JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Synthesis and Insect Antifeedant Activity of Aurones against *Spodoptera litura* Larvae

MASANORI MORIMOTO,* HIROMI FUKUMOTO, TOKI NOZOE, AI HAGIWARA, AND KOICHIRO KOMAI

Department of Applied Biological Chemistry, Faculty of Agriculture, Kinki University, 3327-204 Nakamachi, Nara, Japan

A series of aurones were prepared from various phenols via phenoxy acetic acids and coumaranones and evaluated for insect antifeedant activity against the common cutworm (*Spodoptera litura*). The naturally occurring aurone was most active at an ED_{50} of 0.12 μmol/cm^2. The synthetic precursor, coumaranones, showed that the introduction of methoxyl and methyl groups to the benzene ring increased insect antifeedant activity. Similarly, the tested aurones showed that the introduction of methoxyl group to the A and/or B rings increased the insect antifeedant activity, but 4,5,6- and 3′,4′,5′-trisubstituted compounds did not show this activity in this test. The hydroxylation of aurones in the B ring should be disadvantageous for insect antifeedant activity against *S. litura*. Although the melting points did not correlate well with the insect antifeedant activity, compounds that were nearly inactive had high melting points. A significant correlation was noted between biological activity (pED_{50}) and a hydrogen-bonding parameter calculated from the R_f value obtained from SiOH thin-layer chromatography and a lipophilicity parameter (log k) calculated from the retention time in ODS high-performance liquid chromatography. The respective correlation coefficients (r) were −0.83 and −0.70. The introduction of alkoxy and alkyl groups along with adequate hydrogen bonding seems to contribute to the antifeedant activity of the compounds tested.

KEYWORDS: Aurones; insect antifeedant; SAR; *Spodoptera litura*

INTRODUCTION

In plant−insect interaction, phytophenolics including flavonoids and phenylpropanoids can attract pollinators and provide chemical defense to avoid damage from phytophagous insects (*1*). The flavonoids are some of the most common pigments among naturally occurring phytophenolics. Occasionally, flavones and isoflavones also provide chemical defense against herbivores. Aurones (2-benzylidene-coumaran-3-ones) are flavonoids that are closely associated with the yellow color of flowers; for example, in Scrophulariaceae and Compositae, they are found in heartwood as well as in flowers (*2*). Aurones are obtained from chalcone by aurone synthase as well as through the biosynthesis of other flavonoids (*3*). Aurones have been reported to show cytotoxicity (*4*) and antiparasitic (*5*) and antifungal activity (*6*). 3′,4,4′,6-Tetramethoxyaurone is one of several constituents that has been isolated from the methanolic extract of *Cyperus radians* (Cyperaceae). This Cyperaceae produces large amounts of which polymethylated aurones may be part of a chemical defense system. Because both coumaran (dihydrobenzofuran) and chromene (benzopyran) are known to exhibit insect antifeedant activity (*7*, *8*), a similar corresponding relationship between the chemical structures of flavone (benzopyranone) (*9*) and aurone (benzofuranone) suggests that aurones may show insect antifeedant activity (**Figure 1**). Because natural 3′,4,4′,6-tetramethoxyaurone showed insect antifeedant activity against *Spodoptera litura* larvae, structure−activity relationships are also discussed.

MATERIALS AND METHODS

Synthesis. *General.* ^{1}H and ^{13}C NMR spectra were measured on a JEOL 270EX (270 MHz) spectrometer using tetramethylsilane as an internal standard. Mass spectra were taken at 70 eV (DEI probe) with a JEOL QMS-K9. High-resolution mass spectra (HREIMS) were obtained on a JEOL JMS-700. The synthetic compounds were purified by column chromatography on silica gel, Fuji silysia chemical BW-127ZH and BW-300 (Fuji Silysia Chemical Ltd., Japan). Melting points were measured on a Yanaco model MP apparatus. Thin-layer chromatography (TLC) involved the use of silica gel plates with a fluorescent indicator (Merck Silica Gel 60 F_{254} 0.25 mm thick).

General Procedure for Preparation of Tested Aurones. To a solution of 3,5-dimethoxyphenol (1.086 mmol) in acetone (20 mL) was added Na (8.351 mmol) at room temperature. The solution was kept under the same conditions with stirring until hydrogen was no longer generated. 2-Bromoethylacetate (6.313 mmol) was added to the mixture, and reflux conditions were maintained for several hours. After the starting material had disappeared by TLC analysis, the solution was cooled, ethanol (0.3 mL) was added to dissolve sodium completely, and 0.1 N NaOH(aq) (15 mL) was poured into the solution. The

* To whom correspondence should be addressed. Tel: +81-742-43-7162. Fax: +81-742-43-1445. E-mail: masanori@nara.kindai.ac.jp.

10.1021/jf062562t CCC: $37.00
Published on Web 01/10/2007

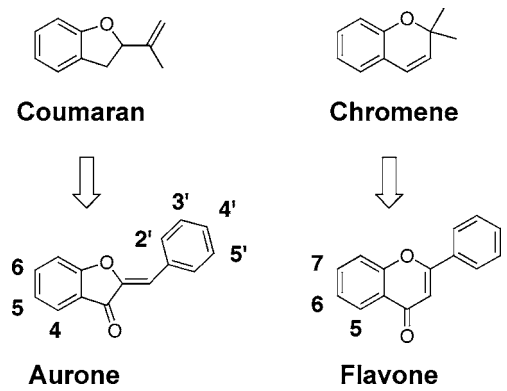


Figure 1. Structural similarity of benzofurans and benzopyranes in this text.

synthetic ester was hydrolyzed at 80 °C. The solution was adjusted to pH 8−9 and washed with chloroform to remove residual ester from the solution. The solution was then adjusted to below pH 3, extracted with chloroform, dried with anhydrous sodium sulfate, and concentrated to dryness to give the 3,5-dimethoxyphenoxyacetic acid (**1**) in 81% yield, which was used directly in the next reaction without further purification. These phenoxy acetic acids were obtained in a yield of 23.9−86.0% in this reaction (*10*).

Coumaranones were prepared by polyphosphoric acid (PPA)-mediated cyclization of the corresponding phenoxyacetic acid. Compound **1** (2.245 mmol) was added to PPA (26.2 g), and the mixture was stirred using a mechanical stirrer at 100 °C for 8 h. The reaction product was then cooled, and distilled water was poured into the same pot. The reaction product was extracted with chloroform, dried with anhydrous sodium sulfate, and concentrated to dryness to give the 4,6-dimethoxycoumaranone (**5**) (0.424 mmol) in 18.9% yield. These coumaranones were obtained in yields of 15.9−36.5% in this cyclization reaction (*10*).

Each aurone was prepared by a known method, and only the *Z* form was obtained (*11*). Basic active alumina for chromatography (Chameleon special reagent for chromatography, 300 mesh, Kishida Chemical Co. Ltd., Japan) (1 g) was added to a dichloromethane solution (1.5 mL) of **5** (0.206 mmol) and benzaldehyde (0.4695 mmol) and allowed to stand overnight at room temperature. The progress of the reaction was monitored by TLC analysis. After the alumina powder was removed by filtration with celite, the solvent was removed under reduced pressure to obtain crude product. Crystallization from chloroform−hexane gave pure aurone, 4,6-dimethoxyaurone (*Z*) (**21**), in 84.3% yield as pale yellow crystals. The determination of *E*−*Z* isomer was achieved by examining the chemical shift value of the C2′ aryl proton in the ^{1}H NMR spectrum. These synthetic aurones were obtained in a yield of 13.2−97.0% in this reaction (**Figure 2**).

3,5-Dimethoxyphenoxyacetic Acid (1). Yield, 81.0%; pale brown crystal; mp, 118−122 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.14 (1H, d, J = 2.0 Hz, C4), 6.10 (2H, d, J = 2.0 Hz, C2, C6), 4.53 (2H, s, −O−CH_2−), 4.43−5.15 (1H, br. s, −COOH), 3.76 (6H, s, Ar−OCH_3 × 2). ^{13}C NMR (270 MHz, CD_3OD): δ 172.7, 163.2 (overlapped), 161.3, 94.7, 94.6 (overlapped), 66.0, 55.9 (overlapped). DEIMS (70 eV) *m*/*z* (relative intensity): 212 (M^+, 57.5%), 167 (7.4%), 137 (13.4%), 107 (7.6%), 95 (9.6%), 69 (100%). HREIMS *m*/*z* (M^+), 212.0684; calcd for $C_{10}H_{12}O_5$, 212.0685.

3,5-Dimethylphenoxyacetic Acid (2). Yield, 35.8%; white crystal; mp, 100−104 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.05−7.24 (1H, br. s, −COOH), 6.66 (1H, s, C4), 6.54 (2H, s, C2, C6), 4.64 (2H, s, −O−CH_2−), 2.29 (6H, s, Ar−CH_3 × 2). ^{13}C NMR (270 MHz, $CDCl_3$): δ 176.3, 159.4, 141.5 (overlapped), 125.9, 114.3 (overlapped), 66.7, 23.4 (overlapped). DEIMS (70 eV) *m*/*z* (relative intensity): 180 (M^+, 61.9%), 163 (6.0%), 135 (29.1%), 105 (42.8%), 91 (29.9%), 58 (100%). HREIMS *m*/*z* (M^+), 180.0780; calcd for $C_{10}H_{12}O_3$, 180.0786.

3,5-Dichlorophenoxyacetic Acid (3). Yield, 86.0%; white crystal; mp, 109−113 °C. ^{1}H NMR (270 MHz, CD_3OD): δ 7.03 (1H, t, J = 1.7 Hz, C4), 6.25 (2H, d, J = 1.7 Hz, C2, C6), 5.64−6.15 (1H, br. s, −COOH), 4.66 (2H, s, −O−CH_2−). ^{13}C NMR (270 MHz, CD_3OD): δ 172.5, 158.5, 135.7 (overlapped), 122.6, 114.0 (overlapped), 65.0. DEIMS (70 eV) *m*/*z* (relative intensity): 220 (M^+, 100%), 175 (79.8%), 145 (32.7%). HREIMS *m*/*z* (M^+), 219.9705; calcd for $C_8H_6O_5Cl_2$, 219.9694.

3,4,5-Trimethoxyphenoxyacetic Acid (4). Yield, 23.9%; pale brown crystal; mp, 96−99 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.50−6.99 (1H, br. s, −COOH), 6.17 (2H, s, C2, C6), 4.63 (2H, s, −O−CH_2−), 3.81 (6H, s, Ar−OCH_3 × 2), 3.77 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 173.3, 154.1, 153.7 (overlapped), 133.0, 92.6 (overlapped), 65.2, 61.0, 56.1 (overlapped). DEIMS (70 eV) *m*/*z* (relative intensity): 242 (M^+, 28.4%), 183 (2.9%), 168 (13.8%), 153 (2.3%), 125 (4.8%), 69 (100%). HREIMS *m*/*z* (M^+), 242.0797; calcd for $C_{11}H_{14}O_6$, 242.0790.

4,6-Dimethoxycoumaranone (5). Yield, 18.9%; yellow crystal; mp, 126−128 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.11 (1H, d, J = 1.8 Hz, C7), 5.96 (1H, d, J = 1.8 Hz, C5), 4.54 (2H, s, −O−CH_2−), 3.87 (3H, s, Ar−OCH_3), 3.83 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 194.8, 177.1, 169.8, 158.9, 104.8, 93.0, 89.0, 75.5, 56.0, 55.9. DEIMS (70 eV) *m*/*z* (relative intensity): 194 (M^+, 16.4%), 165 (6.7%), 151 (5.1%), 48 (100%). HREIMS *m*/*z* (M^+), 194.0583; calcd for $C_{10}H_{10}O_4$, 194.0579.

4,6-Dimethylcoumaranone (6). Yield, 15.9%; yellow crystal; mp, 51−53 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.68 (1H, s, C5), 6.59 (1H, s, C7), 4.51 (2H, s, −O−CH_2−), 2.50 (3H, s, Ar−CH_3), 2.33 (3H, s, Ar−CH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 199.8, 174.8, 149.1, 138.9, 124.6, 116.9, 110.7, 74.7, 22.2, 17.5. DEIMS (70 eV) *m*/*z* (relative intensity): 162 (M^+, 28.1%), 148 (5.0%), 120 (2.0%), 105 (10.5%), 48 (100%). HREIMS *m*/*z* (M^+), 162.0683; calcd for $C_{10}H_{10}O_2$, 162.0681.

4,5,6-Trimethoxycoumaranone (7). Yield, 36.5%; pale brown crystal; mp, 129−131 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.31 (1H, s, C7), 4.56 (2H, s, −O−CH_2−), 4.15 (3H, s, Ar−OCH_3), 3.93 (3H, s, Ar−OCH_3), 3.78 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 195.1, 171.9, 162.5, 150.5, 135.7, 106.6, 90.6, 75.3, 61.9, 61.4, 56.3. DEIMS (70 eV) *m*/*z* (relative intensity): 224 (M^+, 55.3%), 209 (61.2%), 195 (8.9%), 181 (17.2%), 167 (8.4%), 151 (6.5%), 48 (100%). HREIMS *m*/*z* (M^+), 224.0688; calcd for $C_{11}H_{12}O_5$, 224.0685.

Aurone (*Z*) (8). Yield, 22.8%; yellow crystalline; mp, 98−99 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.89−7.93 (2H, m, C2′, C6′), 7.81 (1H, dd, J = 7.6, 1.3 Hz, C4), 7.65 (1H, ddd, J = 8.3, 7.3, 1.3 Hz, C6), 7.36−7.49 (3H, m, C3′, C4′, C5′), 7.32 (1H, d, J = 8.3 Hz, C7), 7.21 (1H, dd, J = 7.6, 7.3 Hz, C5), 6.89 (1H, s, benzylic). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.7, 166.2, 147.0, 136.8, 132.4 (overlapped), 131.5, 129.8 (overlapped), 128.9, 124.7, 123.5, 121.7, 113.0, 112.9. DEIMS (70 eV) *m*/*z* (relative intensity): 222 (M^+, 100%), 134 (36.3%), 120 (19.2%). HREIMS *m*/*z* (M^+), 222.0688; calcd for $C_{15}H_{10}O_2$, 222.0681.

2′-Methoxyaurone (*Z*) (9). Yield, 82.4%; yellow crystal; mp, 167−170 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.31 (1H, dd, J = 7.8, 1.7 Hz, C4), 7.81 (1H, dd, J = 7.9, 1.2 Hz, C7), 7.63 (1H, ddd, J = 7.8, 7.8, 1.2 Hz, C5), 7.48 (1H, s, benzylic), 7.36 (1H, ddd, J = 7.9, 7.8, 1.7 Hz, C6), 7.31 (1H, d, J = 8.3 Hz, C6′), 7.20 (1H, dd, J = 8.2, 6.6 Hz, C4′), 7.06 (1H, dd, J = 8.3, 6.6 Hz, C5′), 6.92 (1H, d, J = 8.2 Hz, C3′), 3.90 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.7, 165.9, 158.8, 146.9, 136.6, 132.0, 131.5, 124.6, 123.3, 121.8, 121.2, 120.8, 112.9, 110.7, 107.3, 55.6. DEIMS (70 eV) *m*/*z* (relative intensity): 252 (M^+, 24.9%), 237 (7.8%), 221 (100%), 92 (17.6%), 76 (11.3%). HREIMS *m*/*z* (M^+), 252.0762; calcd for $C_{16}H_{12}O_3$, 252.0786.

3′-Methoxyaurone (*Z*) (10). Yield, 75.2%; yellow crystal; mp, 117−119 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.81 (1H, dd, J = 7.6, 1.3, Hz, C4), 7.66 (1H, ddd, J = 8.3, 7.3 1.3 Hz, C6), 7.48−7.51 (2H, m, C2′, C6′), 7.37 (1H, dd, J = 8.3, 7.9 Hz, C5′), 7.33 (1H, dd, J = 8.3, 0.7 Hz, C7), 7.22 (1H, ddd, J = 7.6, 7.3, 0.7 Hz, C5), 6.96 (1H, ddd, J = 8.3, 2.6, 1.0 Hz, C4′), 6.86 (1H, s, benzylic), 3.88 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.7, 166.2, 159.9, 147.0, 136.9, 133.6, 129.8, 124.7, 124.3, 123.5, 121.7, 116.6, 115.8, 113.0, 112.9, 55.4. DEIMS (70 eV) *m*/*z* (relative intensity): 252 (M^+, 72.8%), 237 (17.5%), 221 (77.1%), 209 (15.2%), 132 (13.0%), 76 (100%). HREIMS *m*/*z* (M^+), 252.0761; calcd for $C_{16}H_{12}O_3$, 252.0786.

3′-Chloroaurone (*Z*) (11). Yield, 66.2%; pale yellow crystal; mp, 98−99 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.94 (1H, s, C2′), 7.80

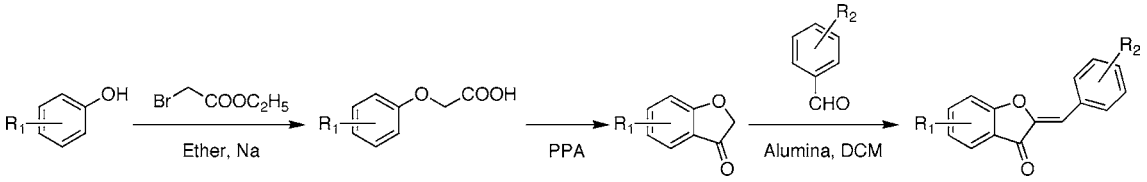


Figure 2. Synthesis of substituted aurones.

(1H, dd, J = 7.6, 1.3 Hz, C4), 7.73 (1H, dd, J = 8.1, 1.7 Hz, C4′), 7.68 (1H, ddd, J = 7.5, 7.3, 1.3 Hz, C6), 7.34−7.42 (3H, m, C5′, C6′, C7), 7.24 (1H, dd, J = 7.3, 7.6 Hz, C5), 6.79 (1H, s, benzylic). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.6, 166.2, 147.3, 137.2, 134.8, 134.0, 130.9, 130.0, 129.7, 129.6, 124.7, 123.7, 121.3, 113.0, 111.1. DEIMS (70 eV) *m/z* (relative intensity): 256 (M^+, 100%), 221 (75.6%), 92 (90.3%), 76 (38.4%). HREIMS *m/z* (M^+), 256.0277; calcd for $C_{15}H_9O_2Cl$, 256.0291.

3′-Bromoaurone (*Z*) (12). Yield, 37.3%; pale yellow crystal; mp, 115−117 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.08 (1H, d, J = 2.0, C2′), 7.80 (1H, d, J = 7.9 Hz, C4′), 7.78 (1H, dd, J = 7.3, 1.3 Hz, C4), 7.66 (1H, ddd, J = 8.3, 7.9, 1.3 Hz, C6), 7.51 (1H, dd, J = 7.9, 2.0 Hz, C6′), 7.34 (1H, d, J = 8.3 Hz, C7), 7.30 (1H, t, J = 7.9 Hz, C5′), 7.22 (1H, dd, J = 7.3, 7.9 Hz, C5), 6.77 (1H, s, benzylic). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.5, 166.3, 147.4, 137.1, 134.4, 133.9, 132.6, 130.3, 129.9, 124.8, 123.7, 123.0, 121.5, 113.0, 110.9. DEIMS (70 eV) *m/z* (relative intensity): 301 (M^+, 25.7%), 221 (64.1%), 120 (61.3%), 92 (100%), 76 (40.2%). HREIMS *m/z* (M^+), 299.9780; calcd for $C_{15}H_9O_2Br$, 299.9786.

4′-Methoxyaurone (*Z*) (13). Yield, 75.3%; yellow crystal; mp, 120−122 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.88 (2H, d, J = 8.7 Hz, C2′, C6′), 7.80 (1H, dd, J = 7.6, 1.3 Hz, C4), 7.62 (1H, ddd, J = 8.3, 7.3, 1.3, Hz, C6), 7.31 (1H, dd, J = 8.3, 0.6 Hz, C7), 7.20 (1H, ddd, J = 7.6, 7.3, 0.6 Hz, C5), 6.98 (2H, d, J = 8.7 Hz, C3′, C5′), 6.88 (1H, s, benzylic), 3.86 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.5, 165.9, 161.1, 145.9, 136.4, 133.4 (overlapped), 125.1, 124.5, 123.2, 122.0, 114.5 (overlapped), 113.3, 112.8, 55.4. DEIMS (70 eV) *m/z* (relative intensity): 252 (M^+, 100%), 237 (29.4%), 221 (38.5%), 135 (62.8%), 77 (73.5%). HREIMS *m/z* (M^+), 252.0772; calcd for $C_{16}H_{12}O_3$, 252.0786.

3′4′-Dimethoxyaurone (*Z*) (14). Yield, 65.8%; yellow crystal; mp, 175−178 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.80 (1H, dd, J = 7.6, 1.3 Hz, C4), 7.63 (1H, ddd, J = 8.3, 7.2, 1.3 Hz, C6), 7.53 (1H, d, J = 2.0 Hz, C2′), 7.49 (1H, dd, J = 8.3, 2.0 Hz, C6′), 7.30 (1H, d, J = 8.3 Hz, C7), 7.21 (1H, dd, J = 7.6, 7.3 Hz, C5), 6.94 (1H, d, J = 8.3 Hz, C5′), 6.89 (1H, s, benzylic), 3.97 (3H, s, Ar−OCH_3), 3.94 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ (ppm) 184.3, 165.8, 151.0, 149.2, 146.0, 136.4, 126.0, 125.4, 124.6, 123.3, 122.0, 114.1, 113.5, 112.8, 114.4, 56.0 (overlapped). DEIMS (70 eV) *m/z* (relative intensity): 282 (M^+, 63.9%), 267 (27.3%), 251 (17.9%), 134 (59.7%), 105 (64.7%). HREIMS *m/z* (M^+), 282.0886; calcd for $C_{17}H_{14}O_4$, 282.0892.

3′,4′-Methylendioxyaurone (*Z*) (15). Yield, 79.9%; yellow crystal; mp, 185−188 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.80 (1H, dd, J = 7.6, 1.7 Hz, C6′), 7.65 (1H, ddd, J = 8.6, 8.3, 1.7 Hz, C6), 7.60 (1H, d, J = 1.7 Hz, C2′), 7.34 (1H, dd, J = 8.3, 1.7 Hz, C4), 7.33 (1H, d, J = 7.6 Hz, C5′), 7.22 (1H, dd, J = 8.3, 8.6 Hz, C5), 6.89 (1H, d, J = 8.3, C7), 6.84 (1H, s, benzylic), 6.05 (2H, s, −OCH_2O−). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.5, 165.8, 149.3, 148.2, 145.9, 136.6, 127.6, 126.6, 124.6, 123.4, 121.8, 113.4, 112.9, 110.6, 108.8, 101.6. DEIMS (70 eV) *m/z* (relative intensity): 266 (M^+, 100%), 252 (19.2%), 146 (20.0%), 120 (35.9%), 92 (59.5%), 76 (28.3%). HREIMS *m/z* (M^+), 266.0561; calcd for $C_{16}H_{10}O_4$, 266.0579.

3′,4′-Dihydroxyaurone (*Z*) (16). Yield, 13.2%; orange crystal; mp, 225−228 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.63−7.92 (2H, m, C4, C6), 7.68 (1H, s, benzylic), 7.53 (1H, d, J = 8.3 Hz, C5′), 7.34−7.45 (2H, m, C5, C7), 6.96 (1H, dd, J = 8.3, 1.5 Hz, C6′), 6.93 (1H, d, J = 1.5 Hz, C2′). ^{13}C NMR (270 MHz, $CDCl_3$): δ 186.0, 167.1, 149.9, 146.8, 146.7, 138.6, 126.9, 125.4, 125.2, 124.7, 122.9, 119.2, 116.7, 116.3, 114.0. DEIMS (70 eV) *m/z* (relative intensity): 254 (M^+, 100%), 237 (26.7%), 134 (5.6%), 120 (18.3%), 92 (33.6%), 76 (21.4%). HREIMS *m/z* (M^+), 254.0564; calcd for $C_{15}H_{10}O_4$, 254.0579.

4′-Hydroxy-3′-methoxyaurone (*Z*) (17). Yield, 82.0%; orange crystal; mp, 199−201 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.82 (1H, dd, J = 7.6, 1.5 Hz, C4), 7.65 (1H, ddd, J = 8.3, 8.2, 1.5 Hz, C6), 7.50 (1H, d, J = 2.0 Hz, C2′), 7.49 (1H, dd, J = 2.0, 8.8 Hz, C6′), 7.32 (1H, d, J = 8.3 Hz, C7), 7.22 (1H, dd, J = 8.2, 7.6 Hz, C5), 7.00 (1H, d, J = 8.8, C5′), 6.87 (1H, s, benzylic), 5.99 (1H, s, Ar−OH), 4.00 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.5, 165.7, 147.8, 146.7, 145.8, 136.5, 126.6, 124.9, 124.6, 123.3, 121.9, 115.0, 113.9, 113.3, 112.8, 56.0. DEIMS (70 eV) *m/z* (relative intensity): 268 (M^+, 100%), 225 (15.9%), 197 (10.3%), 104 (9.8%), 92 (50.7%). HREIMS *m/z* (M^+), 268.0714; calcd for $C_{16}H_{12}O_4$, 268.0736.

3′-Ethoxy-4′-hydroxyaurone (*Z*) (18). Yield, 68.9%; brown crystal; mp, 121−123 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.80 (1H, dd, J = 7.6, 1.3 Hz, C4), 7.63 (1H, ddd, J=8.3, 7.3, 1.3 Hz, C6), 7.47 (1H, d, J = 1.8 Hz, C2′), 7.47 (1H, dd, J = 1.8, 8.7 Hz, C6′), 7.30 (1H, d, J = 8.3 Hz, C7), 7.20 (1H, dd, J = 7.3, 7.6 Hz, C5), 6.99 (1H, d, J = 8.7 Hz, C5′), 6.84 (1H, s, benzylic), 6.07 (1H, s, Ar−OH), 4.21 (2H, q, J = 6.9 Hz, −O−CH_2−), 1.50 (3H, t, J = 6.9 Hz, −CH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.4, 165.8, 148.1, 146.0, 145.8, 136.4, 126.5, 124.8, 124.6, 123.3, 122.0, 115.0, 114.4, 113.9, 112.8, 64.7, 14.8. DEIMS (70 eV) *m/z* (relative intensity): 282 (M^+, 100%), 253 (72.3%), 225 (23.9%), 197 (15.7%), 92(45.4%), 76(16.6%). HREIMS *m/z* (M^+), 282.0865; calcd for $C_{17}H_{14}O_4$, 282.0892.

3′,5′-Dimethoxyaurone (*Z*) (19). Yield, 97.0%; yellow crystal; mp, 153−155 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.79 (1H, d, J = 7.9 Hz, C4), 7.64 (1H, dd, J = 6.9, 8.6 Hz, C6), 7.30 (1H, d, J = 8.6 Hz, C7), 7.21 (1H, dd, J = 6.9, 7.9 Hz, C5), 7.08 (2H, s, C2′, C6′), 6.80 (1H, s, benzylic), 6.53 (1H, s, C4′), 3.85 (6H, s, Ar−OCH_3 × 2). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.6, 166.2, 161.2 (overlapped), 147.0, 136.8, 133.9, 124.7, 123.5, 121.7, 112.9 (overlapped), 109.6 (overlapped), 102.5, 55.4 (overlapped). DEIMS (70 eV) *m/z* (relative intensity): 282 (M^+, 73.0%), 251 (100%), 208 (8.5%), 92 (11.4%), 76 (16.8%). HREIMS *m/z* (M^+), 282.0869; calcd for $C_{17}H_{14}O_4$, 282.0892.

3′,4′,5′-Trimethoxyaurone (*Z*) (20). Yield, 64.2%; yellow crystal; mp, 173−174 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.79 (1H, dd, J = 7.6, 1.3 Hz, C4), 7.63 (1H, ddd, J = 8.3, 8.2, 1.3 Hz, C6), 7.30 (1H, d, J = 8.3 Hz, C7), 7.22 (1H, dd, J = 8.2, 7.6 Hz, C5), 7.19 (2H, s, C2′, C6′), 6.82 (1H, s, benzylic), 3.95 (6H, s, Ar−OCH_3 × 2), 3.93 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.4, 165.9, 153.4 (overlapped), 146.4, 140.5, 136.6, 127.7, 124.6, 123.5, 121.8, 113.2, 112.8, 109.3 (overlapped), 60.9, 56.3 (overlapped). DEIMS (70 eV) *m/z* (relative intensity): 312 (M^+, 100%), 297 (61.1%), 266 (15.5%), 223 (7.9%), 92 (35.3%), 76 (15.1%). HREIMS *m/z* (M^+), 312.0975; calcd for $C_{18}H_{16}O_5$, 312.0998.

4,6-Dimethoxyaurone (*Z*) (21). Yield, 84.3%; pale yellow crystal; mp, 145−146 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.86 (1H, dd, J = 8.3, 2.4 Hz, C2′), 7.87 (1H, dd, J = 7.8, 1.8 Hz, C6′), 7.33−7.47 (3H, m, C3′, C4′, C5′), 6.78 (1H, s, benzylic), 6.39 (1H, d, J = 1.8 Hz, C7), 6.13 (1H, d, J = 1.8 Hz, C5), 3.96 (3H, s, Ar−OCH_3), 3.92 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 180.7, 169.1, 169.0, 159.4, 147.8, 132.5, 131.1 (overlapped), 129.3, 128.8 (overlapped), 110.8, 105.2, 94.0, 89.2, 56.2, 56.1. DEIMS (70 eV) *m/z* (relative intensity): 282 (M^+, 100%), 239 (9.2%), 118 (5.7%), 106 (7.9%), 77 (6.2%). HREIMS *m/z* (M^+), 282.0869; calcd for $C_{17}H_{14}O_4$, 282.0892.

3′,4,4′,6-Tetramethoxyaurone (*Z*) (22). Yield, 71.2%; yellow crystal; mp, 166−168 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.45 (1H, d, J = 2.0 Hz, C2′), 7.43 (1H, dd, J = 8.2, 2.0 Hz, C6′), 6.91 (1H, d, J = 8.2 Hz, C5′), 6.72 (1H, s, benzylic), 6.33 (1H, d, J = 2.0 Hz, C7), 6.12 (1H, d, J = 2.0 Hz, C5), 6.89 (1H, s, benzylic), 3.95 (3H, s, Ar−OCH_3), 3.95 (3H, s, Ar−OCH_3), 3.92 (3H, s, Ar−OCH_3), 3.90 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 180.4, 168.7, 159.4, 150.5, 149.1, 146.9, 125.6, 125.4, 113.9, 111.4, 111.1, 94.0, 89.2, 56.2, 56.0

(overlapped), 55.9. DEIMS (70 eV) *m*/*z* (relative intensity): 342 (M^+, 100%), 311 (56.3%), 296 (8.3%), 77(2.5%). HREIMS *m*/*z* (M^+), 342.1086; calcd for $C_{19}H_{18}O_6$, 342.1103.

3′,4,4′,5,6-Pentamethoxyaurone (*Z*) (23). Yield, 84.7%; yellow crystal; mp, 161−162 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.47 (1H, d, J = 2.0 Hz, C2′), 7.45 (1H, dd, J = 2.0, 8.9 Hz, C6′), 6.93 (1H, d, J = 8.9 Hz, C5′), 6.74 (1H, s, benzylic), 6.51 (1H, s, C7), 4.26 (3H, s, Ar−OCH_3), 3.99 (3H, s, Ar−OCH_3), 3.97 (3H, s, Ar−OCH_3), 3.94 (3H, s, Ar−OCH_3), 3.83 (3H, s, Ar−OCH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 180.6, 163.7, 161.4, 151.6, 150.4, 148.9, 146.6, 136.6, 125.4, 125.3, 113.5, 111.7, 111.1, 107.2, 90.4, 62.4, 61.6, 56.6, 56.0, 55.9. DEIMS (70 eV) *m*/*z* (relative intensity): 372 (M^+, 100%), 357 (77.5%), 314 (7.3%), 299 (7.5%), 195 (17.8%), 167 (36.5%), 151 (10.3%). HREIMS *m*/*z* (M^+), 372.1190; calcd for $C_{20}H_{20}O_7$, 372.1209.

4,6-Dimethoxy-3′,4′-dimethylaurone (*Z*) (24). Yield, 34.5%; yellow crystal; mp, 184−186 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.61 (1H, d, J = 7.6 Hz, C6′), 7.59 (1H, s, C2′), 7.17 (1H, d, J = 7.6 Hz, C5′), 6.72 (1H, s, benzylic), 6.37 (1H, d, J = 1.7 Hz, C7), 6.37 (1H, d, J = 1.7 Hz, C5), 3.94 (3H, s, Ar−OCH_3), 3.90 (3H, s, Ar−OCH_3), 2.31 (3H, s, Ar−CH_3), 2.29 (3H, s, Ar−CH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 180.6, 169.0, 168.8, 159.4, 147.4, 138.5, 136.9, 132.3, 130.2, 130.1, 128.7, 111.1, 105.4, 94.0, 89.2, 56.1, 56.0, 19.8, 19.7. DEIMS (70 eV) *m*/*z* (relative intensity): 310 (M^+, 48.0%), 295 (88.1%), 133 (43.7%), 48 (100%). HREIMS *m*/*z* (M^+), 310.1199; calcd for $C_{19}H_{18}O_4$, 310.1205.

4,6,3′,4′-Tetramethylaurone (*Z*) (25). Yield, 84.1%; yellow crystal; mp, 176−178 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.66 (1H, d, J = 7.6 Hz, C6′), 7.63 (1H, s, C2′), 7.20 (1H, d, J = 7.6 Hz, C5′), 6.93 (1H, s, C5), 6.74 (2H, s, benzylic, C7), 2.62 (3H, s, Ar−CH_3), 2.41 (3H, s, Ar−CH_3), 2.31 (3H, s, Ar−CH_3), 2.30 (3H, s, Ar−CH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 185.0, 166.8, 148.0 (overlapped), 147.0, 139.4, 138.8, 137.0, 132.4, 130.1, 128.9, 126.0, 117.6, 111.9, 110.2, 22.4, 19.9, 19.8, 17.8. DEIMS (70 eV) *m*/*z* (relative intensity): 278 (M^+, 57.3%), 263 (100%), 148 (24.8%), 120 (11.0%). HREIMS *m*/*z* (M^+), 278.1301; calcd for $C_{19}H_{18}O_2$, 278.1307

3′,4′-Dimethoxy-4,6-dimethylaurone (*Z*) (26). Yield, 94.8%; yellow crystal; mp, 134−135 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.53 (1H, d, J = 1.5 Hz, C2′), 7.46 (1H, dd, J = 1.5, 8.5 Hz, C6′), 6.93 (1H, d, J = 8.5 Hz, C5′), 6.91 (1H, s, C5), 6.76 (1H, s, C7), 6.75 (1H, s, benzylic), 3.98 (3H, s, Ar−OCH_3), 3.94 (3H, s, Ar−OCH_3), 2.64 (3H, s, Ar−CH_3), 2.42 (3H, s, Ar−CH_3). ^{13}C NMR (270 MHz, $CDCl_3$): δ 184.8, 166.9, 150.4, 149.0, 147.9, 146.5, 139.5, 126.0, 125.6, 125.5, 117.7, 113.5, 111.9, 111.1, 110.1, 55.9, 55.8, 22.4, 17.7. DEIMS (70 eV) *m*/*z* (relative intensity): 310 (M^+, 100%), 295 (25.1%), 267 (15.5%), 252 (20.7%), 132 (3.4%), 120 (7.2%). HREIMS *m*/*z* (M^+), 310.1193; calcd for $C_{19}H_{18}O_4$, 310.1205.

Insect Antifeedant Assay. *Insects.* Common cutworms (*S. litura* F.) were purchased from Sumika Technoservice Co. Ltd. (Takarazuka, Japan). The insects were reared on an artificial diet (Insecta LF, Nihon Nosan Kogyo Co., Japan) in a controlled environment at 26.5 °C and 60% humidity.

Antifeedant Bioassay. For the insect antifeedant test against common cutworms, leaf disks, 2 cm in diameter, were prepared with a cork borer from fresh sweet potato (*Ipomoea batata* cv. *narutokintoki*) leaves that had been cultivated in the farm at Kinki University (Nara Pref. Japan). Two disks were treated with test compound in an acetone solution, and two other disks were treated with acetone only as a control. After the acetone was completely evaporated, the four disks were set in alternating positions in the same petri dish, 9.5 cm in diameter, with moistened filter paper on the bottom. Fifteen larvae (third instar) were released into the dish. The dishes were then kept in an insect-rearing room at 26.5 °C in the dark for 5−6 h. Partially consumed leaf disks were digitized by a PC scanner. Data were analyzed on a PC using NIH Image (http://rsb.info.nih.gov/nih-image/). For each experiment, the data for an intact disk were measured and compared to those of a treated disk. To measure the activities of test compounds, we used an antifeedant index: AFI = % of treated disks consumed/(% of treated disks consumed + % of control disks consumed) × 100. The AFI value was converted to the inhibitory rate (%): inhibitory rate (%) = (50 − AFI) × 2. The insect antifeedant potency of test compounds was evaluated in terms of the ED_{50} value for the rate of feeding inhibition calculated from the area of the leaf disk consumed. A straight line was fitted to the points obtained by the bioassay, and the ED_{50} was calculated as the dose that corresponded to the midpoint between complete inhibition and no effect.

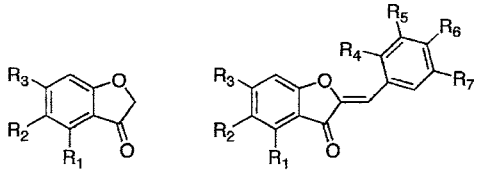
Measurement of Physicochemical Properties of Tested Aurones. The lipophilicity of a substance is closely related to its ability to penetrate a biological membrane. Log *P* is conventionally used to determine lipophilicity by the shaking-flask method using octanol and water. However, this method is difficult to apply to lipophilic substances, such as aurones and flavonoids (*12*). Therefore, we used log *k* to reflect lipophilicity in this paper. Log *k* for the insect antifeedant activity of aurones was calculated from the experimentally determined high-performance liquid chromatography (HPLC) retention time of the aurone toward a marker KI(t_R): $k = (t_R - t_0)/t_0$. HPLC analyses of aurones were performed with a VP10 (Shimadzu, Japan) and a Shimadzu UV/vis detector at 390 nm; column: Imtakt cadenza CD-18 (100 mm × ϕ 4.6 mm). The eluent was acetonitrile:water (6:4) at a flow rate of 1 mL/min.

The TLC R_f values of the tested aurones developed with EtOAc:Hexane (1:1) on a SiOH plate (developing length, 6 cm; Merck Silica Gel 60 F_{254} 0.25 mm thick) were evaluated to assess their effect on biological activity. The hydrogen-bonding parameter (HB) showed that a smaller R_f value meant stronger hydrogen bonding to SiOH; thus, the compound might act strictly at taste receptors or other receptors by hydrogen bonding (*9*).

RESULTS AND DISCUSSION

Previously, we reported that the insect antifeedant activities of benzopyranones, flavones, and chromone against *S. litura* larvae were decreased by the introduction of a hydroxyl group (*9*). In this study, we evaluated the insect antifeedant activities of various aurones (*Z* form) and their synthetic precursors, coumaranones, against *S. litura* larvae by a dual-choice leaf disk bioassay. Among the 23 test compounds, 3′,4,4′,6-tetramethoxyaurone (**22**) was the most active compound with an ED_{50} of 0.12 μmol/cm^2 (**Table 1**). B ring-eliminated compounds, coumaranones, showed that the introduction of methoxyl and methyl groups to a benzene ring increased biological activity, and 4,5,6-trisubstituted compounds showed the strongest activity, with an ED_{50} of 0.41 μmol/cm^2. Similarly, the tested aurones showed that the introduction of methoxyl group to the A and/or B rings increased the insect antifeedant activity, while 4,5,6- and 3′,4′,5′-trisubstituted compounds did not show this activity in this test (**Table 1**). This result differed from that with coumaranone but was similar to previous results using by flavones and chromones (*9*). The methoxyl group located at the 6-position (C6) of flavone, which corresponds to the 5-position (C5) of aurone, was easy to demethylate by *S. litura* larvae (*13*). This suggests that the introduction of a methoxyl group at the C5 of the aurone A ring may have the same effect as introducing a hydroxyl group, and as a result, the biological activity disappeared. While the introduction of 3′- or 4′-monosubstituted, catechol type disubstituted, or methylenedioxy groups to the B ring increased this activity, the introduction of 2′-monosubstituted and electron-withdrawing groups, such as 3′-Br or 3′-Cl derivatives, did not show this activity. In a B ring-substituted derivative, the most effective compounds were 3′-methoxyaurone (**10**) and 3′4′-dimethoxyaurone (**14**) (**Table 1**). It has been reported that the hydrophobic and steric properties of the 6- and 3′-positions of flavone are important for binding to the GABA receptor (*14*). The relationship between compounds that affect the GABA receptor and insect antifeedants has already been reported (*15*). As compared to **14**, the corresponding hydroxylated aurone (**16**) showed remarkably decreased activity, and the addition of a hydroxyl group to an active compound (**10**) gave similar results.

Table 1. Insect Antifeedant Activity of Coumaranones, Aurones, and Salannin on *S. litura* Larvae[a]



coumaranone, 5-7 **8-26**

	A ring			B ring					
compd	R_1	R_2	R_3	R_4	R_5	R_6	R_7	ED_{50} (μmol/cm^2)	pED_{50} (mol/cm^2)
5	OCH_3	H	OCH_3					3.87	5.41
6	CH_3	H	CH_3					0.68	6.17
7	OCH_3	OCH_3	OCH_3					0.41	6.39
coumaranone	H	H	H					inactive	
8	H	H	H	H	H	H	H	inactive	
9	H	H	H	OCH_3	H	H	H	inactive	
10	H	H	H	H	OCH_3	H	H	1.01	6.00
11	H	H	H	H	Cl	H	H	inactive	
12	H	H	H	H	Br	H	H	4.21	5.38
13	H	H	H	H	H	OCH_3	H	2.03	5.69
14	H	H	H	H	OCH_3	OCH_3	H	0.86	6.07
15	H	H	H	H	–O–CH_2–O–		H	1.61	5.79
16	H	H	H	H	OH	OH	H	inactive	
17	H	H	H	H	OCH_3	OH	H	inactive	
18	H	H	H	H	OC_2H_3	OH	H	1.96	5.71
19	H	H	H	H	OCH_3	H	OCH_3	3.45	5.46
20	H	H	H	H	OCH_3	OCH_3	OCH_3	inactive	
21	OCH_3	H	OCH_3	H	H	H	H	0.85	6.07
22	OCH_3	H	OCH_3	H	OCH_3	OCH_3	H	0.12	6.92
23	OCH_3	OCH_3	OCH_3	H	OCH_3	OCH_3	H	inactive	
24	OCH_3	H	OCH_3	H	CH_3	CH_3	H	inactive	
25	CH_3	H	CH_3	H	CH_3	CH_3	H	inactive	
26	CH_3	H	CH_3	H	OCH_3	OCH_3	H	1.02	5.99
salannin								0.066	7.18

[a] Salannin, positive control isolated from neem oil; inactive, antifeedant activity was less than 40% at 0.33 mg (ca. 1.52 μmol)/cm^2 disk treatment.

Table 2. Physicochemical Properties and Insect Antifeedant Activity of Active Compounds against *S. litura* Larvae

	physicochemical properties		
compd	mp	R_f	log *K*
10	118.0	0.61	0.737
12	116.0	0.61	1.047
13	131.5	0.55	0.689
14	154.0	0.54	0.741
15	186.5	0.44	0.624
18	122.0	0.45	0.382
19	154.0	0.54	0.741
21	145.5	0.33	0.560
22	167.0	0.07	0.277

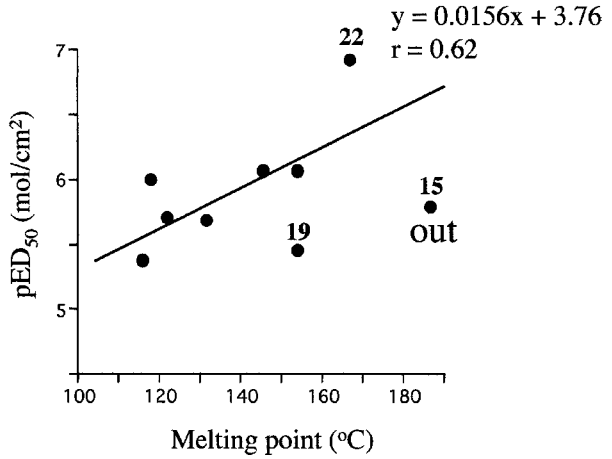


Figure 3. Correlation between insect antifeedant activity and melting point in active compounds.

These results suggest that the hydroxylation of aurones is disadvantageous for insect antifeedant activity against *S. litura* larvae, as well as flavones and chromones.

To determine the structural requirements that are needed for the activity of aurones, biological activities were compared to physicochemical parameters by regression. The biological activities and physicochemical parameters of the nine active compounds are summarized in **Table 2**. While melting points did not show a good correlation with insect antifeedant activity against *S. litura* larvae ($r = 0.62$, with **15** excluded from the data set) (**Figure 3**), compounds that were nearly inactive had high melting points. Despite its high melting point, a methylenedioxy derivative (**15**) showed moderate activity, and we considered that its potent activity may overcome its disadvantageous physicochemical property. Finally, significant correlations were found between biological activity (pED_{50}) and a HB calculated from the R_f value developed with SiOH TLC and a lipophilicity parameter (log *k*) calculated from the retention time in ODS HPLC. The respective correlation coefficients (*r*) were −0.83 and −0.70 (**Figure 4**). There were large differences between 3′-methoxyaurone (**10**) and 3′-ethoxy-4′-hydroxyaurone (**18**) with respect to HB and log *k*. This result suggested that the 3′-position and hydroxyl group in the B ring of aurones were sensitive to the effects of other molecules, SiOH

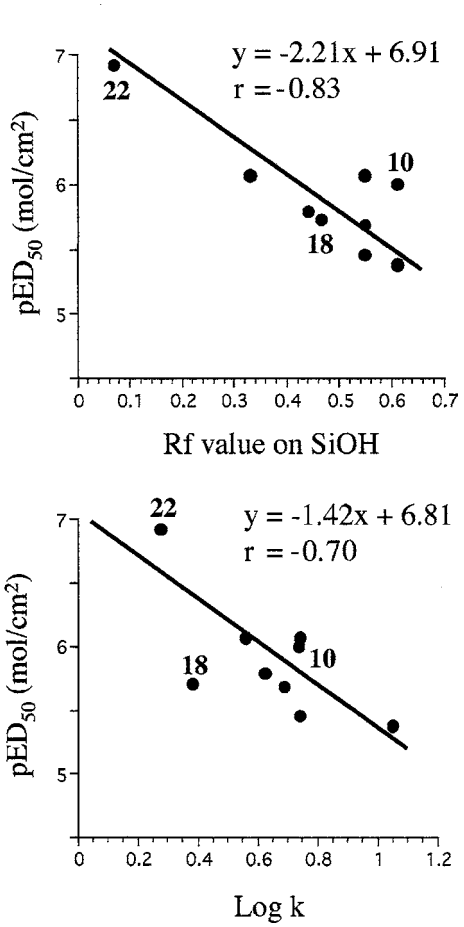


Figure 4. Correlation between insect antifeedant activity and hydrogen-bonding parameter, R_f value and lipophilic parameter log *k* value in active compounds.

and ODS in this case. Similarly, Cao et al. showed that log *P* was an important factor in the quantitative structure−activity relationship of an insect antifeedant, oxa(thia)diazoyl-3(2*H*)-pyridazinones, against armyworm (*Pseudaletia separata*) (*16*). These correlations between physicochemical properties and insect antifeedant activity were similar to previous results with 2,3-dihydrobenzofurans (*7*). This suggests that the antifeedant activity of aurone is strongly dependent on the similarity of the chemical structure between the benzofuran and the benzofuranone moiety of aurone.

In conclusion, the introduction of alkoxy and alkyl groups along with adequate HB seems to contribute to the antifeedant activity of the compounds tested. This could lead to the development of a compound that regulates insect behavior from natural flavonoids.

LITERATURE CITED

(1) Harborne, J. B.; Grayer, R. J. Flavonoids and insects. In *The Flavonoids*; Harborne, J. B., Ed.; Chapman & Hall: London, 1993; pp 589−618.

(2) Mohan, P.; Joshi, T. Two anthochlor pigments from heartwood of *Pterocarpus marsupium*. *Phytochemistry* **1989**, *28*, 2529−2530.

(3) Nakayama, T. Enzymology of aurone biosynthesis. *J. Biosci. Bioeng.* **2002**, *64*, 487−491.

(4) Huang, L.; Wall, M. E.; Wani, M. C.; Navarro, H.; Santisuk, T.; Reutrakul, V.; Seo, E.-K.; Farnsworth, N. R.; Kinghorn, A. D. New compounds with DNA strand-scission activity from the combined leaf ant stem of *Uvaria hamiltonii*. *J. Nat. Prod.* **1998**, *61*, 446−450.

(5) Kayser, O.; Kiderlen, A. F.; Folkens, U.; Kolodziej, H. *In vitro* leishmanicidal activity of aurones. *Planta Med.* **1999**, *65*, 316−319.

(6) Pare, P. W.; Dmitrieva, N.; Mabry, T. J. Phytoalexin aurone induced in *Cephalocereus senilis* liquid suspension culture. *Phytochemistry* **1991**, *30*, 1133−1135.

(7) Morimoto, M.; Urakawa, M.; Fujitaka, T.; Komai, K. Structure-activity relationship for the insect antifeedant activity of benzofuran derivatives. *Biosci., Biotechnol., Biochem.* **1999**, *63*, 840−846.

(8) Isman, M. B.; Proksch, P. Deterrent and insecticidal chromenes and benzofurans from *Encelia* (Asteraceae). *Phytochemistry* **1985**, *24*, 1949−1951.

(9) Morimoto, M.; Tanimoto, K.; Nakano, S.; Ozaki, Y.; Nakano, A.; Komai, K. Insect antifeedant activity of flavones and chromones against *Spodoptera litura*. *J. Agric. Food Chem.* **2003**, *51*, 389−393.

(10) Lawrence, N. J.; Rennison, D.; McGown, A. T.; Hadfield, J. A. The total synthesis of an aurone isolated from *Uvaria hamiltonii*: Aurones and flavones as anticancer agents. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3759−3763.

(11) Varma, R. S.; Varma, M. Alumina-mediated condensation. A simple synsthesis of aurones. *Tetrahedron Lett.* **1992**, *33*, 5937−5940.

(12) Hallgas, B.; Patonay, T.; Kiss-Szikszai, A.; Dobos, Z.; Hollósy, F.; Erös, D.; Örfi, L.; Kéri, G.; Idei, M. Comparison of measured and calculated lipophilicity of substituted aurones and related compounds. *J. Chromatogr. B* **2004**, *801*, 229−235.

(13) Okuno, Y.; Miyazawa, M. Biotransformation of sinesetin by the larvae of the common cutworm (*Spodoptera litura*). *Biol. Pharm. Bull.* **2004**, *27*, 1289−1292.

(14) Marder, M.; Estiú, G.; Blanch, L. B.; Viola, H.; Wasowski, C.; Medina, J. H.; Paladini, A. C. Molecular modeling and QSAR analysis of the interaction of flavone derivatives with the benzodiazepine binding site of the $GABA_A$ receptor complex. *Bioorg. Med. Chem.* **2001**, *9*, 323−335.

(15) Eichenseer, H.; Mullin, C. A. Antifeedant comparisons of GABA/glycinergic antagonists for Diabroticite leaf beetle (Coloptera: Chrysomelidae). *J. Chem. Ecol.* **1997**, *23*, 71−82.

(16) Cao, S.; Wei, N.; Zhao, C.; Li, L.; Huang, Q.; Qian, X. Syntheses, antifeedant activity, and QSAR analysis of new oxa(thia)diazolyl 3(H)-pyridazinones. *J. Agric. Food Chem.* **2005**, *53*, 3120−3125.

Received for review September 6, 2006. Revised manuscript received November 15, 2006. Accepted November 28, 2006.

JF062562T