J Plant Growth Regul (2005) 23:170–178
DOI: 10.1007/s00344-004-0034-2

J P G R
Journal of Plant Growth Regulation

Structural and Biological Diversity of Cyclic Octadecanoids, Jasmonates, and Mimetics

Axel Mithöfer, Mathias Maitrejean, and Wilhelm Boland

Bioorganische Chemie, Beutenberg Campus, Max-Planck-Institut für Chemische Ökologie, Hans-Knöll-Str. 8, D-07745, Jena, Germany

Abstract

The jasmonate family of plant signaling compounds comprises biologically highly active cyclopentenones (for example, 12-oxo-phytodienoic acid) (12-OPDA) and cyclopentanones (for example, jasmonic acid) (JA) of related origin *via* the octadecanoid pathway, and structure. Among others, their biological activities include a broad range of defense-related reactions. Several lines of evidence indicate both common and different biological responses mediated by 12-OPDA and/or JA, suggesting the existence of at least two separate structure-activity groups. Based on the structure of a bacterial phytotoxin, coronatine, with similar biological activities compared with jasmonates, indanoyl isoleucine conjugates have been designed as functional synthetic mimics of octadecanoid-derived signals. The structural diversity of naturally occurring jasmonate-related compounds and synthetic mimics is discussed with respect to their corresponding biological activities. Novel strategies for the synthesis of various indanoyl isoleucine conjugates will be presented.

Key words: Coronatine; Indanoyl isoleucine conjugates; Oxylipins; Signalling molecules

Introduction

In recent years there has been rapid progress in both the identification of lipophilic signals and the understanding of their involvement in signaling processes in higher plants. A large and variable group of highly active lipid-derived signals, referred to as oxylipins, is generated initially by oxidation of unsaturated fatty acids. Oxylipins represent new endogenous signals involved in developmental processes as well as in biotic- and abiotic-induced stress responses in plants (Blee 2002; Weber 2002; Wasternack and Hause 2002; Mithöfer and others 2004). Among these, the best-examined signal molecules belong to the jasmonate family derived from linolenic acid and synthesized *via* the octadecanoid pathway (Schaller and others this issue). Based on structural similarities, these cyclic octadecanoids and derivatives are often discussed as plant analogs of the animal arachidonic acid-derived eicosanoids, implicating high physiological activities and diversity.

(-) - Jasmonic acid (JA) is the lead molecule of the whole octadecanoid-derived family of jasmonate-related phytohormones, which occur in all higher plants (Meyer and others 1984). These compounds are involved in defense against herbivores (Halitschke and Baldwin this issue), bacterial

Received: 27 August 2004; accepted: 2 September 2004; Online publication: 13 January 2005
Corresponding author; e-mail: boland@ice.mpg.de

and fungal pathogens (Pozo and others this issue), as well as in senescence, developmental processes, wounding (Howe this issue), abiotic stress responses, and mechanotransduction (Creelman and Mullet 1997; Weiler 1997; Wasternack and Hause 2002). An exogenous supply of jasmonates, that is JA and its methyl ester (MeJA), or of their biosynthetical precursor, 12-oxo-phytodienoic acid (12-OPDA), induces the biosynthesis of certain proteins and various secondary metabolites most of which are defense or stress related. In many plant species, amino acid conjugates of JA are present. They display activities comparable to those described for JA, as has been shown for induction of gene expression in *Hordeum vulgare* L. (barley) and *Lycopersicon esculentum* Mill. (tomato) (Kramell and others 1997; Wasternack and others 1998) or volatile induction in lima beans (*Phaseolus lunatus* L.) (Krumm and others 1995). Another derivative of jasmonates, *cis*-jasmone, is an airborne product of JA catabolism (Koch and others 1999). For a long time *cis*-jasmone was well known as a flower volatile involved in insect attraction. Recently, it has been identified also as a herbivory-induced insect semiochemical (Birkett and others 2000).

The present overview focuses on structure-activity relationships of the main naturally occurring signaling compounds of the octadecanoid-derived jasmonate family and on the syntheses of mimetics with improved bioactivities.

Diverse Activity Profiles Among Jasmonate-Related Signals

Different octadecanoid pathway-derived compounds, such as the cyclopentenone 12-OPDA and the cyclopentanone JA, clearly vary in their ability to induce plant responses. Results supporting this finding include (i) the induction and accumulation of secondary compounds in various plants, (ii) tendril coiling in *Bryonia dioica* Jacq., and (iii) the expression of responding genes. In soybean (*Glycine max* L.) cell cultures, 12-OPDA was a highly active inducer of the synthesis of isoflavonoid-phytoalexins and glyceollins, compared to jasmonates (Fliegmann and others 2003). In contrast, accumulation of the alkaloid benzo[c]phenanthridine in *Eschscholzia californica* Cham. cell cultures was strongly induced by jasmonates rather than by 12-OPDA (Haider and others 2000). In that study, about 200 jasmonate- and octadecanoid-related compounds were investigated. In *P. lunatus*, the composition of volatiles emitted after treatment with early and late intermediates of the jasmonate biosynthetic pathway differed clearly. Whereas linolenic acid and 12-OPDA elicited the biosynthesis of a homoterpene of diterpenoid origin, JA triggered the synthesis of mono- and sesquiterpenes (Koch and others 1999). The thigmonastic tendril coiling movement in *B. dioica* is induced by mechanical stimulation as well as by exogenously applied linolenic acid, 12-OPDA and jasmonates (Falkenstein and others 1991; Weiler and others 1994). Based on the *B. dioica* tendril coiling response upon treatment with more than 150 different structural analogs of these signaling compounds, Blechert and others (1997, 1999) suggested the presence of two structurally non-overlapping groups of biological activity. The more effective group belongs to the cyclic octadecanoids (12-OPDA) and the other to the jasmonates. However, in *L. esculentum* and *H. vulgare*, both groups of compounds exhibited a more similar activity, although certain sets of genes responded differently to 12-OPDA and jasmonates (Wasternack and others 1998; Kramell and others 2000).

These findings support the hypothesis that at least two separate groups, the 12-OPDA-related and the JA-related signaling compounds (Figure 1), are present, each bearing a certain biological activity to elicit responses in plants besides a shared set of inducible responses (Blechert and others 1997, 1999; Koch and others 1999; Haider and others 2000; Fliegmann and others 2003). Recently the group of octadecanoids was further extended by another class of bioactive compounds, namely, the phytoprostanes (Müller 2004) (Figure 1). Thus, it has been speculated that an 'octadecanoid signature' rather than individual molecules might be responsible for the specificity in the induction of plant responses (Weber and others 1997). In addition, at least two different signaling pathways and/or corresponding receptors might be involved (Blechert and others 1999). Farmer and coworkers suggested that 12-OPDA and JA can participate in the same signaling pathway in a CoI1-dependent manner (see below) because both signal compounds repress and activate the expression of overlapping sets of genes in *Arabidopsis* (Reymond and others 2000). Thus, a distinct additional activity might be present based on electrophilic properties of cyclopentenones, including 12-OPDA (Farmer and others 2003) (Figure 1), as well as other non-JA-related electrophilic species (Almeras and others 2003). This scenario is strongly supported by data from an *Arabidopsis* mutant that is unable to convert 12-OPDA (Stinzi and others 2001). The data available suggest that JA-related as well as 12-OPDA-related compounds can act alone or in concert in a signaling

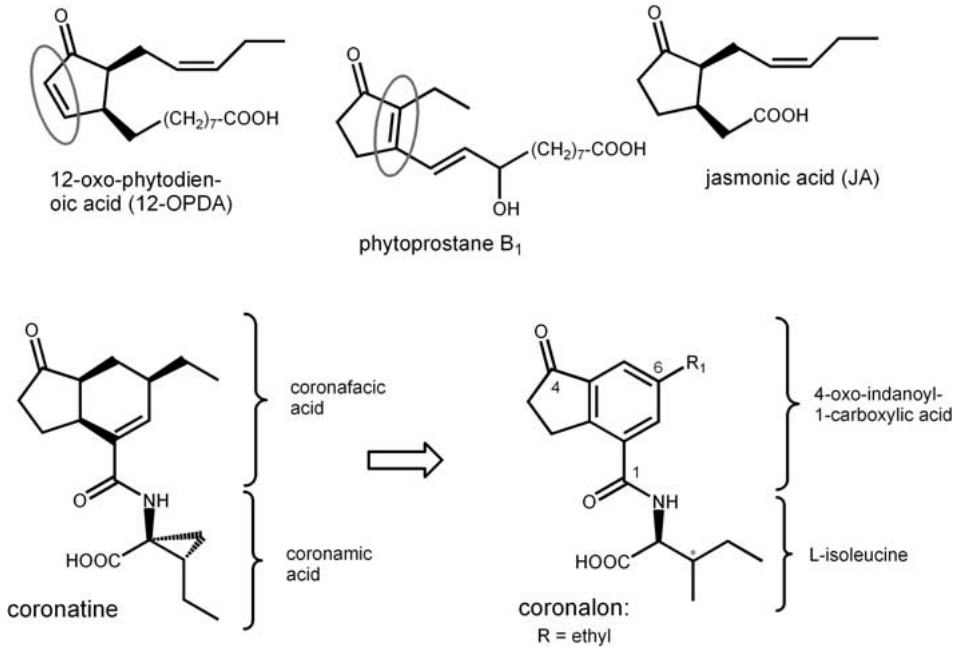

Figure 1. Structures of relevant jasmonate-related compounds and mimics. The electrophilic character of 12-oxo-phytodienoic acid and phytoprostane B_1 in contrast to jasmonic acid is indicated by a circle.

network; however, the underlying molecular mechanism is not known yet.

Coronatine as a Natural Mimic of Jasmonate-Related Signals

Interestingly, the bacterial phytotoxin coronatine (Figure 1) (Ishihara and others 1977), to a certain extent, mimics the biological activities of 12-OPDA and/or JA, respectively. Among others, responses elicited by coronatine include tendril coiling (Weiler and others 1994; Stelmach and others 1998), biosynthesis of terpenoids and other volatiles (Boland and others 1995), expression of genes in *L. esculentum* or *H. vulgare L.* (for example jasmonate-induced proteins, JIPs) (Wasternack and others, 1998), and accumulation of alkaloid- and isoflavonoid-phytoalexins (Haider and others 2000; Fliegmann and others 2003). Moreover, indole glucosinolate accumulation in *Brassica* species has been induced by coronatine (Bodnaryk and Yoshihara 1995). Pautot and others (2001) presented data suggesting that coronatine mimicked the wound response but was insufficient to induce JA-regulated PR genes in tomato. Although some differences between the effects of coronatine, 12-OPDA, and JA have been well documented in those studies, it was obvious that the phytotoxin represents a highly active molecular mimic that matches the activity profiles of both phytohormones, 12-OPDA and JA, to a great extent and in some cases with even higher efficiency. Common structural features are also obvious for a number of the recently discovered phytoprostanes (Müller 2004). In addition, Feys and others (1994) generated the first *coronatine-insensitive* (*coi1*) mutant of *Arabidopsis*. This mutant showed the same insensitivity against treatment with MeJA and coronatine, indicating a similar mode of action of these signaling compounds. Consequently, coronatine became an interesting and valuable compound for studies of octadecanoid- and JA-regulated pathways as well as related responses in plants.

Originally, coronatine was isolated from a fermentation broth of the phytopathogenic bacterium *Pseudomonas syringae* var. *atropurpurea* (Ishihara and others 1977) but is also produced by other pathovars of *P. syringae*, for example, *tomato* and *glycinea*. Unfortunately, neither the fermentation of *Pseudomonas* cultures nor synthetic routes to coronatine represented satisfying practical approaches for the production of large amounts of the compound (Ishihara and Toshima 1999). However, the structure of coronatine has been successfully used as a template to design a set of new coronatine-like molecules that exhibit 12-OPDA- and JA-related biological activities in plants.

Synthesis of Indanoyl Amino Acid Conjugates Resembling Coronatine

Coronatine consists of two molecules from different biosynthetic origins linked *via* an amide bond. The bottom half is the rare amino acid, coronamic acid, derived from isoleucine (Parry and others 1991). The upper half is the polyketide coronafacic acid (Jiralerspong and others 2001). Coronatine displays structural elements resembling jasmonic acid and 12-OPDA. Owing to its high biological activity, coronatine has always been an attractive target for synthesis. However, none of the about 15 published syntheses (Lauchli and Boland 2003) was efficient enough to yield large quantities or a rapid access to structural analogs. Therefore, a new class of aromatic analogs was developed that displayed activities similar to coronatine, but lacked the stereochemical complexity of the fungal metabolite. The coronafacic acid moiety was simplified to 4-oxo-indanoyl carboxylic acid and coronamic acid was replaced by its biosynthetic precursor L-isoleucine by formal ring-opening of the cyclopropane. Despite the amino acid, the aromatic analog (R^1 = H) of coronatine has no chiral center and is easily available in larger quantities by standard chemistry (Krumm and others 1995; Blechert and others 1999).

Although the three-dimensional architecture of the two building blocks, coronafacic acid and 4-oxo-indanoyl-1-carboxylic acid is rather different (Figure 1), both structural types form highly active elicitors of plant secondary metabolism upon conjugation with appropriate amino acids. The bicyclic system of coronafacic is somewhat compact and concave whereas the indanoyl system is almost completely planar and places the relevant functional groups (for example, the keto group of the cyclopentanone) in spatial environment different than coronafacic acid, as independently proven by crystal structure analysis (Schüler and others 2001). A planar structure is also typical for phytoprostanes B_1. Systematic permutation of the amino acid moiety in the indanoyl conjugates demonstrated that the conjugate with L-isoleucine (a conjugate with D-isoleucine is inactive) is the most effective. Its biological activity exceeds even that of a conjugate with authentic coronamic acid (Figure 2). In general, only aliphatic amino acids, resembling the size and polarity of L-isoleucine result in active conjugates; heteroatoms in the amino acid moiety are not tolerated (Krumm and others 1995).

Although coronatine is only active if a free carboxylic acid is present, the indanyol-conjugate with isoleucine can be used as the methyl ester (R = CH_3) (Figure 3). Activated esters such as allyl esters or phenyl esters can also be employed and occasionally display a moderately higher activity than the methyl ester (Krumm and others 1995; Blechert and others 1999). The importance of a free acid for interaction with macromolecular targets is additionally demonstrated by the synthesis of an α-methylated conjugate with leucine or with coronamic acid. In both cases only the free acid was biologically active and induced the biosynthesis of volatiles in *P. lunatus* leaves; the two methyl esters failed (Krumm and others 1995). Apparently the esterase(s) of the plant could not cleave the α-branched esters and, hence, the conjugates remained inactive. Because amide-cleaving enzymes are also hampered by this type of α-branching, these two conjugates additionally prove that the intact

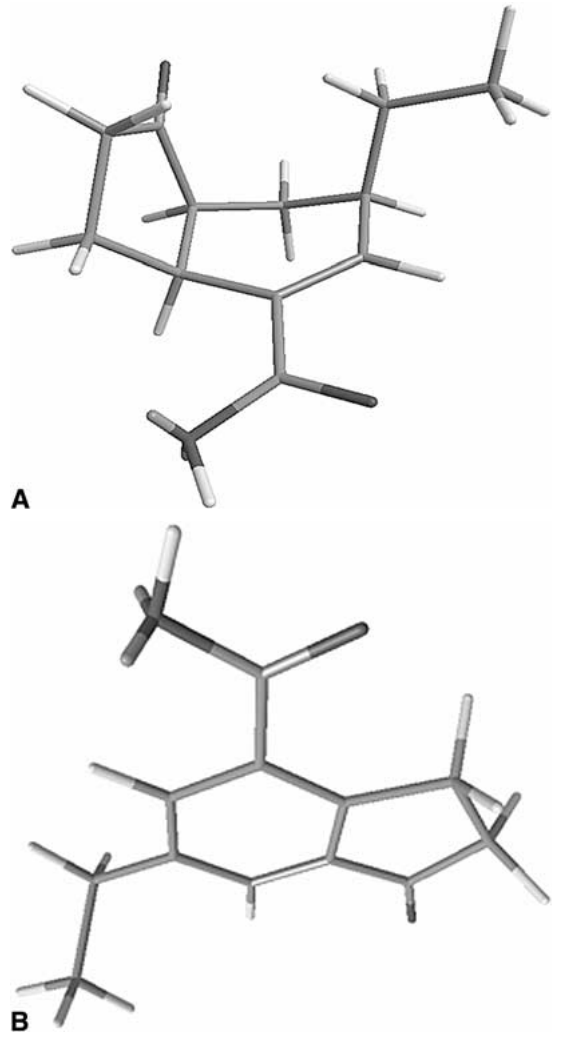

Figure 2. Geometricly optimized structure of (**A**) coronafacic acid and (**B**) 4-oxo-indanoyl-1 -carboxylate.

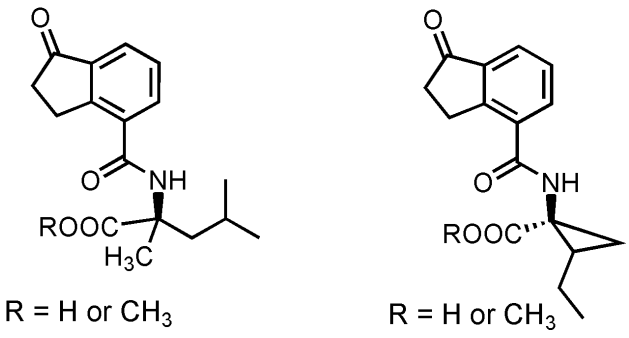

Figure 3. Conjugates of 4-oxo-indanoyl-1-carboxylate with α-branched 2-methyl-leucine (left) and coronamic acid (right). Free acids (R = H) are active, esters (R = CH_3) are not.

molecule rather than a component is required for biological activity. The high activity of the methyl ester of the indanoyl conjugates has, however, practical advantages because the ester, unlike the free acid, easily passes membrane barriers.

Because the isoleucine conjugates of 4-oxo-indanoyl-1-carboxylic acid better match the structures of the corresponding amino acid conjugates of jasmonic acid, for example, jasmonoyl-isoleucin, the hypothesis was suggested that coronatine and the indanoyl conjugates may mimic bioactive JA-conjugates rather than the free hormone (Krumm and others 1995). A systematic study with conjugates of jasmonic acid with L- and D-amino acids demonstrated high activity for such conjugates (Wasternack and others 1998). Recent findings of Staswick and Tiryaki (2004) using *Arabidopsis* wild type and the JA-insensitive *jar1-1* mutant, strongly support this hypothesis.

Even more potent elicitors of plant secondary metabolism were obtained by creating 4-oxo-indanoyl conjugates with L-isoleucine that carry an additional substituent at C-6 of the aromatic nucleus, which corresponds to the position of the ethyl substituent in coronatine. This novel class of indanoyl-elicitors proved to be *i*) generally more active than the simple indanoyl conjugates and *ii*) led to the induction of additional and previously unobserved metabolic activities (*vide infra*). The most active compound of this group, the 6-ethyl indanoyl isoleucine methyl ester conjugate, was named ''coronalon'' (*coro*natine *analog*ue) (Schüler and others 2004) and two different synthetic routes to 6-substituted 4-oxo-indanoylcarboxylic acid have been developed (Schüler and others 2001; Lauchli and others 2002). The additional substituent offered for the first time the unique possibility to optimize an elicitor molecule for optimum performance by simple substituent permutation (Figure 4). The 6-bromo-indanoyl conjugate **4** served a central intermediate, allowing the synthesis of a whole library ''coronalones'' in only few steps. Standard chemistry affords the 3-nitrobenzoic acid **2** which can be transformed to **3** *via* a carefully elaborated protocol of reduction, diazotation, replacement of the diazonium salt by bromide, and a final cyclization in the presence of the *Lewis*-acid $AlCl_3$. The overall yield of the sequence, including conjugation with L-isoleucine, is about 50%. The aromatic halide **4** now serves as the central intermediate that can be alkylated in the presence of Pd(0) with an array of organotin reagents. Following the strategy originally described by Stille (1986) the group transfer to the aromatic nucleus can be achieved in moderate to good yields (30-60%).

The versatile concept also allows the introduction of substituents containing heteroatoms. A 6-azido conjugate (Schüler and others 1999) is a valuable probe that can be used to study the macromolecular binding site of oxylipin hormones such as jasmonates and 12-OPDA. After binding, the photo-labile azide can be flash-activated and converted into a reactive intermediate expected to bind selectively to a nucleophilic group of the macromolecule (Schüler and others 1999). First attempts using a 6-azido-indanoyl conjugate with radioactive L-isoleucine (^{14}C) have been promising (unpublished results). Conjugates with 6-furyl- or 6-thiophenyl-substituents are weakly fluorescent and may serve as the basis for the development of novel highly fluorescent and at the same time bioactive conjugates. The latter could become useful tools for studying transport phenomena and for the localization of binding elements in the plant cell. Unfortunately, the 6-substituent cannot be used to attach the indanoyl conjugate to an affinity column. Bioassays with conjugates of increasing size of the 6-substituent revealed an activity limit, if the side chain is longer than four to five carbons. Derivatives with alkoxy-substituents in this position are also active and promise advantages in practical applications because they display an improved water solubility, which in some cases limits the use of 6-alkyl conjugates (Lauchli and others 2002).

The skeleton of the 4-oxo-indanoyl-1-carboxylic acid can be further modified by introduction of a double bond into the cyclopentanone (unpublished results). This transformation creates an electrophilic moiety and the structure becomes more similar to 12-OPDA. In combination with unsaturated 6-substituents (Figure 5) (R = -$CH{=}CH_2$, -$CH{=}CH{-}CH{=}CH_2$) another series of ''fluorescent elicitors'' can be envisaged. Preliminary bioassays with the simple indenone conjugate (R = H) demonstrate

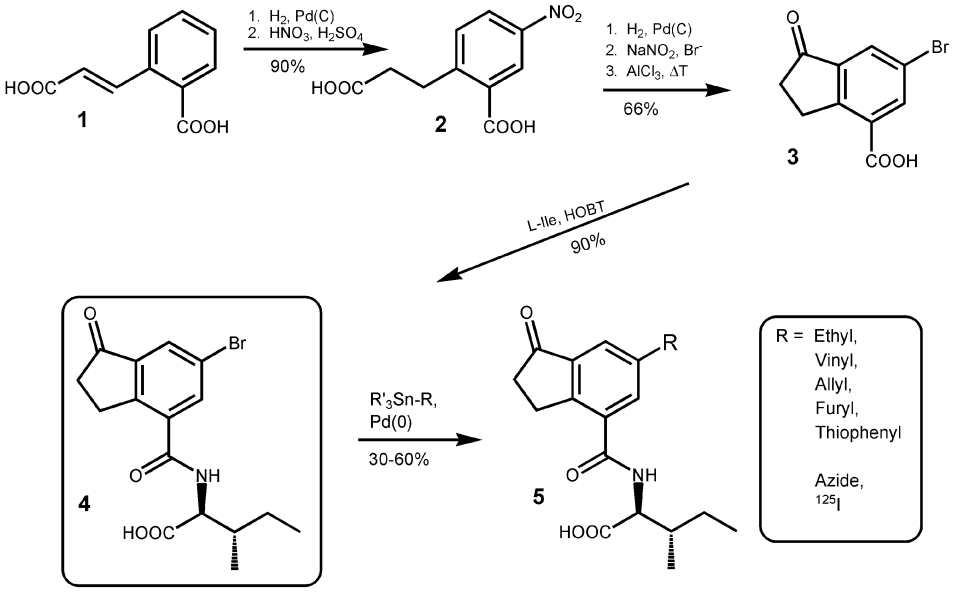

Figure 4. Synthetic route to 6-substituted 4-oxo-indanoyl-isoleucine conjugates. The concept utilizes 6-bromo-indanoyl-isoleucine as a key intermediate for transition metal-catalyzed alkylation reactions.

these compounds to be active, but their profile of bioactivities is different from that of the typical indanones (unpublished results).

Coronalon and Derivatives as Synthetic Mimics of Jasmonate-Related Signals

The indanoyl amino acid conjugates have been developed with respect to their biological activities in typical coronatine responsive assays (Schüler and others 2001; Lauchli and Boland 2002; Lauchli and others 2002). The highly active coronalon obviously combines the activity profiles of the two groups of jasmonate-related compounds, similar to coronatine. For example in *G. max* cell suspension cultures, glyceollin synthesis is mainly induced by the octadecanoid 12-OPDA (Fliegmann and others 2003), just as is the tendril coiling response in *B. dioica* (Weiler and others 1994; Stelmach and others 1998). In contrast, nicotine synthesis (Baldwin and others 1997), benzo[c]phenanthridine synthesis (Haider and others 2000), and *JIP23* gene expression (Kramell and others 2000) are typically jasmonate-triggered reactions. The broad spectrum of biological activities of coronalon in higher plants is given in Table 1 and was originally demonstrated by Schüler and others (2004). However, for a more comparative analysis of the activities of various indanoyl amino acid methyl ester conjugates the *P. lunatus* volatile bioassay has been used. When coronatine was applied, a complex volatile blend was obtained that contained qualitatively and quantitatively more compounds than after stimulation with jasmonate or 12-OPDA alone (Boland and others 1995; Koch and others 1999). This became manifested in the presence (12-OPDA, coronatine) or absence (JA) of the homoterpene 4,8,12-trimethyltrideca-1, 3,7, 11-tetraene (TMTT). Interestingly, certain 6-substituted indanoyl isoleucine methyl ester conjugates, such as the C-6 ethyl- (coronalon), the C-6 allyloxy-, or the C-6 azido-derivative, induced a similar volatile pattern as coronatine (Figure 6). The non-substituted compound elicited a volatile composition similar to JA, and, therefore, in this respect resembled the C-6 methyl and methoxy derivatives (Schüler and others 1999, 2001; Lauchli and others 2002). The latter result was the most

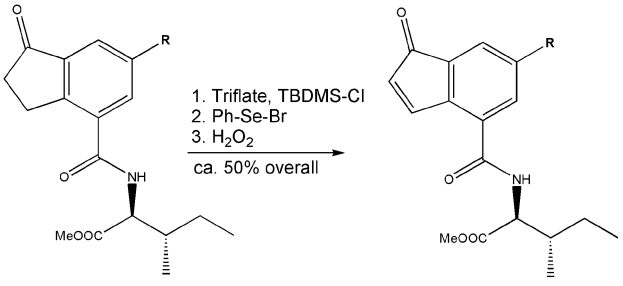

Figure 5. Synthesis of 4-oxo-indenoyl-isoleucine. Introduction of the double bond proceeds with high overall yield and changes the profile of biological activities of the conjugate.

Table 1:. Coronalon-induced Physiological Responses in Higher Plants.

Secondary metabolite synthesis		
Volatile organic compounds	*Phaseolus lunatus*	Krumm and others 1995
Volatile organic compounds	*Medicago truncatula*	Schüler and others 2004
Glyceollins (Isoflavonoids)	*Glycine max*	Fliegmann and others 2003
7, 4′- Dihydroxyflavone	*Glycine max*	Schüler and others 2004
Nicotine	*Nicotiana attenuata*	Schüler and others 2004
Benzo[c]phenanthridines	*Eschscholzia californica*	Schüler and others 2004
Phenylphenalenones	*Wachendorfia thyrsiflora*	Schüler and others 2004
Paclitaxel (Taxol^{R})	*Taxus media*	unpublished
Gene expression		
PIN-2	*Lycopersicon esculentum*	Schüler and others 2004
JIP23	*Hordeum vulgare*	Schüler and others 2004
CHS, CHR	*Glycine max*	Fliegmann and others 2003
Developmental processes		
Tendril coiling	*Bryonia dioica*	Lauchli and Boland 2002
Fruit and leaf drop	*Citrus sinensis*	Lauchli and Boland 2002
Root growth inhibition	*Arabidopsis thaliana*	Schüler and others 2004

PIN: proteinase inhibitor; JIP: jasmonate-induced protein; CHS: chalcone synthase; CHR: chalcone reductase.

surprising one. The methoxy group is about the same size as the ethyl substituent, but in contrast to the 6-ethyl analog, the 6-methoxy derivative was neither able to induce significant amounts of TMTT nor salicylic acid. This might be due to a postulated hydrogen bonding between a macromolecular target and the lone electron pairs of the methoxy oxygen, preventing a conformation necessary for activity (Lauchli and others 2002).

These results again indicate that at least two separate groups with different biological activities are present among the indanoyl isoleucine conjugates. First, a coronalon type which is substituted at C-6 and represented by ethyl-, allyloxy-, and azido-derivatives mimicking the activity-profile of JA along with 12-OPDA; the second type is represented by the nonsubstituted compound mimicking only the activity profile of JA. However, this is not consistent for all bioassays. In the JA-responsive *E. californica* alkaloid-induction assay, only coronalon was active (Lauchli and Boland 2002). In *N. sylvestris*, compounds of both types showed similar activities in the JA-responsive nicotine induction (Zheng and others 1997), and in the 12-OPDA-responsive G. *max*, mainly compounds of the coronalon type induced the response of glyceollin accumulation (Fliegmann and others 2003).

Due to the electrophile criteria mentioned above (Farmer and others 2003), coronatine as well as coronalon should belong to the JA- rather than to the 12-OPDA-type of signal compounds (Figure 1). However, with respect to biological activities, these compounds seem to mimic both 12-OPDA and JA activities. In contrast, the C-6 non-substituted indanoyl isoleucine methyl ester conjugate exhibits a much less-pronounced activity profile covering mostly JA- but never 12-OPDA-effects. Neither coronatine nor coronalon match the structural properties in the form of α, β-unsaturated carbonyl groups as a prerequisite for members of the electrophilic species group. Thus, a hypothesis of two different cyclopentanone- and cyclopentenone-related signals and signaling pathways might not be sufficient. On the other hand, the presence of a small non-charged C-6 substituent in the indanoyl isoleucine conjugates might fit with the structural properties of coronatine, 12-OPDA and JA as well, and could represent the main criteria for their biological activities. However, this cannot explain why the absence of C-6 substituents generates an activity profile similar to JA. Based on the data available, it is still too difficult to make any final conclusion about the molecular features of the two activity groups. The synthesis of new compounds and investigation of their biological activities will help to elucidate what the structural requirements for compounds belonging to the 12-OPDA, coronalon, and coronatine group and for compounds of the JA and indanoyl isoleucine methyl ester conjugate group might be.

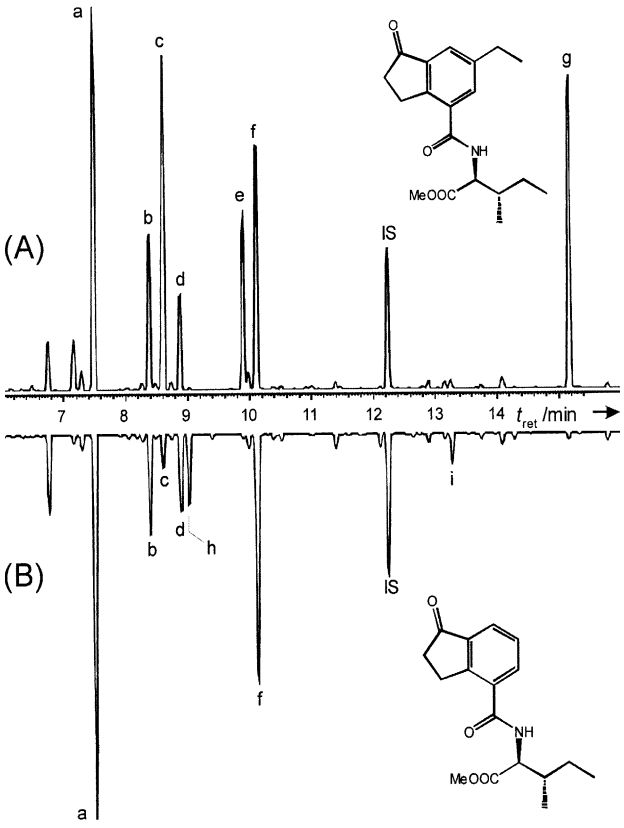

Figure 6. Volatile blends emitted from leaves of the Lima bean *P. lunatus* after treatment with (**A**) the 6-ethyl conjugate and (**B**) the unsubstituted indanoyl conjugate. Identification of compounds: (**a**) β-ocimene, (**b**) linalool, (**c**) 4,8-dimetyl-nona-1,3,7-triene (DMNT), (**d**) $C_{10}H_{14}$, (**e**) methyl salicylate, (**f**) $C_{10}H_{16}O$, IS: internal standard (1-bromodecane), (**g**) 4,8,12-trimethyltrideca-1,3,7, 11-tetraene (TMTT), (**h**) phenyl acetonitrile, (**i**) caryophyllene. Volatiles were collected by absorption onto carbon traps (Donath and Boland 1995). Separation and identification of the compounds were achieved by GLC-MS.

REFERENCES

Almeras E, Stolz S, Vollenweider S, et al. 2003. Reactive electrophile species activate defense gene expression in *Arabidopsis*. Plant J 34:205–226.

Baldwin IT, Zhang Z-P, Diab N, et al. 1997. Quantification, correlations and manipulations of wound-induced changes in jasmonic acid and nicotine in *Nicotiana sylvestris*. Planta 201:397–404.

Blee E. 2002. Impact of phyto-oxylipins in plant defense. Trend Plant Sci 7:315–321.

Birkett MA, Campbell CAM, Chamberlain K, et al. 2000. New roles for *cis*-jasmone as an insect semiochemical and in plant defense. Proc Natl Acad Sci USA 97:9329–9334.

Blechert S, Bockelmann C, Brummer O, et al. 1997. Structural separation of biological activities of jasmonates and related compounds. J Chem Soc Perkin Trans 1:3549–3559.

Blechert S, Bockelmann C, Fußlein M, et al. 1999. Structure-activity analyses reveal the existence of two separate groups of active octadecanoids in elicitation of the tendril-coiling response of *Bryonia dioica* Jacq. Planta 207:470–479.

Bodnaryk R, Yoshihara T. 1995. Structure-activity relationships of cyclopentane analogs of jasmonic acid for induced responses of canola seedlings, *Brassica napus* L. J Chem Ecol 21:1735–1743.

Boland W, Hopke J, Donath J, Nuske F, Bublitz F. 1995. Jasmonic acid and coronatine induce volatile biosynthesis in plants. Angew Chem Int Ed Eng 34:1600–1602.

Creelman RA, Mullet JE. 1997. Biosynthesis and action of jasmonates in plants. Annu Rev Plant Physiol Plant Mol Biol 48:355–381.

Donath J, Boland W. 1995. Biosynthesis of acyclic homoterpenes: enzyme selectivity and absolute configuration of the nerolidol precursor. Phytochemistry 39:785–790.

Falkenstein E, Groth B, Mithöfer A, Weiler EW. 1991. Methyljasmonate and alpha-linolenic acid are potent inducers of tendril coiling. Planta 185:316–322.

Farmer EE, Almeras E, Krishnamurthy V. 2003. Jasmonates and related oxylipins in plant responses to pathogenesis and herbivory. Curr Opin Plant Biol 6:372–378.

Fliegmann J, Schüler G, Boland W, Ebel J, Mithöfer A. 2003. The role of octadecanoids and functional mimics in soybean defense responses. Biol Chem 384:437–446.

Feys BJF, Benedetti CE, Penfold CN, Turner JG. 1994. *Arabidopsis* mutants selected for resistance to the phytotoxin coronatine are male sterile, insensitive to methyl jasmonate, and resistant to a bacterial pathogen. Plant Cell 6:751–759.

Haider G, von Schrader T, Fußlein M, Blechert S, Kutchan TM. 2000. Structure-activity relationships of synthetic analogs of jasmonic acid and coronatine on induction of benzo[c]phenanthridine alkaloid accumulation in *Eschscholzia californica* cell cultures. Biol Chem 381:741–748.

Ishihara A, Shiraishi K, Sato H, et al. 1977. The structure of coronatine. J Am Chem Soc 99:636–637.

Ishihara A, Toshima H. 1999. Coronatine: chemistry and biological activities In: Cutler H, Cutler S Biologically active natural products: agrochemicals Washington DC: CRC Press. pp 93–105.

Jiralerspong S, Rangswamy V, Bender CL, Parry RJ. 2001. Analysis of the enzymatic domains in the modular portion of the coronafacic acid polyketide synthase. Gene 270:191–200.

Koch T, Krumm T, Jung V, Engelberth J, Boland W. 1999. Differential induction of plant volatile biosynthesis in the Lima bean by early and late intermediates of the octadecanoid-signaling pathway. Plant Physiol 121:153–162.

Kramell R, Miersch O, Atzorn R, Parthier B, Wasternack C. 2000. Octadecanoid-derived alteration of gene expression and the ''oxylipin signature'' in stressed barley leaves. Implications for different signaling pathways. Plant Physiol 123:177–187.

Kramell R, Miersch O, Hause B, Ortel B, Parthier B, Wasternack C. 1997. Amino acid conjugates of jasmonic acid induce jasmonate-responsive gene expression in barley (*Hordeum vulgare* L.) leaves. FEBS Lett 414:197–202.

Krumm T, Bandemer K, Boland W. 1995. Induction of volatile biosynthesis in the Lima bean (*Phaseolus lunatus*) by leucine- and isoleucine conjugates of 1-oxo- and 1-hydroxyindan-4-carboxylic acid: evidence for amino acid conjugates of jasmonic acid as intermediates in the octadecanoid signalling pathway. FEBS Lett 377:523–529.

Lauchli R, Boland W. 2002. Indanoyl amino acid conjugates: tunable elicitors of plant secondary metabolism. Chem Rec 3:12–21.

Lauchli R, Schüler G, Boland W. 2002. Selective induction of secondary metabolism in *Phaseolus Iunatus* by 6-substituted indanoyl isoleucine conjugates. Phytochemistry 61:807–817.

Meyer A, Miersch O, Büttner C, Dathe W, Sembdner G. 1984. Occurrence of the plant-growth regulator jasmonic acid in plants. J Plant Growth Regul 3:1–8.

Miersch O, Kramell R, Parthier B, Wasternack C. 1999. Structure-activity relations of substituted, deleted or stereospecifically altered jasmonic acid in gene expression of barley leaves. Phytochemistry 50:353–361.

Mithöfer A, Schulze B, Boland W. 2004. Biotic and heavy metal stress response in plants: evidence for common signals. FEBS Lett 566:1–5.

Müller MJ. 2004. Archetype signals in plants: the phytoprostanes. Curr Opinion Plant Biol 7:441–448.

Parry RJ, Lin MT, Walker AE, Mhaskar SJ. 1991. Biosynthesis of coronatine investigations of the biosynthesis of coronamic acid. J Am Chem Soc 113:1849–1850.

Pautot V, Holzer FM, Chaufaux J, Walling LL. 2001. The induction of tomato leucine aminopeptidase genes (LapA) after *Pseudomonas syringae* pv. *tomato* infection is primarily a wound response triggered by coronatine. Mol Plant-Microbe Interact 14:214–224.

Reymond P, Weber H, Damond M, Farmer EE. 2000. Differential gene expression in response to mechanical wounding and insect feeding in *Arabidopsis*.. Plant Cell 12:707–720.

Schüler G, Goerls H, Boland W. 2001. 6-Substituted indanoyl isoleucine conjugates mimic the biological activity of coronatine: elicitors of plant secondary metabolism V. Eur J Org Chem :1663–1668.

Schüler G, Wasternack C, Boland W. 1999. Synthesis of 6-azido-1-oxo-indan-4-oyl isoleucine: a photoaffinity approach to plant signaling. Tetrahedron 5:3897–3904.

Schüler G, Mithöfer A, Baldwin IT, et al. 2004. Coronalon: a powerful tool in plant stress physiology. FEBS Lett 563:17–22.

Sembdner G, Parthier B. 1993. The biochemistry and the physiological and molecular actions of jasmonates. Annu Rev Plant Physiol Plant Mol Biol 44:569–589.

Staswick PE, Tiryaki I. 2004. The oxylipin signal jasmonic acid is activated by an enzyme that conjugates it to isoleucine in *Arabidopsis*. Plant Cell 16:2117–2127.

Stelmach BA, Müller A, Hennig P, Laudert D, Andert L, Weiler EW. 1998. Quantification of the octadecanoid 12-oxo-phytodienoic acid, a signalling compound in plant mechanotransduction. Phytochemistry 47:539–546.

Stille JK. 1986. The palladium-catalyzed cross-coupling reactions of organotin reagents with organic electrophiles. Angew Chem Int Ed Engl 25:508–524.

Stintzi A, Weber H, Reymond P, Browse J, Farmer EE. 2001. Plant defense in the absence of jasmonic acid: the role of cyclopentenones. Proc Natl Acad Sci USA 98:12837–12842.

Wasternack C, Hause B. 2002. Jasmonates and Octadecanoids: signals in plant stress responses and development. Progr. Nucleic Acid Res. 72:165–221.

Wasternack C, Ortel B, Miersch O, et al. 1998. Diversity in octadecanoid-induced gene expression of tomato. J Plant Physiol 152:345–352.

Weber H. 2002. Fatty acid-derived signals in plants. Trends Plant Sci 7:217–223.

Weber H, Vick BA, Farmer EE. 1997. Dinor-oxo-phytodienoic acid: a new hexadecanoid signal in the jasmonate family. Proc Natl Acad Sci USA 94:10473–10478.

Weiler EW. 1997. Octadecanoid-mediated signal transduction in higher plants. Naturwissenschaften 84:340–349.

Weiler EW, Kutchan TM, Gorba T, Brodschelm W, Niesel U, Bublitz F. 1994. The *Pseudomonas* phytotoxin coronatine mimics octadecanoid signalling molecules of higher plants. FEBS Lett 345:9–13.

Zheng ZP, Krumm T, Baldwin IT. 1997. Structural requirements of Jasmonates and mimics for nicotine induction in *Nicotiana sylvestris*.. J Chem Ecol 23:2777–2789.