Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Molecular Catalysis B: Enzymatic 23 (2003) 145–170
JOURNAL OF MOLECULAR CATALYSIS B: ENZYMATIC
www.elsevier.com/locate/molcatb

Review

Biotransformation using plant cultured cells

Kohji Ishihara [a], Hiroki Hamada [b], Toshifumi Hirata [c], Nobuyoshi Nakajima [d,*]

[a] *Department of Chemistry, Kyoto University of Education, Fushimi-ku, Kyoto 612-8522, Japan*
[b] *Department of Applied Science, Okayama University of Science, Ridai-cho, Okayama 700-0005, Japan*
[c] *Department of Mathematical and Life Sciences, Graduate School of Science, Hiroshima University, Kagamiyama, Higashi-Hiroshima, Hiroshima 739-8526, Japan*
[d] *Department of Nutritional Science, Graduate School of Health and Welfare Science, Okayama Prefectural University, Soja, Okayama 719-1197, Japan*

Received 20 November 2002; received in revised form 4 February 2003; accepted 7 February 2003

Dedicated to Professor Dr. Kenji Soda in honor of his 70th birthday

Abstract

This review outlines the recent progress during the last 25 years concerning the biotransformation of exogenous substrates by plant cultured cells. The plant cultured cells have abilities of the regio- and stereoselective hydroxylation, oxido-reduction, hydrogenation, glycosylation, and hydrolysis for various organic compounds as well as microorganisms. The reaction types and the stereochemistry of the products involved in the biotransformations are described. The development of techniques using immobilized plant cells are also delineated.

Keywords: Biotransformation; Plant cultured cells; Stereoselectivity; Hydroxylation; Oxido-reduction; Hydrogenation; Glycosylation; Hydrolysis

1. Introduction

It is well known that plants are the source of valuable products and some useful basic materials including cellulose, wood, and rubber. In addition, secondary metabolites such as terpenoids, cardenolides, coumarins, anthraquinones, flavonoids, glucosinolates, and alkaloids are also produced by the plants and are used as drugs, flavors, pigments (food ingredients), and agrochemicals. Hitherto some secondary metabolites have been produced using the plant cultured cells (e.g. [1,2]). However, it has been reported that the formation and the accumulation of some secondary metabolites does not normally occur in the cultured cells of higher plants [3–6] and it has proven difficult to harness this potential to organic syntheses or industrial processes.

To overcome these problems, the biotransformation of exogenous substrates by the plant cultured cells has been investigated. The cultured cells have the ability to specifically convert cheap and plentiful substrates into rare and expensive substances. Many studies have recently focused on the ability of the cultured cells to transform xenobiotic compounds [7–11].

The advantages of the using the plant cultured cells as biocatalysts are following. (i) The "plant cultured cells" can be grown in the laboratory. The cultured material is homogenous; experiments can be performed and reproduced the whole year. (ii) The cultured cells

* Corresponding author. Tel.: +81-866-94-2157; fax: +81-866-94-2157.
E-mail address: nakajima@fhw.oka-pu.ac.jp (N. Nakajima).

1381-1177/$ – see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S1381-1177(03)00080-8

can be accumulating high amounts of the products wanted. (iii) The growth cycles are normally between 1 and 2 weeks, which facilities to plant the experiments. (iv) The cultured cells can be grown to an almost unlimited quantity of biological material. Therefore, now, plant cultured cells have been used as a good tool (biocatalyst) for the organic synthesis as well as microorganisms such as yeast, fungi, and bacteria.

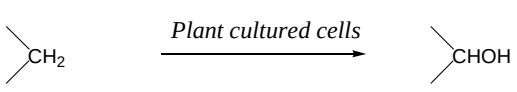
This review summarizes the advances in the biotransformations of exogenous substrates by the cultured cells that have been reported within the past 25 years. Furthermore, in this review, the reaction type, stereospecificity, enantioselectivity involved in the biotransformations of the exogenous substrates by plant cultured cells are summarized according to the chemical reaction classes as follows: hydroxylation, oxidation (of hydroxyl group), reduction (of carbonyl group), hydrogenation (of carbon–carbon double bond), glycosyl conjugation, and hydrolysis. The substrates, products and plant species participating in the biotransformations are listed in Tables 1–15.

2. Hydroxylation

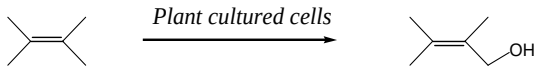
2.1. Regioselectivity of hydroxylation

The regio- and stereoselective hydroxylation of target molecules is one of important categories in the biotransformation of exogenous substrates by plant cultured cells (Scheme 1), because this offers great potential for the production of useful substances.

The hydroxylations of exogenous substrates by plant cultured cells are listed in Tables 1–4. It has been reported that the cultured cells of *Nicotiana tabacum* have the ability to hydroxylate the *trans*-methyl group in the isopropyridene moiety of linalool (**1**), dihydrolinalool (**4**) and their acetate (**3** and **6**) to give the corresponding 8-hydroxy derivatives [12]. Such an ability of the cultured cells is also investigated with monoterpenoids having terminal, endocyclic and exocyclic C–C double bonds, such as *p*-menth-1-en-8-ol



Scheme 1.



Scheme 2.

(α-terpineol) (**7**) and its acetate (**10**) [13,14,16], *c*-*p*-menth-8(9)-en-*r*-1-ol (β-terpineol) (**26**) and its acetate (**29**) [13,17], and 1-acetoxy-*p*-menth-4(8)-ene (γ-terpinyl acetate) (**33**) [18] as substrates. These terpineols are hydroxylated at the carbon atoms allylic to the C–C double bond to yield the corresponding allyl alcohols (Scheme 2).

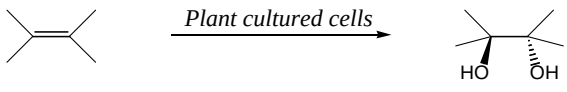
2.2. Stereoselectivity of hydroxylation

Almost the hydroxylations by plant cultured cells are stereoselective: (i) the hydroxylation at C-4 of β-terpineol (**26**) and its acetate (**29**) afforded only *trans*-isomers (**28** and **32**, respectively), (ii) the hydroxylation of the endocyclic linkage of α-terpinyl acetate (**10**) resulted in the predominant formation of a *trans*-diol (**11**), and (iii) the hydroxylation of γ-terpinyl acetate (**33**) predominantly gave a diol (**34**) having the hydroxyl group *trans* to the 1-acetoxyl group. Thus, plant cultured cells possess the ability to hydroxylate the C–C double bond stereospecifically (Scheme 3).

2.3. Substrate specificity of hydroxylation

The enantioselectivity of the hydroxylation by plant cultured cells is tested using enantiomers of α-terpineol (**7**) and its acetate (**10**) [14,16]. The hydroxylation at the six-position of (4*R*)-α-terpineol (**14**) and its acetate (**20**) take place in preference to that of their (4*S*)-isomers. On the other hand, the hydroxylation at the ethylenic linkage of (4*S*)-α-terpinyl acetate (**24**) is in preference to that of its (4*R*)-isomer (Scheme 4).

Hence, the cultured cells discriminate the enantiomers of both substrates and the hydroxylated one of the enantiomers. It is suggested that the differences in



Scheme 3.

Table 1
Regio- and stereoselective hydroxylation with plant cultured cells (part I)

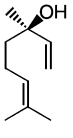
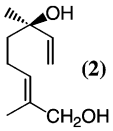
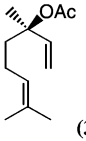
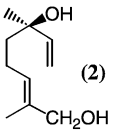
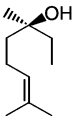
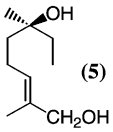
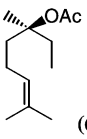
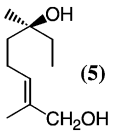
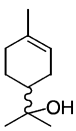
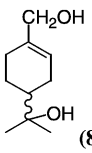
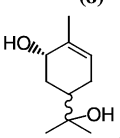
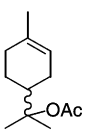
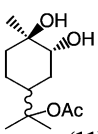
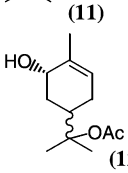
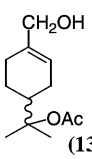
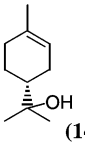
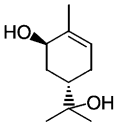
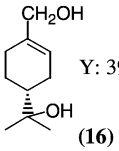
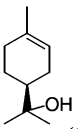
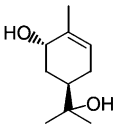
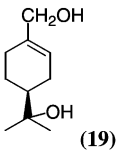
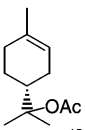
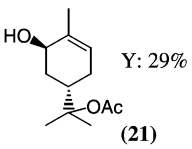
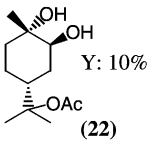
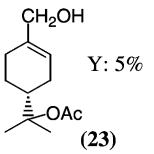
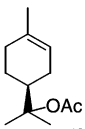
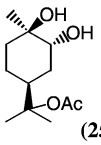
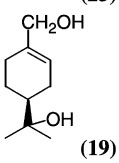
Substrate	Plant species	Products	References
 (1)	*N. tabacum*	 (2)	[12]
 (3)	*N. tabacum*	 (2)	[12]
 (4)	*N. tabacum*	 (5)	[12]
 (6)	*N. tabacum*	 (5)	[12]
 (7)	*N. tabacum*	 (8)	[13,14]
		 (9)	[13,14]
 (10)	*N. tabacum*	 (11)	[14,15]
		 (12)	[14,16]
		 (13)	[14,16]

Table 1 (*Continued*)

Substrate	Plant species	Products	References
 **(14)**	*N. tabacum*	 Y: 44% **(15)**	[14,16]
		 Y: 39% **(16)**	[14,16]
 **(17)**	*N. tabacum*	 **(18)**	[14,16]
		 **(19)**	[14,16]
 **(20)**	*N. tabacum*	 Y: 29% **(21)**	[14,16]
		 Y: 10% **(22)**	[14,16]
		 Y: 5% **(23)**	[14,16]
 **(24)**	*N. tabacum*	 **(25)**	[14,16]
		 **(19)**	[14,16]

Y: Yield in the reference.

Table 2
Regio- and stereoselective hydroxylation with plant cultured cells (part I)

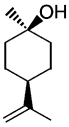
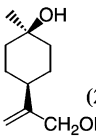
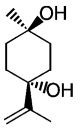
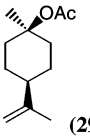
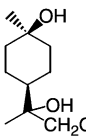
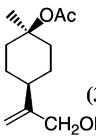
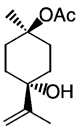
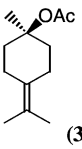
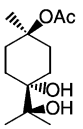
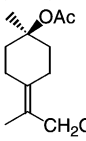
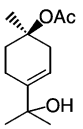
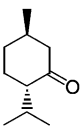
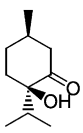
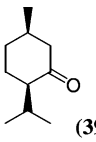
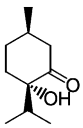
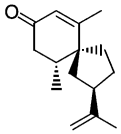
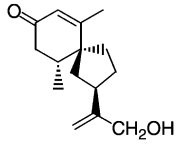
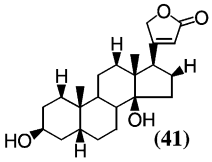
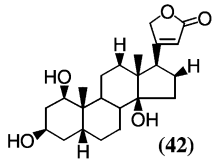
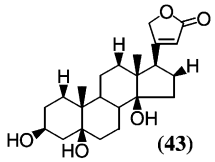
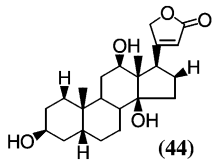
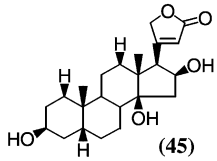
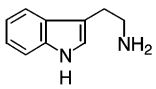
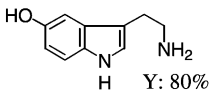
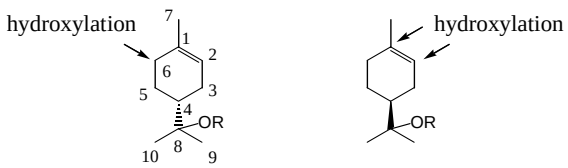
Substrate	Plant species	Products	References
 (26)	*N. tabacum*	 (27)	[13,17]
		 (28)	[13,17]
 (29)	*N. tabacum*	 (30)	[13,17]
		 (31)	[13,17]
		 (32)	[13,17]
 (33)	*N. tabacum*	 (34)	[18]
		 (35)	[18]
		 (36)	[18]
 (37)	*N. tabacum*	 (38)	[19]
 (39)	*N. tabacum*	 (40)	[19]

Table 2 (*Continued*)

Substrate	Plant species	Products	References
	*N. tabacum*		[20]
 (**41**)	*Strophanthus gratus*	 (**42**)	[21,22]
	Strophanthus intermedius	 (**43**)	[21,22]
	Digitarlis lanata	 (**44**)	[21]
	Digitarlis purpurea	 (**45**)	[22]
	*Peganum harmala*	 Y: 80%	[25–27]

Y: Yield in the reference.

the enantioselectivity for the hydroxylation between the allylic position of the C–C double bond and the C–C double bond itself are catalyzed by different enzyme systems in the cultured cells [33].



(4*R*)-α-tepineol (4*S*)-α-tepineol

Scheme 4.

2.4. Glycol formation

The process of glycol formation has been investigated for the biotransformation of γ-terpinyl acetate (**33**) in the cultured cells of *N. tabacum* [18,34]. It was found that glycols are formed from the epoxidation of the C–C double bond, followed by hydrolysis of the resulting epoxides (Scheme 5).

The presence of an epoxidase in the plant cultured cells is also demonstrated by the epoxidation of isopentenol with a cell-free system from the callus tissues of *Jasminum officinale*, though neither callus nor suspension cultures of the cells are able to form any epoxides [35].

Table 3
Regio- and stereoselective hydroxylation with plant cultured cells (part III)

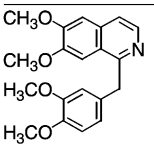
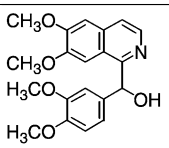
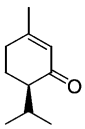
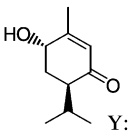
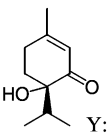
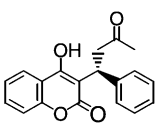
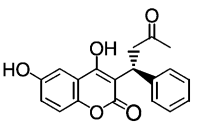
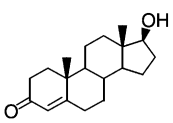
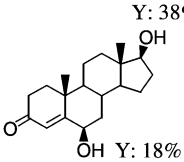
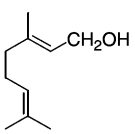
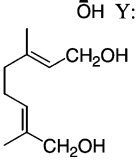
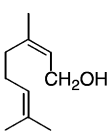
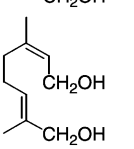
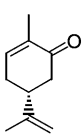
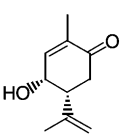
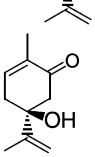
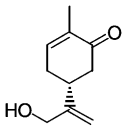
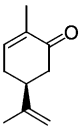
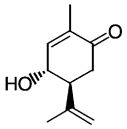
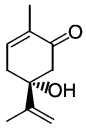
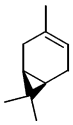
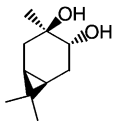
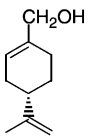
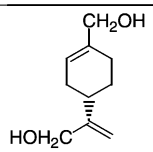
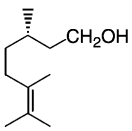
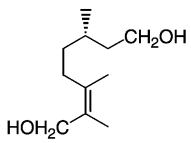
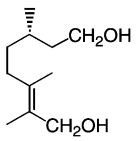
Substrate	Plant species	Products	References
			
	Ochrosia elliptica		[28]
	Saponaria oficinalis	Y: 26%	[29]
	Glycyrrhiza glabra	Y: 32%	[29]
	*Catharanthus roseus*	 Y: 38%	[30]
		 Y: 40%	[30]
	*C. roseus*	 Y: 38%	[31]
	*Marchantia polymorpha*	 Y: 18%	[32]
	*C. roseus*		[37]
	*C. roseus*		[37]
	*C. roseus*		[37]
			[37]

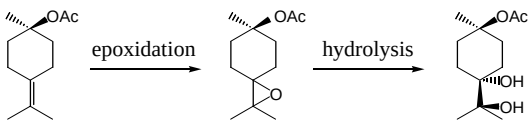
Table 3 (*Continued*)

Substrate	Plant species	Products	References
			[37]
	*C. roseus*		[37]
			[37]
	*N. tabacum*		[38]

Y: Yield in the reference.

Table 4
Regio- and stereoselective hydroxylation with plant cultured cells (part IV)

Substrate	Plant species	Products	References
	*C. roseus*		[39]
	*C. roseus*		[39]
			[39]



γ-terpinyl acetate (**33**) (**34**)

Scheme 5.

2.5. Other types

The other types of hydroxylations, as well as the hydroxylation at the C–C double bond and its allylic position by the plant cultured cells are listed in Tables 1–4. The regio- and stereoselective

Table 5
Stereoselective oxidation with plant cultured cells (part I)

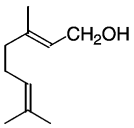
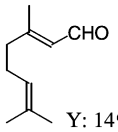
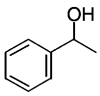
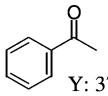
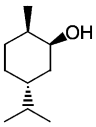
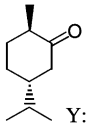
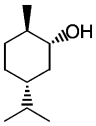
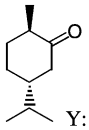
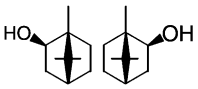
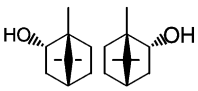
Substrate	Plant species	Products	References
	*Glycine max*	 Y: 14%	[44]
	*Spirodela oligorrhiza*	 Y: 37%	[43]
	*N. tabacum*	 Y: 95%	[40–42]
	*N. tabacum*	 Y: 20%	[40–42]
	*N. tabacum*	 Y: 89%	[40–42]
	*N. tabacum*	 Y: 95%	[40–42]
	*N. tabacum*	 Y: 23%	[44]
	*N. tabacum*	 Y: 24%	[45]
	*N. tabacum*	 Y: 98%	[47]
 (46)	*N. tabacum*	 Y: 96% (47)	[47]
	*N. tabacum*	 Y: 95%	[47]
	*N. tabacum*	 Y: 98%	[47]
	*N. tabacum*	 Y: 97%	[36,48]
	*N. tabacum*		[36,48]

Table 5 (*Continued*)

Substrate	Plant species	Products	References
	*N. tabacum*	 Y: 95%	[36]
	*N. tabacum*	 Y: 96%	[36]
	*N. tabacum*		[38]
			[38]

Y: Yield in the reference.

Table 6
Stereoselective oxidation with plant cultured cells (part II)

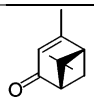
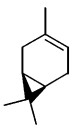
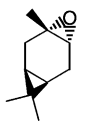
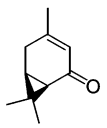
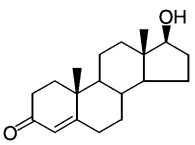
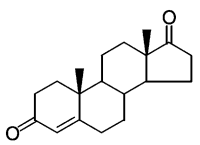
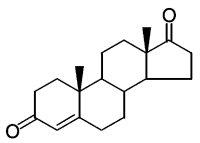
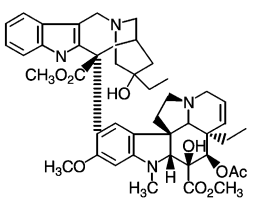
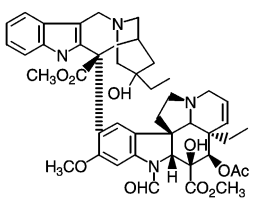
Substrate	Plant species	Products	References
	*N. tabacum*		[38]
	*N. tabacum*		[38]
			[38]
	*Dendrobium phalaenopsis*		[49]
	M. polymorpha		[38]
	*C. roseus*		[50]

Table 7
Regio- and stereoselective reduction with plant cultured cells (part I)

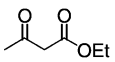
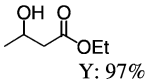
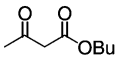
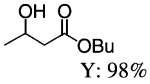
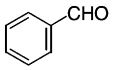
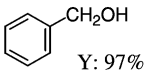
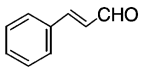
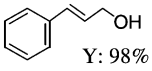
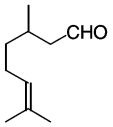
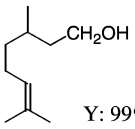
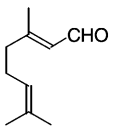
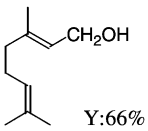
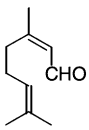
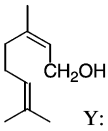
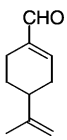
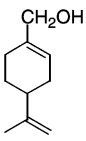
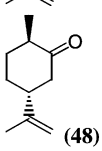
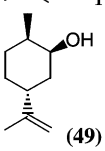
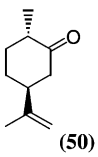
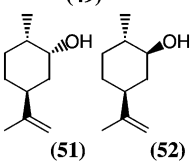
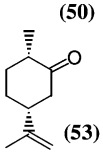
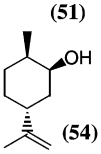
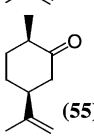
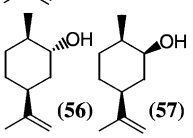
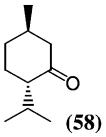
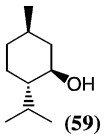
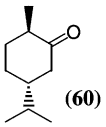
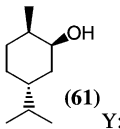
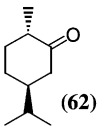
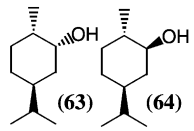
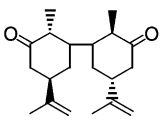
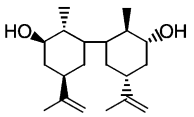
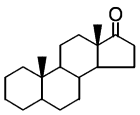
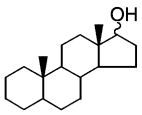
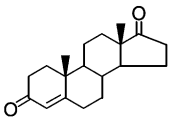
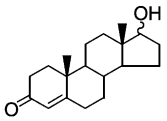
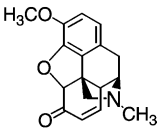
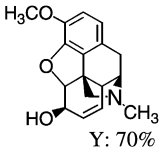
Substrate	Plant species	Products	References
	*N. tabacum*	 Y: 97%	[51]
	*N. tabacum*	 Y: 98%	[51]
	*Lavandula angustifolia*	 Y: 97%	[52]
	*L. angustifolia*	 Y: 98%	[52]
	*L. angustifolia*	 Y: 99%	[52]
	*L. angustifolia*	 Y:66%	[52]
	*L. angustifolia*	 Y: 40%	[52]
	*L. angustifolia*	 Y: 98%	[52]
 (48)	*N. tabacum*	 (49)	[53]
 (50)	*N. tabacum*	 (51) (52)	[53]
 (53)	*N. tabacum*	 (54)	[53]
 (55)	*N. tabacum*	 (56) (57)	[53]

Table 7 (*Continued*)

Substrate	Plant species	Products	References
 **(58)**	*Mentha* sp.	 **(59)**	[54]
 **(60)**	*N. tabacum*	 **(61)** Y: 93%	[45]
 **(62)**	*N. tabacum*	 **(63)** Y: 24% **(64)** Y: 61%	[45]
	*N. tabacum*	 Y: 54%	[55]
	*Dendrobium phalaenopsis*		[51]
	*D. phalaenopsis*		[51]
	*Papaver somniferum*	 Y: 70%	[56]

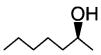
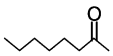
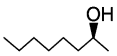
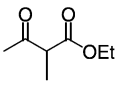
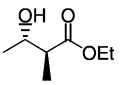
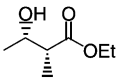
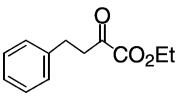
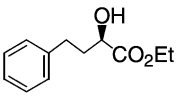
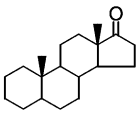
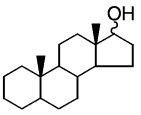
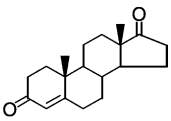
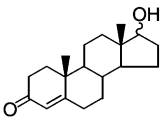
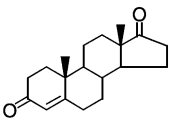
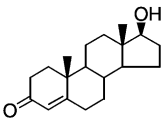
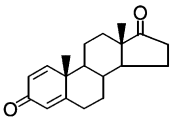
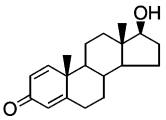
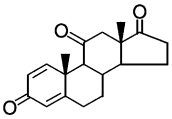
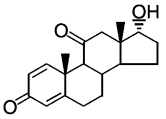
Y: Yield in the reference.

hydroxylations at the C-1 (**42**), C-5 (**43**), C-12 (**44**), and C-16 (**45**) of digitoxigenin (**41**) have been reported [21–24]. Hydroxylation at the α-position to the carbonyl group is found during the biotransformation of the 3-oxo-*p*-menthanes (1*R*,4*S*)- and (1*R*,4*R*)-*p*-menth-3-ones (**37** and **39**) with a suspension culture of *N. tabacum*; the hydroxyl group at the 4-position occupy the same spatial arrangement as that of the leaving methine proton [19]. Interestingly, such hydroxylations do not occur during the biotransformation of the 2-oxo-*p*-menthane derivatives using the same cultured cells [36].

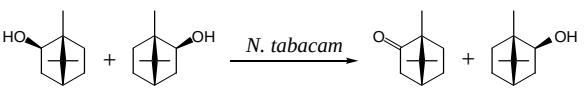
3. Oxidation of hydroxyl group

Alcohols are converted to the corresponding ketones by the plant cell cultures (Tables 5 and 6). The conversion of the mono- and bicyclic monoterpene alcohols by the cultured cells of *N. tabacum* is enantioselective; the cultured cells discriminate the enantiomers of the *p*-menthan-2-ol, bicyclo[2.2.1]heptane-2-ol and bicyclo[3.1.1]heptane-3-ol derivatives, and enantioselectivity oxidized their hydroxy group [36,46]. The transformation of (*RS*)-borneol and (*RS*)-isoborneol with the cultured cells of *N. tabacum*

Table 8
Regio- and stereoselective reduction with plant cultured cells (part II)

Substrate	Plant species	Products	References
	*N. tabacum*		[57]
	*N. tabacum*		[57]
	*M. polymorpha*		[58]
	G. max		[58]
	*Daucus carota*		[59]
	*D. phalaenopsis*		[51]
	*D. phalaenopsis*		[51]
	*M. polymorpha*		[60]
	*M. polymorpha*		[61]
	*M. polymorpha*		[61]

gave (1*R*,4*R*)-camphor (**46**). (1*S*,2*S*,4*R*)-Borneol or (1*S*,2*R*,4*R*)-isoborneol is oxidized to the corresponding ketones, however (1*S*,2*R*,4*S*)-borneol and (1*S*,2*S*,4*S*)-isoborneol are not converted and their optical purities are about 90–95% enantiomeric excess (Schemes 6 and 7) [33,47]. Such an enantioselective oxidation is useful for the preparation of chiral alcohols and ketones from racemic hydroxy compounds.



(*RS*)-borneol

Scheme 6.

4. Reduction of carbonyl group

There are also many reports of the reduction of ketones and aldehydes to the corresponding alcohols with plant cultured cells (Tables 7 and 8). The reductions of the 2- and 3-oxygenated *p*-menthanes, such as (1*R*,4*R*)- and (1*S*,4*S*)-dihydrocarvone (**48** and **50**), (1*S*,4*R*)- and (1*R*,4*S*)-isodihydrocarvones (**53** and **55**)

Table 9
Regio- and stereoselective hydrogenation with plant cultured cells

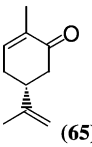
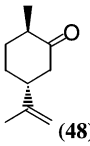
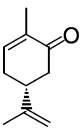
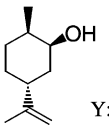
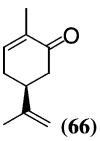
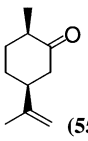
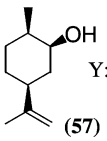
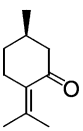
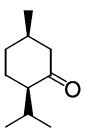
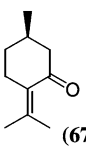
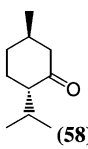
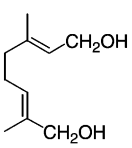
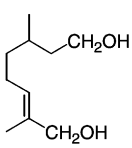
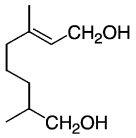
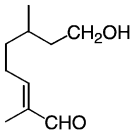
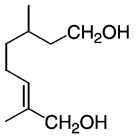
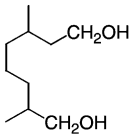
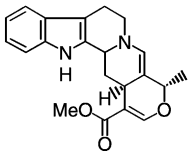
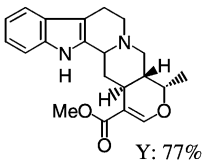
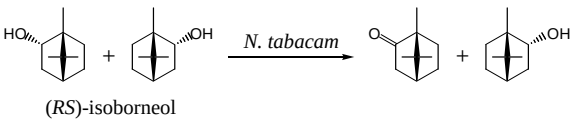
Substrate	Plant species	Products	References
	*Medicago sativa* *G. max* *Vinca minor* *C. roseus*	 Y: 58%	[62] [62] [62] [62]
 **(65)**	*N. tabacum* *M. sativa*	 Y: 27% **(48)**	[53] [62]
 **(65)**	*N. tabacum* *M. sativa*	 Y: 52% **(49)**	[53] [62]
 **(66)**	*N. tabacum*	 Y: 14% **(55)**	[53]
		 Y: 8% **(57)**	[53]
 **(67)**	*Mentha* sp. *N. tabacum*	 Y: 76% **(39)**	[63] [19]
 **(67)**	*Mentha* sp. *N. tabacum*	 Y: 23% **(58)**	[63] [19]
 **(68)**	*N. tabacum*	 Y: 98% **(69)**	[36,48]
	*C. roseus*		[64]

Table 9 (*Continued*)

Substrate	Plant species	Products	References
			[64]
	*C. roseus*		[64]
			[64]
	*C. roseus*	 Y: 77%	[65]

Y: Yield in the reference.

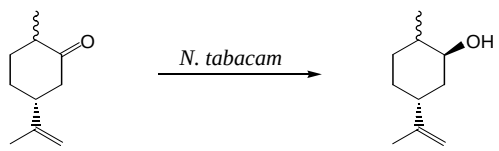


(*RS*)-isoborneol

Scheme 7.

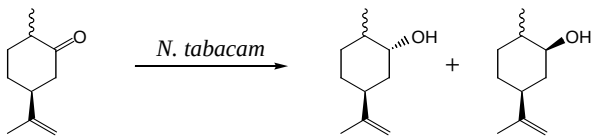
with the cultured cells of *N. tabacam* stereoselectively proceed (Schemes 8 and 9).

(1*R*,4*S*)-Menthone (**58**), (1*R*,4*R*)- and (1*S*,4*S*)-carvomenthones (**60** and **62**) are also stereoselectively reduced by the cells of *N. tabacum*. During the reduction, the hydrogen attack preferentially takes place from the *re*-face of the carbonyl group to give the hydroxy compounds with *S*-chirality at the position bearing the hydroxyl group [36,45,53]. In-



(**47**, **52**) (**48**, **53**)

Scheme 8.



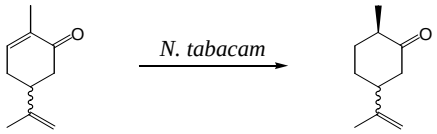
(**49**, **54**) major minor

Scheme 9.

terestingly, the cultured cells discriminate between the 2- and 3-oxygenated *p*-menthanes during their reductive conversions; *p*-menthan-2-ones are converted to their corresponding alcohols in high yield, but this is not the case with the *p*-menthane-3-ones [19]. In addition, the cells stereospecifically reduce (1*R*,4*R*)-2-oxo-*p*-menthanes, whereas the specificity is low in the case of the (4*S*)-epimer [36].

5. Hydrogenation of carbon–carbon double bond

There are several reports of the reduction of a C–C double bond by a plant cultured cells (Table 9). The cultured cells of *N. tabacum* reduce the C–C



(4*RS*)-carvone

Scheme 10.

double bond next to the carbonyl group of (4*R*)- and (4*S*)-carvones (**65** and **66**), but the cell culture does not attack the C–C double bond in the 1-methylethyl group (Scheme 10) [53].

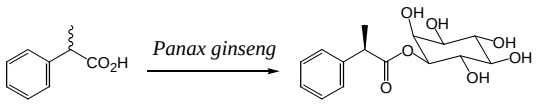
The stereochemistry of the reduction of the endocyclic C–C double bond of (4*R*)-carvone (**65**) was investigated using the cultured cells of *N. tabacum* and enzymes from the cultured cells: (i) the conjugated C–C double bond is regioselectivity reduced; (ii) the reduction stereospecifically occurred by *anti*-addition of hydrogen from the *si*-face at C-1 and the *re*-face at C-6 of carvone to give (1*R*,4*R*)-dihydrocarvone (**48**); (iii) the hydrogen atoms participating in the enzymatic reduction at C-1 and C-6 originate from the medium and the *pro*-4R hydrogen of NADH, respectively [66,67]. Such a stereospecific reduction occurs during the biotransformation of pulegone (**67**) and verbenone (**68**) [19,36,48,64]. In addition, the cell cultures discriminate the enantiomer of verbenone (**68**) and enantioselectively reduce the C–C double bond of only the (1*S*,5*S*)-enantiomer [36,48].

6. Glycosyl conjugation

Glycosyl conjugation is of special interest, because of the possibility of producing new cardenolides, as well as converting water-insoluble substances to water-soluble compounds. Two types of glycosyl conjugations are listed in Tables 10–13. One involves the esterification between the carboxylic acid and sugar moiety. The other one is the ether formation (glycosylation) of the hydroxyl group and sugar moiety.

6.1. Esterification

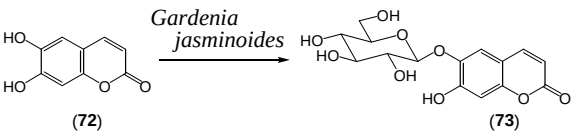
The ester bond formations of propionate derivatives and several sugars, such as glucose, xylose, inositol, and sucrose, have been carried out by using the root cultures of *Panax ginseng* and the cultured cells of *N. tabacum*, *Dioscoreophyllum cummensii*, *Coffea arabica*, and *Coronilla varia* (Scheme 11) [66–70].



(*RS*)-2-phenylpropionic acid

myo-inositol ester

Scheme 11.



(**72**) (**73**)

Scheme 12.

6.2. Glycosylation

When the capacity for glycosylation of plant cultured cells is examined, it was clear that cultured cells have high activity for the glycosylation of phenolic substrates [69–71]. The glycosylation of esculetin (**73**) by cultured cells is highest during the late stationary phase of the cell growth cycle and ca. 10% of the added substrate is converted to 6-*O*-β-D-glycosylesculetin (**74**) in 24 h (Scheme 12) [76].

On the other hand, a higher activity is observed with salicyl alcohol (**70**) during the exponential phase of the growth cycle and about 70% of the administered alcohol is converted to the corresponding glycoside within 4 days [74,75]. Interestingly, a major product of glycosylation with the cultured cells of *Gardenia jasminoides* is salicin (**71**), although other cultured strains derived from different plant species predominantly produce isosalicin (**72**) [74,75]. Furthermore, the glycosyl conjugation of (*RS*)-2-phenylpropionic acid derivatives enantioselectively occurs to give the C-2 chiral products [66,68].

7. Hydrolysis

7.1. Hydrolysis of acetoxy group

The ability of cultured cells to hydrolyze the acetoxy group has been widely investigated (Tables 14

Table 10
Regioselective glycosylation with plant cultured cells (part I)

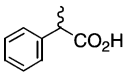
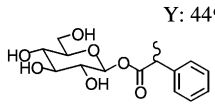
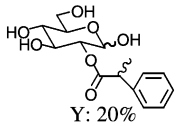
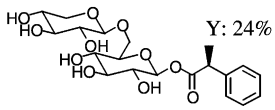
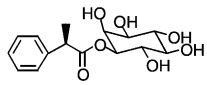
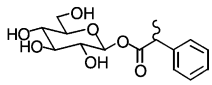
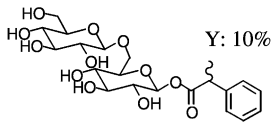
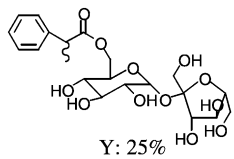
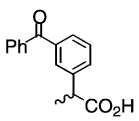
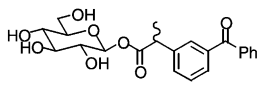
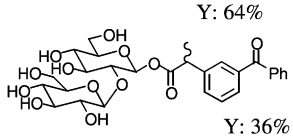
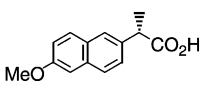
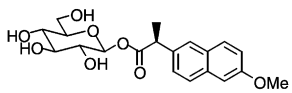
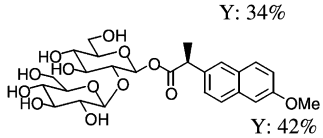
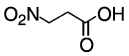
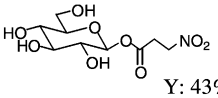
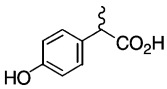
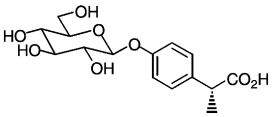
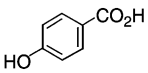
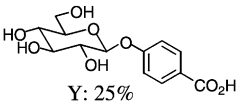
Substrate	Plant species	Products	References
	*Panax ginseng*	 Y: 44%	[66]
	P. ginseng	 Y: 20%	[66]
	P. ginseng	 Y: 24%	[66]
	P. ginseng		[66]
	N. tabacum	 Y: 28%	[67]
	Dioscoreophyllum cummensii	Y: 7%	[67]
	D. cummensii	 Y: 10%	[67]
	Coffea arabica	 Y: 25%	[68]
	*P. ginseng*	 Y: 64%	[69]
		 Y: 36%	[69]
	*P. ginseng*	 Y: 34%	[69]
		 Y: 42%	[69]

Table 10 (*Continued*)

Substrate	Plant species	Products	References
	*Coronilla varia*	 Y: 43%	[70]
	*P. ginseng*		[69]
	*Mallotus japonicus*	 Y: 25%	[71]

Y: Yield in the reference.

Table 11
Regioselective glycosylation with plant cultured cells (part II)

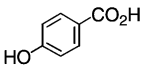
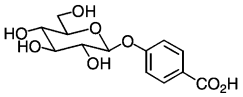
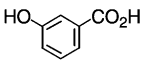
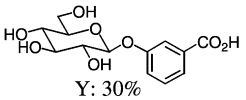
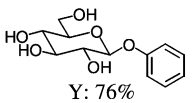
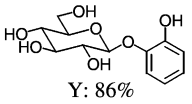
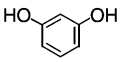
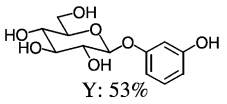
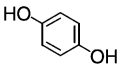
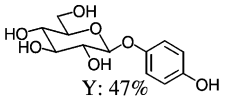
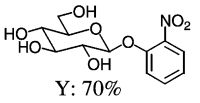
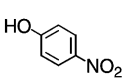
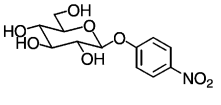
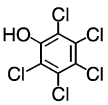
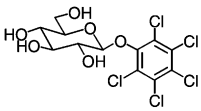
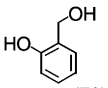
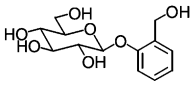
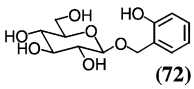
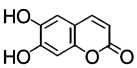
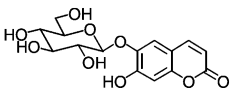
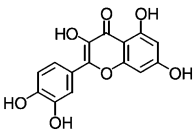
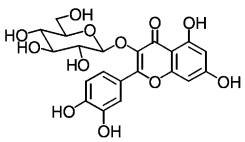
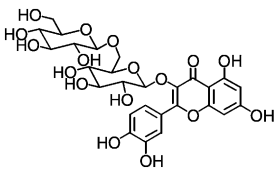
Substrate	Plant species	Products	References
	*Mallotus japonicus*		[71]
	*Datura innoxia*	 Y: 30%	[71]
	Perilla flrutescens	Y: 48%	[71]
	C. roseus	Y: 52%	[71]
	Lithospermun erythrorhizon	Y: 23%	[71]
	*Gardenia jasminoides*	 Y: 76%	[71]
	*G. jasminoides*	 Y: 86%	[72]
	*G. jasminoides*	 Y: 53%	[72]
	*G. jasminoides*	 Y: 47%	[72]
	*G. jasminoides*	 Y: 70%	[72]
	*G. jasminoides*		[72]

Table 11 (*Continued*)

Substrate	Plant species	Products	References
	*G. max*		[73]
	Triticum aestivam		[73]
 (70)	*G. jasminoides*	 (71)	[74,75]
	G. jasminoides	 (72)	[74,75]
 (73)	*G. jasminoides*	 (74)	[76]
	*Cannabis sativa*		[77]
			[77]

Y: Yield in the reference.

Table 12
Regioselective glycosylation with plant cultured cells (part IIII)

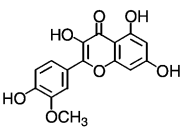
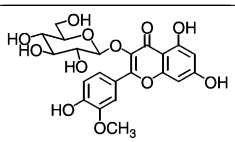
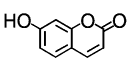
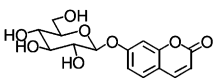
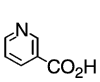
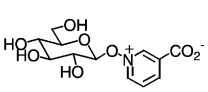
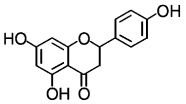
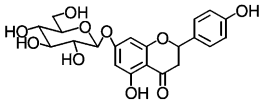
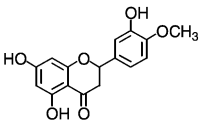
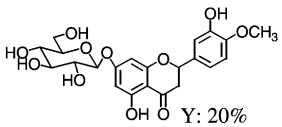
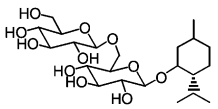
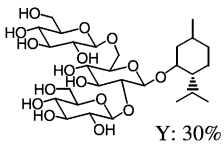
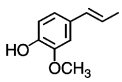
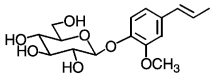
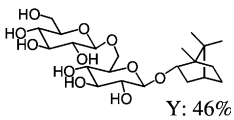
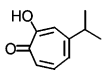
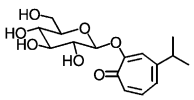
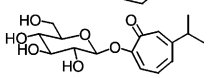
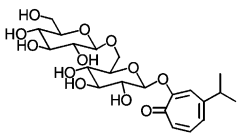
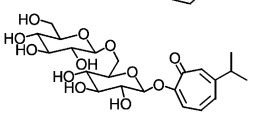
Substrate	Plant species	Products	References
	*C. sativa*		[77]
	*Datura innoxia*	 Y: 90%	[71]
	Perilla flrutescens	Y: 75%	[71]
	C. roseus	Y: 56%	[71]
	Lithospermun erythrorhizon	Y: 46%	[71]
	*Petroselinum hortense*	 Y: 37%	[78]

Table 12

Substrate	Plant species	Products	References
	*Citrus paradisi*		[79,80]
	Citrus limon	Y: 10%	[79,80]
	*C. limon*	 Y: 20%	[79,80]
	*Eucalyptus perriniana*	 Y: 46%	[81]
		 Y: 30%	[81]
	*E. perriniana*		[82]
	*E. perriniana*	 Y: 46%	[83]
	*E. perriniana*		[84]
			[84]
			[84]
			[84]

Y: Yield in the reference.

Table 13
Regioselective glycosylation with plant cultured cells (part IV)

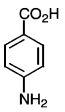
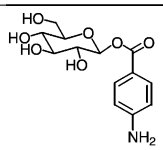
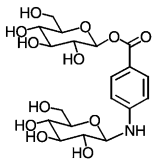
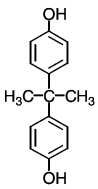
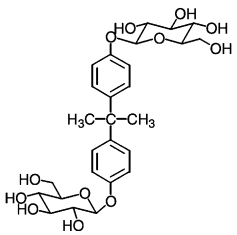
Substrate	Plant species	Products	References
	*E. perriniana*		[85]
			[85]
	*E. perriniana*		[86]

Table 14
Stereoselective hydrolysis with plant cultured cells (part I)

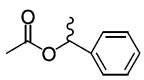
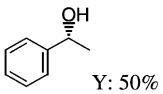
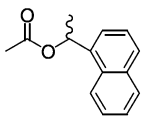
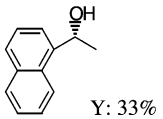
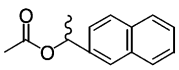
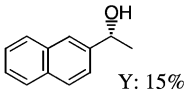
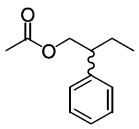
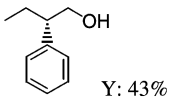
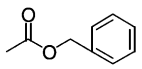
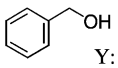
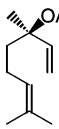
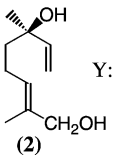
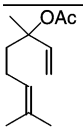
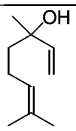
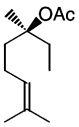
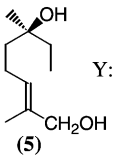
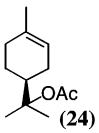
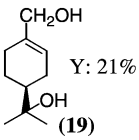
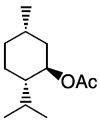
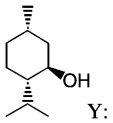
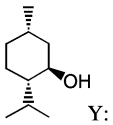
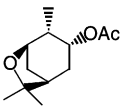
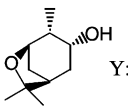
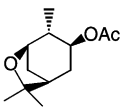
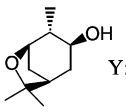
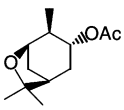
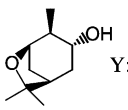
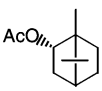
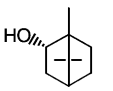
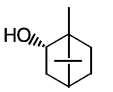
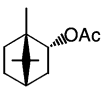
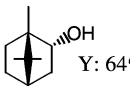
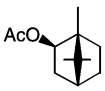
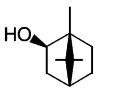
Substrate	Plant species	Products	References
	*Spirodela oligorrhiza*	 Y: 50%	[87]
	*S. oligorrhiza*	 Y: 33%	[87]
	*S. oligorrhiza*	 Y: 15%	[87]
	*S. oligorrhiza*	 Y: 43%	[87]
	*S. oligorrhiza*	 Y: 10%	[87]
 (3)	*N. tabacum*	 Y: 15% (2)	[12]

Table 14 (*Continued*)

Substrate	Plant species	Products	References
	*Lavandula angustifolia*	 Y: 15%	[52]
 **(6)**	*N. tabacum*	 Y: 16% **(5)**	[12]
 **(24)**	*N. tabacum*	 Y: 21% **(19)**	[14,16]
	*S. oligorrhiza*	 Y: 23%	[88]
	Epidendrum ochraceum	 Y: 85%	[49]
	*S. oligorrhiza*	 Y: 22%	[88]
	*S. oligorrhiza*	 Y: 14%	[88]
	*S. oligorrhiza*	 Y: 21%	[88]
	*S. oligorrhiza*	 Y: 75%	[88]
	L. angustifolia	 Y: 80%	[52]
 **(75)**	*N. tabacum*	 Y: 64% **(76)**	[89]
 **(77)**	*N. tabacum*	 Y: 23% **(78)**	[89]

Y: Yield in the reference.

Table 15
Stereoselective hydrolysis with plant cultured cells (part II)

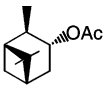
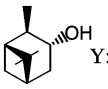
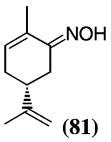
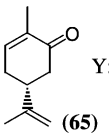
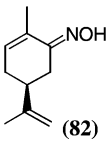
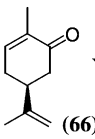
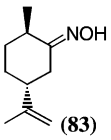
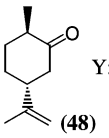
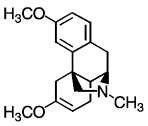
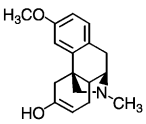
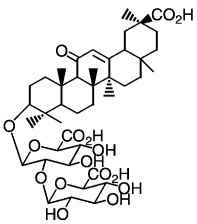
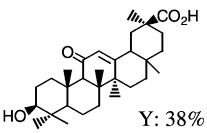
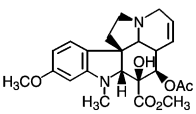
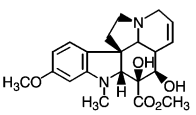
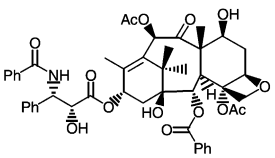
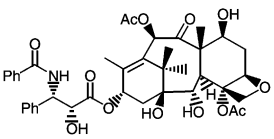
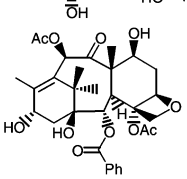
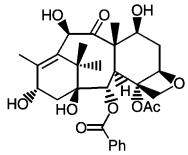
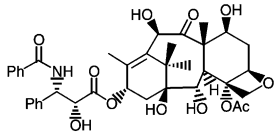
Substrate	Plant species	Products	References
 (79)	*N. tabacum*	 Y: 69% (80)	[89]
 (81)	*N. tabacum*	 Y: 85% (65)	[90]
 (82)	*N. tabacum*	 Y: 82% (66)	[90]
 (83)	*N. tabacum*	 Y: 62% (48)	[90]
 (84)	*Papaver somniferum*	 (85)	[91]
	*C. roseus*	 Y: 38%	[92]
	*C. roseus*		[93]
	*E. perriniana*		[94]
			[94]

Table 15 (*Continued*)

Substrate	Plant species	Products	References
			[94]
	M. Polymorpha		[95]

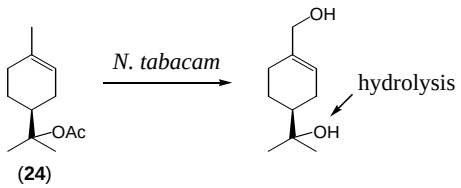
Y: Yield in the reference.

and 15). Enantioselective hydrolysis is of interest, because this type of transformation is considered to be useful for the optical resolution of racemic acetates. The enantiomer (**24**) of α-terpinyl acetate tends to experience enantioselective hydrolysis by the cultured cells of *N. tabacum* (Scheme 13) [14,16].

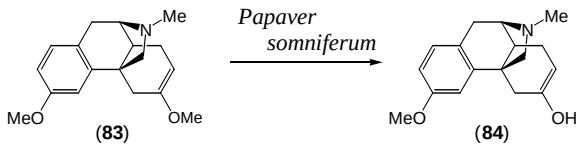
Therefore, the ability of the cultured cells to produce enantioselective hydrolysis is examined for the biotransformation of bornyl acetate (**75**), isobornyl acetate (**77**) and isopinocamphenyl acetate (**79**) by using the cultured cells of *N. tabacum*. The enantiomers with the *R*-configuration at the carbon atom bearing the acetoxy group are preferentially hydrolyzed [89]. Enantioselective hydrolysis is also observed during the biotransformation of (*RS*)-1-phenylethyl acetate and its derivatives with the cultured cells of *Spirodela oligorrhiza* in which the biotransformations give only (*R*)-alcohols [87].

7.2. Hydrolysis of other group

Other examples have been reported for the hydrolysis of the hydroxyimino group and an ether bond; carvoximes (**81** and **82**) and dihydrocaroxime (**83**) are



Scheme 13.



Scheme 14.

hydrolyzed to the corresponding ketones by the cultured cells of *N. tabacum* [90]. Thebaine (**84**) is also converted to the corresponding alcohol by the cultured cells of *Papaver somniferum* (Scheme 14) [91].

8. Biotranfsormation with immobilized plant cultured cells

Untill now, the techniques for immobilization of plant cells have progressed considerably [96–100]. Many studies have been focused on de novo synthesis of useful substances by the immobilized plant cells [99], however, only a few samples have been reported on the biotransformation of foreign substrates by use of the immobilized plant cells [27,51,56,63,65]. Immobilization of the plant cultured cells offers some advantages for the biotransformation of exogenous substrates [96–100]: (i) the cells become resistant to shear damage by immobilization, (ii) the immobilized cells can be used repeatedly over a prolonged period, (iii) high concentrations of biomass are possible, thus giving high conversions of substrate, (iv) the method facilitates recovery of the cell mass and products and (v) sequential chemical treatments are possible.

9. Conclusions

As can be seen from the examples given above, plant cultured cells possess considerable biochemical ability to transform xenobiotic substrates such as various organic compounds. The reaction types and stereochemistry in the biotransformation depends on the functional group in the substrates and the structural moieties in the vicinity of the functional group. Therefore, the biotransformations by plant cultured cells are considered to serve as important tools for the structural modification of molecules to give compounds possessing useful properties. Fundamental information, such as the reaction types, stereospecificity and regioselectivity in the biotransformation of exogenous compounds, is essential for the development of the biotechnology for using higher plant cells. Further investigations, especially the development methods to utilize the multi-reaction processes, will be necessary for the practical applications of biotransformations with plant cultured cells.

References

[1] T. Furuya, Yakugaku Zashi 108 (1988) 675.
[2] Y. Asada, H. Saito, T. Yoshikawa, K. Sakamoto, T. Furuya, Phytochemistry 34 (1993) 1049.
[3] C.-J. Wang, E.J. Staba, J. Pharm. Sci. 52 (1963) 1058.
[4] H. Becker, Biochem. Physiol. Pflanz. 161 (1970) 425.
[5] T. Suga, T. Hirata, Y. Yamamoto, Agric. Biol. Chem. 44 (1980) 325.
[6] H. Bohm, in: Proceedings of the 5th International Congress on Plant Tissue and Cell Culture, 1982, p. 325.
[7] T. Furuya, in: T.A. Thorpe (Ed.), Frontiers of Plant Tissue Culture, University of Calgary, Calgary, 1978, p. 191.
[8] B.V. Charlwood, P.K. Hegatry, K.A. Charlwood, in: P. Morris, A.H. Scragg, A. Stafford, M.W. Fowler (Eds.), Secondary Metabolism in Plant Cell Cultures, Cambridge University Press, London, 1986, p. 15.
[9] G. Lippin, J. Tampion, J. Stride, in: P. Morris, A.H. Scragg, A. Stafford, M.W. Fowler (Eds.), Secondary Metabolism in Plant Cell Cultures, Cambridge University Press, London, 1986, p. 113.
[10] T. Suga, T. Hirata, Phytochemistry 29 (1990) 2393.
[11] H. Hamada, Y. Miyamoto, N. Nakajima, T. Furuya, J. Mol. Catal. B: Enzyme 5 (1998) 187.
[12] T. Hirata, T. Aoki, Y. Hirano, T. Ito, T. Suga, Bull. Chem. Soc. Jpn. 54 (1981) 3527.
[13] T. Suga, T. Aoki, T. Hirata, Y.S. Lee, O. Nishimura, M. Utsumi, Chem. Lett. (1980) 229.
[14] Y.S. Lee, J. Sci. Hiroshima Univ., Ser. A 47 (1983) 21.
[15] T. Hirata, Y.S. Lee, T. Suga, Chem. Lett. (1982) 671.
[16] T. Suga, T. Hirata, Y.S. Lee, Chem. Lett. (1982) 1595.
[17] T. Suga, Y.S. Lee, T. Hirata, Bull. Chem. Soc. Jpn. 56 (1983) 784.
[18] Y.S. Lee, T. Hirata, T. Suga, J. Chem. Soc., Perkin Trans. I (1983) 2475.
[19] T. Suga, T. Hirata, H. Hamada, S. Murakami, Phytochemistry 27 (1988) 1041.
[20] R.M. Zacharius, E.B. Kalan, Plant Cell Rep. 3 (1984) 189.
[21] T. Furuya, K. Kawaguchi, M. Hirotani, Phytochemistry 27 (1988) 2129.
[22] K. Kawaguchi, M. Hirotani, T. Furuya, Phytochemistry 28 (1989) 1093.
[23] A. Joens, I.A. Veliky, Eur. J. Appl. Microbiol. Biotechnol. 13 (1989) 84.
[24] M. Hirotani, T. Furuya, Phytochemistry 19 (1980) 531.
[25] F. Sasse, U. Heckenberg, J. Berlin, Plant Physiol. 69 (1982) 400.
[26] F. Sasse, L. Witte, J. Berlin, Planta Med. 53 (1987) 354.
[27] D. Coutoris, D. Yvernel, B. Florin, V. Petiard, Phytochemistry 27 (1988) 3137.
[28] M. Rideau, P. Marard, C. Gansser, J.C. Chenieux, C. Vial, Pharmazie 43 (1988) 332.
[29] P. Dorisse, J. Gleye, P. Loissau, P. Puig, A.M. Edy, M. Henry, J. Nat. Prod. 51 (1988) 532.
[30] H. Hamada, Y. Fuchikami, Y. Ikematsu, T. Hitara, H.J. Williams, A.I. Scott, Phytochemistry 37 (1994) 1037.
[31] H. Hamada, Y. Fuchikami, R.L. Jansing, L.S. Kaminsky, Phytochemistry 33 (1993) 599.
[32] H. Hamada, H. Konishi, H.J. Williams, A.I. Scott, Phytochemistry 30 (1991) 2269.
[33] T. Suga, T. Hirata, Nippon Kagaku Kaishi (1983) 1385.
[34] T. Hirata, S. Izumi, T. Ekida, T. Suga, Bull. Chem. Soc. Jpn. 60 (1987) 289.
[35] D.V. Banthorpe, M.J. Osborne, Phytochemistry 23 (1984) 905.
[36] H. Hamada, Bull. Chem. Soc. Jpn. 60 (1988) 289.
[37] H. Hamada, H. Yasumune, Y. Fuchikami, T. Hirata, I. Sattler, H.J. Williams, A.I. Scott, Phytochemistry 44 (1997) 615.
[38] T. Hirata, Y. Ikeda, S. Izumi, K. Shimoda, H. Hamada, T. Kawamura, Phytochemistry 37 (1994) 401.
[39] H. Hamada, T. Tanaka, T. Furuya, H. Takahata, H. Nemoto, Tetrahedron Lett. 42 (2001) 909.
[40] T. Suga, H. Hamada, T. Hirata, Plant Cell Rep. 2 (1983) 66.
[41] T. Suga, S. Izumi, T. Hirata, Chem. Lett. (1986) 2053.
[42] S. Izumi, T. Suga, Bull. Chem. Soc. Jpn. 61 (1988) 1725.
[43] P. Pawlowicz, A. Siewinski, Phytochemistry 26 (1987) 1001.
[44] F. Carriere, G. Gil, P. Tapie, P. Chagvardieff, Phytochemistry 28 (1989) 1087.
[45] T. Suga, H. Hamada, T. Hirata, S. Izumi, Chem. Lett. (1987) 903.
[46] T. Suga, S. Izumi, T. Hirata, H. Hamada, Chem. Lett. (1987) 425.
[47] T. Suga, T. Hirata, H. Hamada, M. Futatsugi, Plant Cell Rep. 2 (1983) 186.
[48] T. Suga, H. Hamada, T. Hirata, Chem. Lett. (1987) 471.
[49] A. Mironowicz, K. Kukulczanka, K. Krasinshi, A. Siewinski, Phytochemistry 26 (1987) 1959.

[50] H. Hamada, K. Nakazawa, Biotechnol. Lett. 13 (1991) 805.
[51] Y. Naoshima, Y. Akakabe, F. Watanabe, Agric. Biol. Chem. 53 (1989) 545.
[52] G.J. Lappin, J.D. Stride, J. Tampion, Phytochemistry 26 (1987) 995.
[53] T. Hirata, H. Hamada, T. Aoki, T. Suga, Phytochemistry 21 (1982) 2212.
[54] D. Aviv, E. Krochmal, A. Dantes, E. Galun, Planta Med. 42 (1981) 236.
[55] H. Hamada, N. Nakamura, S. Ito, S. Kawabe, T. Funamoto, Phytochemistry 27 (1988) 3807.
[56] T. Furuya, T. Yoshikawa, M. Taira, Phytochemistry 23 (1984) 999.
[57] H. Hamada, M. Imura, T. Okano, J. Biotechnol. 32 (1994) 89.
[58] K. Nakamura, H. Miyoshi, T. Sugiyama, H. Hamada, Phytochemistry 40 (1995) 1419.
[59] A. Chadha, M. Manohar, T. Soundararajan, T.S. Lokeswari, Tetrahedron: Asymmetry 7 (1996) 1571.
[60] H. Hamada, S. Kawabe, Life Sci. 48 (1991) 613.
[61] H. Hamada, S. Naka, H. Kurban, Chem. Lett. (1993) 2111.
[62] A. Kergomard, M.F. Renard, H. Veschambre, D. Courtois, V. Petiard, Phytochemistry 27 (1988) 407.
[63] E. Galun, D. Aviv, A. Dantes, A. Freeman, Planta Med. 49 (1983) 9.
[64] J. Balsevich, Planta Med. (1985) 128.
[65] H. Flix, P. Brodelius, K. Mosbach, Anal. Biochem. 116 (1981) 462.
[66] T. Furuya, M. Ushiyama, Y. Ashida, T. Yoshikawa, Phytochemistry 28 (1989) 483.
[67] T. Furuya, M. Ushiyama, Y. Ashida, T. Yoshikawa, Phytochemistry 26 (1987) 2983.
[68] T. Furuya, M. Ushiyama, Y. Ashida, T. Yoshikawa, Y. Orihara, Phytochemistry 27 (1988) 803.
[69] M. Ushiyama, T. Asada, T. Yoshikawa, T. Furuya, Phytochemistry 28 (1989) 1859.
[70] B.G. Moyer, D.L. Gustine, Phytochemistry 26 (1987) 139.
[71] M. Tabata, Y. Unetani, M. Oya, S. Tanaka, Phytochemistry 27 (1988) 809.
[72] H. Mizutani, A. Hirano, H. Ohashi, Plant Sci. 48 (1987) 11.
[73] C. Langebartels, H. Harms, Z. Pflanzenphysiol. 113 (1984) 201.
[74] H. Mizukami, T. Terao, A. Amano, H. Ohashi, Plant Cell Physiol. 27 (1986) 645.
[75] H. Mizukami, Syokubutsu Soshiki Baiyo 3 (1986) 35.
[76] M. Tabata, Y. Umetani, K. Shima, S. Tanaka, Plant Cell Tissue Org. Cult. 3 (1984) 3.
[77] R. Braemer, Y. Tsoutsias, M. Hurabielle, M. Paris, Planta Med. 53 (1987) 225.
[78] B. Upmeier, J.E. Thomzik, W. Barz, Phytochemistry 27 (1988) 3489.
[79] E. Lewinson, E. Berman, Y. Mazur, J. Gressel, Phytochemistry 25 (1996) 2531.
[80] E. Lewinson, E. Berman, Y. Mazur, J. Gressel, Plant Sci. 61 (1989) 23.
[81] Y. Orihara, H. Miyatake, T. Furuya, Phytochemistry 30 (1991) 1843.
[82] Y. Orihara, T. Furuya, N. Hashimoto, Y. Deguchi, K. Tokoro, T. Kanisawa, Phytochemistry 31 (1992) 827.
[83] Y. Orihara, T. Furuya, Phytochemistry 34 (1993) 1045.
[84] T. Furuya, Y. Asada, Y. Matsuura, S. Mizobata, H. Hamada, Phytochemistry 46 (1997) 1355.
[85] T. Furuya, Y. Asada, S. Mizobata, Y. Matsuura, H. Hamada, Phytochemistry 49 (1998) 109.
[86] H. Hamada, R. Tomi, Y. Asada, T. Furuya, Tetrahedron Lett. 43 (2002) 4087.
[87] P. Pawlowicz, A. Siewinski, Phytochemistry 26 (1987) 1001.
[88] P. Pawlowicz, K. Piatkowski, A. Siewinski, Phytochemistry 27 (1988) 2089.
[89] T. Suga, T. Hirata, S. Izumi, Phytochemistry 25 (1986) 2791.
[90] T. Suga, T. Hirata, M. Futatsugi, Phytochemistry 23 (1984) 1327.
[91] W.H.J. Tan, W.G.W. Kurz, F. Constabel, K.B. Chatson, Phytochemistry 21 (1982) 253.
[92] H. Hamada, S. Nakata, Plant Tissue Cult. Lett. 9 (1992) 32.
[93] H. Hamada, A.R. Jacobson, H.J. Williams, A.I. Scott, Biotechnol. Lett. 12 (1990) 897.
[94] H. Hamada, K. Sanada, T. Furuya, S. Kawabe, M. Jaziri, Nat. Prod. Lett. 9 (1996) 47.
[95] K. Sanada, A. Kawaguchi, T. Furuya, H. Hamada, Plant Biotechnol. 17 (2000) 321.
[96] P. Brodelius, B. Deus, K. Mosbach, M.H. Zenk, FEBS Lett. 103 (1979) 93.
[97] P. Brodelius, K. Nilsson, FEBS Lett. 122 (1980) 312.
[98] K. Londsey, M.M. Yoeman, G.M. Black, F. Mavituna, FEBS Lett. 155 (1983) 143.
[99] K. Lindsey, in: P. Morris, A.H. Scragg, A. Stafford, M.W. Fowler (Eds.), Secondary Metabolism in Plant Cell Cultures, Cambridge University Press, London, 1986, p. 143.
[100] A. Rosevear, C.A. Lambe, in: P. Morris, A.H. Scragg, A. Stafford, M.W. Fowler (Eds.), Secondary Metabolism in Plant Cell Cultures, Cambridge University Press, London, 1986, p. 156.