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Anodic Oxidation of 4-Hydroxycinnamic Acids and Related Phenols

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Anodic oxidation of 4-hydroxycinnamic acids, 4-hydroxycinnamamides and related phenols was carried out at a controlled potential, using an undivided cell, to afford the corresponding asatone-, isoasatone-, pinoresinol- or podophyllotoxin-type compounds. Furthermore, the corresponding dihydroxy compounds were also electrolyzed at a controlled potential to give different dienones depending on the side chains.

Keywords——neolignan; electrochemical oxidation; Diels–Alder reaction; biomimetic synthesis

In recent years, bioactive lignans and neolignans have been attracting increasing attention.[1,2] In connection with our interest in the asatone- and isoasatone-type neolignans[3] as well as in plant germination inhibitors,[4] anodic oxidation of 4-hydroxycinnamic acids, 4-hydroxycinnamamides and their dihydro derivatives was carried out at a controlled potential, using a glassy carbon beaker as an anode and the tip of a platinum wire as a cathode, without separation.

Results and Discussion

As can be seen in Fig. 1, ferulic acid (**1**) has one anodic peak in its cyclic voltammogram, suggesting that the oxidation potential at the initial step leading to the formation of a cationic radical is nearly equal to or higher than that in the second oxidation step affording the corresponding cation. In such a case, it is expected that both radical and cationic reactions will take place competitively. Thus, a solution of ferulic acid (**1**) (10 mmol/l) in MeOH containing $LiClO_4$ (0.2 mol/l) as a supporting electrolyte was electrolyzed at a controlled potential (+900 mV *vs.* SCE; 1.7 F/mol) to afford a bislactone (**2**) and an asatone-type dimer (**3**) in 11 and 62% yields, respectively. At a low current density (1 mmol/l), however, the asatone-type compound (**3**) was produced from **1** in almost quantitative yield, as judged from high performance liquid chromatography (HPLC) results. Of these two oxidation products, the bislactone (**2**) has already been synthesized from **1** using $FeCl_3$–O_2,[5] an oxidation system with which many lignans have been obtained.[5,6] The identity of the asatone-type dimer (**3**) was deduced on the basis of its spectral data together with some chemical evidence, as follows. On methylation with diazomethane in ether–MeOH (room temp., overnight), this dimer was readily converted into the corresponding dimethyl ester (**4**). As described in the case of the photochemical reaction of demethoxyasatone leading to the formation of demethoxyisoasatone, a cage-compound,[7] the dimethyl ester (**4**) was subjected to photochemical reaction using a Pyrex filter to give an isoasatone-type compound (**5**), which has the same symmetric character as isoasatone and demethoxyisoasatone,[3,7] on the basis of its proton nuclear magnetic resonance (^1H NMR) spectrum δ: 2.88 (2H, s), 3.07 (2H, br d, J=4.5 Hz), 3.24

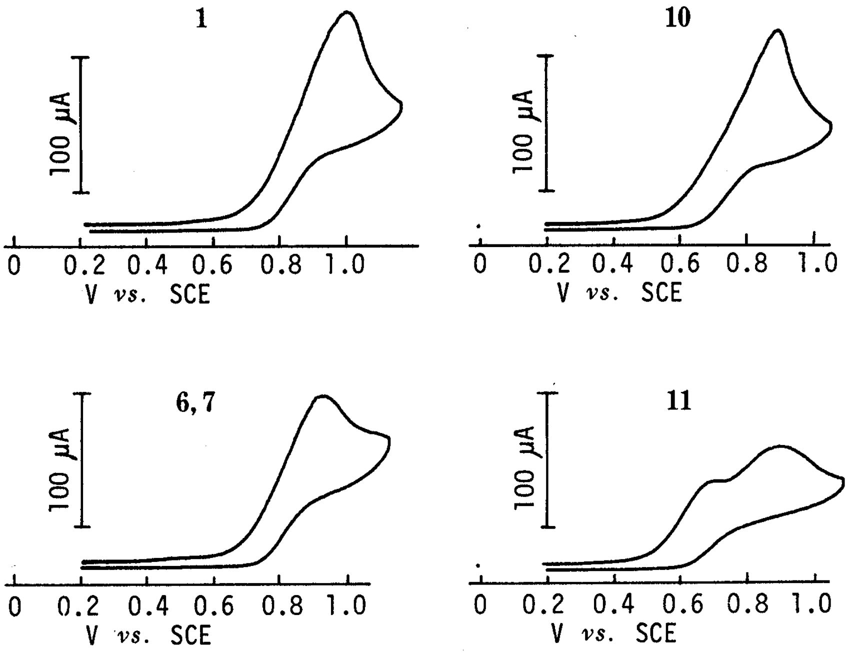
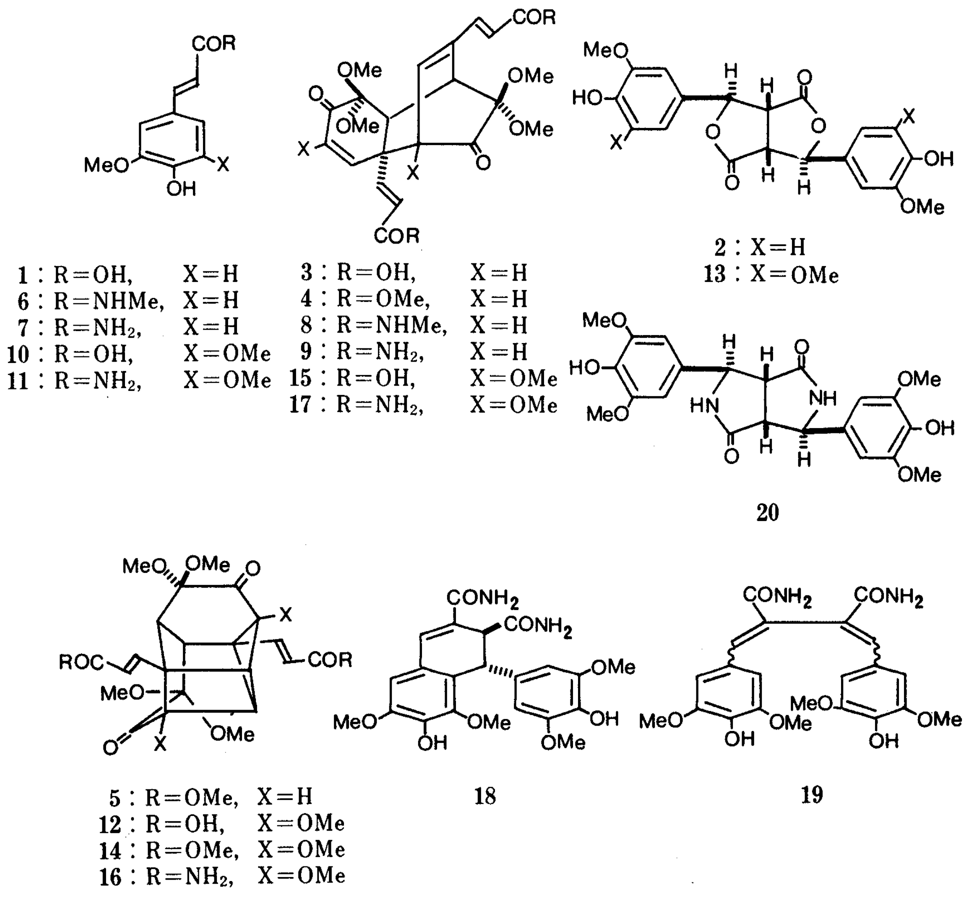


Fig. 1. Cyclic Voltammograms of 5 Phenols (**1**, **6**, **7**, **10** and **11**)

1 (2.0 mM), **6** (2.0 mM), **7** (2.0 mM), **10** (2.0 mM), **11** (2.0 mM); supporter, $LiClO_4$ (0.2 M); solvent, MeOH; WE, glassy carbon disk (0.26 cm^2); sweep rate, 50 $mV \cdot s^{-1}$.



1 : R=OH, X=H
6 : R=NHMe, X=H
7 : $R=NH_2$, X=H
10 : R=OH, X=OMe
11 : $R=NH_2$, X=OMe

3 : R=OH, X=H
4 : R=OMe, X=H
8 : R=NHMe, X=H
9 : $R=NH_2$, X=H
15 : R=OH, X=OMe
17 : $R=NH_2$, X=OMe

2 : X=H
13 : X=OMe

20

5 : R=OMe, X=H
12 : R=OH, X=OMe
14 : R=OMe, X=OMe
16 : $R=NH_2$, X=OMe

18

19

Chart 1

(6H, s), 3.00 (2H, br d, $J=4.5$ Hz), 3.39 (6H, s), 3.77 (6H, s), 5.76 (2H, d, $J=16$ Hz) and 7.11 (2H, d, $J=16$ Hz).

In order to obtain some asatone-type dimers, we further carried out anodic oxidation of 4-hydroxycinnamamides (**6** and **7**) at higher potential (sufficient to form a cation); this reaction could yield a trienone as a plausible precursor of the asatone-type dimer. When electrolyzed at a controlled potential (+1400 mV *vs*. SCE; 2.3 F/mol) in methanol containing $LiClO_4$ as a supporting electrolyte, the amide (**6**) was readily converted into the corresponding asatone-type dimer (**8**) in 71% yield. In the case of **7**,[8] an asatone-type dimer (**9**) was also obtained in 56% yield. The structures of these dimers (**8** and **9**) were elucidated by comparing their ^1H NMR spectra with those of **3** and **4**. Furthermore, anodic oxidation of both sinapic acid (**10**) and 4-hydroxycinnamamide (**11**) was also carried out. On electrolysis at a controlled potential (+800 mV *vs*. SCE), with quenching of the reaction at 2.0 F/mol, sinapic acid (**10**) (11.7 mmol/l) was mainly converted into two dimers (**12** and **13**) in 16 and 68% yields, respectively. Furthermore, analytical HPLC indicated that the relative ratio of the yields of these two dimers varied with concentration of the substrate. In the case of a low current density (1 mmol/l), both **12** and **13** were produced in almost the same yields. Of these two dimers, the known bislactone (**13**) has already been synthesized from sinapic acid (**10**),[5,6] as described in the case of ferulic acid (**1**). The structure of the remaining dimer (**12**) was unambiguously determined on the basis of the spectral data of **12** as well as of its dimethyl ester (**14**), which was obtained on treatment of **12** with diazomethane in ether–methanol; in particular, the ^1H NMR spectra of both **12** and **14**, which show only half of the total protons, are quite similar to that of isoasatone,[3] which has a symmetric structure except for the side chains.

In the cases of 4-hydroxycinnamic acids (**1** and **10**), as shown in Chart 2, the radical [A] initially formed is further oxidized, in competition with the radical dimerization leading to the formation of a plausible bis-*p*-quinonemethide [B], to give the corresponding cation [C], from which the dienone [D] should be produced. Then, further dimerization of this dienone affords the asatone-type dimer (**3** or **15**).[9] Interestingly, in the case of the latter, having one more methoxyl group attached to the double bond conjugated to the carbonyl group, further cyclization may take place in a stepwise manner to afford the corresponding isoasatone-type dimer (**12**).

As can be seen in Fig. 1, the cyclic voltammogram of 4-hydroxy-3,5-dimethoxycinnamamide (**11**) shows two peak potentials at +690 and +900 mV *vs*. SCE, which correspond to the initial oxidation step leading to the formation of a radical cation[10] and to the second oxidation step affording the corresponding cation, respectively. According to the same procedure as described for **1** and **10**, the amide (**11**) having two methoxyl groups on the aromatic ring was also subjected to electrochemical oxidation at a controlled potential (+1000 mV *vs*. SCE; 1.8 F/mol) to give an isoasatone-type dimer (**16**) *via* a plausible intermediate (**17**), in 85% yield.[11] The structure of **16** was determined by comparing its ^1H NMR spectrum with that of **14**. However, a solution of **11** (12 mmol/l) in MeOH containing $LiClO_4$ (0.2 mol/l) was electrolyzed at a lower potential (+650 mV *vs*. SCE) and the reaction was quenched at 1.0 F/mol to afford two radical-coupling dimers (**18** and **19**) in 14 and 19% yields, respectively, in addition to a small amount of **16**.[12] The structures of these two dimers (**18** and **19**) were also supported by their infrared (IR) and ^1H NMR spectra: in particular, the stereostructure of **18** is based on the coupling constant ($J \simeq 0$ Hz) of the methine signal [δ 4.70 (1H, s)], which indicates that the two adjacent methine protons are *trans* to each other.[13] In contrast to the radical coupling dimer (**13**) from sinapic acid (**10**), neither bislactone (**13**) nor bislactam (**20**) was detected, indicating that the $CONH_2$ group at the side chain cannot easily attack the exocyclic double bond in the plausible intermediate [B].

Finally, anodic oxidation of the corresponding dihydro compounds was also examined,

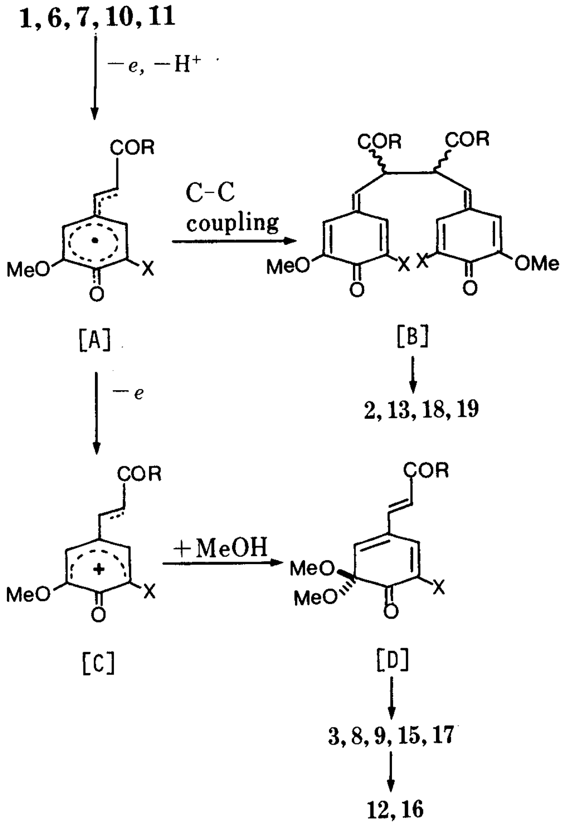


Chart 2

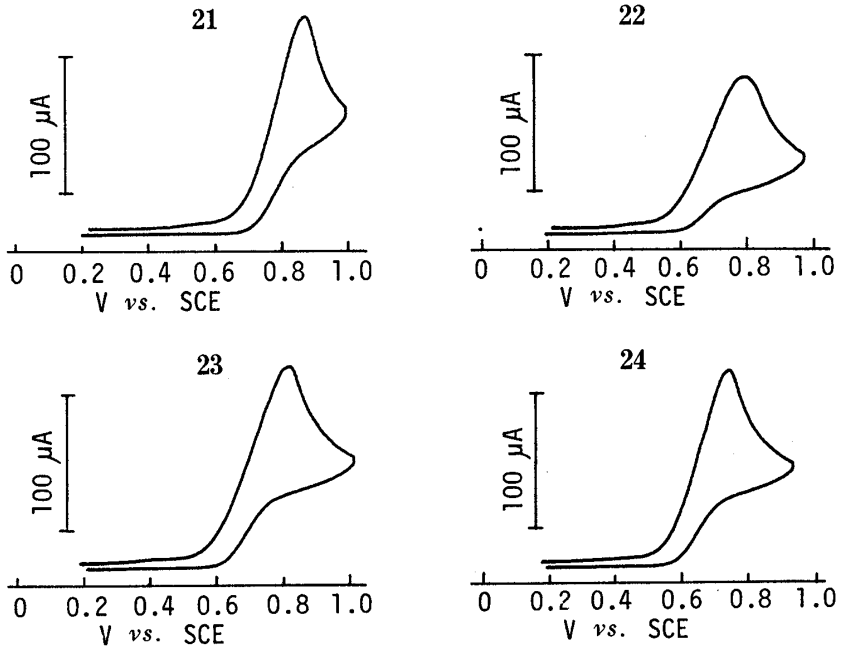
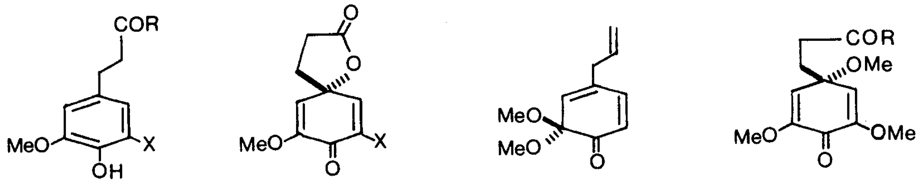


Fig. 2. Cyclic Voltammograms of 4 Phenols (**21**—**24**)

21 (2.0 mM), **22** (2.0 mM), **23** (2.0 mM), **24** (2.0 mM); supporter, $LiClO_4$ (0.2 M); solvent, MeOH; WE, glassy carbon disk (0.26 cm^2); sweep rate, 50 mV·s^{-1}.

as follows. As shown in Fig. 2, each cyclic voltammogram of the four dihydro derivatives (**21**—**24**) suggests that the oxidation potential at the initial step leading to the formation of a cationic radical is higher than that in the second oxidation step affording the corresponding cation. In fact, on electrolysis at a controlled potential (+800 mV *vs.* SCE; 2.0 F/mol) in methanol containing $LiClO_4$ as a supporting electrolyte, dihydroferulic acid (**21**) was readily



21: R=OH, X=H
22: R=OH, X=OMe
23: R=OMe, X=OMe
24: R=NH_2, X=OMe
25: X=H
27: X=OMe
26
28: R=NH_2
29: R=OMe

Chart 3

converted into a spirolactone (**25**) in 51% yield. In the case of eugenol, the conjugated dienone (**26**) was mainly produced and was readily converted into demethoxyasatone.[7]

Anodic oxidation of dihydrosinapic acid (**22**) was also carried out at a controlled potential (+1000 mV *vs.* SCE; 2.0 F/mol) to afford the corresponding spirolactone (**27**) in 47% yield. However, when electrolyzed at a controlled potential (+1000 mV *vs.* SCE; 2.0 F/mol), the amide (**24**) was readily converted into a dienone (**28**) in 91% yield. In this case, no spirolactam was detected in the reaction solution. Under essentially the same conditions as used for **24**, the methyl ester (**23**) of dihydrosinapic acid (**22**) was also oxidized to a dienone (**29**) in 85% yield.

In the present study, asatone- and isoasatone-type dimers have been synthesized from the corresponding 4-hydroxycinnamic acids and 4-hydroxycinnamamides in high yields, in contrast to *E*- and *Z*-isoeugenols, the anodic oxidation of which afforded several different types of dimer.[14] In addition, some bislactones related to known germination inhibitors were also produced from the two acids (**1** and **10**), the yields of which were found to depend on the concentration of the substrate. Finally, whereas the anodic oxidation of 4-allylphenols affords the cyclohexa-2,4-dien-1-ones in good yields, the cyclohexa-2,5-dien-1-ones (**25**, **27**, **28** and **29**) are obtained in high yields from the dihydro derivatives (**21**, **22**, **24** and **23**), respectively, as described herein.

Experimental

All the melting points were measured on a Shimadzu or Mitamura Riken melting point apparatus and are uncorrected. IR spectra were recorded on a Hitachi 215 or Shimadzu IR-400 spectrophotometer. Ultraviolet (UV) spectra were taken on a Hitachi 214 spectrophotometer. ^1H NMR spectra were taken on a JEOL JNM-PS 100 (100 MHz) spectrometer. Chemical shifts are given in ppm from tetramethylsilane (TMS) as an internal standard. Coupling constants are givn in Hz (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). Mass spectra (MS) were obtained on a Hitachi M-52 mass spectrometer operating with an ionization energy of 70 eV. High resolution MS were also taken on a Hitachi M-80 mass spectrometer operating with an ionization energy of 70 eV.

Preparative HPLC was carried out using an APUS-24 (Gasukuro Kogyo Inc.) or a KSU-45 pump (Kyowa Seimitsu Co., Ltd.) and both UV model 502 (Gasukuro Kogyo Inc.) and RI model R-403 (Waters Associates Inc.) detectors.

The instruments used for electrode reactions were as described in the preceding paper. A 200 ml glassy carbon beaker was used as an anode, unless otherwise stated.

Anodic Oxidation of Ferulic Acid (1)——A solution of **1** (194 mg) in MeOH (100 ml) containing $LiClO_4$ (4.3 g) was electrolyzed at a controlled potential (+900 mV *vs.* SCE; 90—20 mA). The reaction was quenched at 1.7 F/mol. The reaction solution was concentrated under reduced pressure and extracted with AcOEt. The AcOEt extract was dried over anhydrous Na_2SO_4 and then filtered. The filtrate was concentrated under reduced pressure and then separated by preparative thin-layer chromatography (TLC) [Kieselgel PF_{254}; 0.5% AcOH/hexane–AcOEt (1 : 4)] to afford **2** (16 mg),[5] **3** (101 mg) and the starting material (52 mg). The spectral data of **2** coincided with those reported for dehydrodiferulic acid bislactone.[5]

3: mp 200 °C (dec.) (from AcOEt). IR (KBr): 3450—2500, 1740, 1710 br, 1685, 1620 cm^{-1}. ^1H NMR (CD_3OD) δ: 3.04 (3H, s), 3.24 (3H, s), 3.45 (6H, s), 3.24—3.45 (3H, overlapped with MeO signals), 5.99 (1H, d, $J=16$ Hz), 6.03 (1H, d, $J=10$ Hz), 6.06 (1H, d, $J=16$ Hz), 6.32 (1H, br d, $J=7$ Hz), 6.44 (1H, d, $J=10$ Hz), 6.94 (1H, d, $J=16$ Hz), 7.18 (1H, d, $J=16$ Hz). High MS (*m*/*e*): Calcd for $C_{22}H_{24}O_{10}$ (M^+): 448.1367, Found: 448.1331.

Usual treatment of **3** with excess CH_2N_2 in ether containing a few drops of MeOH (room temp., overnight) afforded the corresponding methyl ester (**4**) in quantitative yield: mp 181—183 °C (from AcOEt). IR (KBr): 1740, 1715, 1705, 1640, 1605 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ: 3.05 (3H, s), 3.23 (3H, s), 3.45 (6H, s), 3.20—3.45 (3H, overlapped with MeO signals), 3.74 (3H, s), 3.76 (3H, s), 5.94—6.26 (5H, complex), 7.00 (1H, d, $J=16$ Hz), 7.24 (1H, d, $J=16$ Hz). MS *m/e*: 476 (M$^+$) and 238; High MS (*m/e*): Calcd for $C_{24}H_{28}O_{10}$ (M$^+$): 476.1680, Found: 476.1701.

A solution of **4** (50 mg) in hexane (10 ml) in a Pyrex tube was irradiated with a 100 W high pressure mercury lamp at room temperature for 10 h, then concentrated under reduced pressure, and purified by preparative TLC [Kieselgel PF$_{254}$; hexane–AcOEt (1 : 1)] to give **5** (28 mg): mp 191—192 °C (from AcOEt). ^{1}H NMR (CDCl$_3$) δ: 2.88 (2H, s), 3.07 (2H, br d, $J=4.5$ Hz), 3.24 (6H, s), 3.00 (2H, br d, $J=4.5$ Hz), 3.39 (6H, s), 3.77 (6H, s), 5.76 (2H, d, $J=16$ Hz), 7.11 (2H, d, $J=16$ Hz). High MS (*m/e*): Calcd for $C_{24}H_{28}O_{10}$ (M$^+$): 476.1680, Found: 476.1670.

Anodic Oxidation of 4-Hydroxy-3-methoxy-*N*-methylcinnamamide (6)——A solution of **6** (70 mg) in MeOH (21 ml) containing LiClO$_4$ (450 mg) was put into a 40 ml glassy carbon beaker as an anode, and electrolyzed at a controlled potential (+1400 mV *vs.* SCE; 240—10 mA), and the reaction was quenched at 2.3 F/mol. The reaction solution was directly subjected to preparative HPLC (column: 22 mmϕ × 300 mm, HP-255) using MeOH–H$_2$O (55 : 45). The fractions 41—60 (5.5 ml/F) were concentrated under reduced pressure, and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na$_2$SO$_4$ and filtered. The filtrate was concentrated under reduced pressure to give **8** as colorless crystals (57 mg): mp 235 °C (dec.) (from MeOH). IR (KBr): 3400 br, 3280 br, 1735, 1705, 1660, 1620, 1555 br cm^{-1}. ^{1}H NMR (DMSO-d_6) δ: 2.64 (6H, br s), 2.88 (3H, s), 3.12 (3H, s), 3.31 (6H, s), 3.1—3.3 (3H, overlapped with MeO signals), 5.93 (1H, d, $J=10$ Hz), 5.95 (1H, d, $J=16$ Hz), 6.10 (1H, d, $J=16$ Hz), 6.21 (1H, br d, $J=7$ Hz), 6.41 (1H, d, $J=10$ Hz), 6.60 (1H, d, $J=16$ Hz), 6.89 (1H, d, $J=16$ Hz). High MS (*m/e*): Calcd for $C_{24}H_{30}N_2O_8$ (M$^+$): 474.1999, Found: 474.1955.

Anodic Oxidation of 4-Hydroxy-3-methoxycinnamamide (7)——A solution of **7** (128 mg) in MeOH (100 ml) containing LiClO$_4$ (2.2 g) was electrolyzed at a controlled potential (+1400 mV *vs.* SCE; 100—6 mA), and the reaction was quenched at 1.9 F/mol. The reaction solution was directly subjected to preparative HPLC (column: 22 mmϕ × 300 mm, HP-255) using MeOH–H$_2$O (55 : 45). The fractions 16—24 (5.0 ml/F) were concentrated under reduced pressure, and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na$_2$SO$_4$ and then filtered. The filtrate was concentrated under reduced pressure to give **9** as a crystalline solid (68 mg). From fractions 25—35, the starting material (23 mg) was recovered.

9: mp 213 °C (dec.) (from MeOH). IR (KBr): 3430, 3325, 3180, 1730, 1710, 1665, 1610 br cm^{-1}. ^{1}H NMR (CD$_3$OD) δ: 3.02 (3H, s), 3.22 (3H, s), 3.44 (6H, s), 3.2—3.4 (3H, overlapped with MeO signals), 6.01 (1H, d, $J=10$ Hz), 6.15 (1H, d, $J=16$ Hz), 6.23 (1H, d, $J=16$ Hz), 6.26 (1H, br d, $J=7$ Hz), 6.41 (1H, d, $J=10$ Hz), 6.84 (1H, d, $J=16$ Hz), 7.08 (1H, d, $J=16$ Hz); High MS (*m/e*): Calcd for $C_{22}H_{26}N_2O_8$ (M$^+$): 446.1687, Found: 446.1670.

Anodic Oxidation of Sinapic Acid (10)——A solution of **10** (448 mg) in MeOH (170 ml) containing LiClO$_4$ (5.3 g) was electrolyzed at a controlled potential (+800 mV *vs.* SCE; 105—25 mA) and the reaction was quenched at 2.0 F/mol. The reaction solution was concentrated under reduced pressure to *ca.* 10 ml, then water (10 ml) was added. The aqueous solution was directly subjected to preparative HPLC [column: 38 mmϕ × 500 mm, LiChroprep RP-18; MeOH–H$_2$O (50 : 50)]. Fractions 9—25 (15 ml/F) were concentrated under reduced pressure and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na$_2$SO$_4$ and then filtered. The filtrate was concentrated under reduced pressure to leave a solid (134 mg), which was further separated by preparative TLC (Kieselgel PF$_{254}$; 1% AcOH/AcOEt) to afford **12** (77 mg) and the starting material (27 mg). The former was readily converted into the corresponding methyl ester (**14**) in quantitative yield on treatment with CH$_2$N$_2$ in ether containing a few drops of MeOH, as usual.

Fractions 26—52 were also concentrated under reduced pressure and extracted with AcOEt. The AcOEt extract was dried over anhydrous Na$_2$SO$_4$ and then filtered. The filtrate was concentrated under reduced pressure to afford colorless crystals of **13** (283 mg).[5,6] The spectral data of **13** coincided with those reported for dehydrodisinapic acid bislactone.[5]

12 as an Amorphous Powder: IR (KBr): 3200—2500, 1750, 1720, 1710, 1640 cm^{-1}, ^{1}H NMR (DMSO-d_6) δ: 3.02 (6H, s), 3.16 (2H, s), 3.36 (6H, s), 3.47 (8H, br s), 5.90 (2H, d, $J=16$ Hz), 6.88 (2H, br d, $J=16$ Hz). High MS (*m/e*): Calcd for $C_{24}H_{28}O_{12}$ (M$^+$): 508.1578, Found: 508.1551.

14: mp 168—169 °C (from ether). IR (KBr) :1750, 1720 br, 1640 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ: 3.13 (6H, s), 3.30 (2H, s), 3.46 (6H, s), 3.56 (6H, s), 3.75 (6H, s), 3.84 (2H, br s), 5.98 (2H, d, $J=16$ Hz), 7.03 (2H, br d, $J=16$ Hz); High MS (*m/e*): Calcd for $C_{26}H_{32}O_{12}$ (M$^+$): 536.1891, Found: 536.1891.

Anodic Oxidation of 4-Hydroxy-3,5-dimethoxycinnamamide (11) at Higher Potential——A solution of **11** (223 mg) in MeOH (100 ml) containing LiClO$_4$ (2.2 g) was electrolyzed at a controlled potential (+1000 mV *vs.* SCE; 250—7 mA) and the reaction was quenched at 1.8 F/mol. The reaction solution was concentrated under reduced pressure below 40 °C, and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na$_2$SO$_4$, and then filtered. The filtrate was concentrated under reduced pressure and then purified by column chromatography (Kieselgel 60, 50 g) using AcOEt–MeOH (9 : 1) to give **16** as a crystalline solid (214 mg): mp 200 °C (dec.) (from MeOH). IR (KBr): 3410, 3180, 1745, 1715, 1675, 1635, 1600 cm^{-1}. ^{1}H NMR (CD$_3$OD) δ: 3.13 (6H, s), 3.49 (6H, s), 3.56 (6H, s), 3.42—3.56 (4H, overlapped with MeO signals), 6.21 (2H, d, $J=16$ Hz), 6.97 (2H, br d, $J=16$ Hz). High MS (*m/e*): Calcd for $C_{24}H_{30}N_2O_{10}$ (M$^+$): 506.1899, Found: 506.1936.

Anodic Oxidation of 4-Hydroxy-3,5-dimethoxycinnamamide (11) at Lower Potential——A solution of **11** (265 mg) in MeOH (100 ml) containing $LiClO_4$ (2.2 g) was electrolyzed at a controlled potential (+650 mV *vs.* SCE; 100—60 mA) and the reaction was quenched at 1.0 F/mol. The reaction solution was concentrated under reduced pressure, and then separated by preparative HPLC [column: 22 mmϕ × 300 mm, HP-255; MeOH–H_2O (55:45)]. Fractions 32—39 (2.7 ml/F) were concentrated under reduced pressure to afford **18** as a crystalline solid (31 mg): mp 270 °C (dec.) (from MeOH). IR (KBr): 3470, 3360, 3280 br, 1645, 1630, 1600, 1570, 1510, 1500 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 3.48 (3H, s), 3.60 (6H, s), 3.79 (3H, s), 4.70 (1H, s),15) 6.27 (2H, s), 6.71 (1H, s), 7.33 (1H, s). High MS (*m/e*): Calcd for $C_{22}H_{24}N_2O_8$ (M^+): 444.1530, Found: 444.1509.

Fractions 40—75 were also concentrated under reduced pressure, and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na_2SO_4 and then filtered. The filtrate was concentrated under reduced pressure to give a solid (120 mg), which was further separated by preparative TLC (Kieselgel PF_{254}) using AcOEt to afford **16** (10 mg) and **19** (43 mg), in addition to the starting material (43 mg).

19: mp 254 °C (dec.) (from MeOH). IR (KBr): 3450, 3350, 3250 br, 1640, 1600, 1570, 1515 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 3.69 (12H, s), 6.93 (4H, s), 7.69 (2H, s). High MS (*m/e*): Calcd for $C_{22}H_{24}N_2O_8$ (M^+): 444.1530, Found: 444.1503.

Anodic Oxidation of Dihydroferulic Acid (21)——A solution of **21** (392 mg) in MeOH containing $LiClO_4$ (3.9 g) was electrolyzed at a controlled potential (+800 mV *vs.* SCE; 56—20 mA) and the reaction was quenched at 2.0 F/mol. The reaction solution was concentrated under reduced pressure, and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na_2SO_4 and then filtered. The filtrate was concentrated under reduced pressure and separated by preparative TLC (Kieselgel PF_{254}) using AcOEt to afford **25** as colorless crystals (184 mg), in addition to the starting material (26 mg).

25: mp 43—45 °C (from AcOEt). IR (KBr): 1760 br, 1675, 1645, 1620 cm^{-1}. ^1H NMR (CD_3OD) δ: 2.44 (2H, br t, J=7.5 Hz), 2.84 (2H, br t, J=7.5 Hz), 3.67 (3H, s), 6.07 (1H, d, J=3 Hz), 6.19 (1H, d, J=10 Hz), 7.06 (1H, dd, J=10, 3 Hz). High MS (*m/e*): Calcd for $C_{10}H_{10}O_4$ (M^+): 194.0578, Found: 194.0611.

Anodic Oxidation of Dihydrosinapic Acid (22)——A solution of **22** (226 mg) in MeOH (100 ml) containing $LiClO_4$ (2.2 g) was electrolyzed at a controlled potential (+1000 mV *vs.* SCE; 75—44 mA) and the reaction was quenched at 2.0 F/mol. The reaction solution was concentrated under reduced pressure, and then extracted with AcOEt. The AcOEt extract was concentrated under reduced pressure, and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na_2SO_4, and then filtered. The filtrate was concentrated under reduced pressure, and then purified by preparative TLC (Kieselgel PF_{254}; AcOEt) to afford **27** (83 mg), in addition to the starting material (47 mg).

27: mp 130—132 °C (from AcOEt). IR (KBr): 1760 br, 1675, 1665, 1620 cm^{-1}. ^1H NMR (CD_3OD) δ: 2.46 (2H, br t, J=7.5 Hz), 2.87 (2H, br t, J=7.5 Hz), 3.68 (6H, s), 6.11 (2H, s). High MS (*m/e*): Calcd for $C_{11}H_{12}O_5$ (M^+): 224.0684, Found: 224.0694.

Anodic Oxidation of 4-Hydroxy-3,5-dimethoxydihydrocinnamamide (24)——A solution of **24** (97 mg) in MeOH (36 ml) containing $LiClO_4$ (450 mg) was put into a 40 ml glassy carbon beaker as an anode and electrolyzed at a controlled potential (+1000 mV *vs.* SCE; 120—30 mA), and the reaction was quenched at 2.0 F/mol. The reaction solution was concentrated under reduced pressure and directly subjected to preparative HPLC [column: 22 mmϕ × 300 mm, HP-255; MeOH–H_2O (55:45)] to afford **28** (57 mg) and the starting material (42 mg).

28: mp 125—128 °C (from AcOEt). IR (KBr): 3390, 3180, 1670 br, 1650 br, 1620 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 1.99 (4H, s), 3.05 (3H, s), 3.59 (6H, s), 5.69 (2H, s). High MS (*m/e*): Calcd for $C_{12}H_{17}NO_5$ (M^+): 255.1104, Found: 255.1088.

Anodic Oxidation of Dihydrosinapic Acid Methyl Ester (23)——A solution of **23** (240 mg) in MeOH (100 ml) containing $LiClO_4$ (2.2 g) was electrolyzed at a controlled potential (+1000 mV *vs.* SCE; 240—140 mA) and the reaction was quenched at 2.0 F/mol. The reaction solution was concentrated under reduced pressure and then extracted with AcOEt. The AcOEt extract was dried over anhydrous Na_2SO_4, and then filtered. The filtrate was concentrated under reduced pressure and separated by preparative TLC [Kieselgel PF_{254}; benzene–AcOEt (1:1)] to afford **29** (101 mg) and the starting material (134 mg).

29: mp 84 °C (from AcOEt). IR (KBr): 1725, 1675, 1655, 1620 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.0—2.5 (4H, m), 3.16 (3H, s), 3.62 (3H, s), 3.69 (6H, s), 5.39 (2H, s). High MS (*m/e*): Calcd for $C_{13}H_{18}O_6$ (M^+): 270.1102, Found: 270.1106.

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8) The reaction was quenched at 1.9 F/mol.
9) The possibility cannot be ruled out that the dimeric compound (**3** or **15**) is produced in the course of separation of the reaction mixture.
10) Deprotonation seems to occur very rapidly.
11) This compound was produced in almost quantitative yield, as judged from analytical HPLC of the reaction mixture.
12) At higher concentrations of **11**, this dimer (**16**) was not detected by analytical HPLC.
13) The remaining methine signal overlaps with one of the MeO signals.
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15) One of the two methine signals overlaps with one of the MeO signals. In addition, the coupling constant ($J \simeq 0$ Hz) of the signal at δ 4.70 indicates that the two adjacent methine protons are *trans* to each other.