.1 (1C, -SiC(CH$_3$)$_3$), 20.9 (1C, -CH$_2$CH$_3$), 25.0 (1C, -CH=CHCH$_2$CH=CH-), 25.9 (1C, -CH=CHCH$_2$CH=CH-), 26.1 (3C, -SiC(CH$_3$)$_3$), 27.6 (1C, -CH$_2C$H$_2$CH=CH-), 29.7 (1C, -CH$_2C$H$_2$CH$_2$-), 29.8 (1C, -CH$_2C$H$_2$CH$_2$-), 29.89 (4C, -

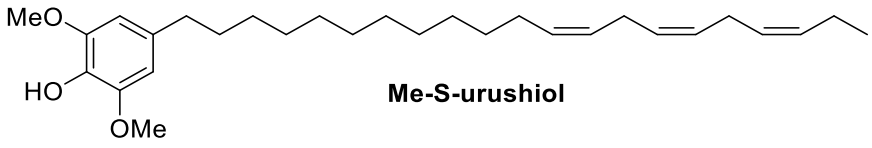
$CH_2CH_2CH_2$-), 29.95 (1C, -$CH_2CH_2CH_2$-), 30.01 (1C, -$CH_2CH_2CH_2$-), 38.6 (1C, Ar$COCH_2$-), 56.2 (2C, -OCH_3), 106.0 (2C, ^{2,6}Ar), 127.5 (1C, -*C*H=CH-), 128.0 (1C, -*C*H=CH-), 128.6 (1C, -*C*H=CH-), 128.7 (1C, -*C*H=CH-), 130.2 (1C, ^{1}Ar), 130.8 (1C, -CH_2CH_2CH=CH-), 132.3 (1C, -CH=*C*HCH_2CH_3), 139.8 (1C, ^{4}Ar), 151.7 (2C, ^{3,5}Ar), 199.7 (Ar*C*O-); HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{35}H_{59}O_4Si$ 571.4177, found 571.4173; Anal. Calcd for $C_{35}H_{58}O_4Si$ 0.3AcOEt C, 72.79; H, 10.19. Found C, 72.58; H, 10.20.



Me-G-urushiol

4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]-2-methoxypnehol (Me-G-urushiol)

To a solution of (12*Z*,15*Z*,18*Z*)-1-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl)henicosa-12,15,18-trien-1-one (**G-3**, 2.16 g, 4.0 mmol) in TFA (6.12 mL, 79.9 mmol) was added triethylsilane (1.59 mL, 10.0 mmol) at 0 °C. After reaction mixture was stirred at ambient temperature for 4 h. To the reaction mixture was added CH_2Cl_2 (22 mL). The solution was neutralized by adding a sat. aqueous $NaHCO_3$, and the organic layer was washed with brine, dried over $MgSO_4$, filtered and evaporated to give a brown oil. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a pale yellow oil of **Me-G-urushiol** (1.08 g, 65 %); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 0.97 (t, *J* = 7.4 Hz, 3H, -OC*H*$_3$), 1.20–1.40 (m, 12H, -CH(C*H*$_2$)$_6$$CH_2$-), 1.55–1.57 (m, 2H, -$CH_2$C*H*$_2$$CH_2$-), 2.04–2.08 (m, 4H, -$CH_2$C*H*$_2$CH=CH-, -CH=CHC*H*$_2$$CH_3$), 2.52 (t, *J* = 8.1 Hz, 2H, Ar-C*H*$_2$$CH_2$-), 2.79–2.83 (m, 4H, -CH=C*H*$_2$CH=CH-), 3.88 (s, 3H, -OC*H*$_3$), 5.30–5.43 (m, 6H, -C*H*=C*H*-), 6.64–6.70 (m, 2H, Ar-^{3,6}*H*), 6.82 (d, *J* = 8.5 Hz, 1H, Ar-^{5}H); ^{13}C NMR ($CDCl_3$, 98.5 MHz) δ 14.6 (1C, -CH_2*C*H$_3$), 20.9 (1C, -*C*H$_2$$CH_3$), 25.9 (1C, -CH=CH*C*H$_2$CH=CH-), 26.0 (1C, -CH=CH*C*H$_2$CH=CH-), 27.6 (1C, -CH_2*C*H$_2$CH=CH-), 29.7 (2C, -CH_2*C*H$_2$$CH_2$-), 29.89 (2C, -$CH_2$*C*H$_2$$CH_2$-), 29.97 (2C, -$CH_2$*C*H$_2$$CH_2$-), 30.00 (2C, -$CH_2$*C*H$_2$$CH_2$-), 32.2 (Ar$CH_2$*C*H$_2$-), 36.0 (1C, Ar*C*H$_2$-), 56.2 (1C, -O*C*H$_3$), 111.3 (1C, ^{3}Ar), 114.4 (1C, ^{6}Ar), 121.2 (1C, ^{5}Ar), 127.5 (1C, -*C*H=CH-), 128.0 (1C, -*C*H=CH-), 128.6 (1C, -*C*H=CH-), 128.7 (1C, -*C*H=CH-), 130.8 (1C, -CH_2*C*H$_2$CH=CH-), 132.3 (1C, -CH=*C*HCH_2CH_3), 135.3 (1C, ^{4}Ar), 143.8 (1C, ^{1}Ar), 146.6 (1C, ^{2}Ar); HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{28}H_{44}O_2Na$ 435.3234, found 435.3228; Anal. Calcd for $C_{29}H_{50}O_3$. 0.3EtOAc C, 79.87; H, 10.65; N, 0.00. Found C, 79.97; H, 10.74; N, 0.00; Anal. Calcd for $C_{27}H_{42}O_2$ 0.2AcOEt C, 80.14; H, 10.51; N, 0.00. Found C, 80.07; H, 10.67; N, 0.00.

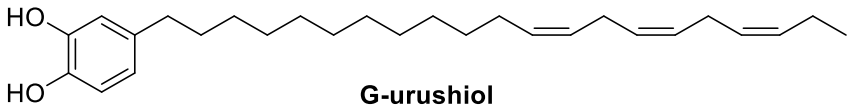


Me-S-urushiol

2,6-Dimethoxy-4-[(12*Z*,15*Z*,18*Z*)-henicosa-12,15,18-trienyl]pnehol (Me-S-urushiol)

To a solution of (12*Z*,15*Z*,18*Z*)-1-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethoxyphenyl)-

henicosa-12,15,18-trien-1-one (**S-3**, 5.85 g, 10.2 mmol) in TFA (15.7 mL, 204.9 mmol) was added triethylsilane (4.1 mL, 25.6 mmol) at 0 °C. After reaction mixture was stirred at ambient temperature for 2.5 h. To the reaction mixture was added CH_2Cl_2 (60 mL). The solution was neutralized by adding a sat. aqueous $NaHCO_3$, and the organic layer was washed with brine, dried over $MgSO_4$, filtered and evaporated to give a yellow oil. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a pale yellow oil of **Me-S-urushiol** (2.7 g, 59 %); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 0.97 (t, *J* = 7.4 Hz, 3H, -CH_2CH_3), 1.27–1.37 (m, 12H, -$CH_2(CH_2)_6CH_2$-), 1.54–1.60 (m, 2H, Ar-CH_2CH_2-), 2.00–2.12 (m, 4H, -CH_2CH_2CH=, =$CHCH_2CH_3$), 2.52 (t, *J* = 7.6 Hz, 2H, Ar-CH_2CH_2-), 2.77–2.85 (m, 4H, =$CHCH_2CH$=), 3.88 (s, 6H, -OCH_3), 5.28–5.43 (m, 6H, -C*H*=C*H*-), 6.40 (s, 2H, Ar-^{2,6}*H*); ^{13}C NMR ($CDCl_3$, 98.5 MHz) δ 14.6 (1C, -CH_2CH_3), 20.9 (1C, -CH_2CH_3), 25.9 (1C, -CH=CHCH_2CH=CH-), 26.0 (1C, -CH=CHCH_2CH=CH-), 27.6 (1C, -CH_2CH_2CH=CH-), 29.67 (1C, -$CH_2CH_2CH_2$-), 29.70 (1C, -$CH_2CH_2CH_2$-), 29.90 (2C, -$CH_2CH_2CH_2$-), 29.97 (2C, -$CH_2CH_2CH_2$-), 30.01 (2C, -$CH_2CH_2CH_2$-), 32.2 (ArCH_2CH_2-), 36.6 (1C, ArCH_2-), 56.6 (1C, -OCH_3), 105.3 (2C, ^{2,6}Ar), 127.5 (1C, -CH=CH-), 128.0 (1C, -CH=CH-), 128.61 (1C, -CH=CH-), 128.64 (1C, -CH=CH-), 130.8 (1C, -CH_2CH_2CH=CH-), 132.3 (1C, -CH=CHCH$_2$CH$_3$), 133.0 (1C, ^{1}Ar), 134.5 (1C, ^{4}Ar), 147.2 (2C, ^{2,6}Ar); HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{29}H_{47}O_3$ 443.3520, found 443.3517; Anal. Calcd for $C_{29}H_{46}O_3$ 0.3AcOEt C, 77.32; H, 10.40; N, 0.00. Found C, 77.28; H, 10.62; N, 0.00.

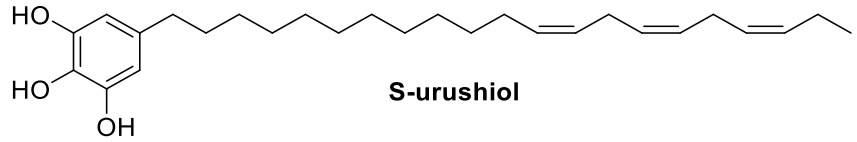


G-urushiol

4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]catechol (G-urushiol)

A mixture of 2-methoxy-4-((12Z,15Z,18Z)-henicosa-12,15,18-trien-1-yl)phenol (**Me-G-urushiol**, 50 mg, 0.12 mmol), ethyl ether solution of methylmagnesium iodide (0.3 mL, 2 M, 0.6 mmol) in diglyme (2.5 mL) was stirred at 170 °C for 23 h. To the reaction mixture was added EtOAc (100 mL), then to the mixture was added 1 M aqueous HCl (2 mL) and water (20 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and evaporated to give a dark brown oil. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a pale white oil of **G-urushiol** (25 mg, 52 %); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 0.98 (t, *J* = 7.4 Hz, 3H, -OCH_3), 1.26–1.40 (m, 12H, -$CH(CH_2)_6CH_2$-), 1.51–1.58 (m, 2H, Ar$CH_2CH_2CH_2$-), 2.03–2.10 (m, 4H, -CH_2CH_2CH=CH-, -CH=CHCH_2CH_3), 2.48 (t, *J* = 7.6 Hz, 2H, Ar-CH_2CH_2-), 2.76–2.85 (m, 4H, -CH=CHCH_2CH=CH-), 4.86–5.20 (br, 2H, ArO*H*), 5.28–5.43 (m, 6H, -C*H*=C*H*-), 6.61 (dd, *J* = 8.1, 1.8 Hz, 1H, Ar-^{6}*H*), 6.70 (d, *J* = 1.8 Hz, Ar-^{2}*H*), 6.76 (d, *J* = 8.1 Hz, Ar-^{5}*H*); ^{13}C NMR ($CDCl_3$, 98.5 MHz) δ 14.6 (1C, -CH_2CH_3), 20.9 (1C, -CH_2CH_3), 25.9 (1C, -CH=CHCH_2CH=CH-), 26.0 (1C, -CH=CHCH_2CH=CH-), 27.6 (1C, -CH_2CH_2CH=CH-), 29.58 (1C, -$CH_2CH_2CH_2$-), 29.67 (1C, -$CH_2CH_2CH_2$-), 29.86 (1C, -$CH_2CH_2CH_2$-), 29.89 (1C, -$CH_2CH_2CH_2$-), 29.93 (1C, -$CH_2CH_2CH_2$-), 29.99 (3C, -$CH_2CH_2CH_2$-), 32.0 (ArCH_2CH_2-), 35.6 (1C, ArCH_2-), 115.6 (1C, ^{6}Ar), 115.8 (1C, ^{3}Ar), 121.1 (1C, ^{5}Ar), 127.5 (1C, -CH=CH-), 127.9 (1C, -CH=CH-), 128.6 (1C, -CH=CH-), 128.7 (1C, -

*C*H=CH-), 130.8 (1C, -CH_2*C*H_2CH=CH-), 132.3 (1C, -CH=*C*HCH$_2$CH$_3$), 136.7 (1C, ^{4}Ar), 141.5 (1C, ^{2}Ar), 143.7 (1C, ^{1}Ar) ; HRMS (ESI-FT-ICR): *m/z* $[M+H]^+$ calcd for $C_{27}H_{42}O_2Na$ 399.32576, found 399.32567.



S-urushiol

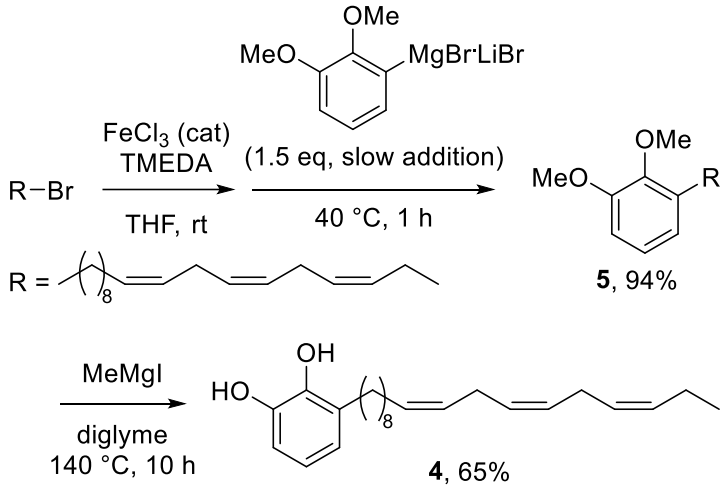
4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]pyrogallol (S-urushiol)

A mixture of 2,6-dimethoxy-4-((12Z,15Z,18Z)-henicosa-12,15,18-trien-1-yl)phenol (**Me-S-urushiol**, 50 mg, 0.11 mmol), ethyl ether solution of methylmagnesium iodide (0.65 mL, 2.8 M, 1.8 mmol) in mesitylene (1 mL) was stirred at 170 °C for 3 h. To the reaction mixture was added EtOAc (100 mL), then to the mixture was added 1 M aqueous HCl (1.6 mL) and water (20 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and evaporated to give brown oil. The residue was subjected to silica gel column chromatography, where the major fraction was collected to afford a brown oil of **S-urushiol** (24 mg, 51 %); ^{1}H NMR ($CDCl_3$, 392 MHz) δ 0.98 (t, *J* = 7.4 Hz, 3H, -CH_2CH_3), 1.26–1.35 (m, 16H, -CH_2(CH_2)$_8$$CH_2$CH=), 1.51–1.56 (m, 2H, Ar-CH_2CH_2-), 2.02–2.12 (m, 4H, -CH_2CH_2CH=, =CHCH_2CH_3), 2.43 (t, *J* = 7.6 Hz, 2H, Ar-CH_2CH_2-), 2.77–2.82 (m, 4H, =CHCH_2CH=), 5.04 (br, 3H, ArO*H*), 5.30–5.45 (m, 6H, -C*H*=C*H*-), 6.31 (s, 2H, Ar-^{2,6}*H*); ^{13}C NMR ($CDCl_3$, 98.5 MHz) δ 14.6 (1C, -CH_2CH_3), 20.9 (1C, -*C*H_2CH_3), 25.9 (1C, -CH=CH*C*H_2CH=CH-), 26.0 (1C, -CH=CH*C*H_2CH=CH-), 27.6 (1C, -CH_2*C*H_2CH=CH-), 29.6 (1C, -CH_2*C*H_2CH_2-), 29.7 (1C, -CH_2*C*H_2CH_2-), 29.86 (1C, -CH_2*C*H_2CH_2-), 29.89 (1C, -CH_2*C*H_2CH_2-), 29.93 (1C, -CH_2*C*H_2CH_2-), 29.99 (3C, -CH_2*C*H_2CH_2-), 31.8 (ArCH_2*C*H_2-), 36.0 (1C, Ar*C*H_2-), 108.4 (2C, ^{2,6}Ar), 127.5 (1C, -*C*H=CH-), 128.0 (1C, -*C*H=CH-), 128.6 (1C, -*C*H=CH-), 128.7 (1C, -*C*H=CH-), 129.7 (1C, ^{1}Ar), 130.8 (1C, -CH_2*C*H_2CH=CH-), 132.3 (1C, -CH=*C*HCH_2CH_3), 135.9 (1C, ^{4}Ar), 144.0 (2C, ^{2,6}Ar); HRMS (ESI-FT-ICR): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{42}O_3Na$ 437.30262, found 437.30250; Anal. Calcd for $C_{10}H_{12}O_4$ C, 61.22; H, 6.17; N, 0.00. Found C, 61.12; H, 6.12; N, 0.00.

Synthesis of Urushiol Analog Bearing Trienyl Side Chain at the 3-Position of Catechol.

For the investigation on the relationship between molecular structure and polymerization properties, a different type of urushiol analog **4** was also synthesized by introducing trienyl side chain to the 3-position of catechol (Scheme S2). We previously developed iron-catalyzed cross-coupling reactions between alkyl halides and aryl Grignard reagents,[6] which were applied to the synthesis of the urushiol analog **4**. The reaction conditions were optimized by screening ligands and catalyst precursors, revealing that the combination of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) and catalytic amount of $FeCl_3$ gives the highest yield for this reaction.[7] The aryl Grignard reagent, 2,3-dimethoxyphenylmagnesium bromide lithium bromide was cross-coupled with linelenyl bromide in the presence of catalytic amount of $FeCl_3$, affording the methoxy-protected urushiol derivative **5** quantitatively. The following methoxy-deprotection gave the urushiol analog **5** in 65% yield. Through the two-step reactions, the retention of all-*cis* configuration of the trienyl side chain was confirmed by ^1H and ^{13}C NMR. The same urushiol analog was previously synthesized by cross-coupling reaction using equimolar amount of copper salt.[8] This is the first report of a catalytic approach to the synthesis of urushiol analog **4**.

Scheme S3. Synthesis of Urushiol Analog by Iron-Catalyzed Cross Coupling



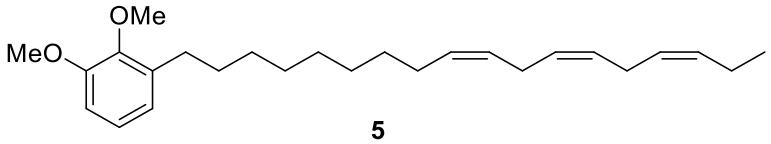
[6] (a) M. Jin, L. Adak and M. Nakamura, *J. Am. Chem. Soc.,* 2015, **137,** 7128–7134. (b) T. Hatakeyama, Y.-I. Fujiwara, Y. Okada, T. Itoh, T. Hashimoto, S. Kawamura, K. Ogata, H. Takaya and M. Nakamura, *Chem. Lett.,* 2011, **40,** 1030–1032. (c) M. Nakamura, K. Matsuo, S. Ito and E. Nakamura, *J. Am. Chem. Soc.,* 2004, **126,** 3686–3687.

[7] (a) S. Nakajima, H. Takaya and M. Nakamura, *Chem. Lett.,* 2017, **46,** 711–714. (b) M. Nakamura, T. Hatakeyama, T. Hashimoto, S. Nakajima and N. Nakagawa, Jpn. Kokai Tokkyo Koho JP 2013180991, 2013.

[8] Y. Kamiya, in *Progress of Urushi Chemistry*, eds. T. Miyakoshi, K. Nagase and T. Yoshida, IPC, Tokyo, 2000, pp 259–288.

Preparation of 2,3-dimethoxyphenylmagnesium bromide lithium bromide.

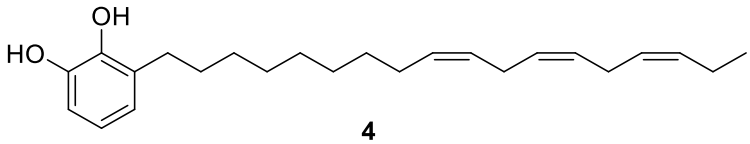
To a solution of dimethoxybenzene (11.9 g, 86.0 mmol) in THF (25 mL) was added slowly a solution of BuLi in hexane (53.7 mL, 1.60 M, 86.0 mmol) at 0 ºC. After the mixture was stirred at room temperature for 1 h, the resulting reaction mixture was added to a solution of $MgBr_2$ in THF (400 mL, 0.26 M, 103 mmol) at –78 ºC. After stirring at room temperature for 1 h, the resulting reaction mixture was filtered through Celite and titrated before use.



5

1,2-Dimethoxy-3-[(12*Z*,15*Z*,18*Z*)-octadeca-12,15,18-trienyl]benzene (5).

A solution of 2,3-dimethoxyphenylmagnesium bromide lithium bromide complex in THF (0.84 mL, 0.53 M, 0.45 mmol) was added to a mixture of $FeCl_3$ (2.4 mg, 0.015 mmol), TMEDA (54 μL, 0.36 mmol), undecane (31.6 mg, 0.20 mmol) and linolenyl bromide (97.8 mg, 0.30 mmol) in 0.36 mL of THF at 40 ºC by using a syringe pump. After cooling to room temperature, the reaction mixture was quenched with aqueous HCl (1 N) and the aqueous layer was extracted with ethyl acetate. The organic layer was filtered through a pad of Florisil. The product yield was determined by GC analysis (>99% yield) using undecane as an internal standard. The large-scale synthesis was also carried out according to the typical procedure on a 6.0 mmol scale. After the addition of 2,3-dimethoxyphenylmagnesium bromide lithium bromide complex in THF, aqueous HCl (1N) was added to the reaction mixture at 0 ºC. The aqueous layer was extracted with ethyl acetate three times. The combined organic layers were filtered through a Florisil pad and concentrated under reduced pressure to give the crude product. The crude product was purified by silica gel column chromatography with a step gradient of 0–9 % ethyl acetate in hexane (R_f = 0.50) to give the title compound **5** (2.20 g, 95%) as a colorless oil; ^{1}H NMR (392 MHz, $CDCl_3$) δ 0.98 (t, J = 7.8 Hz, 3H, -C*H*$_3$), 1.26–1.36 (m, 10H, -C*H*$_2$-), 1.58 (quint, J = 7.5 Hz, 2H, C_6H_3-CH_2-C*H*$_2$-), 2.02–2.12 (m, 4H, CH_3-C*H*$_2$-CH=CH-, -CH=CH-C*H*$_2$-CH_2-), 2.61 (t, J = 7.5 Hz, 2H, C_6H_3-C*H*$_2$-), 2.81 (t, J = 6.3 Hz, 4H, -CH=CH-C*H*$_2$-CH=CH-C*H*$_2$-CH=CH-), 3.81, (s, 3H, 2-OC*H*$_3$) 3.85 (s, 3H, 1-OC*H*$_3$), 5.28–5.43 (m, 6H, -C*H*=C*H*-CH_2-C*H*=C*H*-CH_2-C*H*=C*H*-), 6.75 (d, J = 3.1 Hz, 1H, 6-C_6H_3-), 6.78 (d, J = 2.7 Hz, 1H, 4-C_6H_3-), 6.97 (t, J = 7.8 Hz, 1H, 5-C_6H_3-); ^{13}C NMR (99 MHz, $CDCl_3$) δ 14.42, 20.70, 25.69, 25.78, 27.40, 29.48, 29.64 (2C), 29.77, 29.82, 29.96, 30.96, 55.82 (1-O*C*H$_3$), 60.76 (2-O*C*H$_3$), 110.06, 122.04, 123.80, 127.28, 127.78, 128.4, 128.46, 130.56, 132.11, 136.94, 147.26, 152.88; IR (neat, cm^{-1}) 2926, 2853, 1718, 1474, 1268, 1085, 1011, 747; HRMS (EI) m/z $[M]^+$ calcd for $C_{26}H_{40}O_2$ 384.3028, found 384.3031; Anal. calcd for $C_{26}H_{40}O_2$ C, 81.20; H, 10.48, found, C, 81.17; H, 10.57.



4

3-[(12*Z*,15*Z*,18*Z*)-Octadeca-12,15,18-trienyl]catechol (4).

A solution of methyl magnesium iodide in diethyl ether (0.43 mL, 2.80 M, 1.2 mmol) was placed in a reaction vessel and then concentrated under the reduced pressure to remove the solvent. The substrate **5** (55.0 mg, 0.14 mmol) and diglyme (1.0 mL) were added to methyl magnesium iodide at room temperature. After the mixture was stirred at 140 ºC for 4 h, aqueous NH_4Cl was added to the reaction mixture at 0 ºC. The aqueous layer was extracted with ethyl acetate three times. The combined organic layers were filtered through a pad of Florisil and concentrated under reduced pressure to give the crude product. The crude product was purified by silica gel column chromatography with a step gradient of 0–10 % ethyl acetate in hexane (R_f = 0.18) to afford the title compound **4** (32.9 mg, 65%) as a colorless oil; ^{1}H NMR (392 MHz, $CDCl_3$) δ 0.97 (t, J = 7.1 Hz, 3H, -C*H*$_3$), 1.26–1.33 (m, 10H, -C*H*$_2$-), 1.61 (quint, J = 6.7 Hz, 2H, C_6H_3-CH_2-C*H*$_2$-), 2.02–2.12 (m, 4H, CH_3-C*H*$_2$-CH=CH-, -CH=CH-C*H*$_2$-CH_2-), 2.60 (t, J = 7.5 Hz, 2H, C_6H_3-C*H*$_2$-), 2.81 (t, J = 5.5 Hz, 4H, -CH=CH-C*H*$_2$-CH=CH-C*H*$_2$-CH=CH-), 5.13, (s, 2H, -O*H*), 5.28–5.42 (m, 6H, -C*H*=C*H*-CH_2-C*H*=C*H*-CH_2-C*H*=C*H*-), 6.72–6.72 (m, 3H, C_6H_3-). ^{13}C NMR (99 MHz, $CDCl_3$): δ 14.42, 20.70, 25.69, 25.77, 27.39, 29.44, 29.64 (3C), 29.80, 29.91 (2C), 113.01, 120.23, 122.23, 127.28, 127.79, 128.42 (2C), 129.49, 130.54, 132.12, 142.03, 143.17; IR (neat, cm^{-1}) 3449, 3010, 2926, 2854, 1737, 1475, 1459, 1366, 1278, 969, 730; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{24}H_{36}O_2$ 356.2715, found 356.2713.

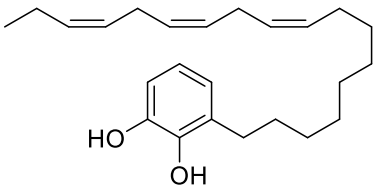
General procedure for preparing artificial *urushi* film

Prior to the preparation of artificial *urushi* film, a laccase solution was prepared. To a centrifuge tube was added laccase-adsorbed dextran (3.0 g, Amano Enzyme Inc.) and deionized water (3.0 mL). The mixture solution was stirred using a spatula for 20 s, capped, and left in the refrigerator for 1 h. Then, the solution was centrifuged at 2,000 rpm for 5 min to remove dextran. The supernatant solution was used for preparing the artificial *urushi* film. A powder of commercially available protein hydrolysate (1.5 g) was mixed with deionized water (1.5 mL). The mixture was heated by an electric microwave oven to dissolve the protein hydrolysate. The protein hydrolysate solution (40 mg) was mixed with urushiol analog compound (200 mg) and the laccase solution (40 μL), stirred well using a spatula to prepare an *urushi* sap-like liquid. The prepared mixture liquid was coated on a cleaned glass plate using a film applicator (50 μm thickness, 50 mm width, Taiyu Kizai, Japan). The natural *urushi* films were also prepared following the same procedure using extracted urushiol or thitsiol instead of the artificial urushiol.

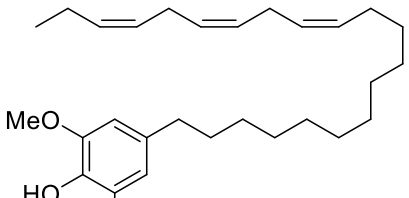
Measurement of curing property of artificial *urushi* films

The time-course curing property of the prepared film was recorded on an automatic drying time recorder (Dry Time Tester, Taiyu Kizai, Japan) at 30 °C in 80 % relative humidity. The curing time was usually described as the set-to-touch time which was needed for the marks of the needle of the automatic drying time recorder to appear on the sample's surface.[9]

Table S1. Martens Hardness of Thermally Cured Artificial *urushi* Films and Commercially Available Polymer Films



4



Me-S-urushiol

entry	compound	curing condition	Martens hardness (N/mm^2)
1	**4**	30 °C, 120 d	140.4 ± 1.5
2	**4**	180 °C, 30 min	195.2 ± 6.2
3	**Me-S-urushiol**	180 °C, 30 min	161.3 ± 3.5
4	Chinese urushiol	180 °C, 30 min	183.2 ± 0.8
5	PMMA	-	208.6 ± 1.8
6	PVC	-	144.6 ± 0.4
7	Polycarbonate	-	126.4 ± 1.1
8	ABS	-	124.4 ± 0.6
9	PP	-	100.4 ± 0.4

[9] Yang, J.; Deng, J.; Zhu, J.; Liu, W.; Zhou, M.; Li, D. *Prog. Org. Coat.* **2016,** *94*, 41–48.

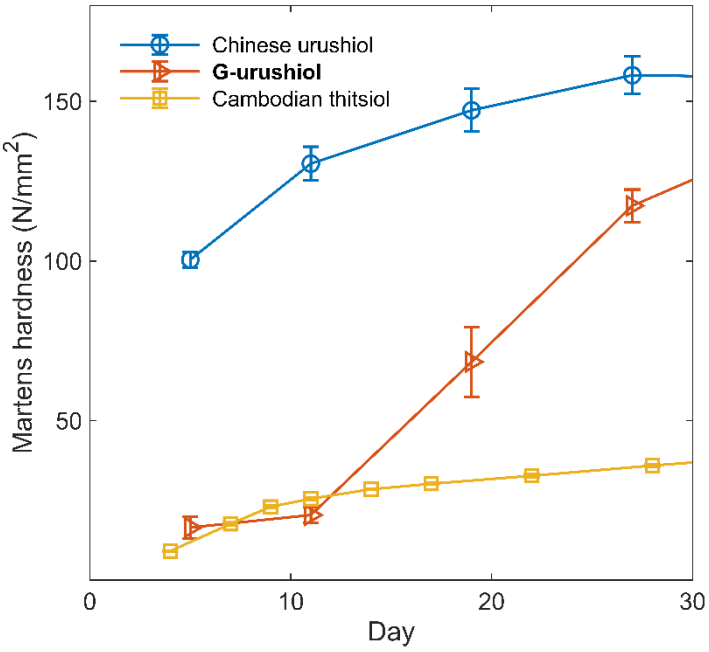


Figure S1. Magnified initial steps of time-course curing property of film obtained from **G-urushiol** (red line), natural Chinese urushiol (blue line) and natural Cambodian thitsiol (yellow line).

DFT calculation of vibration modes of artificial urushiol 10

Geometry optimization of artificial urushiol **G-urushiol** was studied through DFT calculation using the B3LYP functional. Basis set used was 6-31G(d). Structural optimization was carried out followed by frequency calculation to confirm that the optimized structures had no imaginary frequencies, indicating that they were located at the local/global minima of the potential energy surface. The calculated IR spectrum was obtained from the frequency calculation. The similar vibration modes were also obtained from 4-methylcatechol. All calculations were conducted using the Gaussian 16 program.[10]

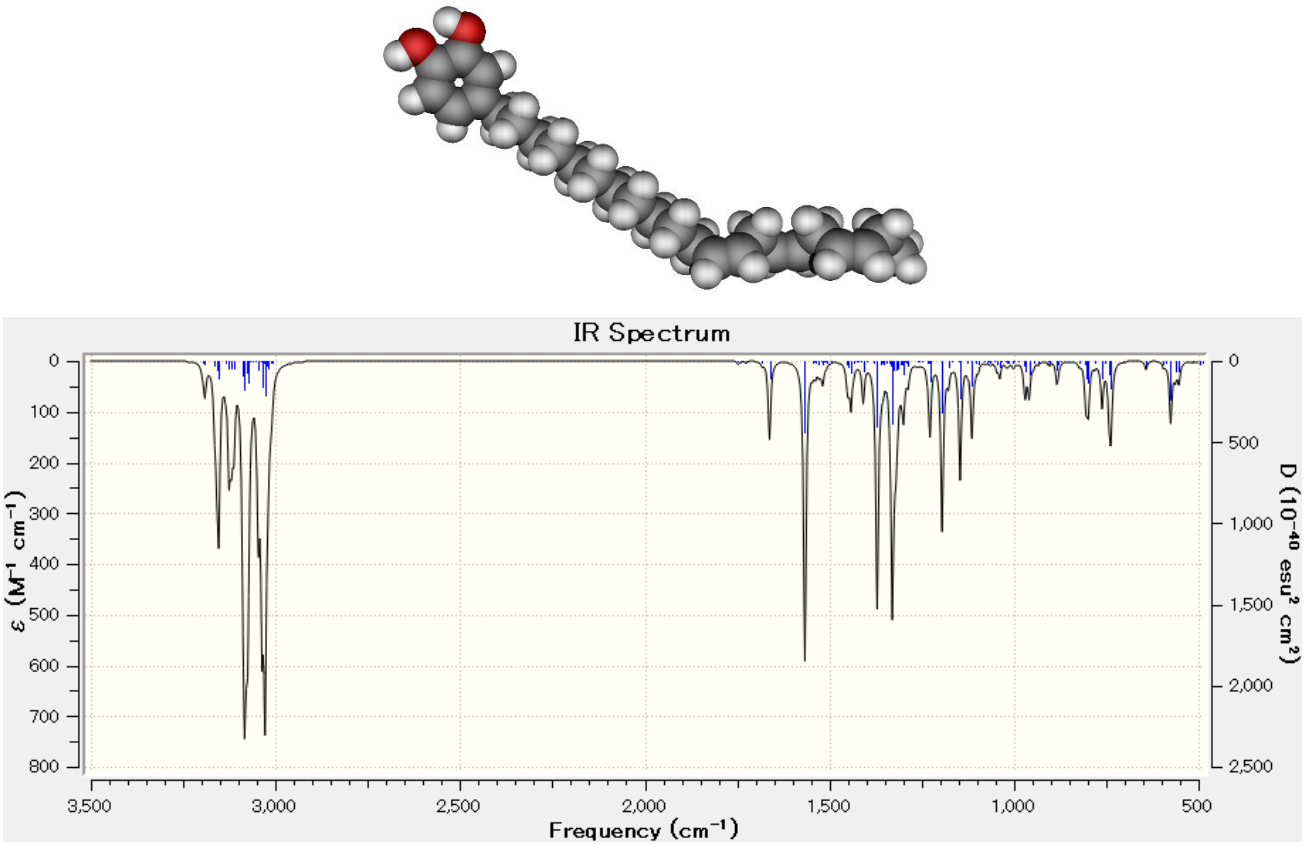


Figure S2. DFT-calculated structure and IR spectrum of **G-urushiol**.

[10] Gaussian 16, Revision C.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2016.

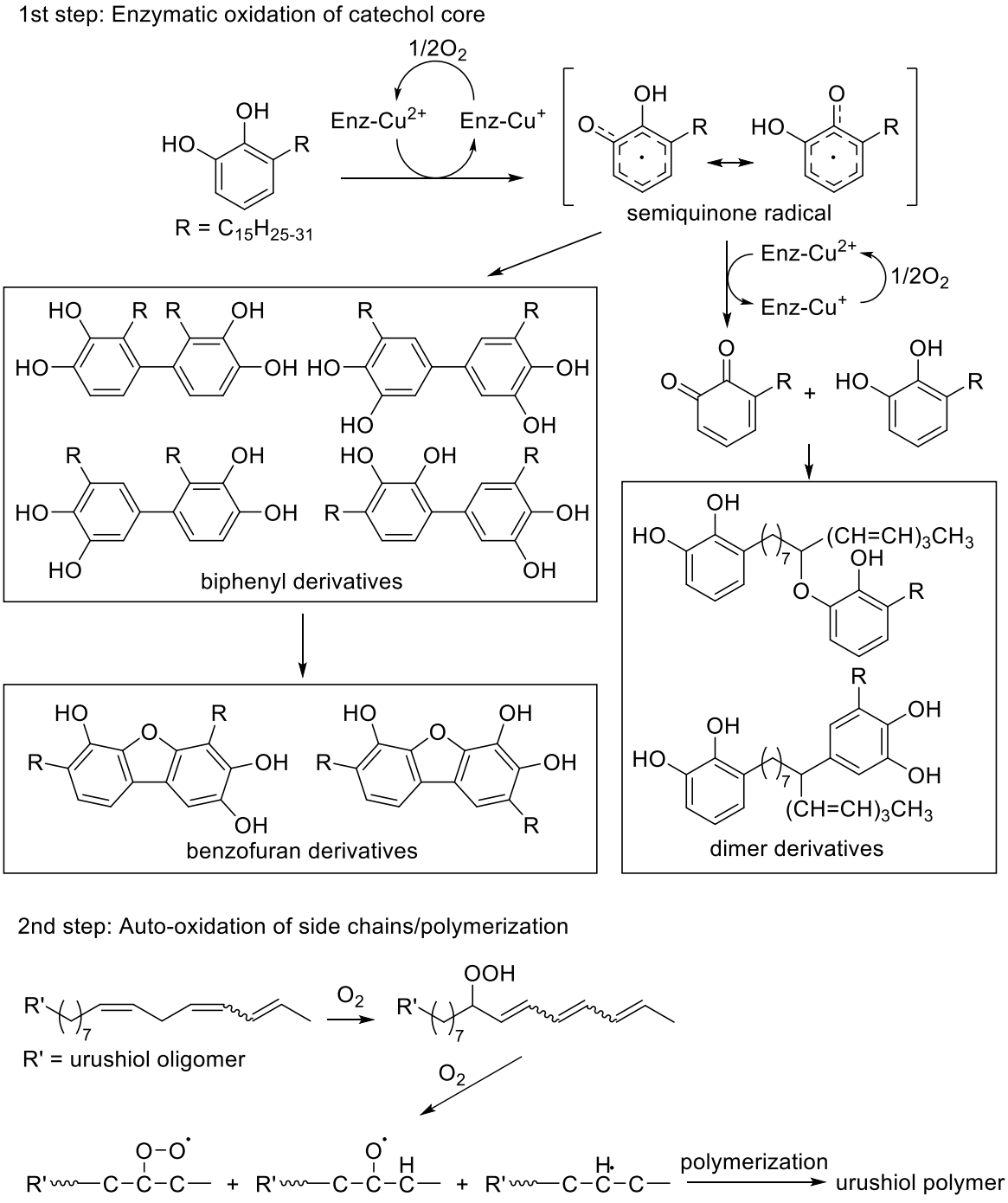


Figure S3. Proposed mechanism of urushiol polymerization.[11]

[11] (a) Lu, R.; Yoshida, T.; Miyakoshi, T. *Pol. Rev.* **2013,** *53*, 153. (b) Kumanotani, J. *Prog. Org. Coat.* **1998,** *34*, 135.

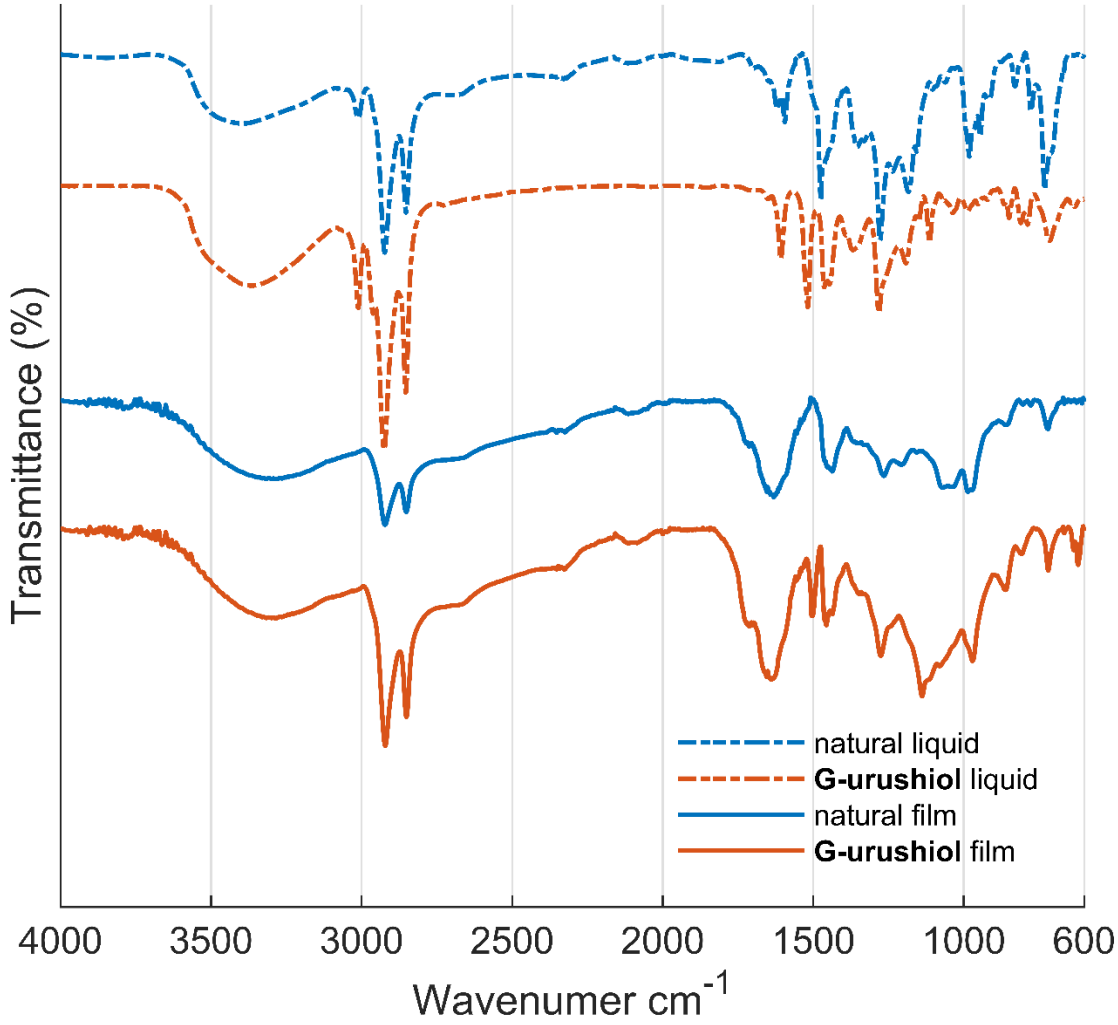
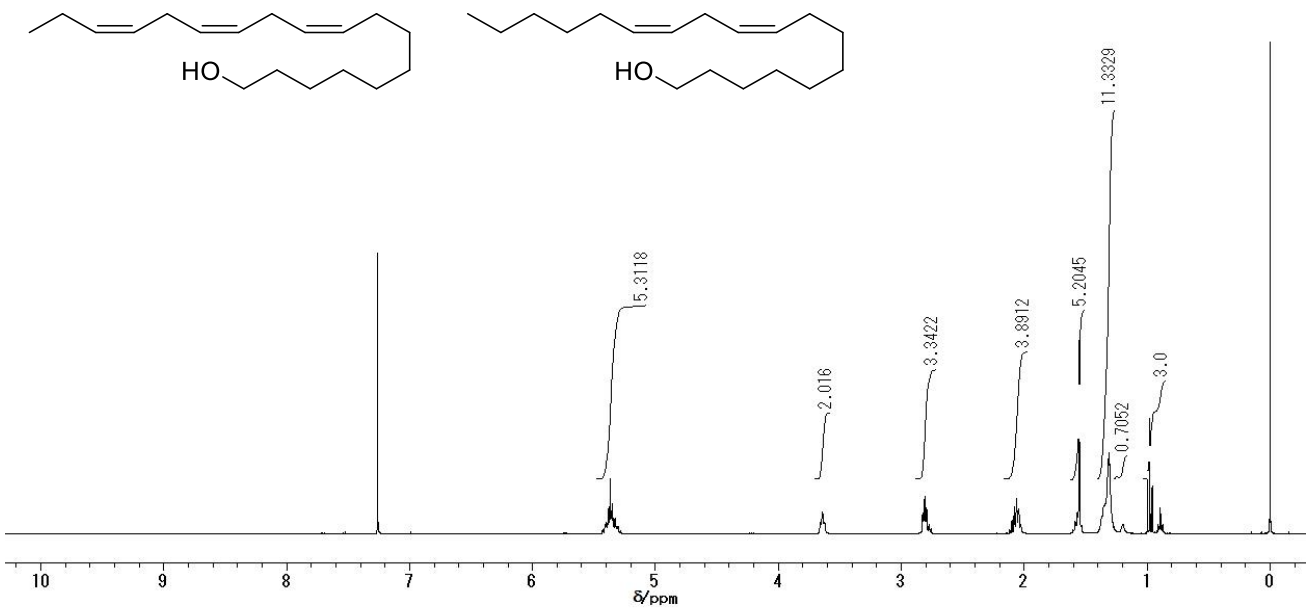
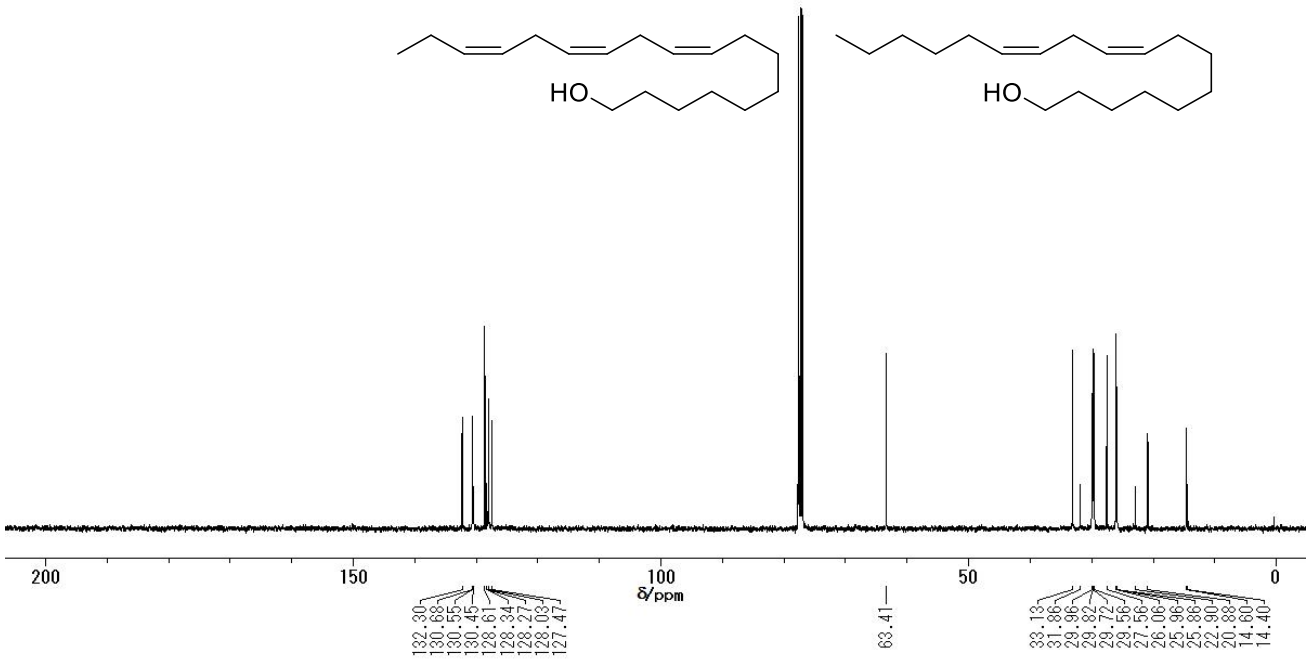


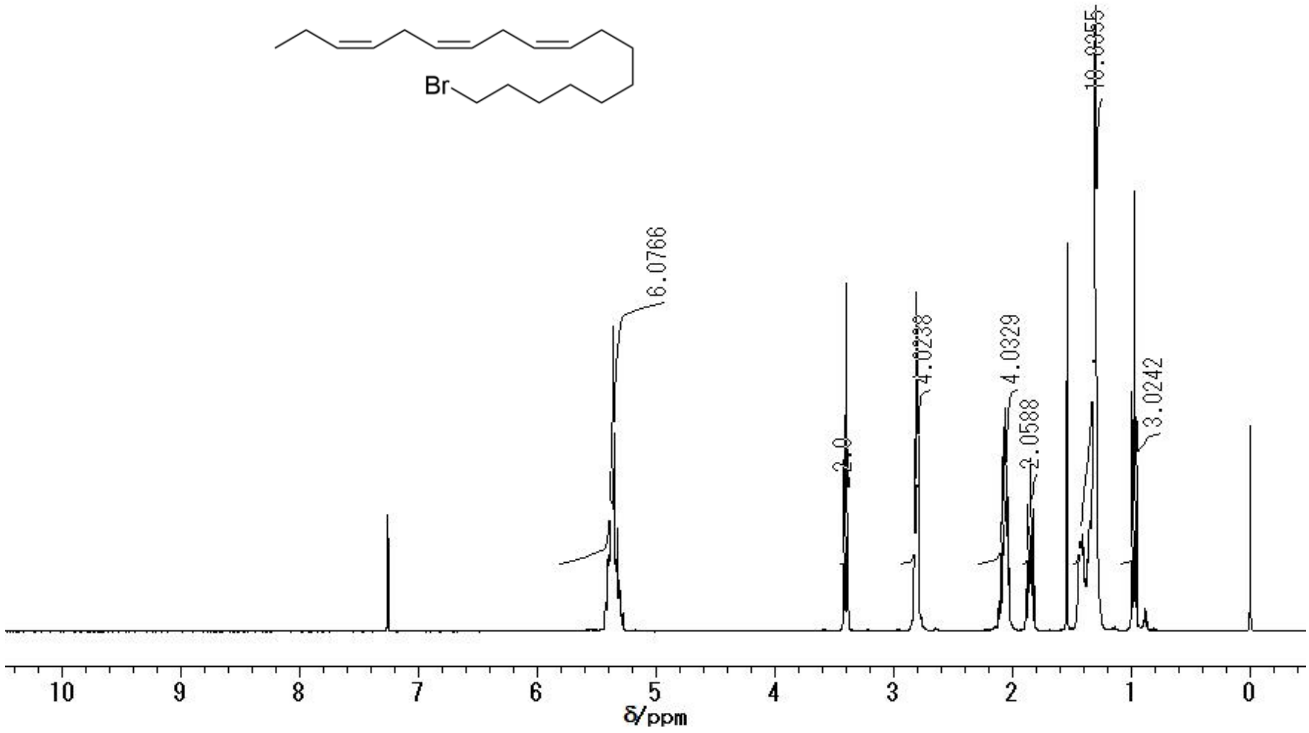
Figure S4. Full-range IR spectra of liquid state (dotted line) and cured film (solid line) obtained from natural Chinese urushiol (blue line) and **G-urushiol** (orange line). All spectra have been shifted and normalized for clarity.



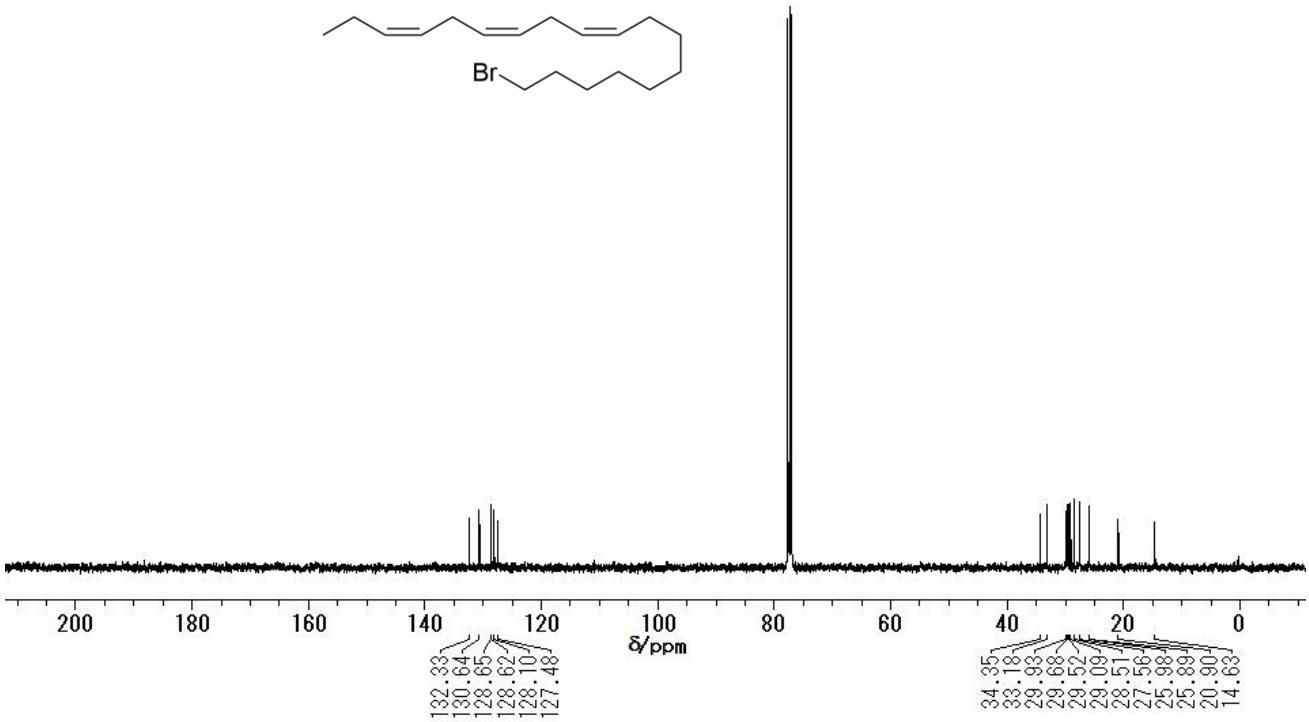
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of the mixture of linolenyl alcohol and linoleyl alcohol.



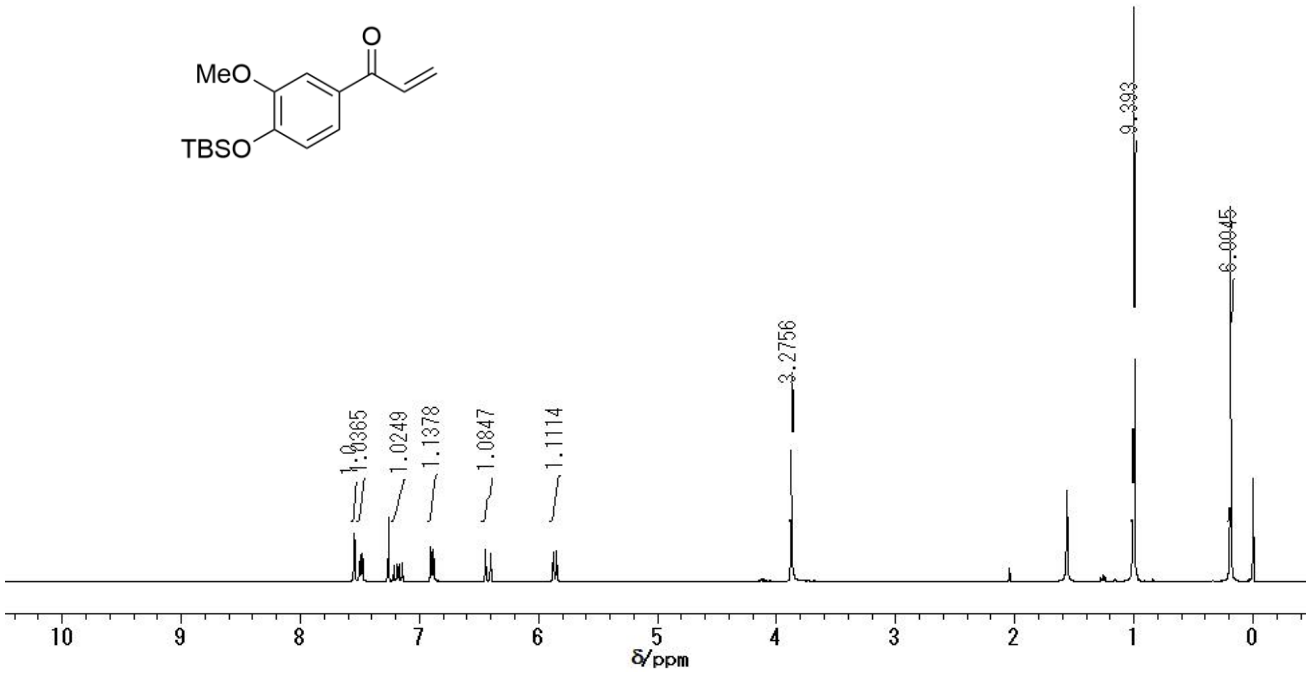
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of the mixture of linolenyl alcohol and linoleyl alcohol.



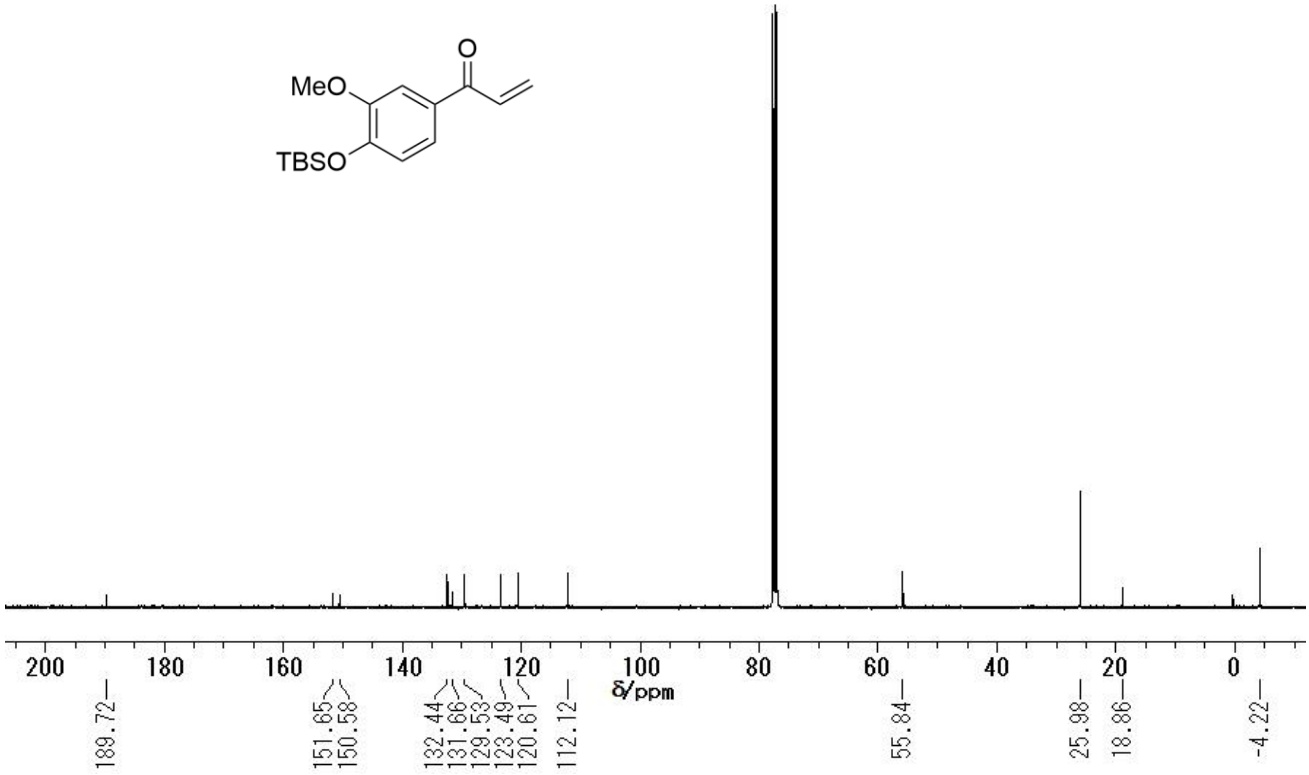
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of (3*Z*,6*Z*,9*Z*)-18-bromooctadeca-3,6,9-triene.



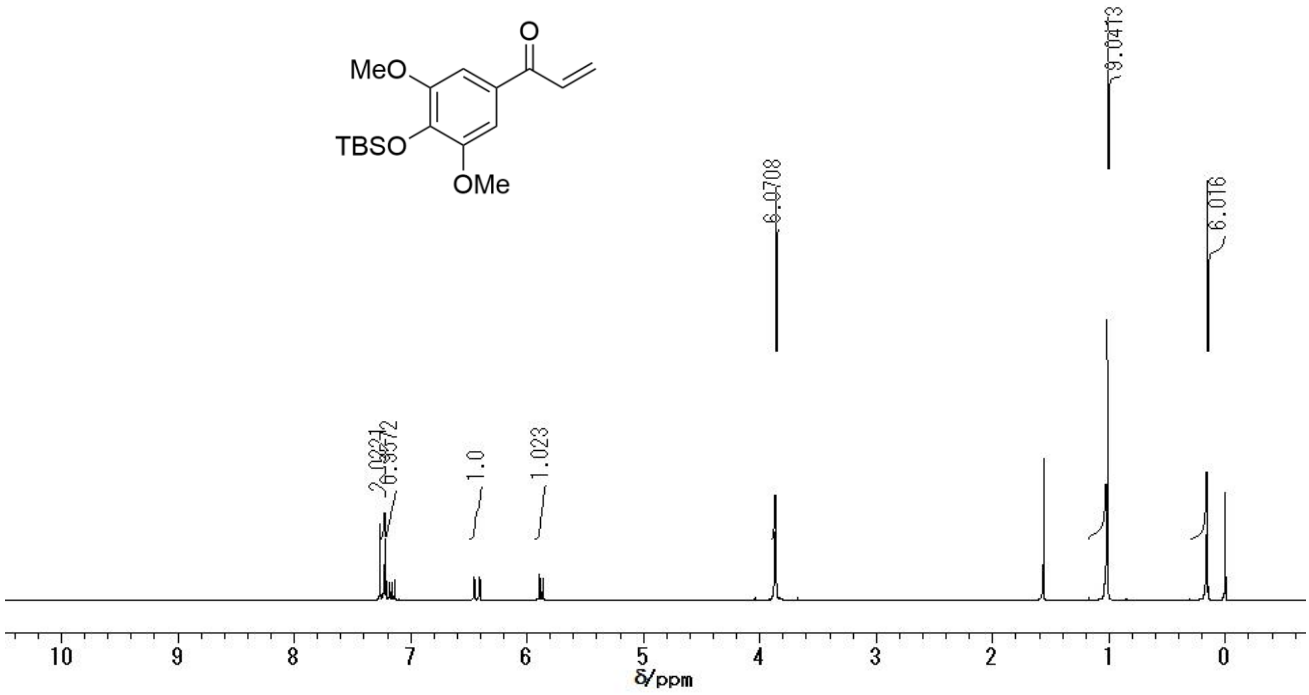
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of (3*Z*,6*Z*,9*Z*)-18-bromooctadeca-3,6,9-triene.



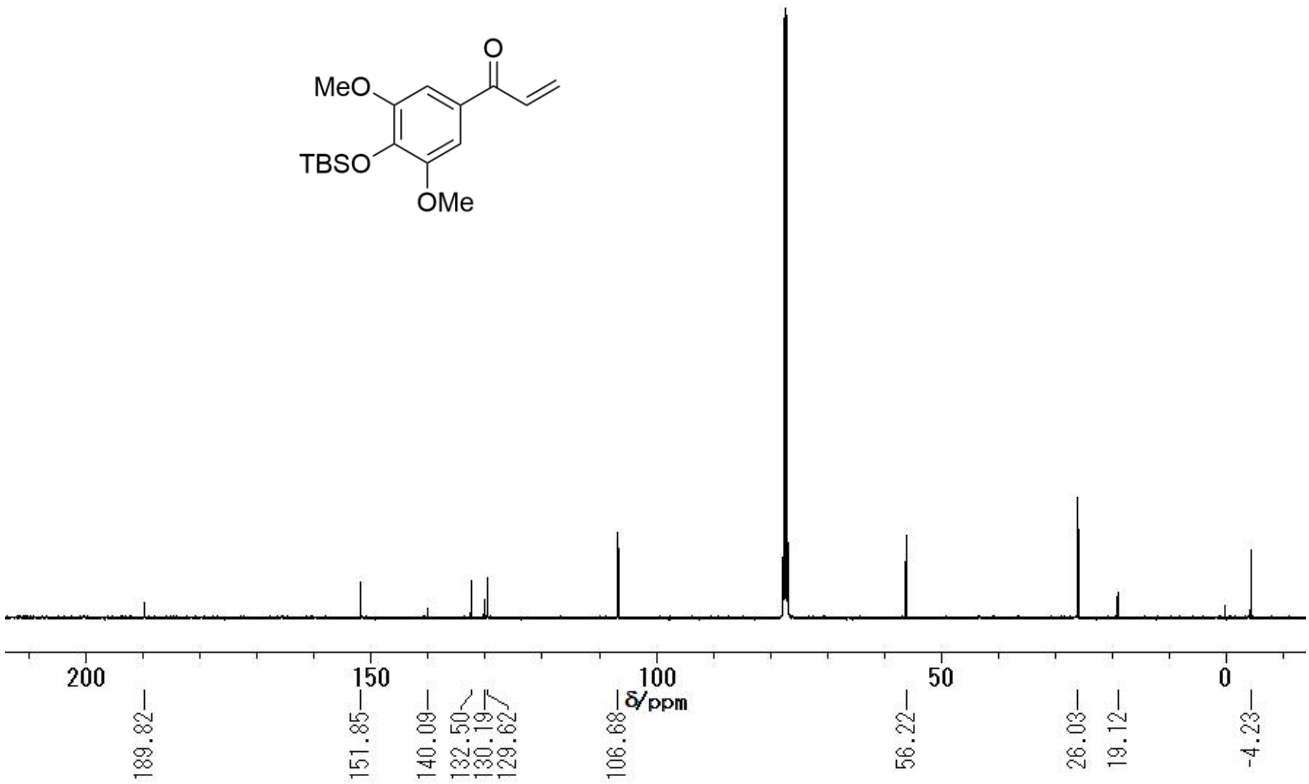
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of 1-[4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl]-propen-1-one (**G-2**).



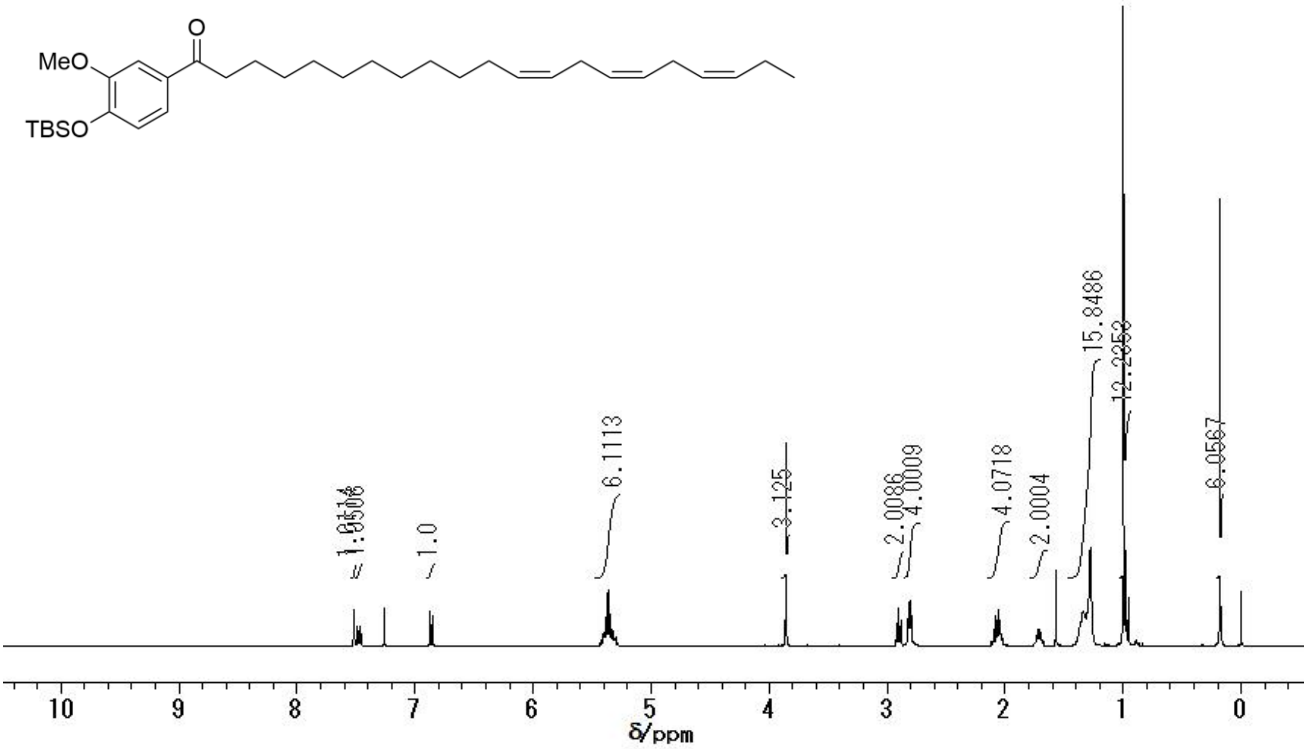
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of 1-[4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl]-propen-1-one (**G-2**).



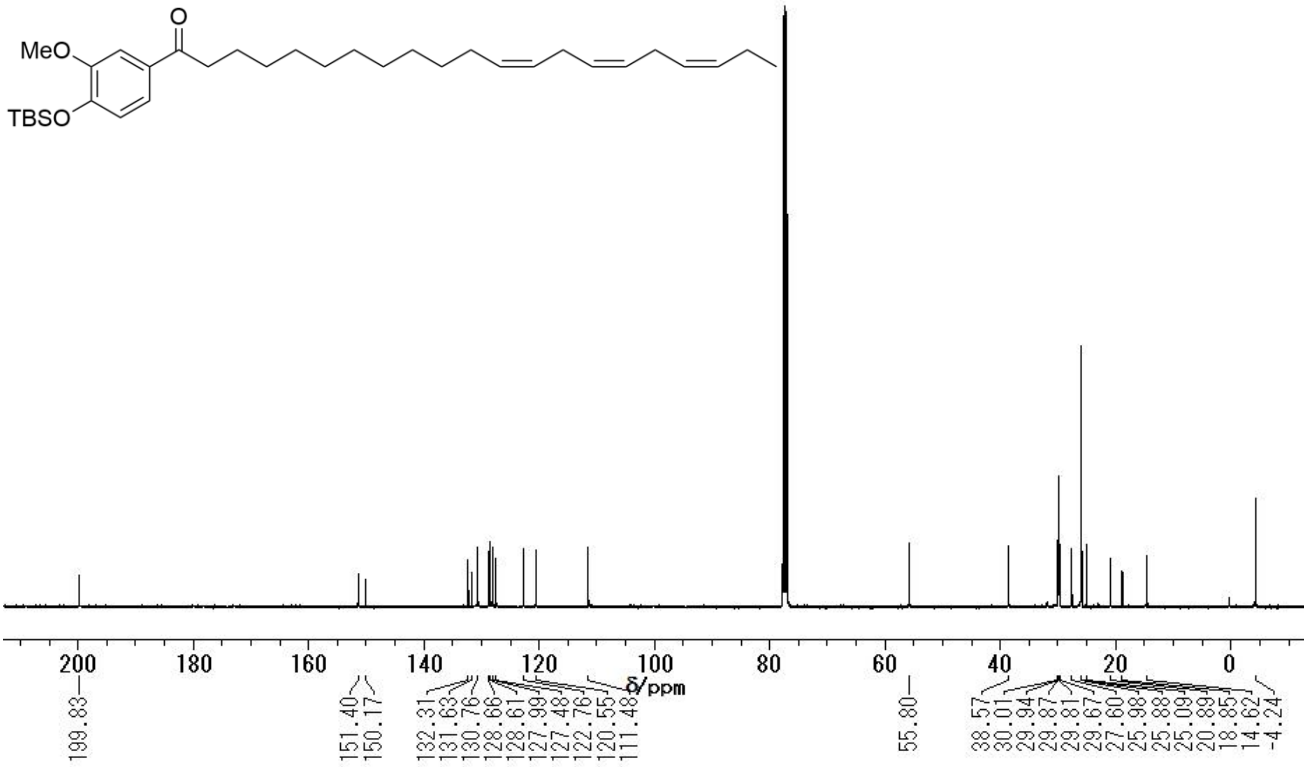
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of 1-[4-(*tert*-Butyldimethylsilyloxy)-3,5-dimethoxyphenyl]-propen-1-one (**S-2**).



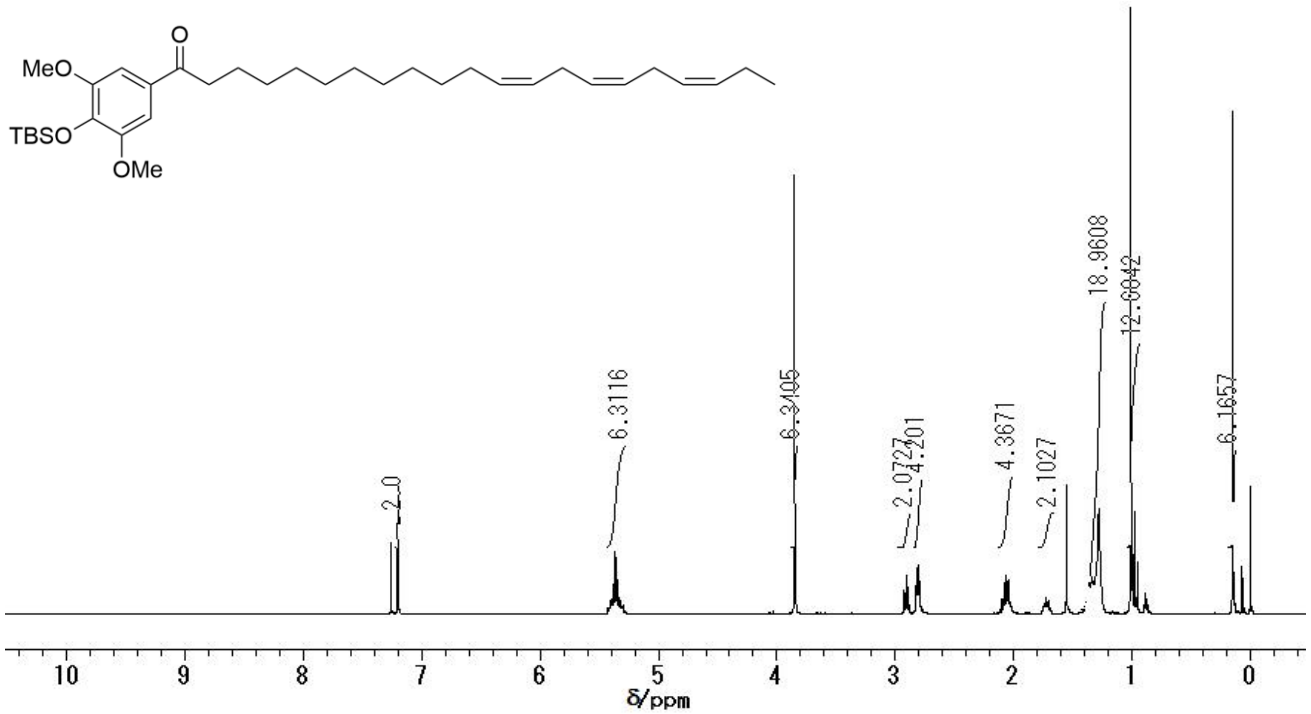
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of 1-[4-(*tert*-Butyldimethylsilyloxy)-3,5-dimethoxyphenyl]-propen-1-one (**S-2**).



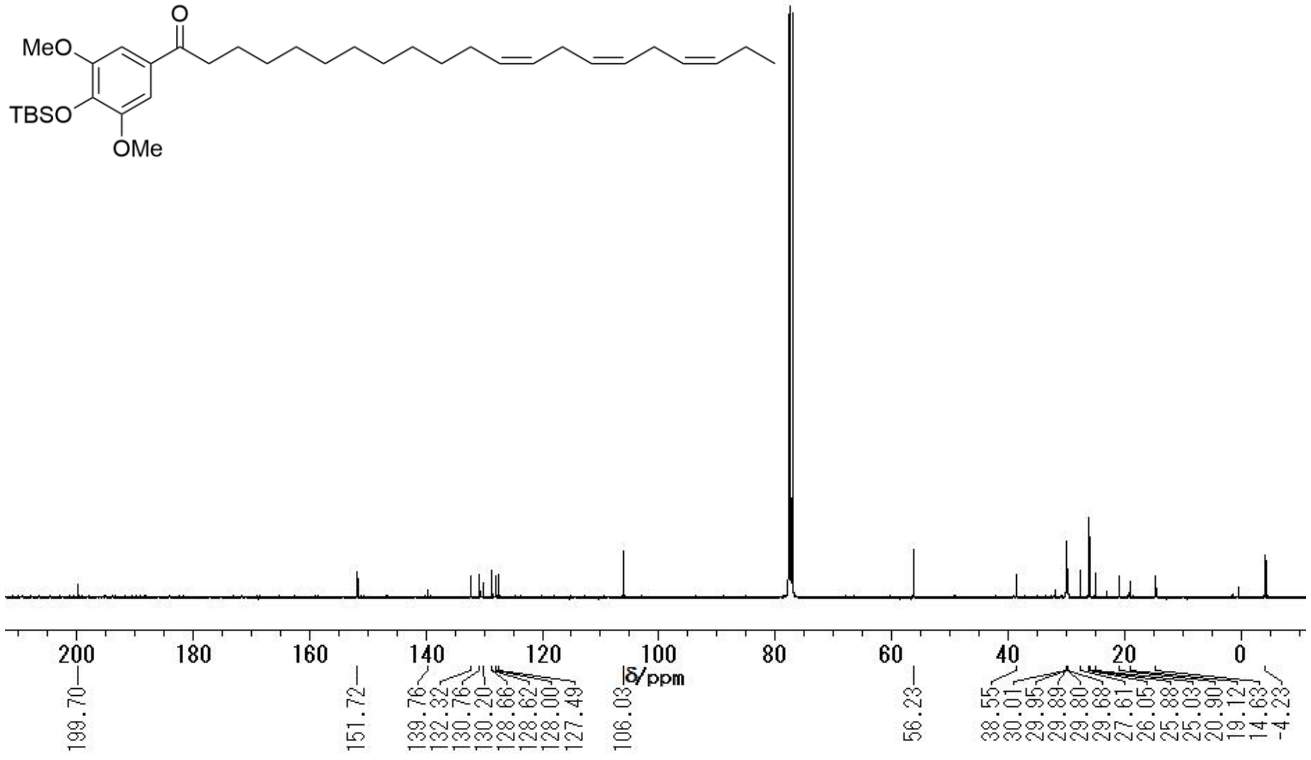
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of (12*Z*,15*Z*,18*Z*)-1-[4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl]henicosa-12,15,18-trien-1-one (**G-3**).



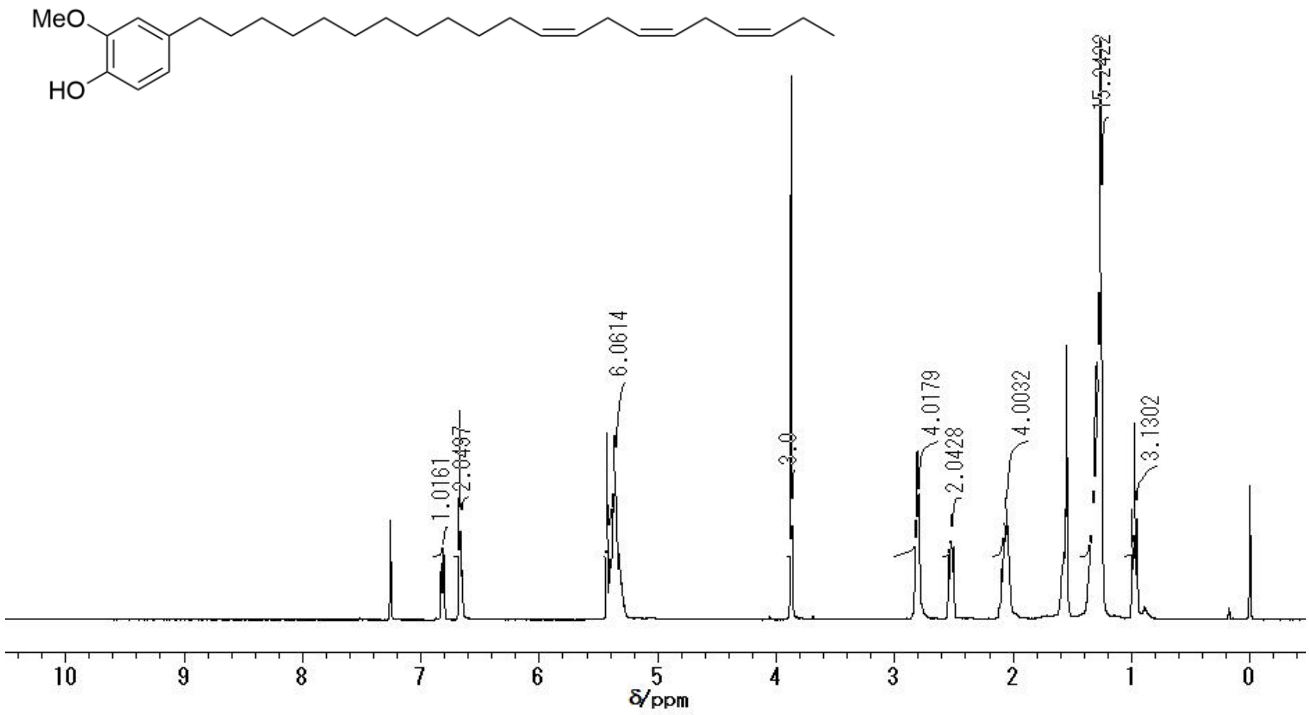
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of (12*Z*,15*Z*,18*Z*)-1-[4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl]henicosa-12,15,18-trien-1-one (**G-3**).



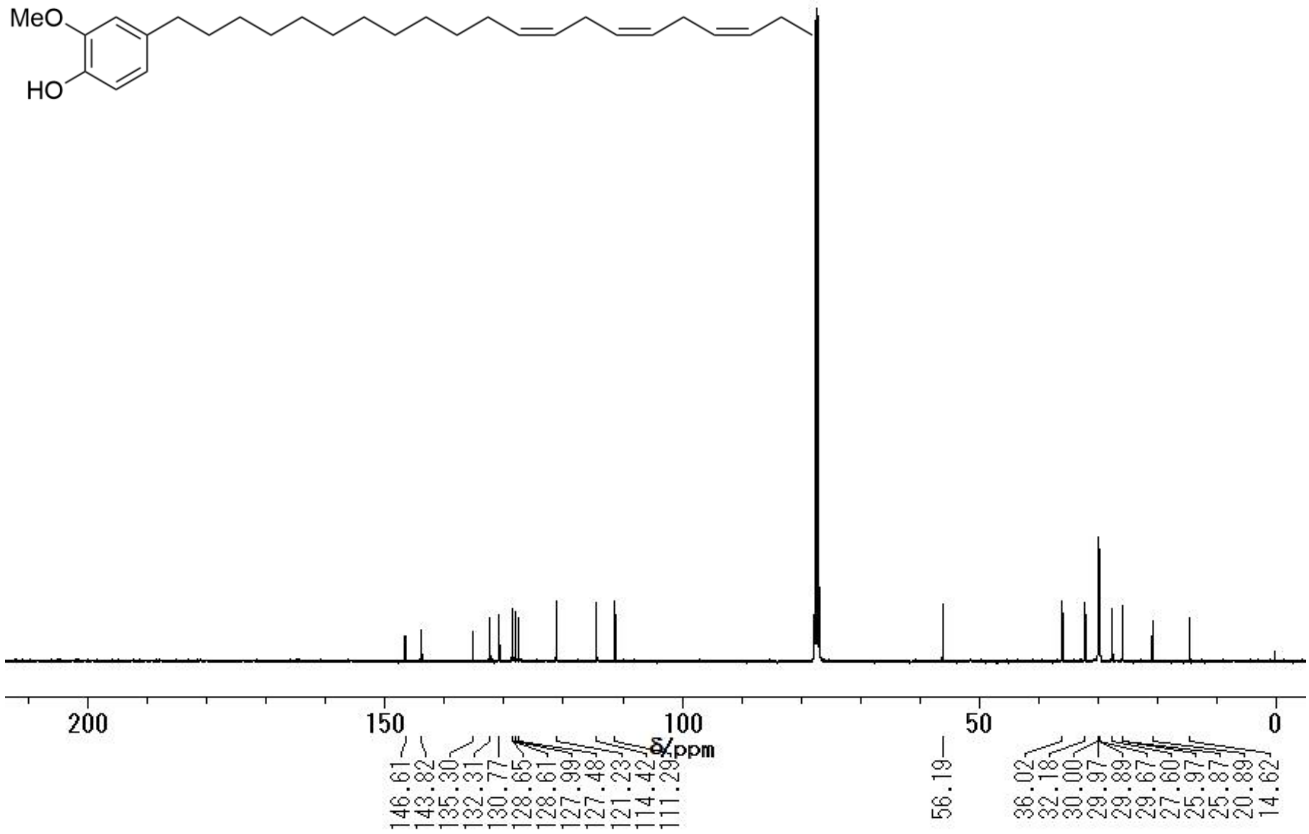
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of (12*Z*,15*Z*,18*Z*)-1-[4-(*tert*-Butyldimethylsilyloxy)-3,5-dimethoxyphenyl]henicosa-12,15,18-trien-1-one (**S-3**).



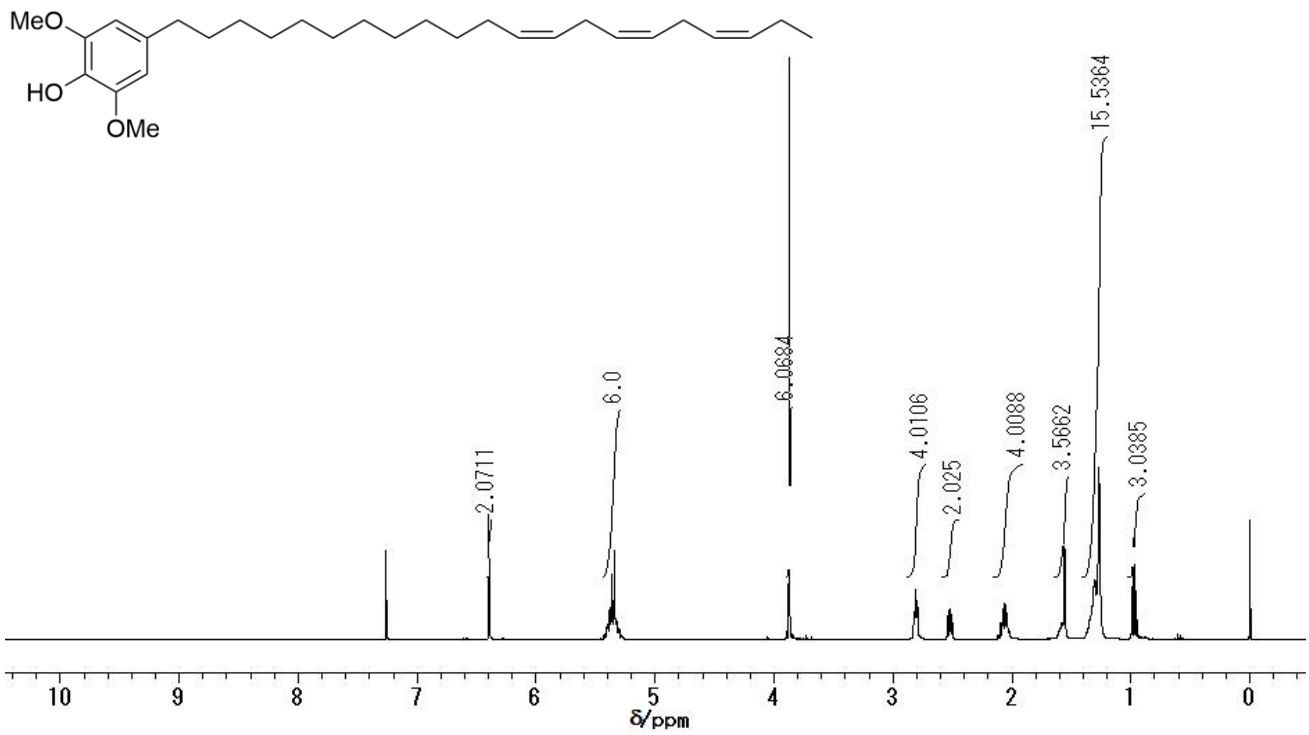
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of (12*Z*,15*Z*,18*Z*)-1-[4-(*tert*-Butyldimethylsilyloxy)-3,5-dimethoxyphenyl]henicosa-12,15,18-trien-1-one (**S-3**).



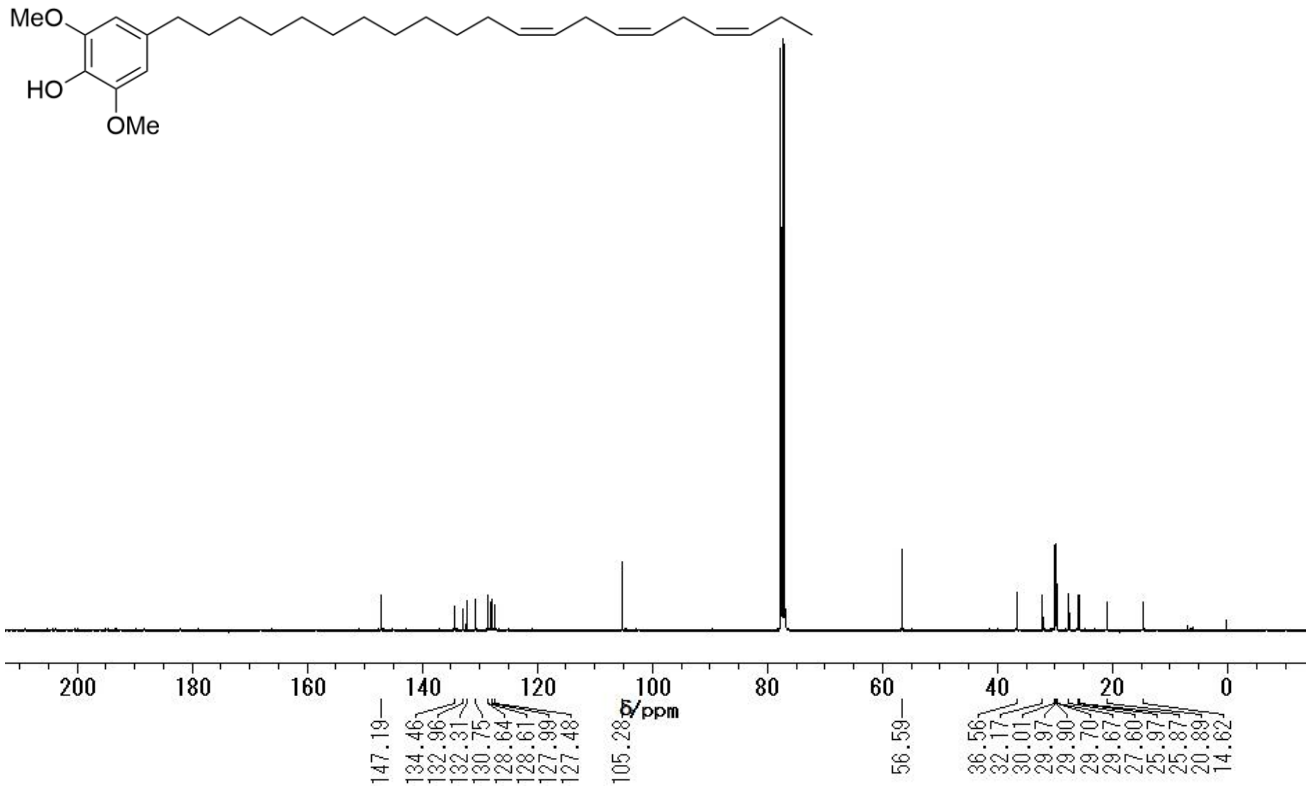
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of 4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]-2-methoxypnehol (**Me-G-urushiol**).



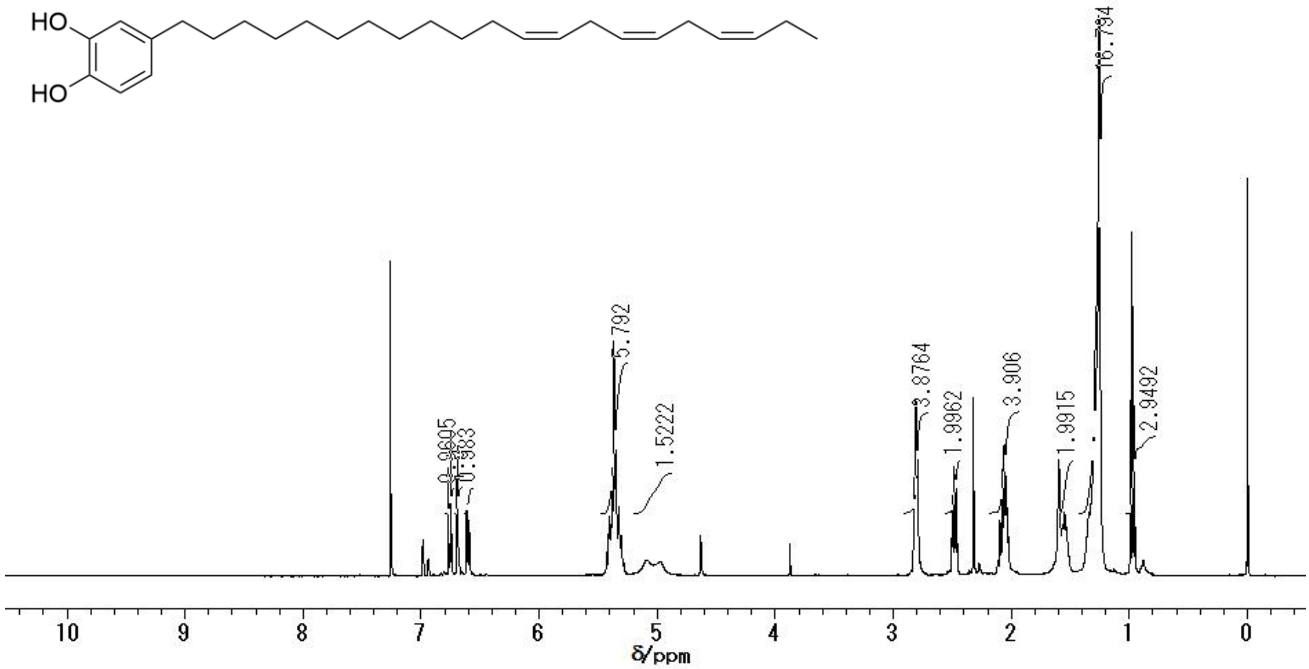
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of 4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]-2-methoxypnehol (**Me-G-urushiol**).



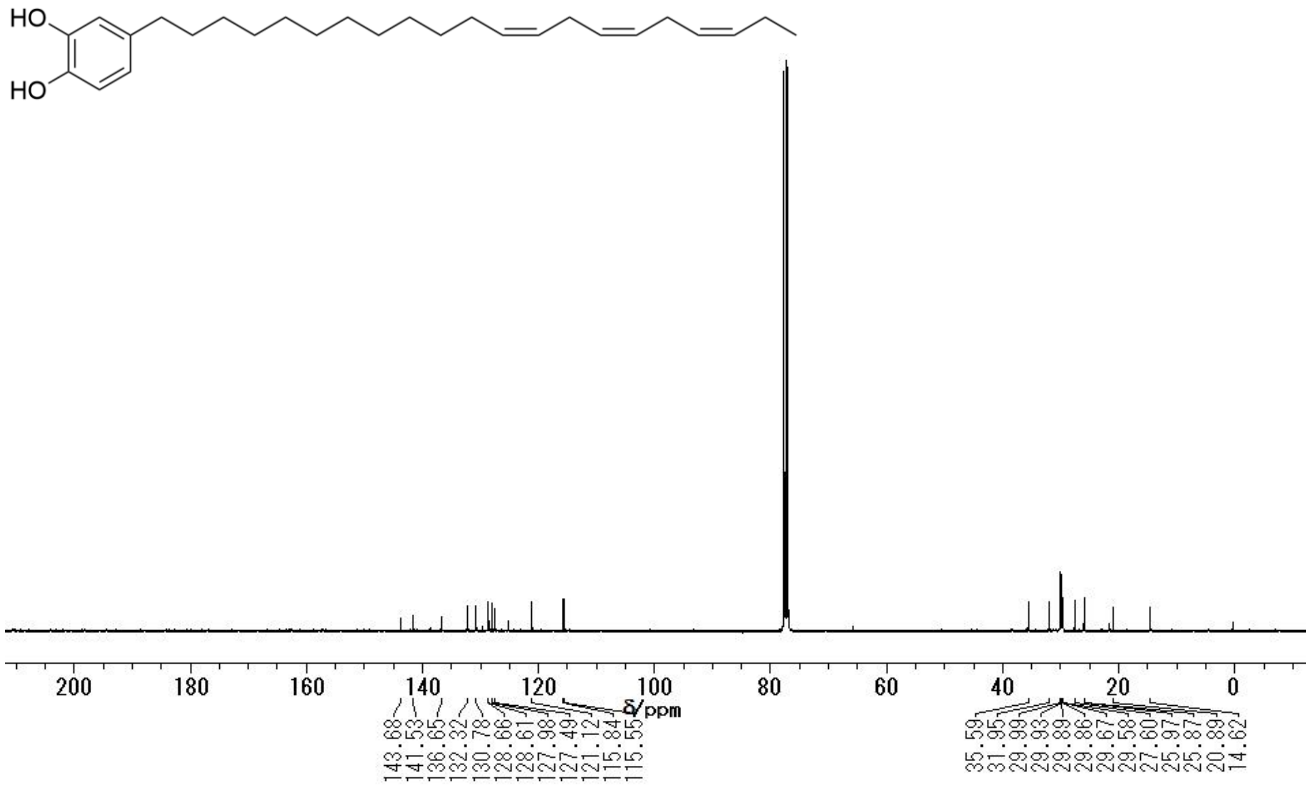
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of 2,6-Dimethoxy-4-[(12*Z*,15*Z*,18*Z*)-henicosa-12,15,18-trienyl]phenol (**Me-S-urushiol**).



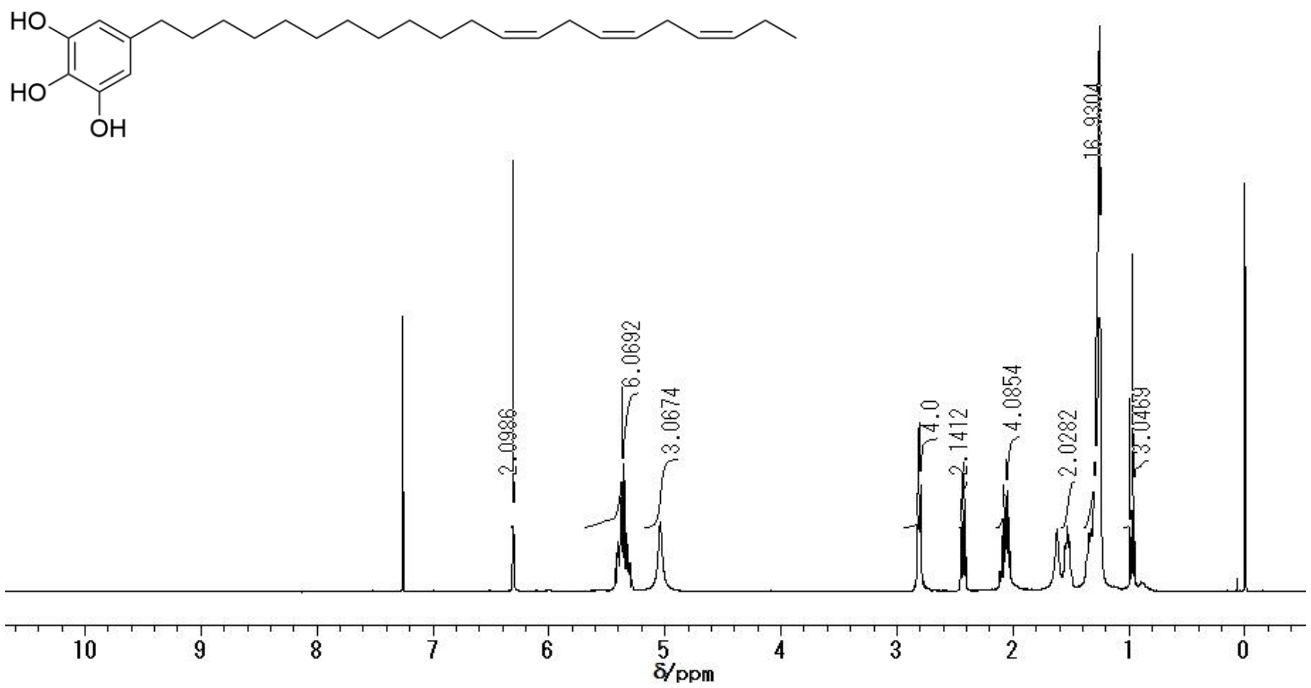
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of 2,6-Dimethoxy-4-[(12*Z*,15*Z*,18*Z*)-henicosa-12,15,18-trienyl]phenol (**Me-S-urushiol**).



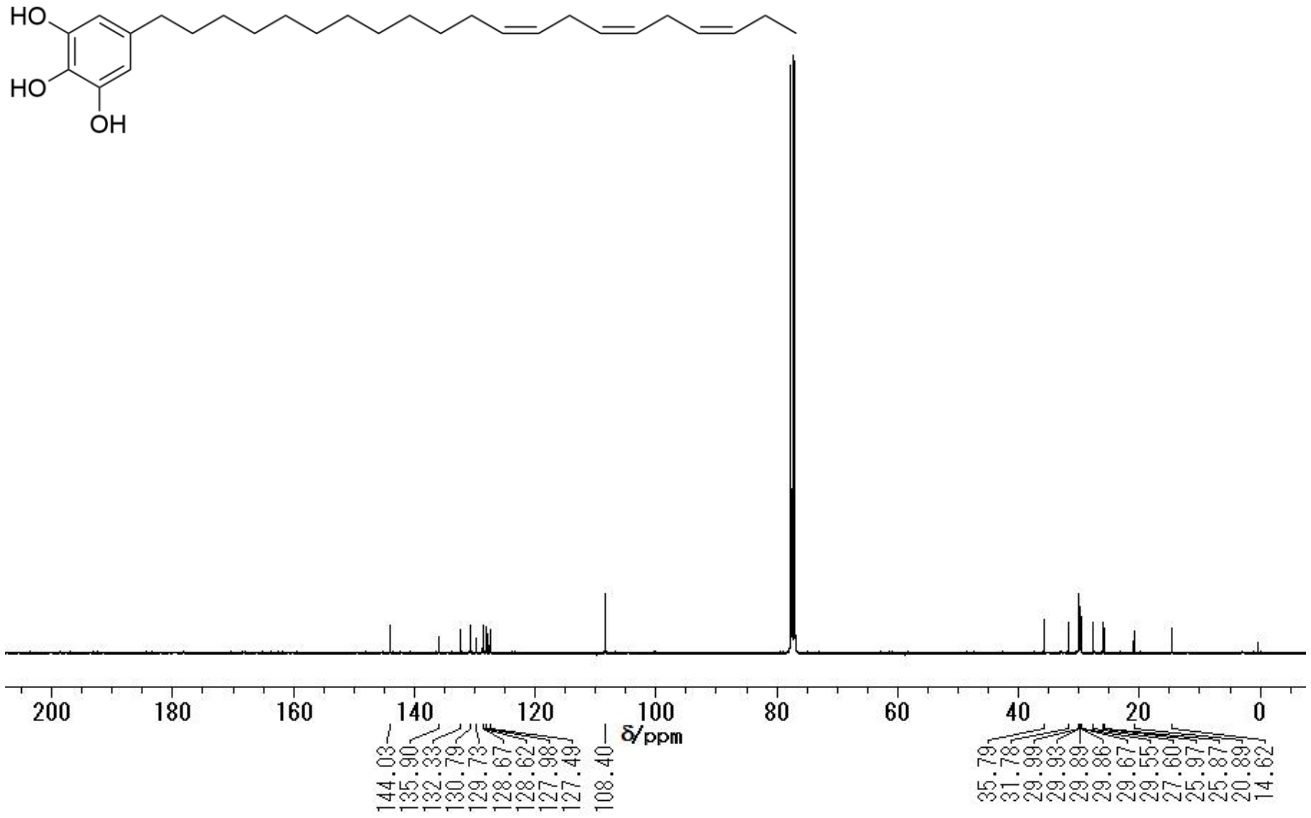
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of 4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]catechol (**G-urushiol**).



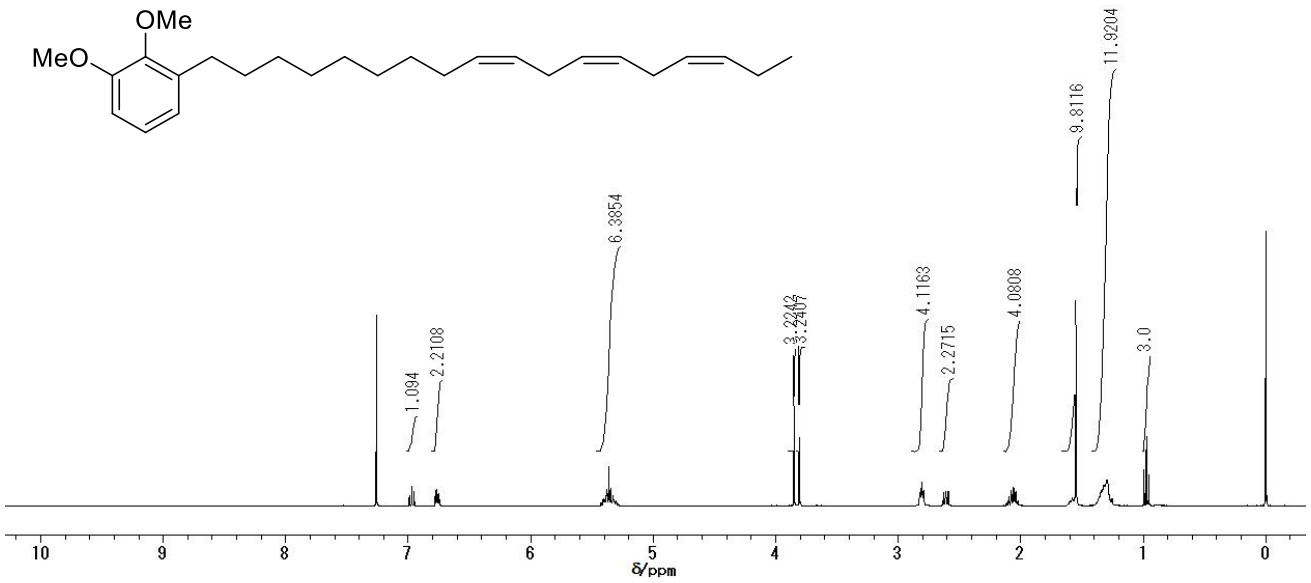
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of 4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]catechol (**G-urushiol**).



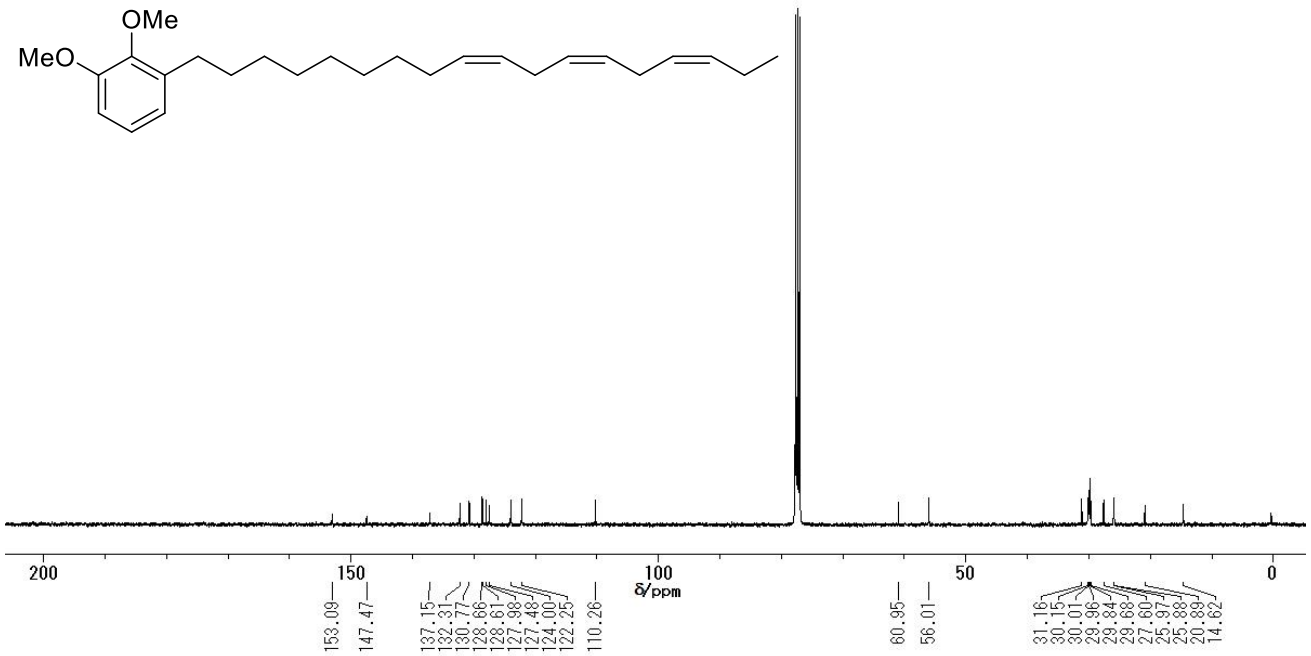
^{1}H NMR spectrum (391.8 MHz, $CDCl_3$) of 4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]pyrogallol (**S-urushiol**).



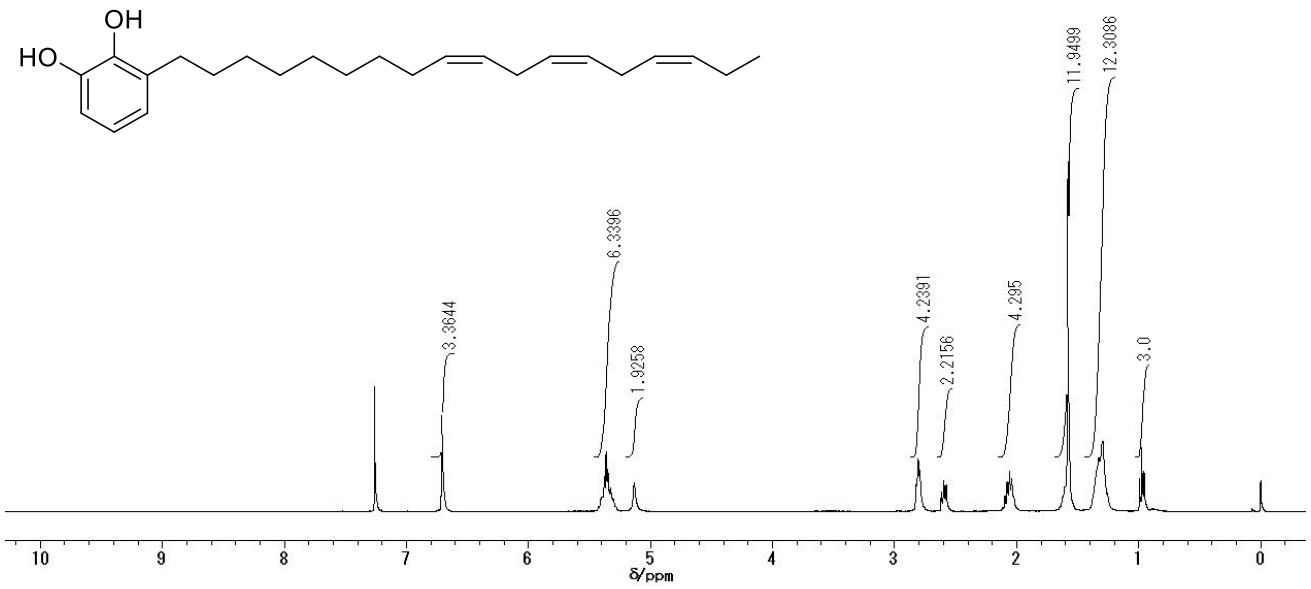
^{13}C NMR spectrum (98.5 MHz, $CDCl_3$) of 4-[(12*Z*,15*Z*,18*Z*)-Henicosa-12,15,18-trienyl]pyrogallol (**S-urushiol**).



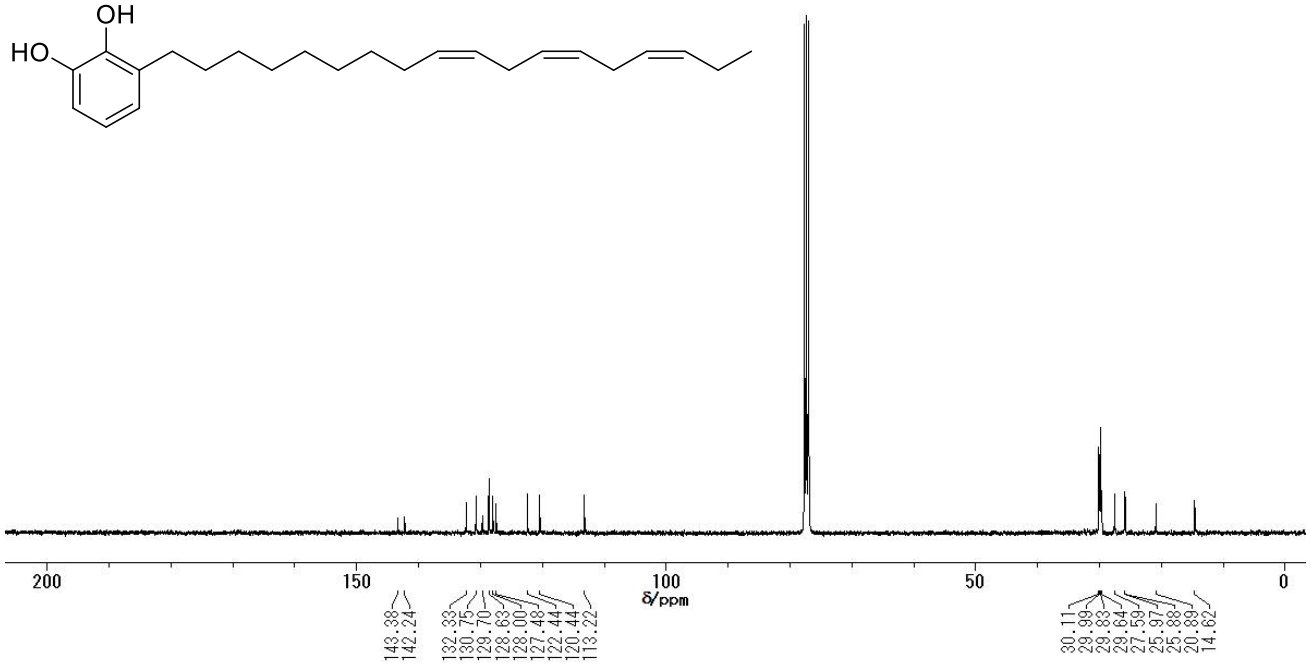
^{1}H NMR spectrum of 1,2-Dimethoxy-3-[(12*Z*,15*Z*,18*Z*)-octadeca-12,15,18-trienyl]benzene (**5**).



^{13}C NMR spectrum of 1,2-Dimethoxy-3-[(12*Z*,15*Z*,18*Z*)-octadeca-12,15,18-trienyl]benzene (**5**).



^{1}H NMR spectrum of 3-[(12*Z*,15*Z*,18*Z*)-Octadeca-12,15,18-trienyl]catechol (**4**).



^{13}C NMR spectrum of 3-[(12*Z*,15*Z*,18*Z*)-Octadeca-12,15,18-trienyl]catechol (**4**).