Biosynthesis of Lepidopteran Sex Pheromones

I. Introduction: Experimental methods to elucidate a biosynthetic pathway

II. Biosynthetic studies with the silk moth

III. Biosynthetic pathways of lepidopteran sex pheromones

  A) Biosynthesis of Type I pheromones

  B) Biosynthesis of Type II pheromones

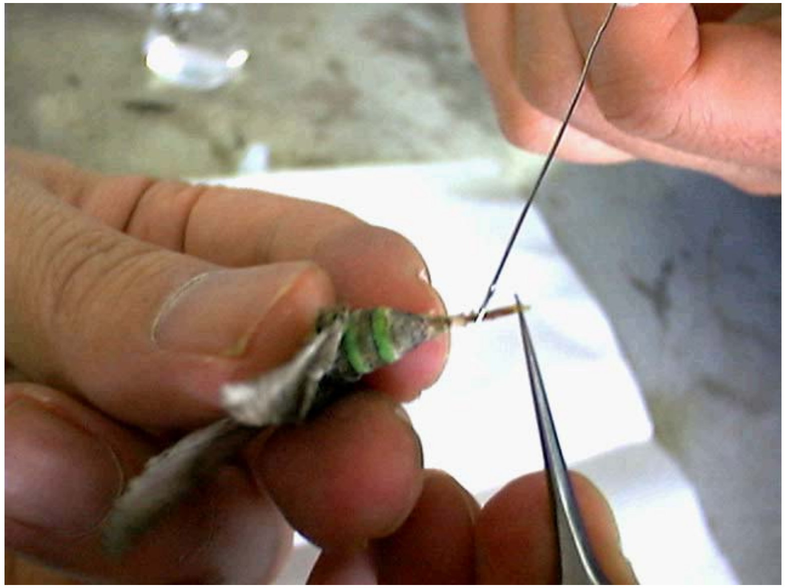
IV. Enzymatic studies on the biosynthesis of sex pheromones

  A) Desaturases

  B) Acyl reductases

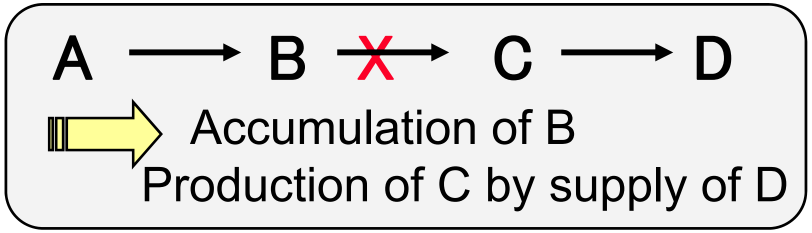
V. Inhibitors of sex pheromone biosynthesis

VI. Biosynthesis of methyl-branched pheromones

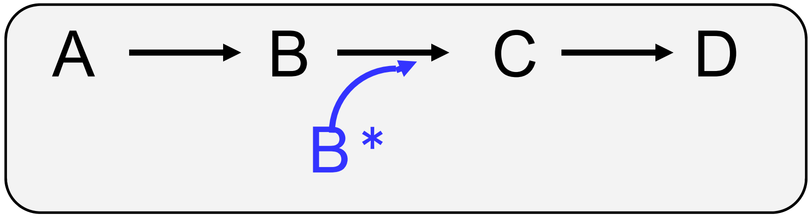


I. Introduction: Experimental methods for elucidation of biosynthetic pathway

1. Use of mutants



2. Feeding experiments of a labeled precursor



Stable isotope ^{2}H (D), ^{13}C

Analysis by GC-MS or NMR

Radio isotope ^{3}H (T), ^{14}C, ^{11}C

Analysis by autoradiography → Chemical structure？

→ problem

Pheromone component： ultra trace substance → problem

Application of an exogenous precursor

→ Possible disturbance of original biosynthetic system

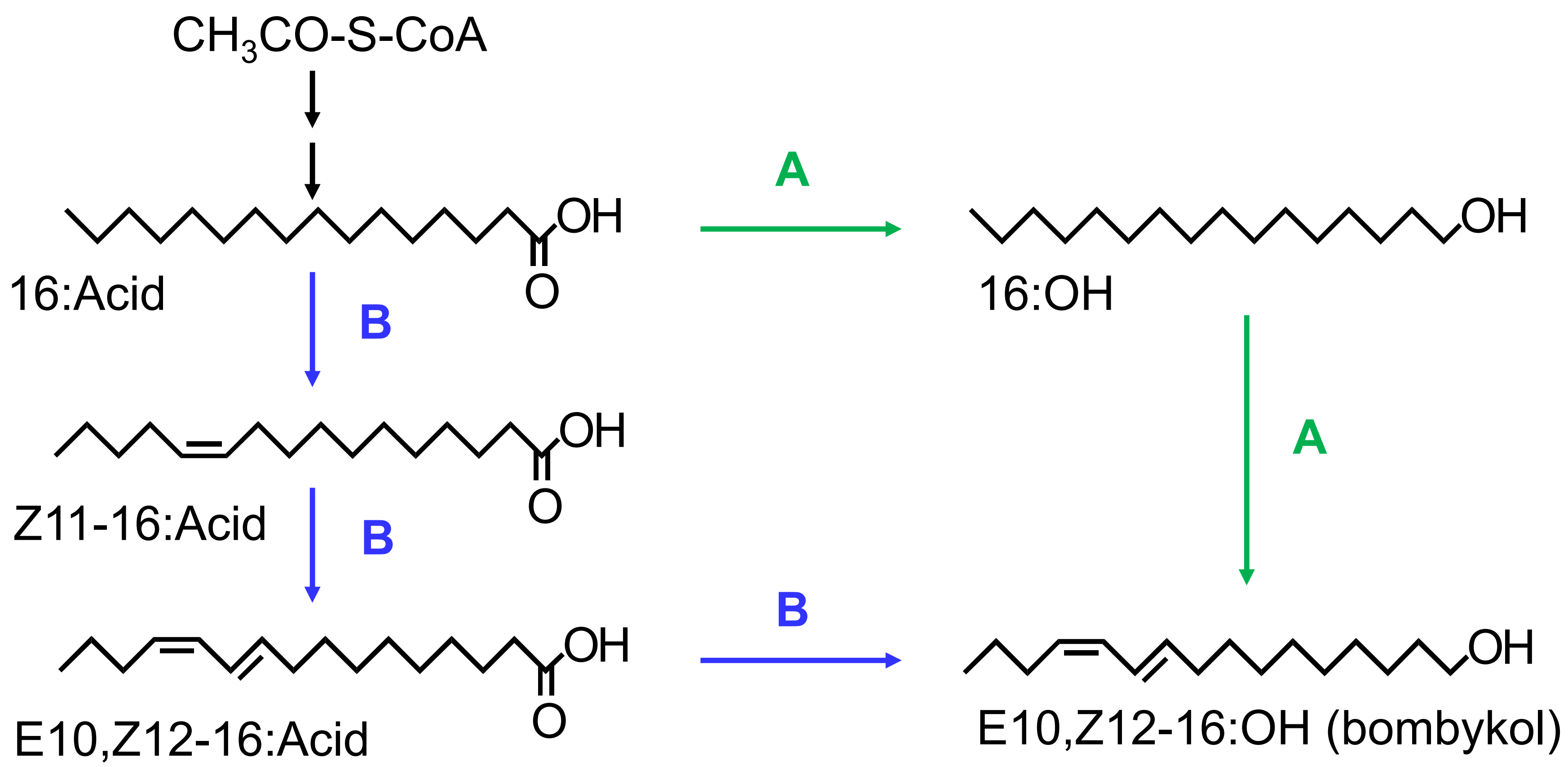
Ex） In the case of 1% incorporation of palmitic acid

^{14}C-label（specific activity 50 mCi/mmol） 500 dpm → 50,000 dpm ＝ 100 ng

D-label 10 ng → 1000 ng = 1 mg

II. Biosynthetic studies with the silk moth

a) Proposed biosynthetic pathways of bombykol

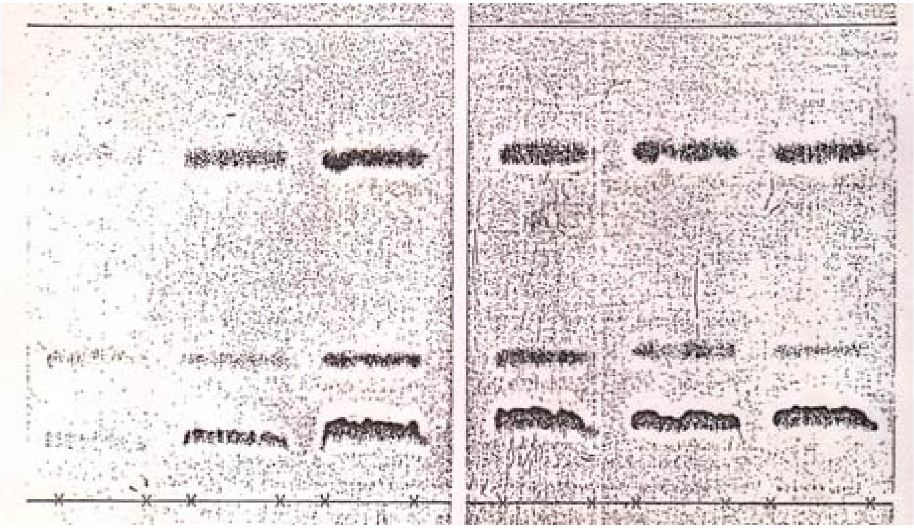


A Inoue & Hamamura, 1972. *Nippon Nogeikagaku Kaishi,* **46**: 645

B Yamaoka *et al.*, 1984. *Experientia,* **48**: 80
Bjostad & Roelofs, 1984. *Insect Biochem.*, **14**: 275

b) Conversion of palmitic acid (16:Acid)

TLC (autoradiography)



solvent: benzene + ethyl acetate (4:1)

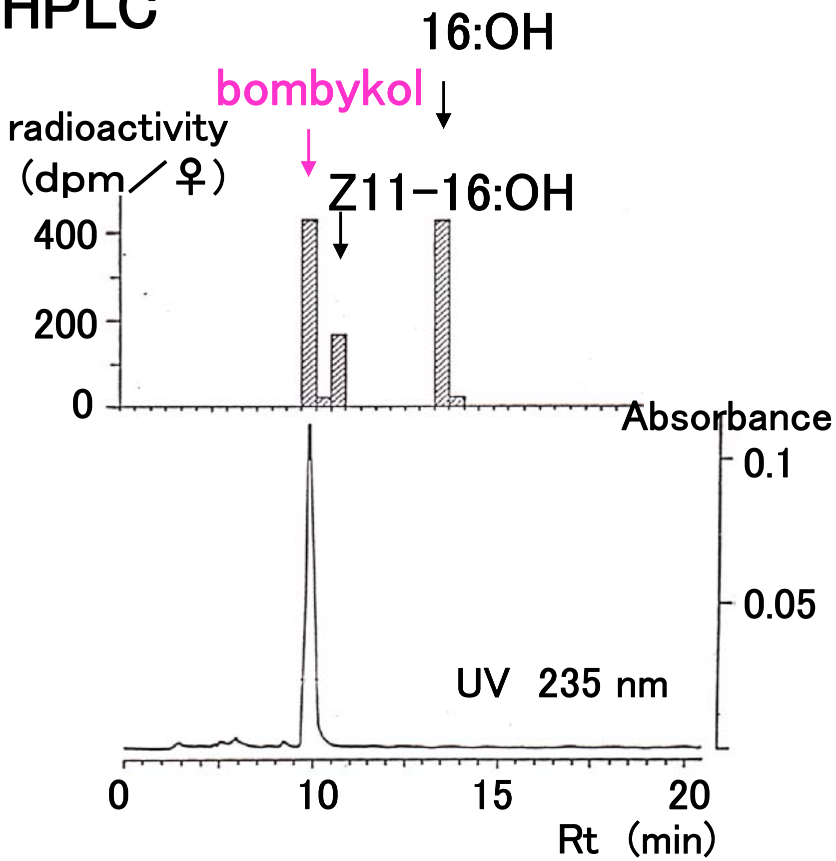
i [1–^{14}C]12:Acid
ii [1–^{14}C]14:Acid
iii [1–^{14}C]16:Acid
iv [16–^{14}C]16:Acid
v [1–^{14}C]18:Acid
vi [18–^{14}C]18:Acid

A: triacylglycerols

B: alcohols

C: acids (recovery)

HPLC



column: ODS (8 mm X 15 cm)
solvent: MeOH + H_2O (93:7)

Ando *et al.*, 1988. *Agric. Biol. Chem.*, **52**: 141

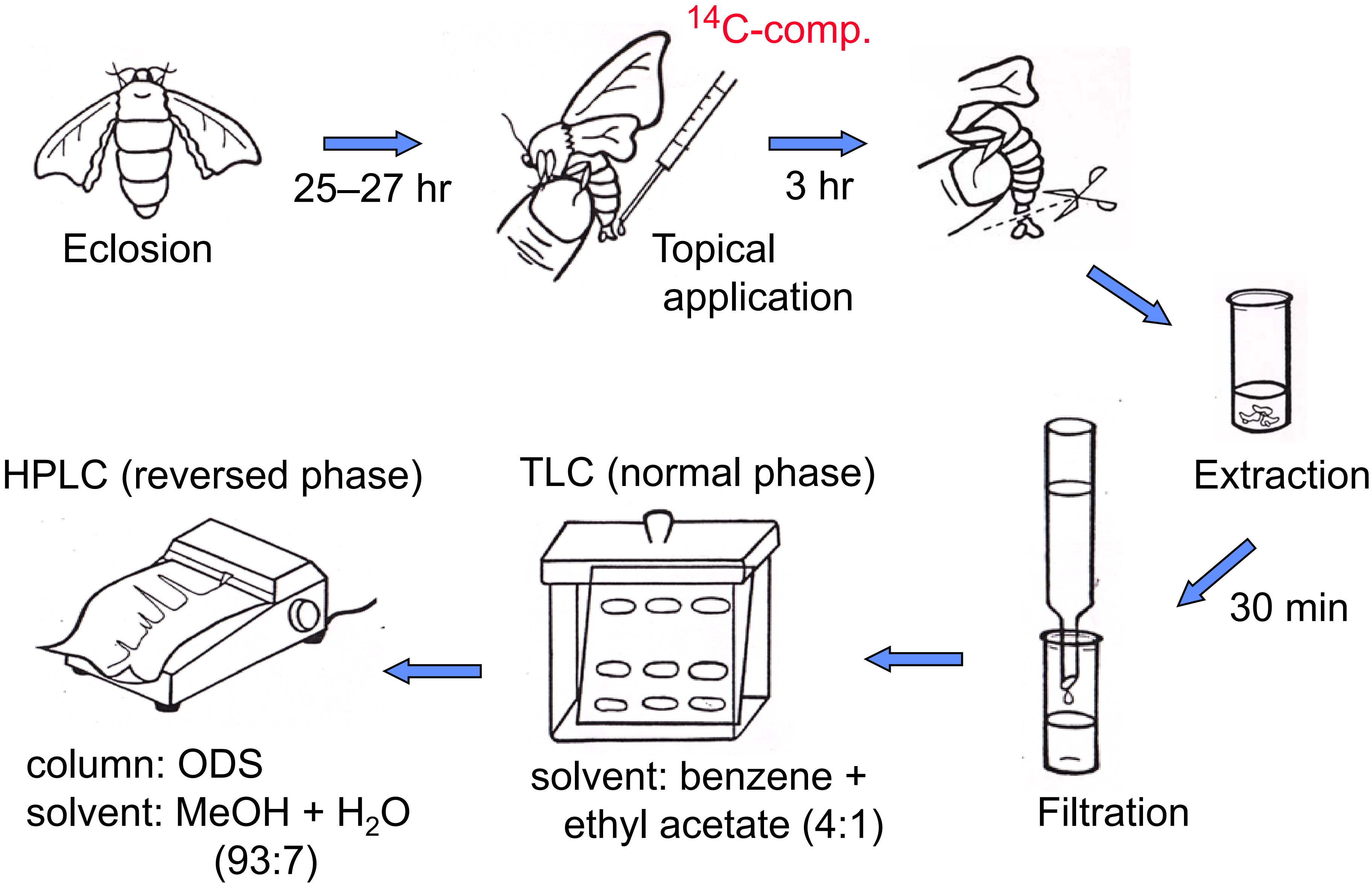
c) Optimum incubation time for the incorporation

Incorporation ratios (%) of [16-^{14}C]hexadecanoic acid at different incubation times

	Incubation time (hr)				
	1	3	6	24	48
Band A (triacylglycerol)	7.2 ± 0.4	7.8 ± 0.9	4.3 ± 0.7	1.6 ± 0.4	1.1 ± 0.1
Fr. B-I (Bombykol)	1.5 ± 0.3	1.5 ± 0.4	1.1 ± 0.1	0.7 ± 0.3	0.4 ± 0.1
Fr. B-II (Z11-16:OH)	1.0 ± 0.2	0.9 ± 0.3	0.5 ± 0.2	0.2 ± 0.1	0.1 ± 0.0
Fr. B-III (16:OH)	1.7 ± 0.4	1.6 ± 0.4	0.9 ± 0.3	0.5 ± 0.2	0.3 ± 0.1
Band C (unconversion)	17.1 ± 2.0	11.1 ± 0.8	7.5 ± 1.2	5.2 ± 2.2	3.2 ± 0.8

Ando *et al.*, 1988. *Agric. Biol. Chem.*, **52**: 141

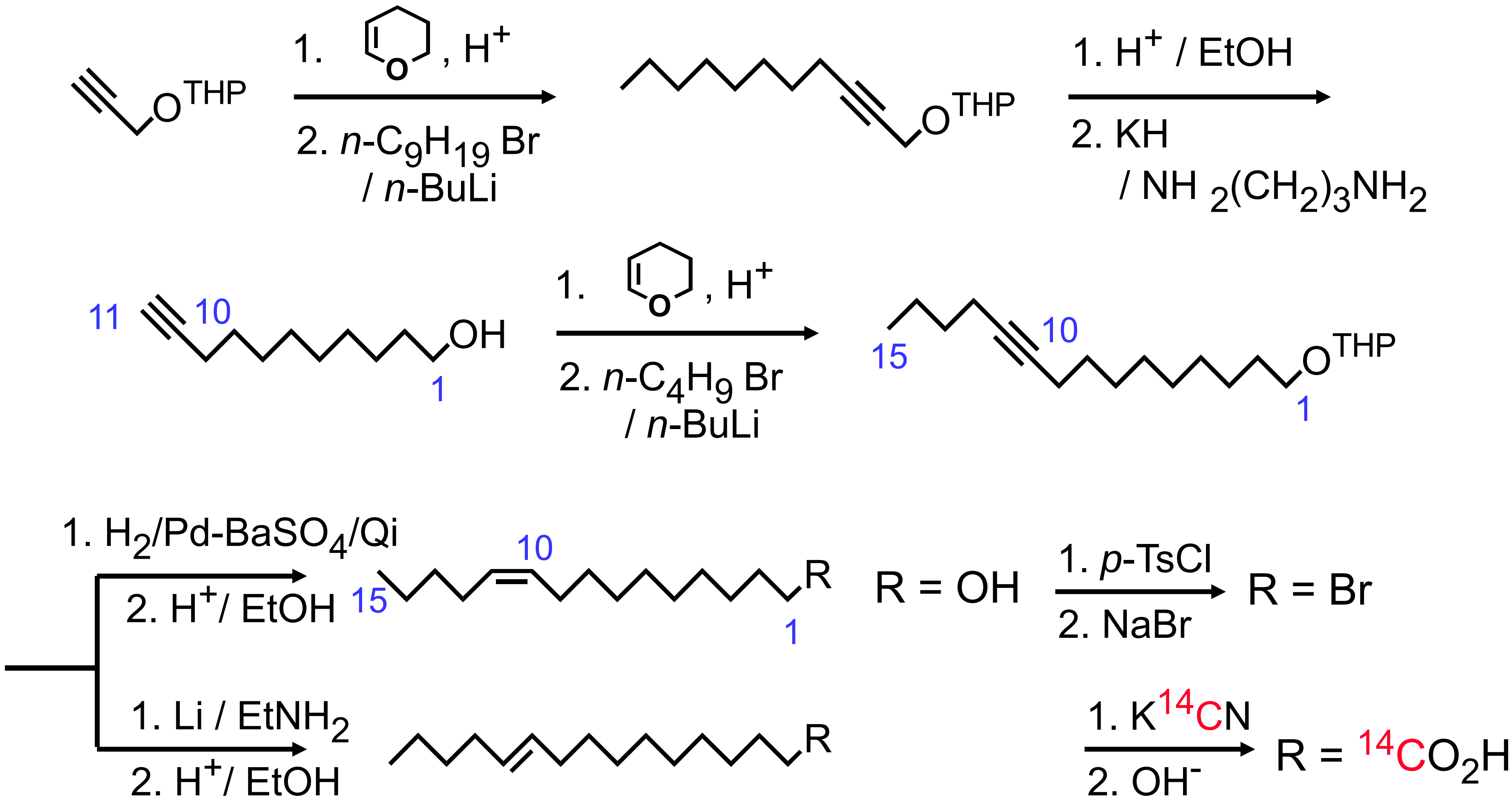
d) Experimental procedure



e) Synthesis of labeled precursor

Rule: Introduction of a label at the final step

Synthesis of [1-^{14}C](*Z*)-11-hexadecenoic acid



Ando *et al.*, 1988. *Agric. Biol. Chem.*, **52**: 473

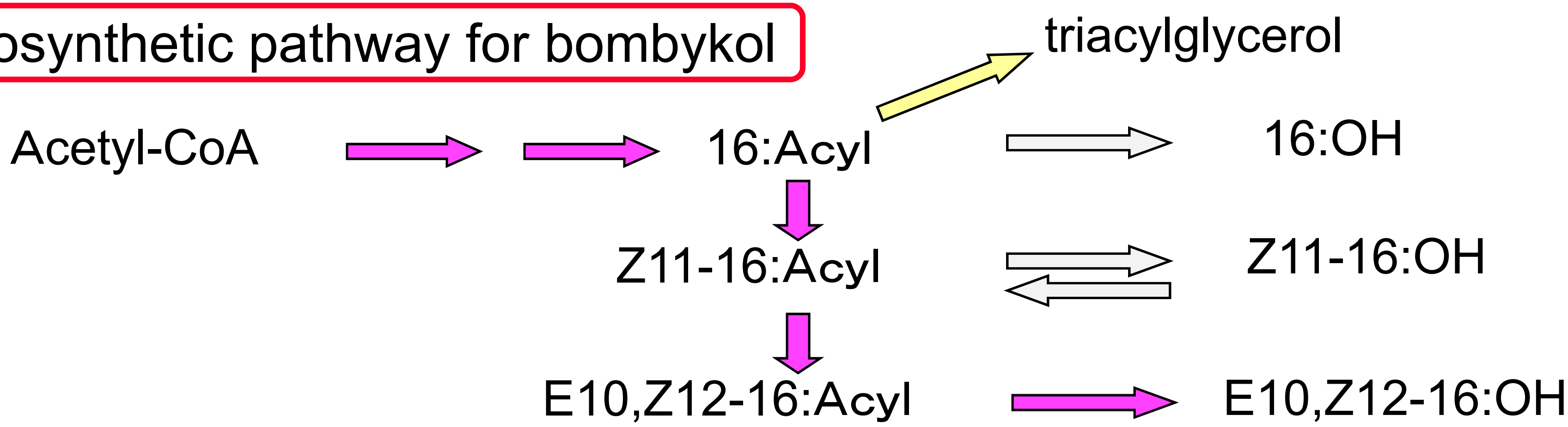
f) Comparing the incorporation of labeled compounds

	^{14}C-Labeled compound	Incorporatin ratio (%)
[a]	12:Acid	0. 2
	14:Acid	0. 1
	16:Acid	1. 7
	18:Acid	0. 1
[b]	16:OH	0. 2
	Z11-16:OH	0. 9
	Z11-16:Acid	3. 3

	^{14}C-Labeled compound	Incorporatin ratio (%)
[c]	Z10-16:Acid	0. 3
	E10-16:Acid	0. 4
	E11-16:Acid	0. 2
	Z12-16:Acid	0. 4
	E12-16:Acid	0. 5

Ando *et al.*, 1988. *Agric. Biol. Chem.*, **52**: 473

Biosynthetic pathway for bombykol



III. Biosynthetic pathways of lepidopteran sex pheromones

A) Biosynthesis of Type I pheromones

Acetyl CoA → 16:Acyl → (Δ11-desaturation) → Z11-16:Acyl → (reduction, acetyration) → Z11-16:OAc

Z11-16:Acyl ↓ (β-oxidation)

Z9-14:Acyl → Z9-14:OAc

↓

Z7-12:Acyl → Z7-12:OAc

Δ11-desaturaze

Cloning of a gene from the cabbage looper, *Trichoplusia ni*

Gene expression in yeast（Knipple *et al*., *ProNAS USA*, **95**: 15287, 1998）

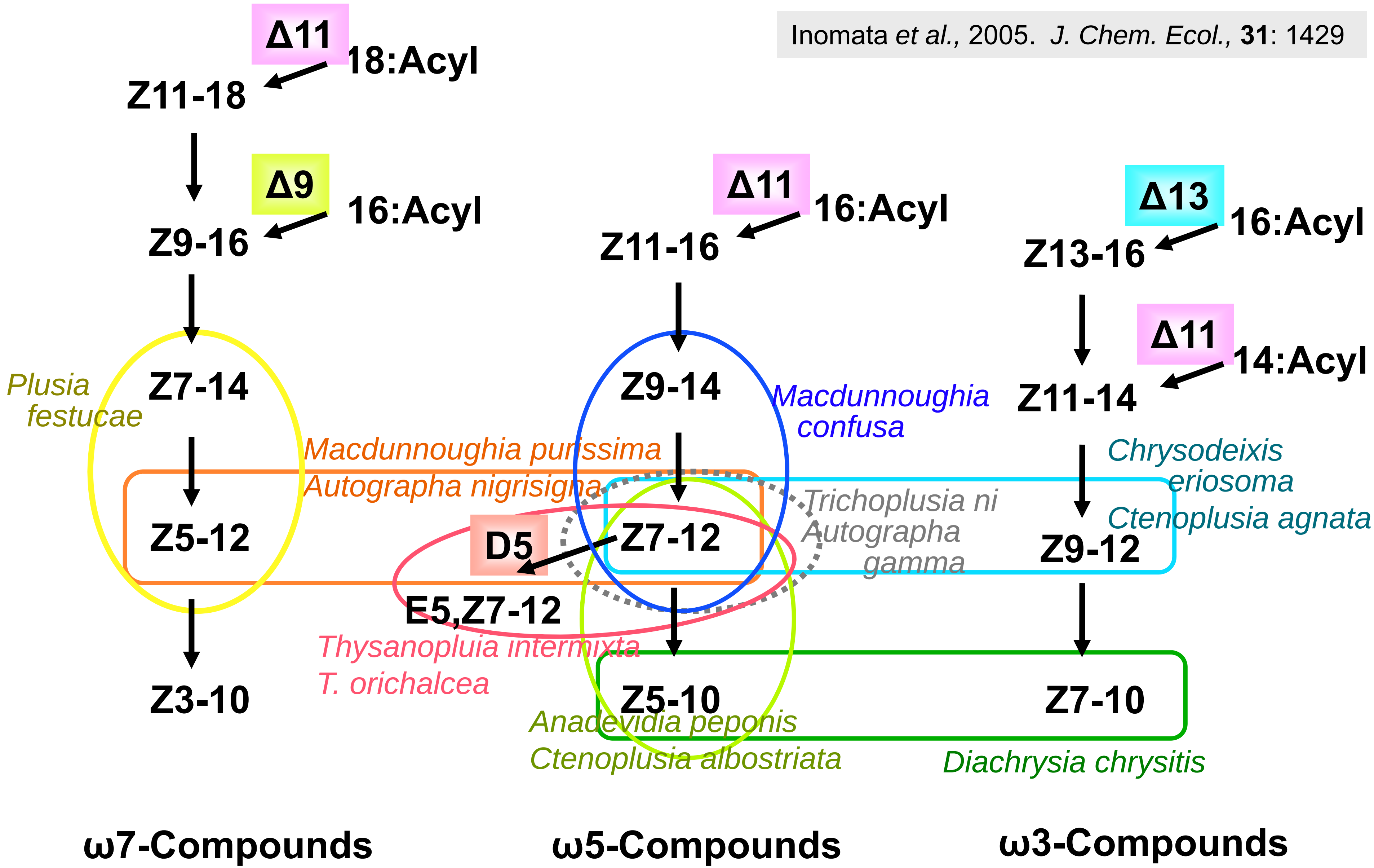
β-oxidaze？

reductase, acetyl transferase ← low substrate specificity

Further subjects： Mechanism of desaturation with positional specificity and controlling a ratio of the pheromone blend

a) Biosynthetic pathways of Plusiinae pheromones

Inomata *et al.*, 2005. *J. Chem. Ecol.*, **31**: 1429



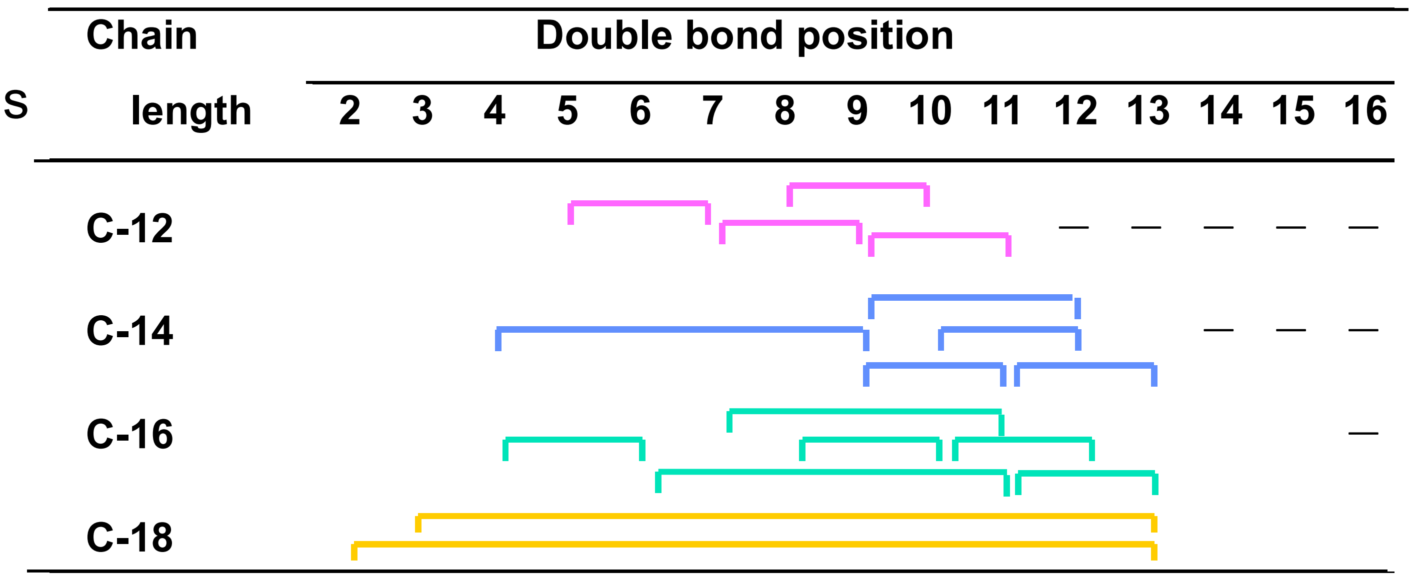
b) Double-bond positions of monoenyl pheromones

Ando *et al.*, 2004. *Top. Curr. Chem.*, **239**: 51

(i) Monoene compounds

Chain length	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
C-10				○		○			–	–	–	–	–	–	–
C-12		○		○		○	○	○		○	–	–	–	–	–
C-14				○		○	○	○		○	○		–	–	–
C-16						○		○	○	○					–
C-18										○		○			

(ii) Diene compounds



c) Biosynthesis of dienyl pheromones ①

(i) α-monoene → α,γ-diene

α β γ δ

$-CH=CH-CH_2-CH_2-$

↓

$-CH=CH-CH=CH-$

α β γ δ

Spodoptera littoralis (Noctuidae)
E11-14 → Z9,E11-14:OAc

Epiphyas postvittana (Tortricidae)
E11-16 → E9-14 → E9,E11-14:OAc

Thysanoplusia intermixta (Noctuidae)
Z11-16 → Z7-12 → E5,Z7-12:OAc

Dendrolimus punctatus (Lasiocampidae)
Z11-18 → Z9-16 → Z9,E11-16
→ Z5,E7-12:OH

(ii) β-monoene → α,γ-diene

α β γ δ

$-CH_2-CH=CH-CH_2-$

↓

$-CH=CH-CH=CH-$

α β γ δ

Bombyx mori (Bombycidae)
Z11-16 → E10,Z12-16:OH

Manduca sexta (Sphingidae)
Z11-16 → E10,Z12-16:Ald,
\+ E10,E12-16:Ald

Cydia pomonella (Tortricidae)
E9-12 → E8,E10-12:OH

c) Biosynthesis of dienyl pheromones ② (References)

(i) α-monoene → α,γ-diene

Spodoptera littoralis (Noctuidae) E11-14 → Z9,E11-14:OAc
Dunkelblum & Kehat, 1987. *Insect Biochem.*, **17**: 877
Martinez *et al.*, 1990. *J. Biol. Chem.*, **265**: 1381

Epiphyas postvittana (Tortricidae) E11-16 → E9-14 → E9,E11-14:OAc
Foster & Roelofs, 1990. *Experientia*, **46**: 269

Thysanoplusia intermixta (Noctuidae) Z11-16 → Z7-12 → E5,Z7-12:OAc
Ono *et al.*, 2002. *IBMB*, **32**: 701

Dendrolimus punctatus (Lasiocampidae) Z11-18 → Z9-16 → Z9,E11-16 → Z5,E7-12:OH
Zhao *et al.*, 2004. *IBMB*, **34**: 261

(ii) β-monoene → α,γ-diene

Bombyx mori (Bombycidae) Z11-16 → E10,Z12-16:OH
Yamaoka *et al.*, 1984. *Experientia*, **40**: 80
Roelofs & Bjostad, 1984. *Bioorg. Chem.*, **12**: 279
Ando *et al*., 1988. *Agric. Biol. Chem.*, **52**: 473

Manduca sexta (Sphingidae) Z11-16 → E10,Z12-16:Ald, E10,E12-16:Ald
Fang *et al.*, 1995. *IBMB*, **25**: 39

Cydia pomonella (Tortricidae) E9-12 → E8,E10-12:OH
Löfstedt & Bengtsson, 1988. *JCE*, **14**: 903

B) Biosynthesis of Type II pheromones

Z9,Z12,Z15-18:Acyl —reduction→ Z3,Z6,Z9-18:H —epoxidation→ epo3,Z6,Z9-18:H

↓

Z9,Z12,Z15-20:Acyl —decarboxylation→ Z3,Z6,Z9-19:H → epo3,Z6,Z9-19:H

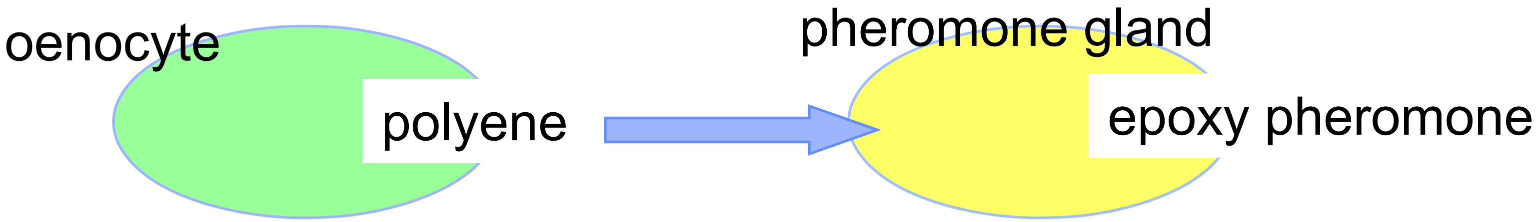
↓

Reductase ? decarboxylase ?

epoxidase （P_{450}-dependent mono-oxygenase）

High-selective attack of a double-bond under low substrate specificity

Unsaturated hydrocarbons (polyenes) are combined with lipophorin and moved to a pheromone gland



Ando *et al.*, 2008. *J. Pestic. Sci.*, **33**: 17

Further subject：Experimental confirmation of steps for hydrocarbon formation

IV. Enzymatic studies on the biosynthesis of sex pheromones

A) Desaturases

a) History of the research ①

Δ11-Desaturase   Knipple *et al*., 1998. *PNAS*, **95**: 15287

Cloning of a gene from the cabbage looper, *Trichoplusia ni*

pheromone: Z7-12:OAc ← Z11-16:Acyl

primers: Δ9-desaturases of rat and yeast

Gene expression in yeast, a desaturase deficient strain,

because of the desaturation helped by two other enzymes,

NADH-cytochrome *b*5 reductase (flavoprotein)

and cytochrome *b*5 (hemoprotein)

Following related studies

Δ11-Desaturase of the silk moth   Yoshiga *et al*., 2000. *Gene,* **246**: 339

Δ9-Desaturase of the cabbage looper   Liu *et al*., 1999. *IBMB,* **29**: 435

Δ 9- and Δ11-Desaturase of the corn earworm (*Helicoverpa zea*)

Rosenfield *et al*., 2001. *IBMB,* **31**: 949

a) History of the research ②

Δ9- and Δ10-Desaturase of *Planotortrix octo, a* leafroller in New Zealand

Hao *et al*., 2002. *IBMB*, **32**: 961

pheromone (Z8-14:OAc) with a unusual structure
← common pheromone component of leafrollers: Z11-14:OAc

Homology (%)	Plo-Z9	Trn-Z9	Hez-9	Trn-Z11	Hez-Z11
Plo-Z9	-	73	80		
Plo-Z10	62	62	61	66	66

Studies until 2007 [see e) List ① & ②]

Helicoverpa assulta Jeong *et al*., 2003. *IBMB,* **33**: 609

Choristoneura parallela Liu *et al*., 2004. *Gene,* **342**: 303 *etc.*

Noctuidae	5 species
Tortricidae	5 species
Crambidae	2 species
Bombycidae	1 species

b) Formation of (*E*)-double bonds

Biosynthesis of typical pheromones of leafroller moths

Δ11-Desaturase of *Argyrotaenia velutinana,* redbanded leafroller

Liu *et al*., 2002. *IBMB,* **32**: 1489

Pheromone: Z11-14:OAc + E11-14:OAc (92:8)

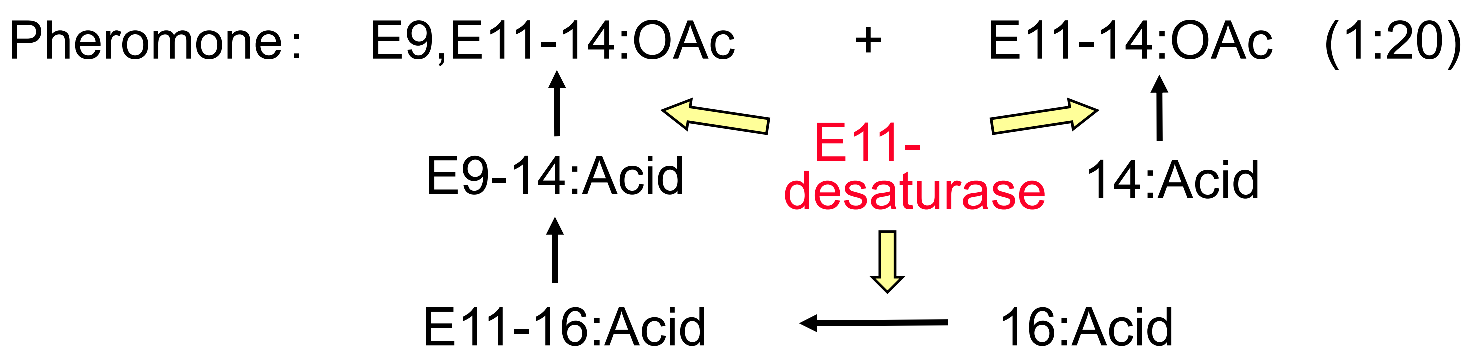
Unsaturated fatty acid: 3:2 Z/E ratio ⟵ 14:Acid (substrate)

Gene expression of Δ11-desaturase in yeast ⇒ 6:1 Z/E ratio

E11-Desaturase of *Epiphyas postvittana*, lightbrown apple moth

Liu *et al*., 2002. *PNAS*, **99**: 620

Cloning of desaturases ⇒ two genes (E9 and Z9) from pheromone glands
one gene (Z9) from fat bodies



c) Desaturases of a noctuid moth, *Spodoptera littoralis*

Rodriguez *et al*., 2004. *IBMB,* **34**: 1315

Pheromone: Z9,E11-14:OAc (main) + E10,E12-14:OAc (minor)

14:Acid —Δ11→ E11-14:Acid —Δ9→ Z9,E11-14:Acid ⟶ ⟶ main comp.

Cloning of desaturases ⇒ four genes

#1 from fat bodies, #2 - #4 from pheromone glands

Feeding experiments with three fatty acids (14:Acid, 16:Acid, and 18:Acid)

#1 (Δ9) Z9-16/Z9-18 = 1 : 4.5 (also 14:Acid → Z9-14)

#2 (Δ9) Z9-16/Z9-18 = 1.5 : 1 (also 14:Acid → Z9-14)

However, 14:Acid + E11-14:Acid → only Z9,E11-14:Acid

#3 (Δ11) E11-14/Z11-14/Z11-16/Z11-18 = 5 : 4 : 60 : 31

#4 (?) no functions

Serra *et al*., 2006. *IBMB,* **36**: 634

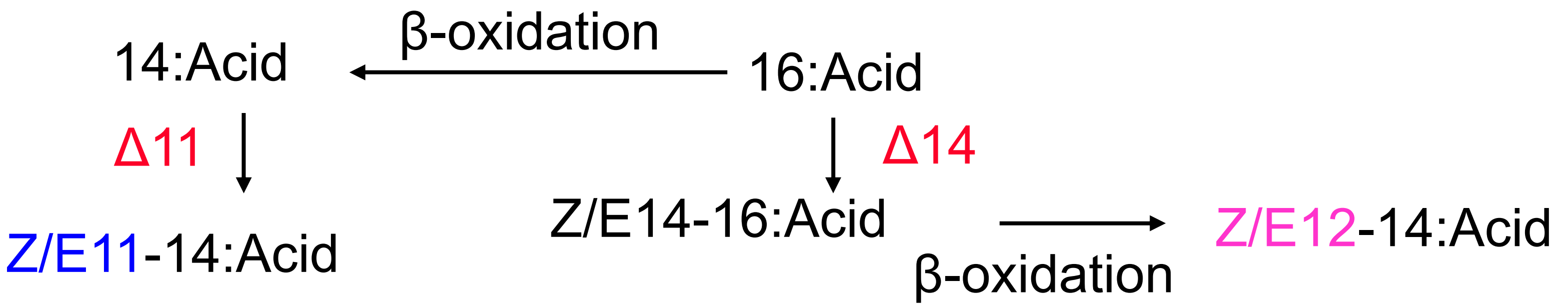
Z11-14:Acid —#3 (Δ11)→ E10,E12-14:Acid ⇒ bifunctional enzyme

d) Desaturases of corn bores, *Ostrania* spp. (Pyraloidea: Crambidae)

Roelofs *et al*., 2002. *PNAS*, **99**: 13621

European corn borer (*Ostrinia nubilalis*) pheromone: Z/E11-14:OAc

Asian corn borer (*Ostrinia furnacalis*) pheromone: Z/E12-14:OAc



Their host plants are same, but reproductive isolation is accomplished by geometrical and pheromone system.

Which is an original species? Is it speculaed by enzymatic analysis?

Cloning of genes from pheromone glands

⇒ Presence of similar thee cDNAs (Δ11-, Δ14-, and Δ9-desaturases) in the both species

Expression of Δ11-gene in *O. nubilalis*, and Δ14-gene in *O. furnacalis*

e) List of identified desaturase genes ①

Published until 2007

Desaturation		Species	(Family)	Reference
Z9	← 16	*Helicoverpa zea*	(Noct.)	Rosenfield *et al*., 2001
		Helicoverpa assulta	(Noct.)	Jeong *et al*., 2003
	← E11-14	*Spodopteta littoralis*	(Noct.)	Rosenfield *et al*., 2004
Z10	← 14	*Planotortrix octo*	(Tort.)	Hao *et al*., 2002(a)
Z11	← 16	*Trichoplusia ni*	(Noct.)	Knipple *et al*., 2001
		H. zea	(Noct.)	Rosenfield *et al*., 2001
		H. assulta	(Noct.)	Jeong *et al*., 2003
		Bombyx mori	(Bomb.)	Moto *et al*., 2004
		Manduca sexta	(Sphi.)	Matouskova *et al*., 2007
E11	←14,16	*Epiphyas postvittana*	(Tort.)	Liu *et al*., 2002
	← E9-14	*E. Postvittana*	(Tort.)	Liu *et al*., 2002
	← 14	*Choristoneura parallela*	(Tort.)	Liu et al., 2004

e) List of identified desaturase genes ②

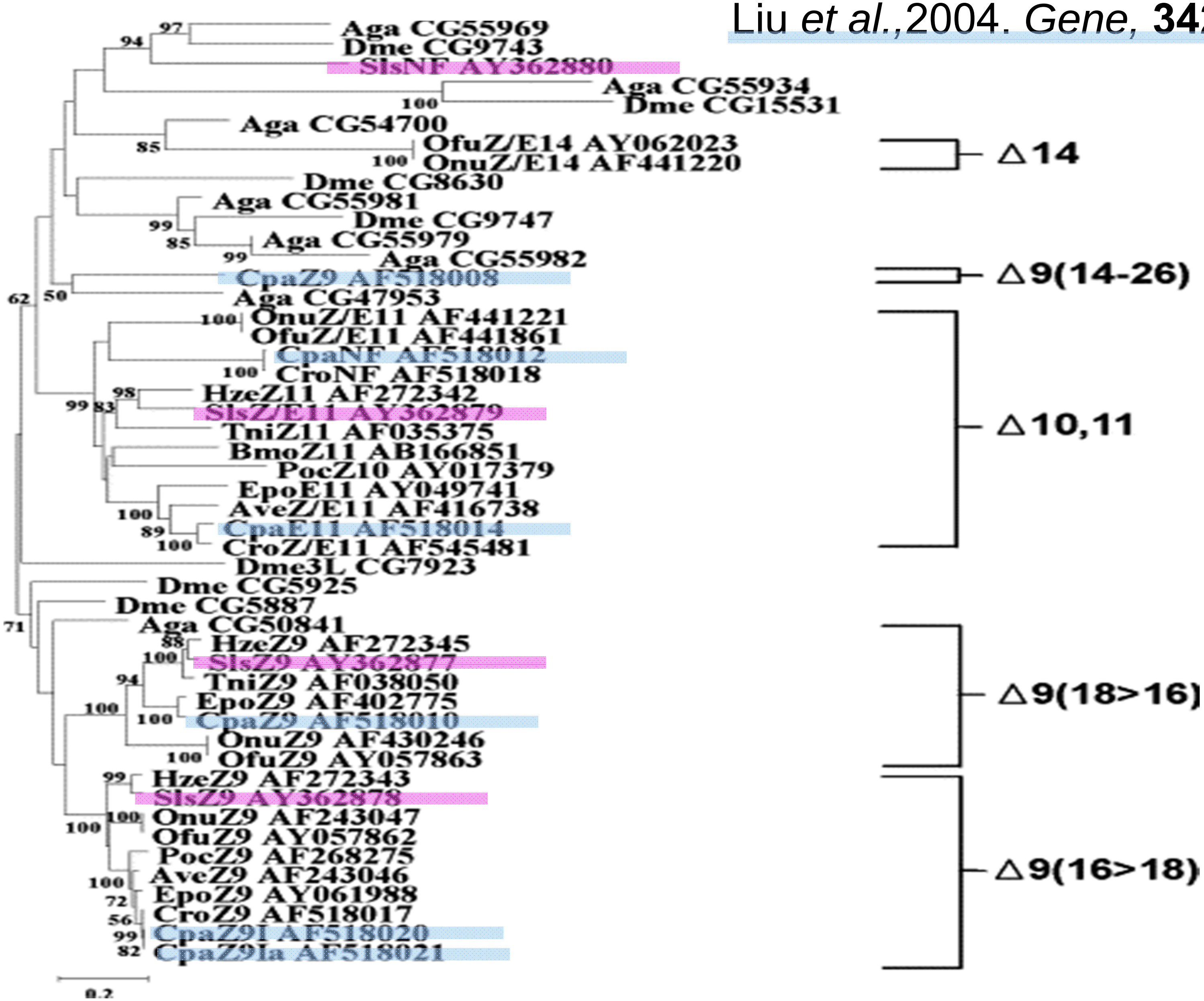
Published until 2007

Desaturation		Species	(Family)	Reference
Z/E11	←14	*Argyrotaenia velutinana*	(Tort.)	Liu *et al*., 2002
		Choristoneura rosaceana	(Tort.)	Hao *et al*., 2002(b)
		Ostrinia furnacalis	(Cram.)	Roelofs *et al*., 2002
		Ostrinia nubilalis	(Cram.)	Roelofs *et al*., 2002
		S. littoralis	(Noct.)	Rodriguez *et al*., 2004
		Ostrinia scapulalis	(Cram.)	Fukuzawa *et al*., 2006
Z/E14	←16	*O. furnacalis*	(Cram.)	Roelofs *et al*., 2002
		O. nubilalis	(Cram.)	Roelofs *et al*., 2002
E10,Z12	←16	*B. mori*	(Bomb.)	Moto *et al*., 2004
	← Z11-16	*M. sexta*	(Sphi.)	Matouskova *et al*., 2007

f) Phylogeny

Rodriguez *et al.*, 2004. *IBMB* **34**: 1315

Liu *et al.*,2004. *Gene,* **342**: 303



B) Acyl reductase

Identification from silk moth

Moto *et al*., 2003. *PNAS*, **100**: 9156

PCR experiment with a primer of a plan reductase gene

➡ Cloning of the cDNA encoding 460 amino acids, which include an NAD(P)H-binding motief

➡ Gene expression in yeast in order to detect the enzymatic activity

Substrate specificity

Saturated fatty acids

16:Acid, 15:Acid >> 17:Acid >> 14:Acid

Monoenyl fatty acids

Z11-16:Acid, E11-16:Acid > E9-16:Acid > Z9-16:Acid

Dienyl fatty acids

E10Z12-16:Acid >> E10,E12-16:Acid

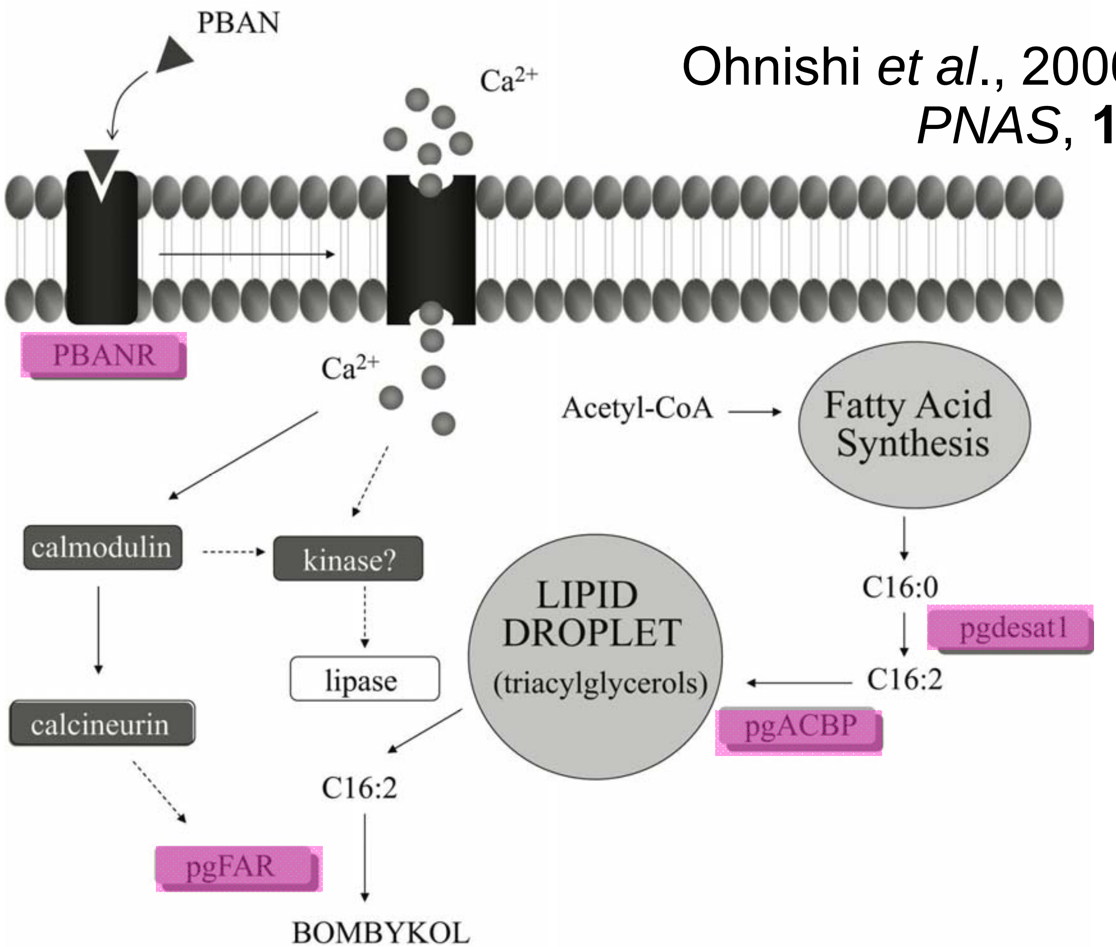
C) RNAi (gene knockdown effects of RNA interference)

Experiment with the silk moth

Targeted genes related to the pheromone biosynthesis

desaturase (pgdesat1), Acyl-CoA binding protein (pgACBP)
reductase (pgFAR), PBAN receptor (PBANR)

Ohnishi *et al*., 2006. *PNAS*, **103**: 4399

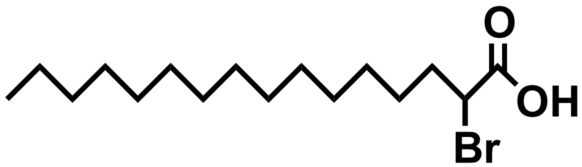


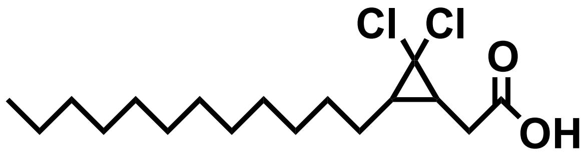
V. Inhibitors of sex pheromone biosynthesis

A) Inhibitors of β-oxidation

Rosell *et al.*, 1992. *IBMB*, **22**: 679

Hernanz *et al.*, 1997. *J. Lipid Res.*, **38**: 1988





B) Inhibitors of desaturation

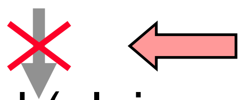
Norflurazon (inhibitor of phytoene in plants): no inhibition

a) Cyclopropenyl compounds

Fogerty *et al.*, 1972. *Lipids*, **7**: 335

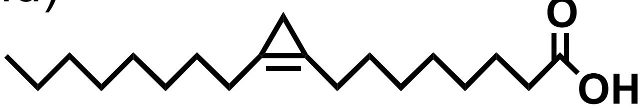
18:Acid (stearic acid)

Δ9-desaturation



Z9-18:Acid (oleic acid)

sterculic acid



Inhibition of pheromone biosynthesis

Spodoptera littoralis (Noctuidae)

pheromone: Z9,E11-14:OAc

R: CO_2H

Arsequell *et al.,* 1989. *Insect Biochem.,* **19**: 949

Gosalbo *et al*., 1992. *IBMB,* **22**: 687

1994. *Arch. Insect Biochem. Physiol.*, **26**: 279

Fabrias *et al*., 1996. *J. Lipid Res.,* **37**: 1503

R: CH_2OH

Rodriguez *et al*., 2004. *IBMB,* **34**: 283

Thaumetopoea pityocampa (Notodontidae)

pheromone: ≡11,Z13-16:OAc

R: CO_2H

Rodriguez *et al*., 2004. *IBMB.,* **34**: 283

Bombyx mori (Bombycidae)

pheromone: E10,Z12-16:OH

R: CO_2H, CO_2NH_2

Ando *et al.,* 1995. *J. Pestic Sci.,* **20**: 25

1996. *J. Agric. Food Chem.*, **44**: 3350

1998. *Arch. Insect Biochem. Physiol.*, **37**: 8

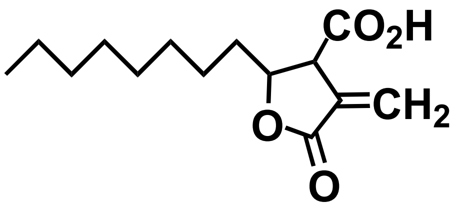
b) Fluorinated compounds

Spodoptera littoralis (Noctuidae)   14:Acid → E11-14:Acid

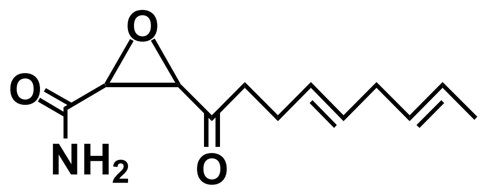
Abad *et al.*, 2003.   *Lipids*, **38**: 865

C) Effect of lipid biosynthesis inhibitors

Choi & Jurenka, 2006.   *J. Asia-Pacific Entonol*., **9**: 43



cerulenin

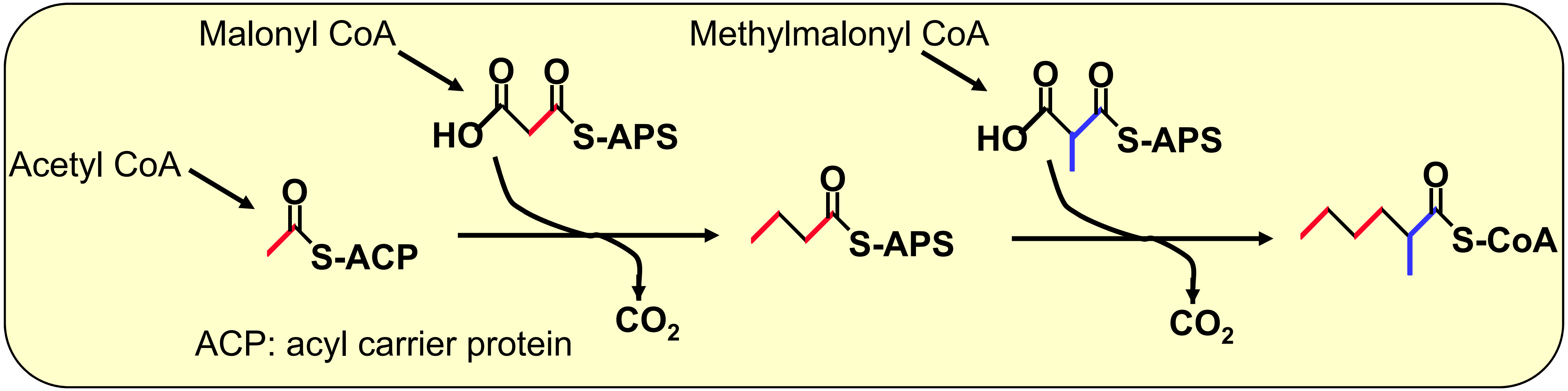


C75

VI. Biosynthesis of methyl branched pheromones

Questions for the biosynthesis of non-terpene pheromones
1) Construction of a carbon skeleton
   From which compound a methyl branch is derived?
2) Formation of a functional group

A) Incorporation of propanoate chains (propanogenins)



Most common process to introduce a methyl branch of non-terpene compounds, which is catalyzed by polyketide synthases (PKS) or fatty acid synthases (FAS)

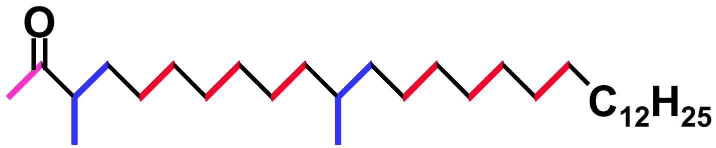
a) German cockroach

Chase *et al.*, 1992. *PNAS,* **89**: 6050

acetyl CoA X 1
malonyl CoA X 6
methylmalonyl CoA X 2
→ Me8,Me16-18:CoA

malonyl CoA X 6 → Me20,Me28-30:CoA —($- CO_2$)→ Me3,Me11-29:H

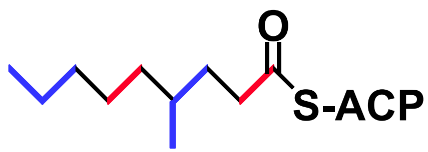
→ Me3,Me11-29:2-OH → Me3,Me11-29:2-one



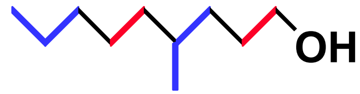
b) Mealworm beetle (*Tenebrio molitor*)

Islam *et al.*, 1999. *BMB,* **29**: 201

propionyl CoA X 1
malonyl CoA X 3
methylmalonyl CoA X1
→



→ Me4-9:OH

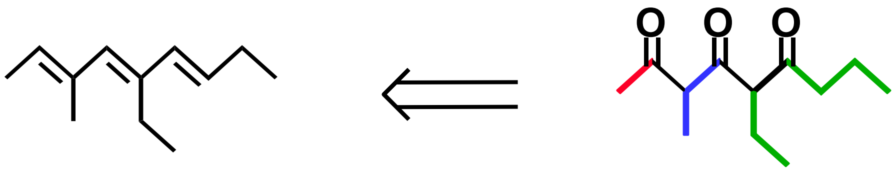


ACP: acyl carrier protein

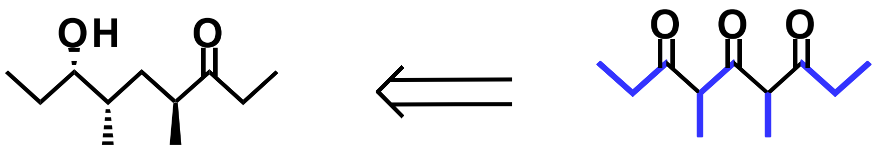
Feeding experiments of diets with ^{2}H- and ^{13}C-labeled acids

B) Polyketide origin

a) Sap beetle (*Carpophilus davidsoni*)

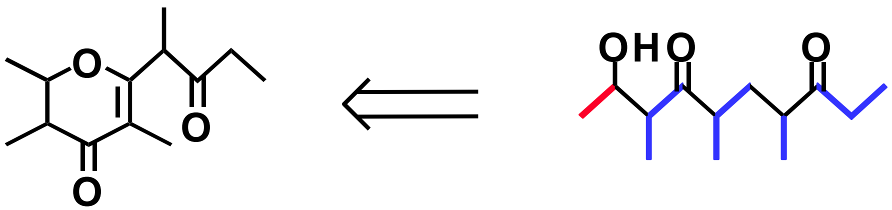


b) Cigarette beetle (*Lasioderma srricorne*)



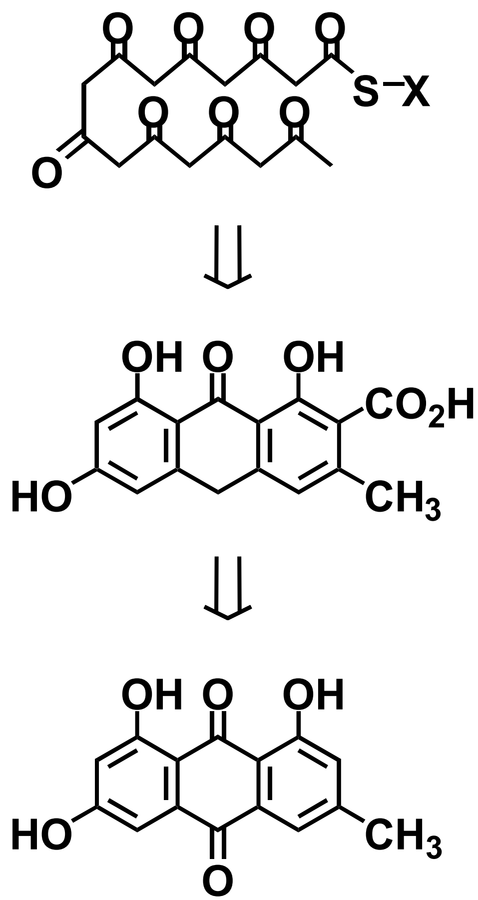
serricornin

c) Drugstore beetle (*Stegobium paniceum*)



stegobinone

Quinone produced by a plant

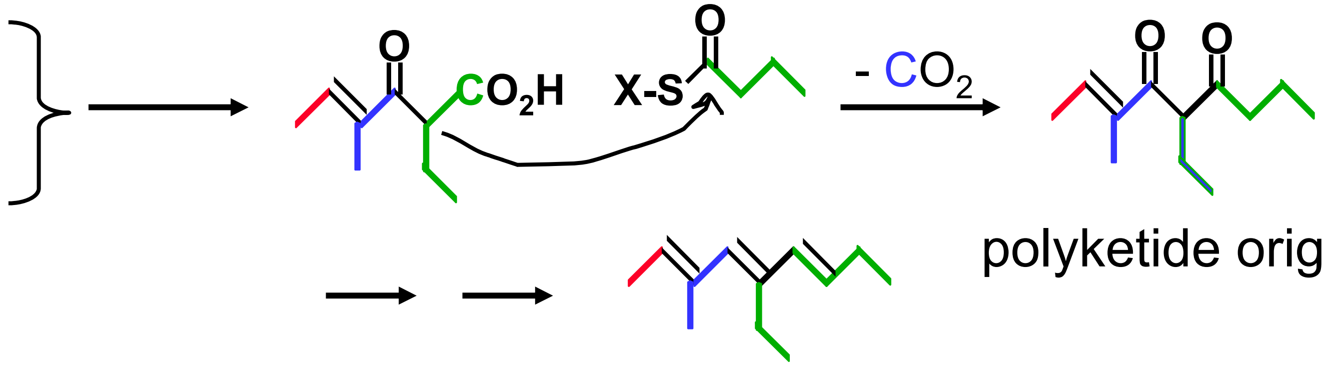


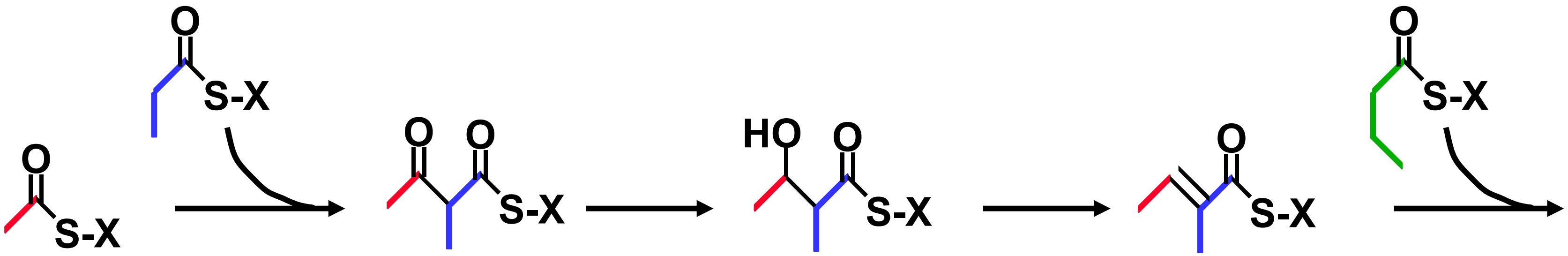
emodin

d) **Sap beetle** (*Carpophilus davidsoni*)

Petroski *et al.*, 1994. *IBMB*, **24**: 69

mcetyl CoA X 1
propionyl CoA X 1
butyryl CoA X 2





C) Incorporation of a amino acid

Gypsy moth (*Lymantria disper*)

Jurenka *et al.*, 2003. *PNAS,* **100**: 809

valine
→ isobutyryl CoA X 1
malonyl CoA X 8
} →

Me18-19:CoA

→ Me18,Z12-19:CoA —($- CO_2$)→ Me2,Z7-18:H

—(epoxidation)→ Me2,epo7-18:H

Other *Lymantria* species

Me2,epo7,17-18:H

Me2,epo7-20:H

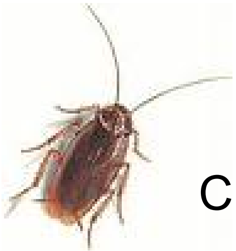
propyl CoA
?

epo7-18:H

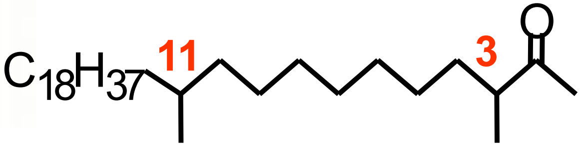
D) Biosynthesis of methyl-branched 2-ketones

a) Typical known pheromones

Blattodea



Blattella germanica
(German cockroach)



Me3,Me11-29:2-one

Nishida *et al.*, 1974. *Experientia*, **30**: 978

Lepidoptera

Lyclene dharma dharma
(Lithosiinae moth)

Me6-18:2-one
Me14-18:2-one
Me6,Me14-18:2-one

Yamamoto *et al.*, 2007. *BBB*, **71**: 2860

Coleoptera

Diabrotica balteata
(banded cucumber beetle)

Me6,Me12-15:2-one

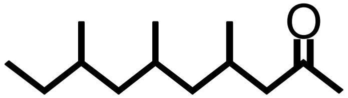
Chuman *et al.*, 1987. *JCE*, **13**: 1601

Diabrotica undecimpunctata
(spotted cucumber beetle)
Me10-13:2-one

Guss *et al.*, 1983. *JCE*, **9**: 1363

Arachnida (Acari)

Chortoglyphus arcuatus
(storage mite)



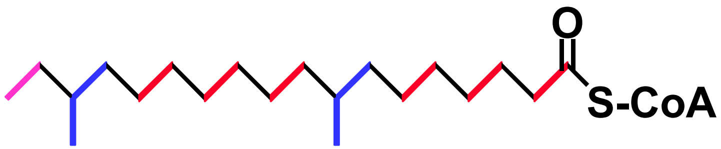
chortolure
Me4,Me6,Me8-10:2-one

Schulz *et al.*, 2004. *Chembiochem*, **5**: 1500

b) German cockroach

Chase *et al.*, 1992. *PNAS*, **89**: 6050

acetyl CoA X 1
malonyl CoA X 6
methylmalonyl CoA X 2
→



Me8,Me16-18:CoA

malonyl CoA X 6 → Me20,Me28-30:CoA —($- CO_2$)→ Me3,Me11-29:H

2-hydroxylation → Me3,Me11-29:2-OH

Recognition of the 2-position based on the 3-methyl group

oxidation → Me3,Me11-29:2-one

Branched hydrocarbons → 2-Ketones

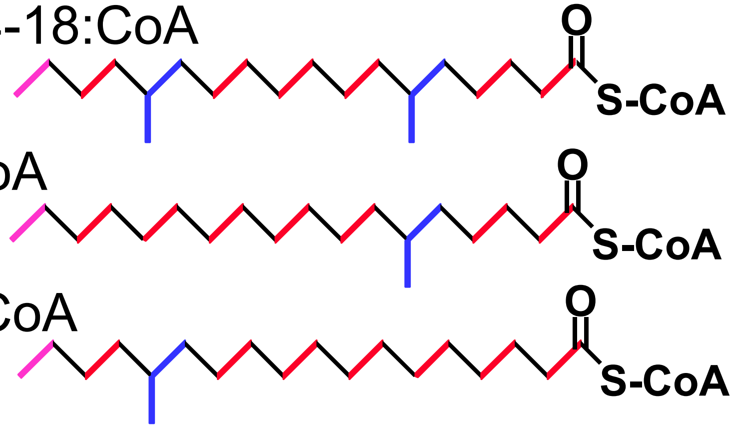
← General route ?

c) **Lichen moth** (speculation) ①

acetyl CoA X 1
malonyl CoA X 6 or 7
methylmalonyl CoA X 2 or 1

→

Me6,Me14-18:CoA
Me6-18:CoA
Me14-18:CoA



? →

Me6,Me14-18:H (Me5,Me13-18:H)
Me6-18:H (Me13-18:H)
Me14-18:H (Me5-18:H)

In hemolymph ?
(not analyzed)

X →

Me5,Me13-18:2-one
Me5-18:2-one
Me13-18:2-one

undetected

→

pheromone
Me6,Me14-18:2-one
Me6-18:2-one
Me14-18:2-one

Not general route

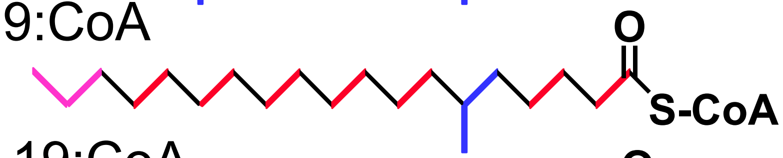
Branched hydrocarbons	→	2-Ketones

c) Lichen moth (speculation) ②

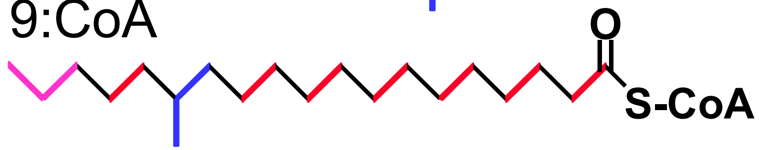
propyl CoA X 1
malonyl CoA X 6 or 7
methylmalonyl CoA X 2 or 1
→

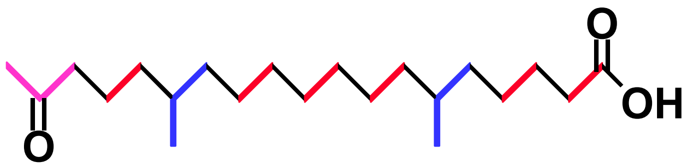
Me6,Me14-19:CoA

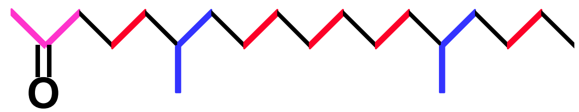
Me6-19:CoA



Me14-19:CoA







ω1-oxydation →

- Me6,Me14,18-keto-19:Acid
- Me6,18-keto-19:Acid
- Me14,18-keto-19:Acid

$- CO_2$ →

- Me6,Me14-18:2-one
- Me14-18:2-one
- Me6-18:2-one

ω1-Oxydation of fatty acid in honey bee

Plettner *et al.*, 1996. *Science*, **271**: 1851
1998. *IBMB*, **28**: 31

18:Acid →

17-OH-18:Acid

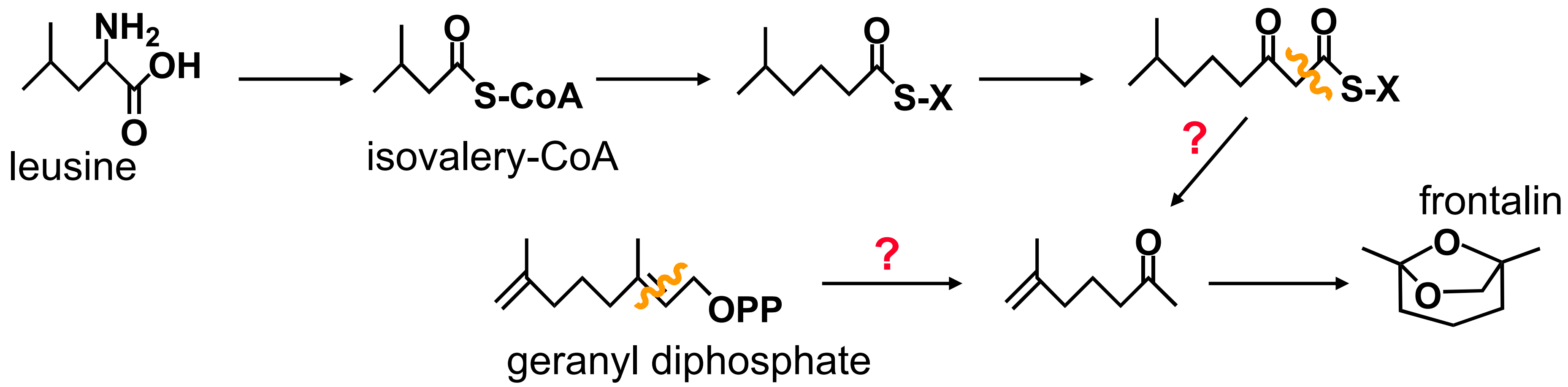
chain shorting →

9-OH,E2-10:Acid —oxidation→

9-keto,E2-10:Acid

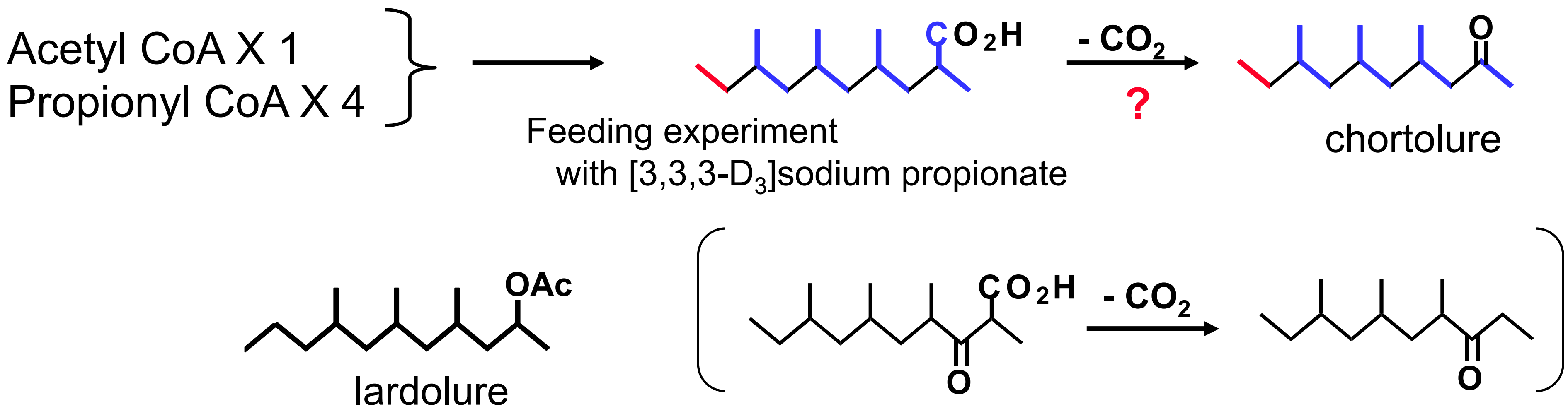
d) Bark beetle

Barkawi *et al.*, 2003. *IBMB*, **33**: 1773



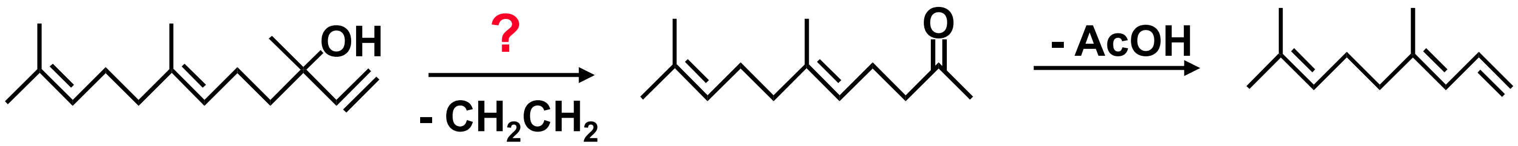
e) Storage mite

Schulz *et al.*, 2004. *Chembiochem*, **5**: 1500



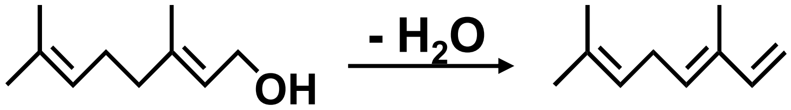
f) Intermediate of homoteropene

Boland *et al.*, 1998. *Tetrahedron*, **54**: 14725



nerolidol geranylacetone C_{11} homoterpenel

farnesol



geraniol β-ocimene