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Iridodials: enantiospecific synthesis and stereochemical assignment of the pheromone for the golden-eyed lacewing, *Chrysopa oculata*

Kamlesh R. Chauhan,[a,*] Qing-He Zhang[a,b] and Jeffrey R. Aldrich[a]

[a]*USDA-ARS Chemicals Affecting Insect Behavior Laboratory, B-007, BARC-West, Beltsville, MD 20705, USA*
[b]*Department of Entomology, University of Maryland, College Park, MD 20742, USA*

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Abstract—1*R*,2*S*,5*R*,8*R*; 1*R*,2*S*,5*R*,8*S*; 1*S*,2*S*,5*R*,8*R*; and 1*S*,2*S*,5*R*,8*S*-Iridodials have been prepared in five steps from 4a*S*,7*S*,7a*R* and 4a*S*,7*S*,7a*S*-nepetalactones, major components of catnip oil. 1*R*,2*S*,5*R*,8*R*-Iridodial has been identified as a male-produced male-aggregation pheromone for *Chrysopa oculata*, the first pheromone of any kind identified for lacewings.

Lacewings, especially green lacewings (Chrysopidae), are some of the most common predators of aphids and other soft-bodied insects.[1] Furthermore, because of their commercial availability and resistance to insecticides, chrysopids are among the most commonly released predators for augmentative biological control,[2] albeit with differing degrees of success. While green lacewings are increasingly being released for biocontrol, methods are still needed to retain the predators near augmentation sites and/or to attract wild predators to target areas.[3] Intra-specific chemical signals, namely pheromones, may have practical potential for managing lacewings, and would be of great economic importance. In our efforts[4] to search for pheromones of *Co. oculata* (*Co.* = *Chrysopa*), one of the most common lacewings in the eastern United States, a single isomer of iridodial was discovered to be the key pheromone component. The initial identification of iridodial occurred during gas chromatography-electroantennogram detection (GC-EAD) and GC–mass spectrometry (GC–MS)[5,6] analyses of nepetalactol **3**, which contained iridodials **1a** and **1b** as impurities (5–8%). Subsequent analyses of extracts from the 1st to 8th abdominal segments of *Co. oculata* males revealed the presence of iridodial **1a**.

Iridodials have been identified from many other natural sources such as ants, especially the *Iridomyrmex* spp.,[7] as well as from rove beetles and a stick insect.[8] In all these cases, iridodials serve as defensive compounds. Citronellal has been explored as a starting material for the synthesis of iridodial and iridomyrmecin,[9] however to date synthesis of enantiomerically pure iridodial diastereomers with four asymmetric centers has not been reported. To establish absolute configuration, and to prepare sufficient quantities of isomerically pure iridodial **1a**, a convenient synthesis was developed (Fig. 2).

Availability of 4a*S*,7*S*,7a*R*(*Z*,*E*) **2a** and 4a*S*,7*S*,7a*S*(*E*,*Z*) **2b** nepetalactone [major components of catnip oil (*Nepeta*

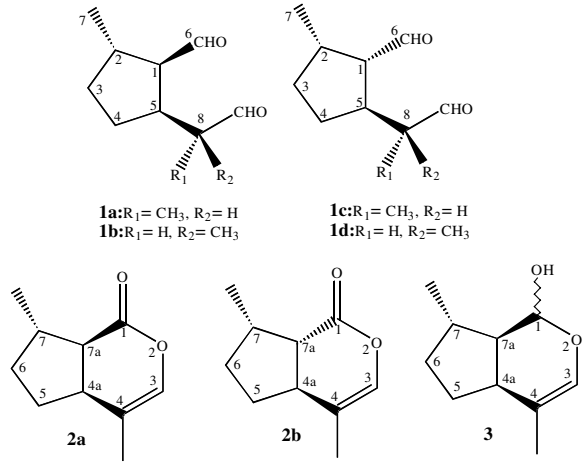

Figure 1. Monoterpene-iridoids: **1a**: 1*R*,2*S*,5*R*,8*R*-iridodial; **1b**: 1*R*,2*S*,5*R*,8*S*-iridodial; **1c**: 1*S*,2*S*,5*R*,8*R*-iridodial; **1d**: 1*S*,2*S*,5*R*,8*S*-iridodial; **2a**: 4a*S*,7*S*,7a*R*(*Z*,*E*)-nepetalactone; **2b**: 4a*S*,7*S*,7a*S*(*E*,*Z*)-nepetalactone; **3**: 4a*S*,7*S*,7a*R*(*Z*,*E*)-nepetalactol.

Keywords: Iridodials; Nepetalactone; Lacewing.
* Corresponding author. Tel.: +1-3015045166; fax: +1-3015046580; e-mail: chauhank@ba.ars.usda.gov

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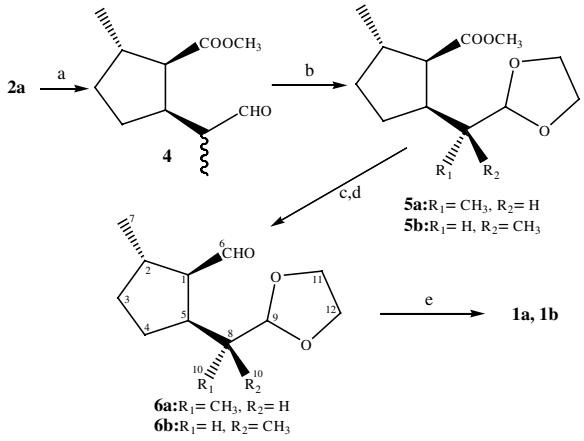

Figure 2. Synthesis of iridodial **1a/1b**. Reagents and conditions: (a) $NaHCO_3$ (5%), $MeOH/H_2O$ (95:5), rt; (b) ethane-1,2-diol, toluene, cat. TsOH, azeotropic dehydration; (c) DIBAL, toluene, −78 to 0 °C; (d) PDC, dry DCM, rt; (e) THF, 2 N HCl, rt.

cataria), quantitatively isolated by chemical separation][10] was the key to this synthetic approach. Methanolysis of **2a** at room temperature in 5% methanolic $NaHCO_3$ solution (95:5 methanol/water) gave an isomeric mixture of methyl ester–aldehyde **4**, which was quantitatively protected to the cyclic acetals **5a** and **5b** by azeotropic dehydration with ethane-1,2-diol in 94% yield over the two steps. Cyclic acetals **5a** and **5b** were separated by flash column chromatography.[11] DIBAL reduction followed by PDC oxidation of **5a** and **5b** individually afforded mono-protected dialdehydes **6a** and **6b** in 78% yield over two steps. At this stage, the absolute configuration at the C-8 asymmetric center of each isomer was established by NMR spectroscopy (^1H, ^{13}C-APT, and COSEY)[12,13] of mono-protected iridodials to avoid interference of lactol formation in free iridodials. Deprotection of the cyclic acetal was carried out under mild acidic hydrolysis at room temperature to conclude the synthesis of iridodials **1a** in 65% and **1b** in 48% overall yields.

Repetition of the foregoing sequence using 4a*S*,7*S*,7a*S*-nepetalactone **2b** proceeded analogously and with comparable yields to give **1c** and **1d** (Fig. 1). When injected as a mixture for GC analyses, only synthetic iridodial **1a** co-eluted with the natural iridodial extracted from the 1st to 8th abdominal segments of *Co. oculata*, and **1a** was identical to the natural product by GC–MS.

In conclusion, 1*R*,2*S*,5*R*,8*R*-iridodial **1a**, along with three isomeric iridodials,[14,15] have been conveniently prepared in five steps from readily available starting materials. Iridodial **1a** attracts conspecific males and possibly females in the field. The availability of synthetic 1*R*,2*S*,5*R*,8*R*-iridodial will facilitate further efforts to semiochemically promote biocontrol involving this and other lacewing species.

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11. Ethyl acetate (5%) in hexane as mobile phase and 230–400 mesh silica gel as stationary phase.
12. Mono-protected iridodial **6a**: ^1H NMR ($CDCl_3$, 300 MHz): δ 9.75 (1H, d, $J = 3.8$, H6), 4.71 (1H, d, $J = 3.7$ Hz, H9), 3.85 (4H, m, H11, H12), 2.54 (1H, ddd, $J = 3.8$, 3.0, 12.9 Hz, H1), 2.2 (2H, m, H2, H8), 1.92 (2H, m, H5, H3), 1.41 (1H, m, H3), 1.15 (2H, m, H4), 1.01 (3H, d, $J = 7.19$ Hz, H7), and 0.91 (3H, d, $J = 6.81$ Hz, H10) ppm; $J = 13.2$ Hz at H5–H8, indicating *threo* or *trans* configuration.[13] ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.5 (C6), 106.8 (C9), 64.9 (C11), 64.7 (C12), 60.41 (C1), 44.0 (C8), 36.9 (C2), 35.3 (C5), 32.9 (C3), 30.6 (C4), 21.4 (C7), and 13.7 (C10) ppm.
6b: ($CDCl_3$, 300 MHz): δ 9.69 (1H, d, $J = 4.5$, H6), 4.82 (1H, d, $J = 3.0$ Hz, H9), 3.85 (4H, m, H11, H12), 2.43 (1H, ddd, $J = 4.1$, 3.7, 12.6 Hz, H1), 2.0 (4H, m, H2, H3, H5, H8), 1.47 (1H, m, H3), 1.24 (2H, m, H4), 1.01 (3H, d, $J = 6.81$ Hz, H7), and 0.91 (3H, d, $J = 6.71$ Hz, H10) ppm; $J = 11.3$ Hz at H5–H8, confirming *erythreo* or *cis* configuration.[13] ^{13}C NMR ($CDCl_3$, 75 MHz) δ 203.8 (C6), 105.9 (C9), 65.1 (C11), 65.0 (C12), 60.6 (C1), 45.8 (C8), 37.4 (C2), 33.9 (C5), 33.8 (C3), 30.6 (C4), 21.4 (C7), and 12.2 (C10) ppm.
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