

CHAPTER II

HISTORICAL

Chemical Aspects in *Usnea* spp

Members of the genus *Usnea* are found to contain a wide range of chemical constituents: depsides, depsidones, dibenzofurans, aliphatic acids, xanthenes, anthraquinones, sterols, triterpenes, polyols and vitamins.

A list of compounds found in various species of *Usnea* genus is shown in table 1.

Among lichen constituents; the largest numbers of these substances are usnic acid, depsides and depsidones.

Table 1 : Chemical investigations of *Usnea* spp.

Botanical Origin	Chemical substances	Category	Reference
<i>Usnea abissina</i> Mot.	norstictic acid	depsidone	Swins & Krog (1988)
<i>U. acanthera</i> Mot.	protocetraric acid	depsidone	Swins & Krog (1988)
<i>U. aciculifera</i> Vain.	stictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. acromelana</i>	norstictic acid	depsidone	Culberson(1969)
var. <i>decipiens</i> (Lamb.) Lamb.	usnic acid	dibenzofuran	"
<i>U. alata</i>	caperatic acid	depsidone	Keeton &
	norstictic acid	depsidone	Keogh (1973)
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. albomaculata</i> Mot.	conpsoromicacid	depsidone	Swins & Krog
	fumarprotocetraric acid	depsidone	(1988)
	norstictic acid	depsidone	"
	psoromic acid	depsidone	'
	salazinic acid	depsidone	"
<i>U. aliphatica</i>	α -(15-hydroxyhexadecyl)itaconic acid	aliphatic acid	Keogh &
	norstictic acid	depsidone	Zurita (1977)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. angulata</i> Ach.	diffraitaic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. angulata</i> Ach.	norstictic acid	depsidone	Mendondo(1972)
ssp. <i>alata</i> Mot.	(+)usnic acid	dibenzofuran	

Table 1 : (continued)

<i>U. antarctica</i> Du Rietz	fumarprotocetraric acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. antiqua</i> Swins & Krog	psoromic acid	depsidone	Swins & Krog (1988)
	usnic acid	dibenzofuran	Culberson(1969)
<i>U. arguta</i> Mot.	barbatic acid	depside	Swins & Krog (1988)
<i>U. aristata</i> Mot.	fumaprotocetraric acid	depsidone	"
	protocetraric acid	depsidone	Culberson(1969)
<i>U. arizonica</i> Mot.	salazinic acid	depside	Culberson(1969)
<i>U. articulata</i> (L.)Hoffm.	barbatic acid	depside	Culberson(1969)
	diffraitaic acid	depside	"
	fumaprotocetraric acid	depsidone	"
	galbinic acid	depsidone	"
	norstictic acid	depsidone	"
	potassium oxalate	miscellaneous	"
	protocetraric acid	depsidone	"
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"
	(+)-usnic acid	dibenzofuran	"
	<i>U. articulata</i>	stictic acid	depsidone
<i>var.asperula</i> Mull. Arg.	usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. articulata</i>	articulatic acid	miscellaneous	Culberson(1969)
<i>var.intestiniformis</i> (Ach.)Cromb.	barbatic acid	depside	"
<i>U. asahinai</i> Mot.	norstictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. aspera</i> (Eschw.)Vain.	norstictic acid	depsidone	Culberson(1969)
	psoromic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. aurantiaco-ater</i> (Jacq.)Bory	norstictic acid	depsidone	Culberson(1969)
<i>U. aureola</i> Mot.	salazinic acid	depsidone	Culberson(1969)
	(+)usnic acid	dibenzofuran	"
<i>U. baileyi</i> (Stirton)	diffRACTaic acid	depside	Swins & Krog
<i>var.baileyi</i> Zahlbr.	norstictic acid	depsidone	(1988)
	salazinic acid	depsidone	"
<i>var.pinnatifida</i> Swins & Krog.	pigment	miscellaneous	"
	protocetraric acid	depsidone	"
<i>var.planiuscula</i> Swins&Krog.	pigment	miscellaneous	"
	protocetraric acid	depsidone	"
<i>U. bakongoensis</i> Duvign.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. barbata</i> (L.)Wigg.	ascorbic acid	vitamin	Culberson(1969)
	barbatic acid	depside	"
	barbatolic acid	benzyl ester	"

Table 1 : (continued)

	D-arabitol	polyol	Culberson(1969)
	ergosterol	sterol	"
	fatty acid	organic acid	"
	lichenin	polysaccharide	"
	lobaric acid	miscellaneous	"
	norstictic acid	depsidone	"
	salazinic acid	depsidone	"
	(+)-usnic acid	dibenzofuran	"
<i>U. bicolorata</i> Mot.	alectorialic acid	miscellaneous	Swins & Krog
	barbatic acid	depside	(1988)
	protocetraric acid	depsidone	"
<i>U. bismolliuscula</i> Zahlbr.	salazinic acid	depsidone	Culberson(1969)
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. bismolliuscula</i>	baeomycesic acid	depside	Culberson(1969)
<i>ssp.pseudomolliuscula</i>	thamnolic acid	depside	"
Asah.	usnic acid	dibenzofuran	"
<i>U. bornmuelleri</i> Steiner.	fumaprotocetraric acid	depsidone	Swins & Krog
	conpsoromic acid	depsidone	(1988)
	norstictic acid	depsidone	"
	protocetraric acid	depsidone	"
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"

Table 1 : (continued)

<i>U. californica</i> Herre	usnic acid	dibenzofuran	Culberson(1969)
<i>U. campestris</i> Sant.	(+)usnic acid	dibenzofuran	Mendiondo(1972)
<i>U. canariensis</i> (Ach.)	atranorin	depside	Culberson(1969)
Du Reitz	canarion	quinone	"
	canariondimethylether	quinone	"
	diacetylcanarion	quinone	"
	khellin	quinone	"
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. capilliformis</i> Asah.	protocetraric acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. ceratina</i> Ach.	barbatic acid	depside	Culberson(1969)
	diffRACTAIC acid	depsidone	"
	D-arabitol	polyol	"
	norstictic acid	depsidone	"
	potassium oxalate	miscellaneous	"
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. chilensis</i> Mot.	usnic acid	dibenzofuran	Culberson(1969)
<i>U. chloreoides</i> (Wainio)	diffRACTAIC acid	depsidone	Swins & Krog
Mot.	salazinic acid	depsidone	(1988)

Table 1 : (continued)

<i>U. comosa</i> (Ach.)Rohl.	folic acid	vitamin	Culberson(1969)
	folinic acid	vitamin	"
	mannitol	polyol	"
	obtusatic acid	depside	"
	squamatic acid	depside	"
	thamnolic acid	depside	"
	usnic acid	dibenzofuran	"
	vitamin B ₁₂	vitamin	"
<i>U. comosa</i>	decarboxythamnolic acid	depside	Culberson(1969)
<i>ssp.colorans</i> Asah.	thamnolic acid	depside	"
	usnic acid	dibenzofuran	"
	salazinic acid	depside	Culberson(1969)
<i>U. comosa</i>	usnic acid	dibenzofuran	"
<i>ssp.melanopoda</i> Asah.	norstictic acid	depsidone	Culberson(1969)
<i>U. comosa</i>	usnic acid	dibenzofuran	"
<i>ssp.praetervisa</i> Asah.	conpsoromic acid	depsidone	Swins & Krog
<i>U. complanata</i> (Mull.Arg.) Mot.	fatty acid	organic acid	(1988)
<i>(U. barbata</i> <i>var. strigosa)</i> Mull. Arg.	galbinic acid	depsidone	"
	norstictic acid	depsidone	"
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. confusa</i> Asah.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. confusa</i> <i>ssp.rubroreagens</i> Asah.	protocetraric acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. contorta</i> Jatta	protocetraric acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. cornuta</i> Korb.	barbatic acid	depside	Culberson(1969)
	potassium oxalate	miscellaneous	"
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. creberrima</i> Vain.	diffRACTAIC acid	depsidone	Culberson(1969)
	norstictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. cristata</i> Mot.	diffRACTAIC acid	depsidone	Swins & Krog
	salazinic acid	depsidone	(1988)
<i>U. croceorubescens</i> Vain.	usnic acid	dibenzofuran	Culberson(1969)
<i>U. dasy-poga</i> (Ach.) Rohl.	ascorbic acid	vitamin	Culberson(1969)
	barbatolic acid	benzyl ester	"
	enzyme	enzyme	"
	salazinic acid	depsidone	"
	thamnolic acid	depside	"
	usnellin	miscellaneous	"
	(+)usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. dasypoga</i>	diffraitaic acid	depsidone	Culberson(1969)
<i>var. plicata f. annulata</i> (Mull. Arg.) Hue	usnic acid	dibenzofuran	"
<i>U. deminuta</i> Mot.	diffraitaic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. densirostra</i> Taylor	norstictic acid	depsidone	Mendiondo(1972)
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. diffracta</i> Vain.	barbatic acid	depside	Culberson(1969)
	d-usnic acid	dibenzofuran	"
	dehydrobarbatic acid	depside	"
	diffraitaic acid	depside	"
	lichenin	polysaccharide	"
	salazinic acid	depsidone	"
<i>U. diffracta</i> <i>ssp. subdiffracta</i> Asah.	usnic acid	dibenzofuran	Culberson(1969)
			"
<i>U. diplotypus</i> Vain.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. dorogawensis</i> Asah.	stictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. dusenii</i> Du Rietz	usnic acid	dibenzofuran	Culberson(1969)
<i>U. eizanensis</i> Asah.	thamnolic acid	depside	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. elata</i> Mot.	diffraitaic acid	depside	"

Table 1 : (continued)

<i>U. elongata</i> Mot.	hirtinic acid	miscellaneous	Culberson(1969)
	protocetraric acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. eulychiniae</i>	thamnolic acid	depside	Huneck&
	(+)usnic acid	dibenzofuran	Follmann(1968)
<i>U. exasperata</i> (Mull.Arg.) Mot.	alectorialic acid	miscellaneous	Swins & Krog (1988)
<i>(U. dasypogoides</i> <i>var. exasperata</i> Mull.Arg.)	conpsoromic acid	depsidone	"
	diffRACTAIC acid	depside	"
	echinocarpic acid	miscellaneous	"
	fumarprotocetraric acid	depsidone	"
	protocetraric acid	depsidone	"
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"
<i>U. fasciata</i> Torrey	fumarprotocetraric acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. firmula</i> (Stirton)Mot.	norstitic acid	depsidone	Swins & Krog (1988)
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
<i>U. flexilis</i> Stirt.	alanine	amino acid	Culberson(1969)
	barbatic acid	depside	"
	barbatinic acid	miscellaneous	"

Table 1 : (continued)

<i>U. florida</i> (L.)Wigg.	glycine	amino acid	Culberson(1969)
	norstictic acid	depsidone	"
	salazinic acid	depsidone	"
	threonine	amino acid	"
	tyrosine	amino acid	"
	(+)usnic acid	dibenzofuran	"
	atranorin	depside	Culberson(1969)
<i>U. fulvoreaens</i> (Ras.)Ras.	barbatic acid	depside	"
	potassium oxalate	miscellaneous	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
	thamnolic acid	depside	"
<i>U. galbinifera</i> Asah.	usnic acid	dibenzofuran	"
	usnic acid	dibenzofuran	Culberson(1969)
	galbinic acid	depsidone	Culberson(1969)
<i>U. gigas</i> Mot.	norstictic acid	depsidone	"
	usnic acid	dibenzofuran	"
	barbatic acid	depside	Swins & Krog (1988)
	constitic acid	depsidone	"
	diffRACTAIC acid	depsidone	"
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"

Table 1 : (continued)

<i>U. glabrata</i>	barbatic acid	depside	Culberson(1969)
<i>ssp.pseudoglabrata</i> Asah.	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. glabrescens</i>	norstictic acid	depsidone	Culberson(1969)
(Nyl.ex.Vain.)Vain.	usnic acid	dibenzofuran	"
<i>U. glabrescens</i>	salazinic acid	depsidone	Culberson(1969)
<i>ssp.asiatica</i> Asah.	usnic acid	dibenzofuran	"
<i>U. glabrescens</i>	thamnolic acid	depside	Culberson(1969)
<i>ssp.pseudocolorans</i> Asah.	usnic acid	dibenzofuran	"
<i>U. goniodes</i> (Stirton)	caperatic acid	aliphatic acid	Swins & Krog
Swins & Krog			(1988)
<i>U. hakonensis</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. haumanii</i> Mot.	fatty acid	organic acid	Swins & Krog
	fumarprotocetraric acid	depsidone	(1988)
	protocetraric acid	depsidone	"
<i>U. hirta</i> (L.)Wigg.	atranorin	depside	Culberson(1969)
	hirtinic acid	miscellaneous	"
	potassium oxalate	miscellaneous	"
	salazinic acid	depsidone	"
	thamnolic acid	depside	"
	(+)usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. hondoensis</i> Asah.	barbatic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. hossei</i>	diffRACTAIC acid	depsidone	Culberson(1969)
<i>f.subtrichodea</i> Asah.	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. implicita</i> (Stirt) Zahlbr.	norstictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. incrassata</i> Mot.	protocetraric acid	depsidone	Swins & Krog
	psoromic acid	depsidone	(1988)
	salazinic acid	depsidone	"
<i>U. indigena</i> Mot.	stictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. intexta</i> Stirt.	norstictic acid	depsidone	Culberson(1969)
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. intumescens</i> Asah.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. japonica</i> Vain.	barbatolic acid	benzyl ester	Culberson(1969)
	norstictic acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. kinkiensis</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. koyana</i> Asah.	decarboxythamnolic acid	depside	Culberson(1969)
	thamnolic acid	depside	"
	usnic acid	dibenzofuran	"
<i>U. kurokawae</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. kushiroensis</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. kushiroensis</i> <i>ssp. subasiriensis</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
<i>U. kyotoensis</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. lacerata</i> Mot.	protocetraric acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. laricina</i> Vain.ex Ras.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. leprosa</i> Mot.	galbinic acid	depsidone	Swins & Krog
	norstictic acid	depsidone	(1988)
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"
<i>U. lethariiformis</i>	diffRACTic acid	depside	Swins & Krog
	usnic acid	dibenzofuran	(1988)
<i>U. liechtensteinii</i> Steiner	protocetraric acid	depsidone	Swins & Krog (1988)
<i>U. longissima</i> Ach.	atranorin	depside	Culberson(1969)
	ascorbic acid	vitamin	"
	barbatic acid	depside	"
	D-arabitol	polyol	"
	dehydrobarbatic acid	depside	"
	diffRACTic acid	depsidone	"
	evernic acid	depside	"
	fumarprotocetraric acid	depsidone	"
	isolichenin	polysaccharide	"
	lichenin	polysaccharide	"
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
(+)usnic acid	dibenzofuran	"	

Table 1 : (continued)

<i>U. longissima</i>	diffrataic acid	depsidone	Culberson(1969)
<i>ssp. ambigua</i> Asah.	(+)-usnic acid	dibenzofuran	"
<i>U. longissima</i>	evernic acid	depside	Culberson(1969)
<i>ssp. jesoensis</i> Asah.	(+)usnic acid	dibenzofuran	"
<i>U. longissima</i>	atranorin	depside	Culberson(1969)
<i>ssp. persensibilis</i> Asah.	fumarprotocetraric acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. longissima</i>	atranorin	depside	Culberson(1969)
<i>ssp. persensibilis</i>	fumarprotocetraric acid	depsidone	"
<i>f. tingens</i> Asah.	usnic acid	dibenzofuran	"
<i>U. longissima</i>	salazinic acid	depsidone	Culberson(1969)
<i>ssp. sensibilis</i> Asah.	usnic acid	dibenzofuran	"
<i>U. longissima</i>	barbatic acid	depside	Culberson(1969)
<i>ssp. vulgata</i> Asah	usnic acid	dibenzofuran	"
<i>U. longissima</i> Ach.	d-usnic acid	dibenzofuran	Culberson(1969)
<i>var. jesoensis</i> Asah.	salazinic acid	depsidone	"
<i>U. ludicra</i> Rizz.	barbatic acid	depside	Culberson(1969)
	norstictic acid	depsidone	"
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. lunaria</i> Mot.	(+)usnic acid	dibenzofuran	Culberson(1969)
<i>U. maculata</i> Stirton	protocetraric acid	depsidone	Culberson(1969)

Table 1 : (continued)

<i>U. merrillii</i> Mot.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. microcarpa</i> Pers.	barbatic acid	depside	Culberson(1969)
	potassium oxalate	miscellaneous	"
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. misaminensis</i> (Vain.) Mot.	hydroxyanthraquinone	anthraquinone	Culberson(1969)
	stictic acid	depsidone	"
<i>U. monstrosa</i> Vain.	usnic acid	dibenzofuran	Culberson(1969)
<i>U. montis-fuji</i> Mot.	atranorin	depside	Culberson(1969)
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. montis-fuji</i> f. <i>cinerea</i> Asah.	atranorin	depside	Culberson(1969)
	salazinic acid	depsidone	"
<i>U. mutabilis</i> Stirt.	usnic acid	dibenzofuran	"
	usnic acid	dibenzofuran	Culberson(1969)
<i>U. nipparensis</i> Asah.	stictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. nodulosa</i> Swins&Krog	constictic acid	depsidone	Swins & Krog
	fatty acid	organic acid	(1988)
	norstictic acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"

Table 1 : (continued)

<i>U. orientalis</i> Mot.	barbatic acid	depside	Culberson(1969)
	caperatic acid	aliphatic acid	"
	ergosterol	sterol	"
	psoromic acid	depsidone	"
	stictic acid	depsidone	"
	(+)-usnic acid	dibenzofuran	"
<i>U. orientalis</i> <i>f. esorediosa</i> Asah.	salazinic acid	depsidone	Culberson(1969)
<i>U. pectinata</i> Tayl.	usnic acid	dibenzofuran	"
	barbatic acid	depside	Culberson(1969)
	D-arabitol	polyol	"
	hydroxyanthraquinone	anthraquinone	"
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. perhispidella</i>	ventosic acid	miscellaneous	"
	galbinic acid	depsidone	Swins & Krog (1988)
	norstictic acid	depsidone	"
	psoromic acid	depsidone	"
	stictic acid	depsidone	"
<i>U. perplexans</i> Stirt.	barbatic acid	depside	Culberson(1969)
	constictic acid	depsidone	"
	fatty acid	organic acid	"
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. picta</i> Steiner	constictic acid	depsidone	Swins & Krog
	norstictic acid	depsidone	(1988)
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
<i>U. plicata</i> (L.) Wigg.	pliatric acid	miscellaneous	Culberson(1969)
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. poeppigii</i>	divaricatic acid	depside	Swins & Krog
	usnic acid	dibenzofuran	(1988)
<i>U. pseudintumescens</i>	psoromic acid	depepsidone	Culberson(1969)
Asah.	usnic acid	dibenzofuran	"
<i>U. pseudomontis-fuji</i>	atranorin	depside	Culberson(1969)
	fumarprotocetraric acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. pseudorubescens</i> Asah.	stictic acid	depsidone	Culberson(1969)
<i>U. pulvinata</i> Fr.	barbatic acid	depside	Swins & Krog
	fumarprotocetraric acid	depsidone	(1988)
	norstictic acid	depsidone	"
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"

Table 1 : (continued)

<i>U. pulvinulata</i> Dodge	diffractaic acid	depside	Swins & Krog
	norstictic acid	depsidone	(1988)
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
<i>U. pusilla</i>	usnic acid	dibenzofuran	Swins & Krog (1988)
<i>U. pygmaea</i> ssp. <i>kitamiensis</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. roseola</i> Vain.	barbatic acid	depside	Culberson(1969)
	diffractaic acid	depside	"
	usnic acid	dibenzofuran	"
<i>U. roseola</i> ssp. <i>pseudoroseola</i> Asah.	barbatic acid	depside	Culberson(1969)
	diffractaic acid	depside	"
	usnic acid	dibenzofuran	"
<i>U. rubescens</i> Stirt.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. rubescens</i> ssp. <i>aberrans</i> Asah.	stictic acid	depsidone	Culberson(1969)
<i>U. rubicunda</i> Stirt.	barbatic acid	depside	Culberson(1969)
	constictic acid	depsidone	"
	ergosterol	sterol	"
	galbinic acid	depsidone	"

Table 1 : (continued)

	norstictic acid	depsidone	Culberson(1969)
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. rubicunda</i>	norstictic acid	depsidone	Culberson(1969)
<i>ssp.aberrans</i> Asah.	salazinic acid	depsidone	"
<i>U. rubicunda</i>	stictic acid	depsidone	Swins & Krog
<i>var.primarin</i>	usnic acid	dibenzofuran	(1988)
<i>U. rubiginea</i> (Michx)	norstictic acid	depsidone	Culberson(1969)
Mass.	(+)usnic acid	dibenzofuran	"
<i>U. rugulosa</i> Vain.	usnic acid	dibenzofuran	Culberson(1969)
<i>U. ruwenzoriana</i> Mot	alectorialic acid	depsidone	Swins & Krog
	barbatic acid	depside	(1988)
	protocetraric acid	depsidone	"
	squamatic acid	depside	"
<i>U. sanguinea</i> Swins&	norstictic acid	depsidone	Swins & Krog
Krog	salazinic acid	depsidone	(1988)
<i>U. scabrata</i> Nyl.	barbatic acid	depside	Culberson(1969)
	potassium oxalate	miscellaneous	"
	salazinic acid	depsidone	"
	(+)usnic acid	dibenzofuran	"
<i>U. shikokiana</i> Asah.	stictic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. similis</i> (Mot)Ras.	usnic acid	dibenzofuran	Culberson(1969)
<i>U. sorediifera</i> (Arn.)Lyng.	(+)usnic acid	dibenzofuran	Culberson(1969)
<i>U. solediosula</i> Mot.	protocetraric acid	depsidone	Swins & Krog (1988)
<i>U. spinigera</i> Asah.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. stirtoniana</i> Zahlbr.	ascorbic acid	vitamin	Culberson(1969)
	calcium	element	"
	iron	element	"
	isolichenin	polysaccharide	"
	lichenin	polysaccharide	"
	riboflavin	vitamin	"
	<i>U. strigosa</i> (Ach) A. Eat.	norstictic acid	depsidone
psoromic acid		depsidone	"
usnic acid		dibenzofuran	"
<i>U. subcristata</i> Dodge	diffraactaic acid	depside	Swins & Krog (1988)
	salazinic acid	depsidone	(1988)
<i>U. subcilliata</i> (Mot.) Swins&Krog	fatty acid	organic acid	Swins & Krog (1988)
	norstictic acid	depsidone	(1988)
	salazinic acid	depsidone	"

Table 1 : (continued)

<i>U. subflorida</i> (Zahlbr)Mot.	barbatic acid	depside	Swins & Krog
(<i>U. steineri</i> .	norstictic acid	depsidone	(1988)
var. <i>subflorida</i> Zahlbr)	pigment	miscellaneous	"
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
<i>U. subfusca</i> Stirt.	norstictic acid	depsidone	Culberson(1969)
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. submollis</i> Steiner	alectorialic acid	depsidone	Swins & Krog
	barbatic acid	depside	(1988)
	fatty acid	organic acid	"
	galbinic acid	depsidone	"
	norstictic acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
<i>U. sulphurea</i> (Kon.)	norstictic acid	depsidone	Culberson(1969)
Th. Fr.	usnic acid	dibenzofuran	"
<i>U. thomsonii</i> Stirt.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. trachycarpa</i>	norstictic acid	depsidone	Swins & Krog
	usnic acid	dibenzofuran	(1988)
<i>U. trichodea</i> Ach.	evernic acid	depside	Culberson(1969)
	(+)usnic acid	dibenzofuran	"

Table 1 : (continued)

<i>U. trichodeoides</i>	barbatic acid	depside	Culberson(1969)
Vain. ex. Mot.	norstictic acid	depsidone	"
	protocetraric acid	depsidone	"
	salazinic acid	depsidone	"
	usnic acid	dibenzofuran	"
<i>U. undulata</i> Stirton	conpsoromic acid	depsidone	Swins & Krog (1988)
	constictic acid	depsidone	"
	galbinic acid	depsidone	"
	norstictic acid	depsidone	"
	protocetraric acid	depsidone	"
	psoromic acid	depsidone	"
	salazinic acid	depsidone	"
	stictic acid	depsidone	"
<i>U. venosa</i> Mot.	barbatic acid	depside	Culberson(1969)
	carotene	carotene	"
	ergosterol	sterol	"
	glycine	amino acid	"
	leucine	amino acid	"
	salazinic acid	depsidone	"
	threonine	amino acid	"
	(+)usnic acid	dibenzofuran	"
	valine	amino acid	"

Table 1 : (continued)

<i>U. wasmuthii</i> Ras.	salazinic acid	depsidone	Culberson(1969)
	usnic acid	dibenzofuran	"
<i>U. welwitschiana</i>	protocetraric acid	depsidone	Swins & Krog (1988)
<i>U. yakushimensis</i> Asah.	thamnolic acid	depside	Culberson(1969)
	usnic acid	dibenzofuran	"



ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

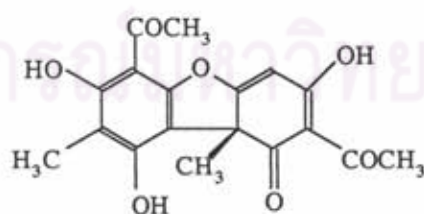
1. Usnic acid

Usnic acid is a well-known and widely occurring lichen substance and it was first isolated more than 120 years back from *Usnea barbata*. However its chemistry was understood only during the thirties of the present century. The structure now accepted is due to Robertson, 1937 as well as Schopt, 1941 and a number of detailed reviews are available on the chemistry of the substance.

1.1 Chemistry

Usnic acid. 2,6-Diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH) dibenzofurandione: usnic acid; usnein; usniacin $C_{18}H_{16}O_7$ mol. wt. 344.31 C 62.79%, H 4.68%, O 32.53%. Yellow orthorhombic prisms from acetone, m.p. 204° . $[\alpha]_D^{16} +509.4$ ($c=0.697$ in chloroform). Monobasic acid. Soly at $25^{\circ}C$ (g/100 ml), in water <0.01; acetone 0.77; ethyl acetate 0.88; ethanol 0.02; methyl Cellosolve 0.22; ethyl Cellosolve 0.32; furfural 7.32; furfuryl alcohol 1.21.

Usnic acid is somewhat unusual in that it has been isolated in both the D- and L- forms as well as a racemic mixture.



(+) USNIC ACID

1.2 Biological Activities

1.2.1 Antibacterial activities

The biological activities of the usnic acid enantiomorphs were the same (Stoll *et al*, 1947). These activities were active against gram-positive bacteria such as *Bacillus subtilis*, *B. mycooides*, *Sarcina lutea*, *Streptococcus faecalis*, *Staphylococcus aureus*, *Micrococcus lysodeiktitous*, *Corynebacterium diphtheriae*, *Haemophilus pertussis* and the acid-fast organism *Mycobacterium tuberculosis* at about 1 part per million. Most gram-negative bacteria, filamentous fungi and yeasts were not inhibited. There was very little work on its mechanism of action. One report stated that 30 µg/ml usnic acid inhibited the induction of β-galactosidase in *Staphylococcus aureus* (Shaw, 1967).

2.2 Effect on Respiration

The study of the effects on respiration in washed rat kidney particles was usnic acid at 10^{-6} M caused slightly inhibit oxygen uptake with succinate, fumarate and citrate. Respiration was increased or there was no effect with glutamate, α-keto glutarate, malate, pyruvate plus fumarate or *cis*-aconitrate as the substrate. At 10^{-4} M, the oxidation of all these substrates was inhibited from 55 to 89% (Prukudom, 1993).

Usnic acid at 10^{-6} M caused a slight in inorganic phosphate uptake by liver homogenates with pyruvate as the substrate. Inhibition occurred at higher antibiotic concentrations and was nearly complete at 1.6×10^{-5} M. These was little effect on oxygen consumption at these concentrations.

The mechanism of action of usnic acid would appear to be at some site in the terminal electron transport system. It inhibits respiration and uncouples oxidation phosphorylation so inhibition may be associated with the energy transforming system in the terminal respiratory pathway (Shaw, 1967).

1.2.3. Tumor Inhibition

In the course of searching for tumor inhibitors indicated that both L- and D-usnic acid were active as tumor inhibitors (Kupchan and Kopperman, 1975).

Usnic acid, a lichen antibiotic, showed low-level activity in the Lewis lung carcinoma test system. In an effort to produce new agents of potential use in the treatment of lung cancer, derivatives of the natural product were synthesized and evaluated with a cytotoxicity assay. Structure-activity analysis of the cytotoxicity data indicated the importance of the lipophilicity and the β -triketone moiety of usnic acid on cytotoxicity (Takai, Uehara and Beisler, 1979).

1.2.4 Antituberculous activities

Usnic acid has been extensively studied for antituberculous activities in Finland, Japan, Spain and U.S.A. An interesting finding was that both the optically active forms of usnic acid and the racemic one are microbiologically active. Virtanen, (1955) prepared a number of derivatives of usnic acid by reacting with aminocompounds, particularly those which were clinically accepted tuberculostatic agents, and studied their antituberculous activities. One of the derivatives, designated as USNO has attracted much

attention since it was claimed to be the most potent water-soluble derivative of usnic acid so far tested. It was prepared by reacting usnic acid with the surface-active agent, benzothonium chloride (Hyamin, 1622). It might therefore be concluded that the traditional use of tincture prepared from lichens in the treatment of pulmonary infections was not justification.

1.3 Biogenesis of Usnic acid

The biogenetical hypothesis of usnic acid which would be formed in lichen by the condensation of two molecules of methylphloroacetophenone. The results of the feeding experiments performed that synthesis of DL-usnic acid by the phenol oxidative coupling of methylphloroacetophenone (Taguchi and Sankawa, 1969).

The labelling pattern of usnic acid clearly indicated that two unit of C₈-polyketide were involved in the biosynthesis. Two methyl groups in the usnic acid molecule, aromatic and angular ones, were confirmed to be derived from C₁-unit. The results of the degradation of the feeding experiment clearly indicated that the methyl group of methylphloroacetone was not introduced into phloroacetophenone but into C₈-polyketide prior to its cyclization. However the oxidative coupling of methylphloroacetone should be stereospecific, since usnic acid occurred mainly in an optically active form. Moreover it seemed probable to assume, not only the position and steric factor of oxidative coupling but also the formation of ether linkage was controlled by enzymes, because the occurrence of isousnic acid was found in many lichens along with usnic acid.

The final stage of the biosynthesis of usnic acid was the dehydration of hydrated usnic acid. This step was also confirmed by the conversion of ³H-labelled hydrated usnic acid. From these experiments the pathway of the biosynthesis of usnic acid had been

established as summarized in Figure 2.

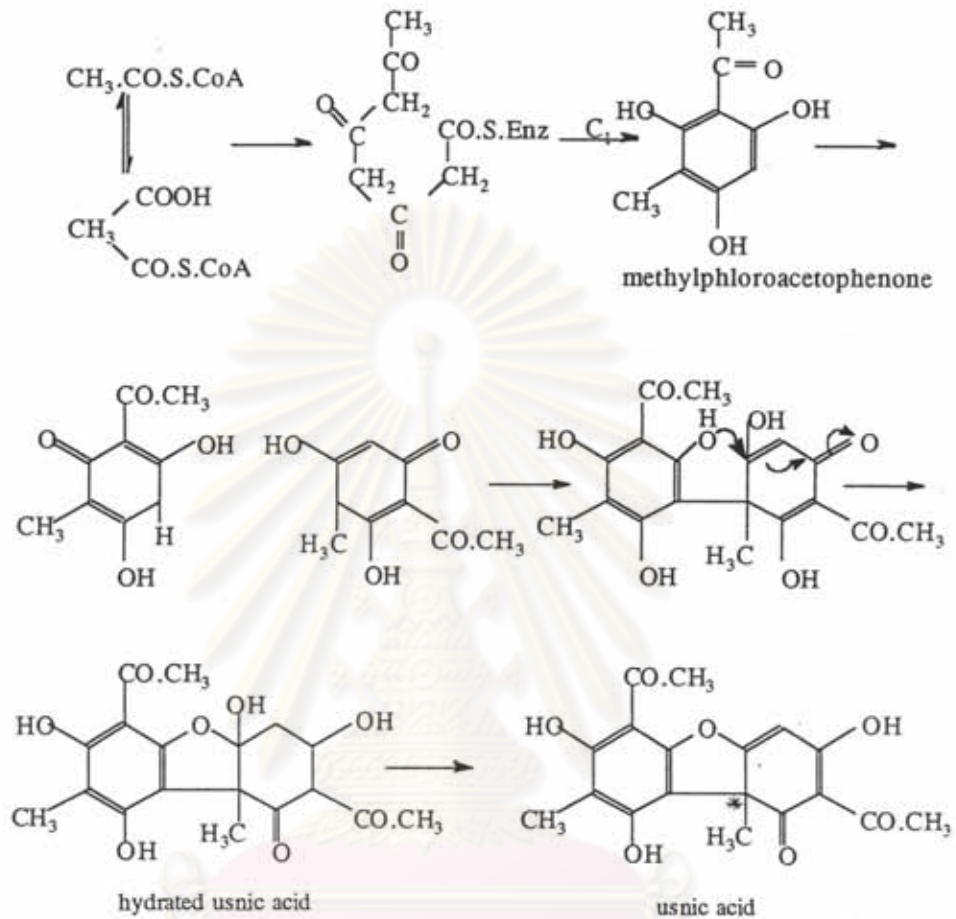


Figure 2 Biogenesis of usnic acid

It might be noted that the structure of usnic acid could be written in tautomeric keto-enol forms and with the possibility of intramolecular hydrogen bonds. Infrared and proton magnetic resonance spectroscopic studies (Forsen, 1962) have revealed the existence of three intramolecular hydrogen bonds in usnic acid. This would explain its pronounced lipophilic properties like solubility in benzene and chloroform in spite of its high oxygen content.

A remarkable property of optically active usnic acid was its ease of racemisation (involving the quarternary carbon marked *) under neutral conditions (boiling with toluene or xylene). This has been explained by involving a homolytic fission of the bond (a) in usnic acid to a structure centre, could recyclise to the racemate.

1.4 Optical, Crystallographic and X-Ray Diffraction Data

1.4.1 Optical and Crystallographic Properties

Crystals of usnic acid were rectangular tablets having beveled ends and sides. The refractive indices were determined by immersion methods. The crystals dissolved slowly in some of the immersion liquid used, but a good value could be obtained by examining the sample immediately after adding the immersion liquid or by saturating the immersion liquid with the usnic acid and redetermining the index of the resulting solution. The indices of the liquids used were checked on a refractometer. Ordinary views of the crystals showed a centered obtuse bisectrix interfere Figure 3, Table 2 summarized the optical data. The combination of properties required that this compound belong to the orthorhombic crystal system (Jones and Palmer, 1950).

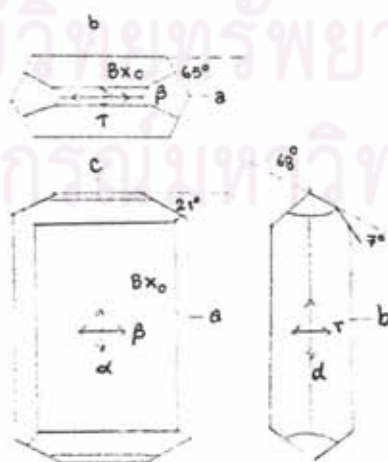


Figure 3 Optic orientation of usnic acid

Table 2 : Optical Properties of Usnic Acid

Author	F.T.Jones	A.N.Winchell
$11^{25}D \alpha$	1.611+0.001	1.4627
β	1.710+0.002	1.6531
γ	1.772+1.002	1.7798
2 v Obs.	72.1	-
Calcd.	73	60
Dispersion	(v>r)strong	(v>r)
Optical character	(-)	(+)
Pleochroism	None	Green-yellow
Crystal system	Orthorhombic	Orthorhombic

1.4.2 X-Ray Diffraction Analysis

Usnic acid crystals suitable for X-ray diffraction analysis were obtained by recrystallization from chloroform. The Weissenberg photographs confirmed the orthorhombic symmetry of the crystal. The results obtained were given in Table 3. The density of an usnic acid crystal was measured by flotation in a mixture of ethylenebromide and toluene and found to be 1.46 g/cc. There were, therefore, eight molecules with the empirical formula $C_{18}H_{16}O_7$ in the unit cell.

Since the space group deduced for usnic acid has only four general positions there must be either two crystallographically different sets of four molecules with

of Signer using acetone as a solvent. The molecular weight so determined agrees with the formula $C_{18}H_{16}O_7$ and there must be, therefore, two crystallographically different sets of four molecules each in the unit cell of usnic acid (Jones and Palmer, 1950).

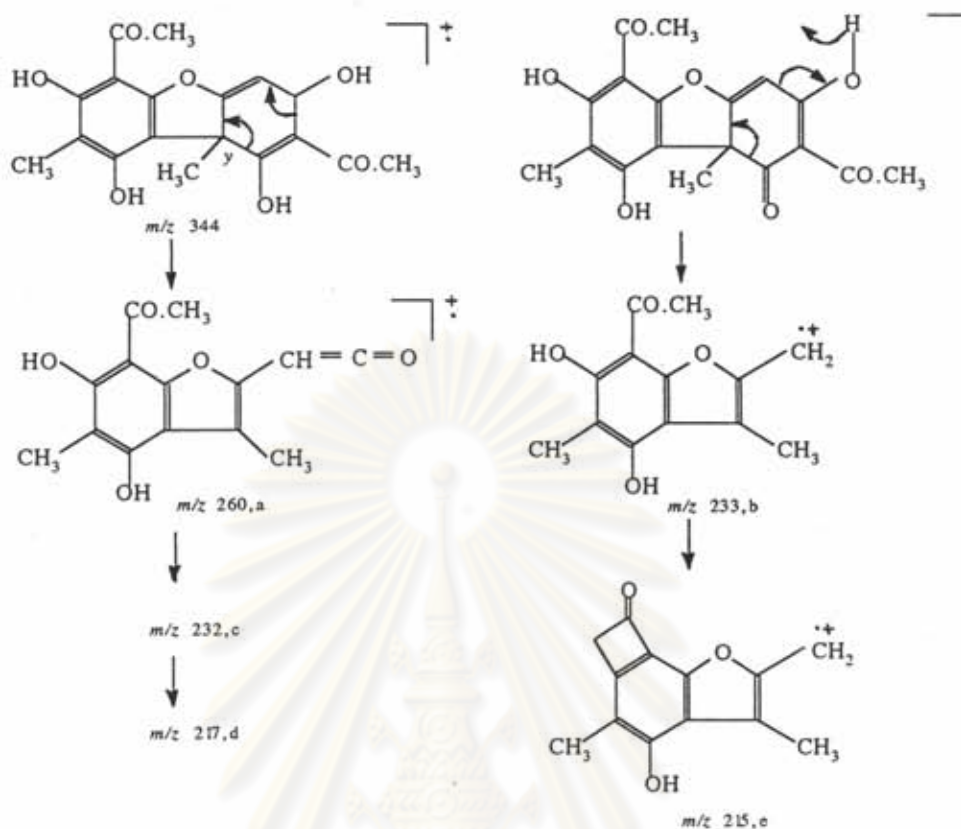
Table 3 : X-Ray Diffraction Results for Uronic Acid

a/β	b/γ	c/α
19.10 A	20.39 A	8.09 A
Density 1.46 g/cc		
Eight molecules ($C_{18}H_{16}O_7$) per unit cell		
Axial ratio $a:b:c = 0.937:1:0.397$		

1.5 Structure Elucidation of Uronic Acid

1.5.1 Mass Spectrum

The fragmentation of usnic acid under electron impact conditions was somewhat similar to its chemical degradation, since in both processes the bond 'y' in usnic acid was easily broken. The mass spectrum of usnic acid also showed two prominent fragment ions, *a* at m/z 260 ($C_{14}H_{12}O_5^+$) and the base peak *b* at m/z 233 ($C_{13}H_{13}O_4^+$), which arise from the keto- and enol- forms as shown in Scheme 1. Ion *a* fragments further through successive loss of CO giving *c* (m/z 232), and methyl giving ion *d* at m/z 217 ($C_{12}H_9O_4^+$). As expected, *b* loses water to give ion *e* (m/z 215) (Letcher, 1968).



Scheme 1 The fragmentation of usnic acid

1.5.2 Infrared Spectrum

The IR spectrum of usnic acid showed a number of peaks in the carbonyl region (Forsen *et al*, 1962).

(1) The conjugated chelated carbonyl of the enolised β -tricarbonyl grouping gave a broad band near 1540 cm^{-1} .

(2) The enol ether double bond absorbed near 1610 cm^{-1} and the absorption of the aromatic ring could also be expected in this region.

3) The aromatic C-acetyl group absorbed near 1620 cm^{-1} . The corresponding band coalesced with the enol ether band and a very intense absorption was observed.

(4) The dienone carbonyl absorbed near 1670 cm^{-1} .

(5) The O-acetyl groups, as expected, absorbed near 1780 cm^{-1} .

The hydroxyl stretching absorptions of enolised β -tricarbonyl compounds were broad, of low extinction and displaced towards unusually low frequencies. It revealed that usnic acid contained three quite distinct hydrogen bonds of different character. Spectra recorded for different concentrations showed no significant changes and it was therefore evident that these hydrogen bonds were intramolecular.

1.5.3 Nuclear Magnetic Resonance Spectra

1.5.3.1 The PMR Spectrum

Table 4 : $^1\text{H-NMR}$ of Usnic Acid (δ -value) (Takahashi and Tanaka, 1975)

	ang- CH_3	- CH_3	COCH_3	=CH-	chelated aromatic OH	chelated enol OH
Usnic acid	1.8(s)	2.2(s)	2.7(s) 6H	6.0(s)	13.3(C ₇) 11.0(C ₉)	18.8(C ₃)

*abbreviation :s:singlet

The PMR spectra were very distinct. The signals from the hydroxyl protons afford straight-forward information about the hydrogen bonding (Forsen *et al*, 1962).

(1) The hydroxyl proton of the triketone chelate gave a signal very low field at $\delta = 9.20$ ppm. The signal was shifted somewhat towards higher field on acetylation of the phenolic hydroxyl groups, especially that in the 5-position.

(2) The phenolic proton of the aromatic conjugated chelate gave a signal at surprisingly low field ($\delta = 3.28$ ppm). The position of the signal implied that the hydrogen bonds in the aromatic chelates were rather strong. It should be remembered, however, that diamagnetic anisotropic effects of the aromatic system contribute to the low-field position.

(3) The signal at 1.03 ppm was obviously due to the phenolic hydroxyl group in the 5-position. Its position at a fairly low field indicated that it was engaged in a hydrogen bond. This was in agreement with the infrared hydroxyl absorption pattern.

(4) The signal at 4.05 ppm, which recurred in all spectra, was obviously due to the proton in the 1-position.

The signals from the methyl groups were generally well separated. It indicated that these signals in usnic acid were coinciding signals from the C-acetyl groups, the aromatic methyl and the angular methyl group.

1.5.3.2 The Carbon-13 NMR Spectrum

The assignments for the phenolic protons in usnic acid were confirmed by selective INEPT experiments. These studies established that the C(9)-OH was two or three bonds from the C(8), C(9a) and C(9) carbons, and C(7) carbons. It should be noted that some of the ^{13}C -assignment for usnic acid made by the previous workers have been corrected here. Thus, using two dimensional ^{13}C - ^1H correlation (HETCOR) and

selective INEPT experiments, the carbon resonances of usnic acid were established (McPhail, 1992).

Table 5 : ^{13}C -NMR Chemical Shift Assignments in CDCl_3 relative to TMS

(+)-Usnic Acid	
Carbon	ppm
1	197.98
2	105.19
3	191.64
4	98.26
4a	179.20
5a	155.15
6	101.46
7	163.82
8	109.24
9	157.43
9a	103.90
9b	59.03
10	32.08
11	201.69
12	27.82
13	200.24
14	31.21
15	7.49

In the solid state, hydroxy groups at C(7) and C(9) were involved in intramolecular O-H...O hydrogen bonds to the adjacent carbonyl oxygen atoms at C(15) and C(1). The absolute configuration at the C-9b position of (+)-usnic acid was determined to be R and S configuration at this asymmetric center.

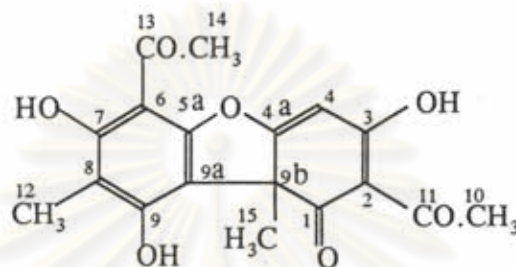


Figure 4 ^{13}C -NMR chemical shift assignment of usnic acid

1.6 Pharmacokinetic of Usnic Acid

The pharmacokinetics of D(+)-usnic acid was studied in rabbits following intravenous or oral administration of 5 and 20 mg/kg body weight doses, respectively. Plasma samples were collected at different time intervals and usnic acid was determined by HPLC. Plasma usnic acid levels following intravenous administration showed a triexponential elimination with a mean \pm sd terminal half-life of 10.7 \pm 4.6 hr. The volume of distribution of the central compartment and systemic clearance were 43.9 \pm 21.3 ml/kg and 12.2 \pm 3.0 ml/hr/kg, respectively. Plasma concentration data obtained after oral administration were analyzed using a noncompartmental method. Peak plasma level (C_{max}) of 32.5 \pm 6.8 $\mu\text{g/ml}$ was achieved in 12.2 \pm 3.8 hr (t_{max}). Mean absolute bioavailability of usnic acid following oral administration was 77.8% (Krishna and Venkataramana, 1992).



1.7 Toxicology

1.7.1 Hypersensitivity

Mitchell (1966) studying cedar poisoning in lumber workers in British Columbia, found D-usnic acid to be an antigen in the bark lichens. Champion (1971) also found D-usnic acid sensitivity in some, but not all patients with lichen sensitivity. In a group of atopic individuals who developed exacerbation of eczema, as well as asthma and rhinitis, after exposure to lichens, three patients had positive patch tests with lichens, notably *Lecanora* spp. In addition to D-usnic acid, the L-enantiomer (mirror image molecule) can also sensitive (Salo *et al*, 1981).

1.7.2 Antifeedant Activity

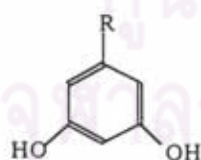
Both enantiomers of usnic acid were studied for toxicity and antifeedant activity against larvae of the polyphagous insect herbivore *Spodoptera littoralis*. They provoked strong mortality as well as significant growth retardation and a pronounced increase of the larval period in chronic feeding experiments with neonate larvae at concentrations comparable to or even significantly below their natural concentrations in various lichens. LD₅₀ of the most active compound (-)-usnic acid was observed at 8.6 μmolg^{-1} dry weight whereas the LD₅₀ of the (+)-enantiomer amounted to 90.8 and 111.0 μmolg^{-1} dry weight, respectively (Emmerich *et al*, 1993).

2. Depsides

2.1 History

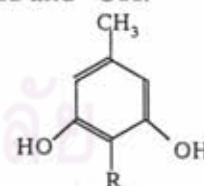
The largest number of lichen substances belong to the groups, depsides and depsidones. Depsides are esters of phenol carboxylic acids and have a phenyl benzoate skeleton. Two phenolic parts of a depside may be distinguished by referring the two units as the acid component and the phenolic component. Most of the lichen depsides are didepsides but a few are tridepsides. They are further classified into *para*-depsides and *meta*-depsides depending upon whether the hydroxyl group involved in the depside formation is *para* or *meta* to the carbonyl group of the phenolic component. In the case of *meta*-depsides the 3'-hydroxyl group or the 5'-hydroxyl group may be involved in the depside formation. No *ortho*-depsides are known so far to occur in nature (Neelakantan, 1969).

Lichen depsides may be grouped into (i) orcinol and (ii) β -orcinol derivatives. A variation commonly met with is the lengthening of the side chain of orcinol nucleus. The side chain contains an odd number of carbon atoms of varying length and in some cases ketonic groups are incorporated. In the case of β -orcinol derivatives, no such chain lengthening is noticed. However, the methyl group in between the two hydroxyls is often found in various stages of oxidation such as $-\text{CH}_2\text{OH}$, $-\text{CHO}$, $-\text{COOH}$ and $-\text{OH}$.



(i) Orcinol

R = CH_3 , C_3H_7 , C_5H_{11} , C_7H_{14}



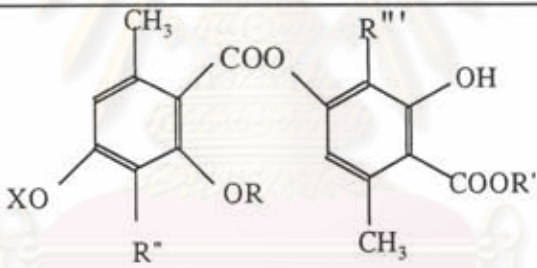
(ii) β -Orcinol

R = CH_3 , CH_2OH , CHO , COOH , OH

2.2 Chemistry

A survey of pertinent literature of the genus *Usnea* was made and it was noted that the antibiotic usnic acid (1) is the principal constituent of members of this lichen genus. In the Indian (Nair *et al*, 1953, Dhar *et al*, 1959, Murty *et al*, 1959, Aghoramurthy *et al*, 1961), Japanese (Asahina *et al*, 1926; 1932; 1933;1934), Australian (Briner *et al*, 1960) and Brazilian (Mors *et al*, 1960) Usneaceae, it (1) occurs together with various depsides as barbatic acid (2), ramalic acid (3), evernic acid (4), atranorin (5), diffractaic acid (6), thamnolic acid (7) (Culberson, 1969).

Table 6 Depsides found in Usneaceae

						
		R	R'	R''	R'''	X
Barbatic acid	2	H	H	CH ₃	CH ₃	CH ₃
Ramalic acid	3	H	H	CH ₃	H	CH ₃
Evernic acid	4	H	H	H	H	CH ₃
Atranorin	5	H	CH ₃	CHO	CH ₃	H
Diffractaic acid	6	CH ₃	H	CH ₃	CH ₃	CH ₃

2.3 Chemical Reaction

2.3.1 Hydrolyzation

The depsides are esters of aromatic hydroxy acids, in which the carboxyl group of an acid is linked to the hydroxy group of another cyclic compound. The ester linkage is quite labile. If it forms the only linkage between two rings, the complex compound is easily hydrolyzed into degradation products containing one ring each. Boiling with alcohol readily causes splitting of the depsides and a simultaneous ester exchange. On steam distillation, or on extraction of the lichens with a solvent containing hydroxy groups, the lichen acids pass into the extract either as such, or partially decomposed (hydrolyzed). For this reason it is of fundamental importance to be well acquainted with the depsides occurring in oak moss and tree moss, viz., evernic acid, atranorin, barbatinic acid and chloro-atranorin (Guenther, 1960).

(a) Evernic acid : On treatment with water, it undergoes these reactions :

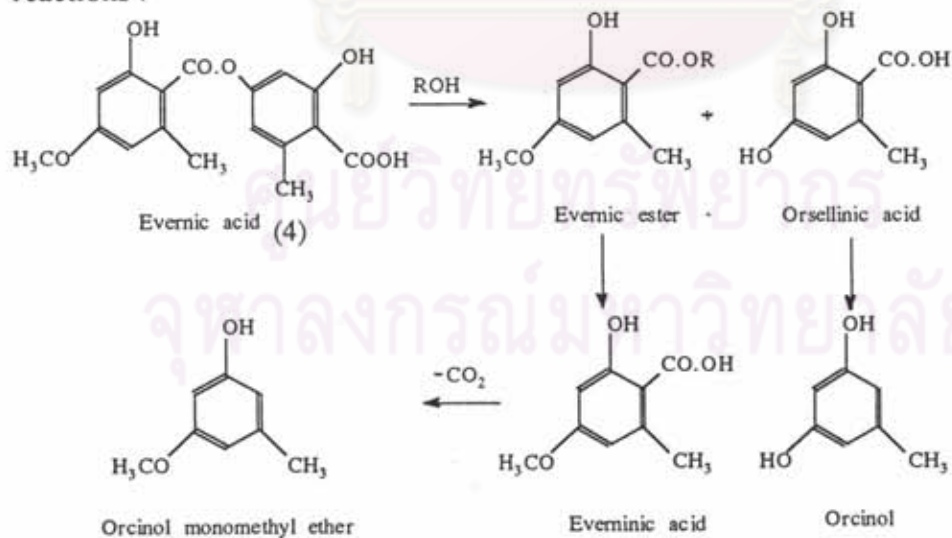


Figure 5 Hydrolyzation of evernic acid

(b) Barbatinic acid : a higher homolog of evernic acid, occurs in the lichen *Usnea ceratina* Ach. Barbatinic acid, if treated similarly to evernic acid, undergoes these reactions :

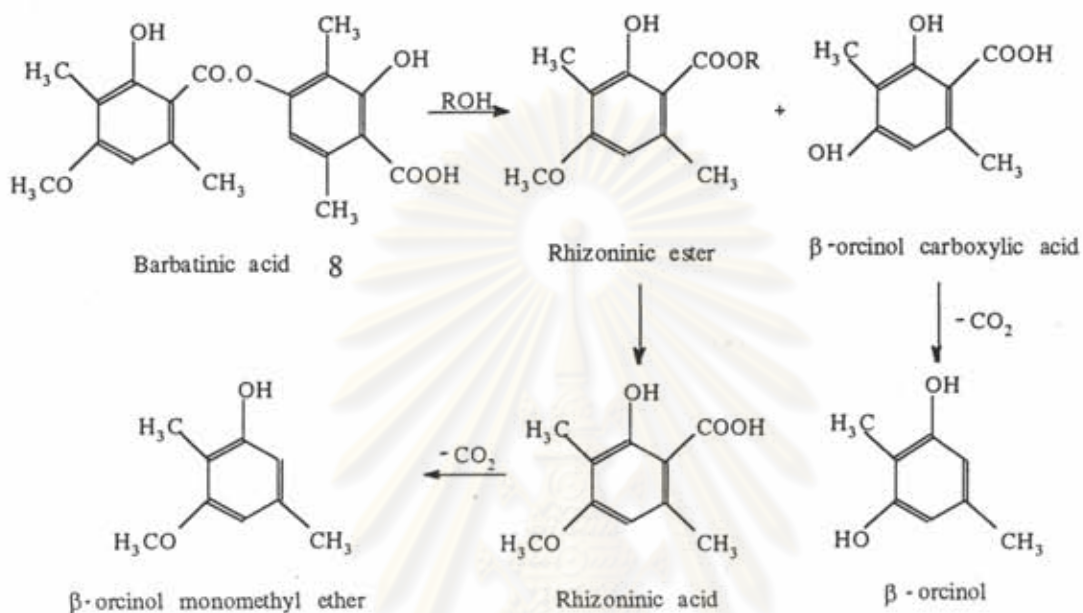


Figure 6 Hydrolyzation of barbatinic acid

(c) Atranorin: Similarly , atranorin and chloroatranorin undergoes the following reactions :

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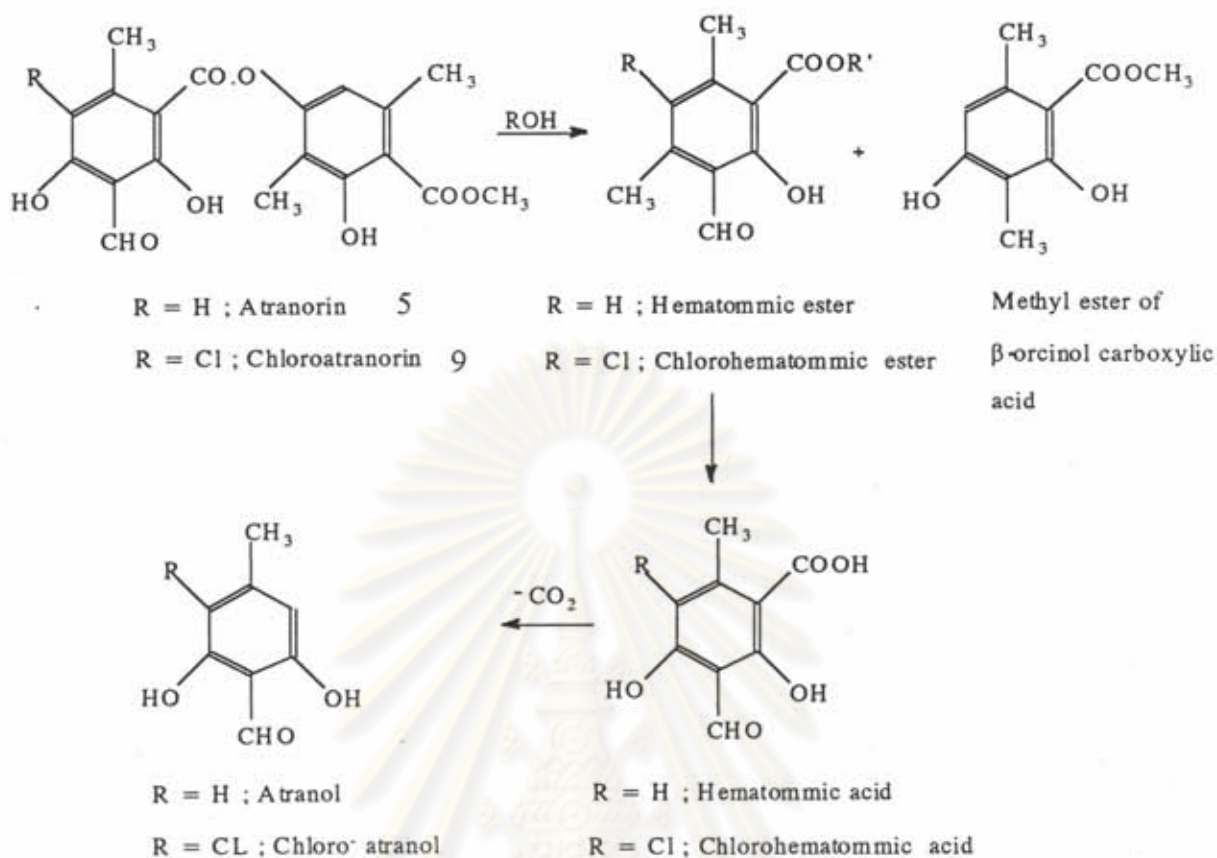


Figure 7 Hydrolyzation of atranorin

2.3.2 Thermal Degradation

A few lichen depsides, however, are known to undergo partial decomposition in the herbarium. For example; products detected by TLC after thermal decomposition of atranorin (5), anziaiaic acid (10) and perlatolic acid (11) in thalli of *Hypotrachyna partita* are shown in Figure 8.

After thermal decomposition, in addition to atranorin (5), anziaic acid (10), and a trace of perlatolic acid (11), the collection contained substantial amounts of anziol (12), a new depside proven to be decarboxylated anziaic acid, olivetolcarboxylic acid

(13), and olivetol (15) in addition to traces of 4-O-methylolivetolcarboxylic acid (14) and O-methyl olivetol (16) (Culberson *et al*, 1977).

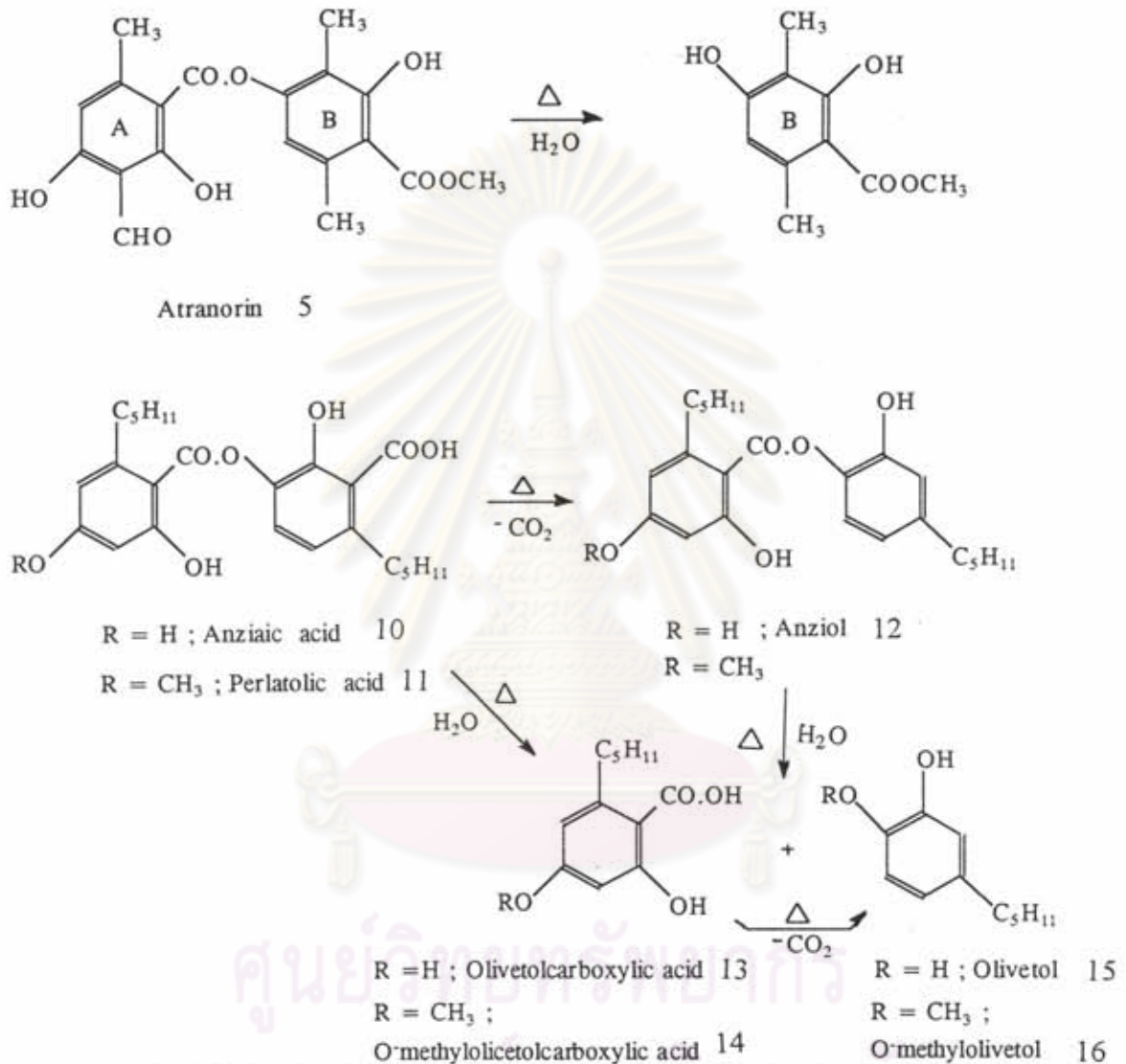


Figure 8 Thermal degradation of depsides

2.4 Biosynthesis

Lichen are known to produce several phenolic compounds, such as depsides, depsidones, and anthraquinones, which show a systemic structural interrelation suggesting that they are occurring by a mutual biogenetic scheme as acetate-malonate pathway (Shibata, 1965).

The biosynthetic experiment has been designed at first to test the turnover rate of carbon metabolism in lichen. ^{14}C -labeled carbon dioxide was fixed and carried out by spraying aqueous solution of acetate- ^{14}C and formate- ^{14}C . The results showed that acetate is a mutual precursor of the depsides, whereas formate is incorporated only into atranorin and chloroatranorin to reveal that it participates as a C_1 -fragment to form CH_3 and CHO groupings. The high radioactivity of atranorin seemed to suggest the C_1 -fragment incorporation occurs prior to the completion of aromatic ring.

The participation of 1 mole of acetate and 4 moles of malonate in orsellinic acid in *Penicillium* sp. has been established by Mosbach, 1960 and by Bentley and Keil, 1962. The present experiment has revealed that this scheme can be extended to the depsides in lichens. The co-occurrence of orcinol and β -orcinol type depside in the same lichen as has happened in the case would be noted from biogenetic view point.

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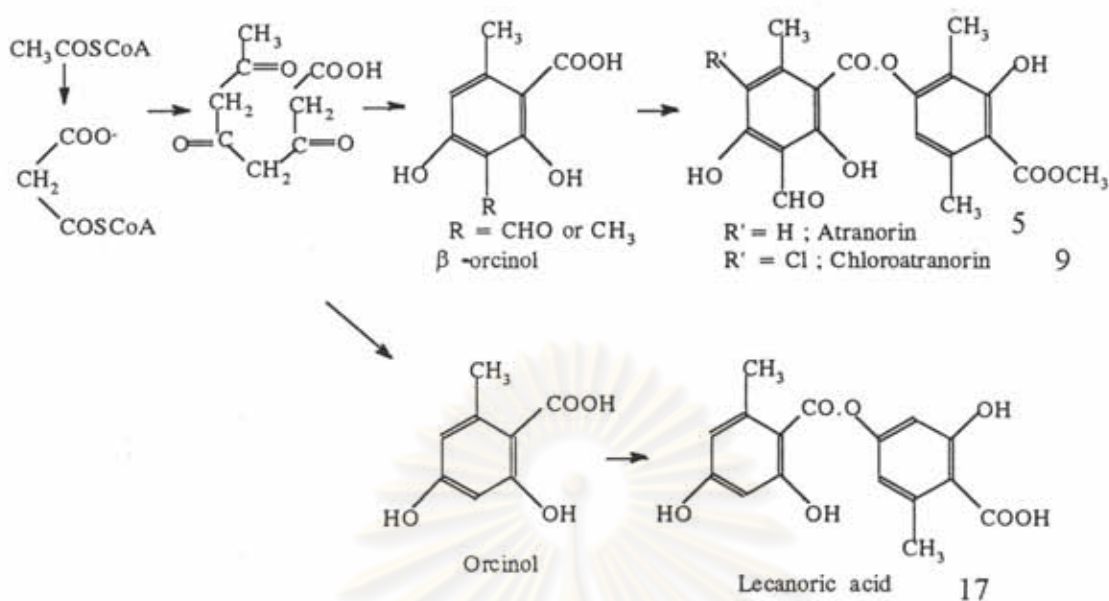


Figure 9 Biogenesis of depsides

2.5 Synthesis

Lichen depsides have now been synthesized by making use of two reagents ; N-N'-dicyclohexylcarbodiimide (DCC) and trifluoroacetic anhydride. The use of DCC for the condensation of a hydroxy compound like a phenol or an alcohol with organic acids was first tested with simple examples. The reaction was carried out by taking equimolecular quantities of the carbodiimide. With benzoic acid and phenol, phenyl benzoate was obtained only in poor *p*-nitrophenyl benzoate in good yield with the appropriate alcohols. Among the lichen depsides, the following were synthesized by making use of this reagent.

Bourne *et al* (1949) reported the use of trifluoroacetic anhydride for the preparation of phenolic as well as alcoholic esters of both aliphatic and aromatic carboxylic acids and as the reagent may also be used as a solvent, it enables the components to react directly under mild conditions. While preparing depsides using this reagent, Brown *et al*

(1960) reported the preparation by this method of a depside intermediate, needed in the synthesis of diploicin. Taub *et al* (1963) have subsequently used it for the condensation of acids with phenols to yield ketones and they have reported the formation of esters as by-products. Excess of acid component has been avoided in order to simplify the purification procedure and a slight excess of the anhydride used to dissolve the reactants completely.

The suitability of this method was first examined by preparing phenyl benzoate using equimolecular quantities of benzoic acid and phenol when the ester was obtained in good yield. Similarly by condensing haematommic acid (18) and methyl β -orcinoic carboxylate (19) in the presence of a slight excess of trifluoroacetic anhydride and purifying the reaction product on a column of silicic acid, pure atranorin (5) was obtained in satisfactory yield. The synthetic depside was characterized by its m.p. and mixed m.p. with an authentic sample, colour reactions and reaction (Asahina, 1933) to methyl nor-barbatate (20) (Neelakantan *et al*, 1965).

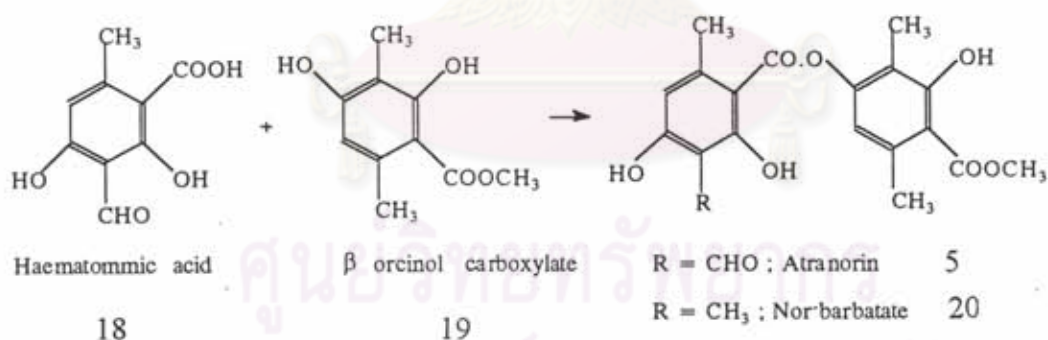
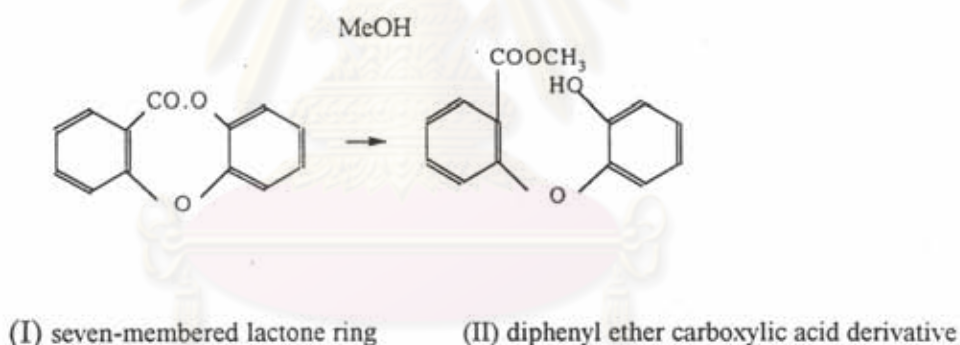


Figure 10 Synthesis of depsides

3. Depsidones

3.1 History

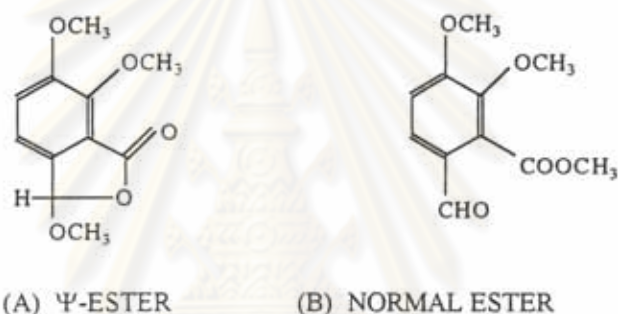
Compounds belonging to the depsidone group have a seven-membered lactone ring (I) and may be considered as derivatives of both depsides and diphenyl ethers. The name 'depsidone' was first given by Asahina and Asano (1933). The numbering of the different positions in the depsidone skeleton has been proposed by Neelakantan *et al* (1962) and starts with the free position *ortho* to the carbonyl; this was based on the analog of numbering in xanthones. Because of the extra oxygen bridge, depsidones, unlike depsides, do not yield two aromatic halves by methanolysis but only a hydroxydiphenyl ether carboxylic acid derivative (II)



A large number of compounds belonging to the group of depsidones have been isolated and their structures elucidated. Till recently, these were considered to be obtainable only from lichens, but of late a few have been isolated as products of mold metabolism (e.g. nidulin from *Aspergillus nidulans*). Like depsides, depsidones also exhibit a number of variations in the structures and may be classified into orcinol, β -orcinol and mixed derivatives. Four of the lichen depsidones, viz., pannarin, diploicin, gangaleoidin and vicanicin also contain chlorine (Neelakantan, 1960).

3.2 Chemistry

The depsidones have a lactone ring in the A-part of the molecule. The lactone structure is tautomeric with the O-aldehyde carboxylic acid structure and hence two esters are possible : the Ψ -ester and the normal ester, as demonstrated for the first time by Wegscheider (1980) who showed that opianic acid (2,3-dimethoxy-6-formyl-benzoic acid) gave on heating with methanol the Ψ -ester (A) in the absence of mineral acids and the normal ester(B) in the presence of mineral acids.



3.3 Chemical Reaction

3.3.1 Hydrolyzation

The reaction of depsidones with alcoholic solvent has been investigated by Huneck and Tabacchi(1987). Stictic acid (1) gave on boiling with methanol a mixture from which it was possible to isolate 8'-O-methylstictic acid (2) identical with methylstictic acid. On treatment of (2) with acetic anhydride/pyridine 2'-O-acetyl-8'-O-methylstictic acid(4) was formed while reaction of 3 with acetic anhydride/sulfuric acid gave a compound identical with 9,9,2',8'-tetra-O-acetylstictic acid (5). Methylation of stictic acid with methyl iodide and silver oxide in acetone yield 2',8'-di-O-methylstictic acid (6) in agreement with

the work of Curd and Robertson (1935). Methylation of norstictic acid with dimethyl sulphate and potassium carbonate in dimethylformamide gave 2'-O-methylstictic acid(7).

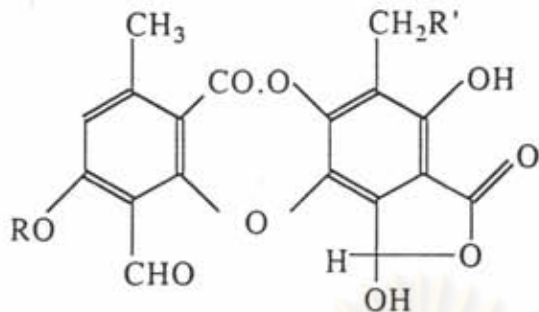
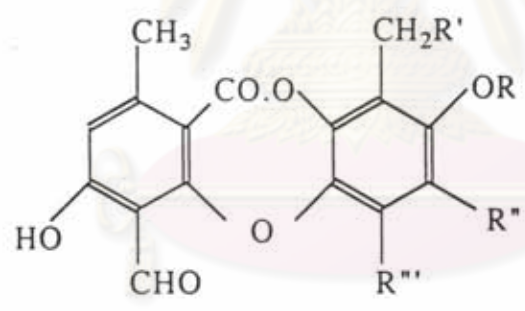
Acetylation of the 8'-OH group, as shown in the case of pentaacetylnorstictic acid, shifted the signal of the 8-proton in the NMR spectrum to 7.85 ppm. The ^1H -NMR spectrum of (4) does not show a signal in this region, which proved that methylation had occurred at the 8'-OH group.

Heating stictic acid with ethanol gave 8'-O-ethylstictic acid (8) which was acetylated by acetic anhydride/pyridine to 2'-O-acetyl-8'-O-ethylstictic acid (9) and by acetic anhydride/sulfuric acid to 9,9,2'-tri-O-acetyl-8'-O-ethylstictic acid (10). Methylation of 8 with dimethyl sulphate/potassium carbonate in dimethylformamide gave 2'-O-methyl-8'-O-ethylstictic acid(11).

The reaction of norstictic acid (15) with methanol and ethanol. Boiling (15) with methanol yielded 8'-O-methylnorstictic acid (16) which was acetylated with acetic anhydride/pyridine to 4,2'-O-acetyl-8'-O-methylnorstictic acid (17) and with acetic anhydride/sulphuric acid to 4,9,9,2'-tetra-O-acetyl-8'-O-methylnorstictic acid (18). From the mother liquor of (15), after saturation with hydrochloric acid, the diphenylether (19) was isolated; it gave a red colour with sodium hypochlorite, proving the presence of two free, metahydroxyl groups. On acetylation with acetic anhydride/pyridine (19) gave the triacetate (20). Prolonged reaction of diazomethane on norstictic acid gave the diphenylether (21). The ^1H NMR spectrum of (21) showed a signal at 2.54 which corresponded to the additional methyl group at C-8'.

The results of the experiments demonstrate that depsidones which a lactone ring react with hot alcohols and consequently extraction of lichens with alcohols or solvents contained with alcohols (e.g. CHCl_3) should be avoided (Huneck and Tabacchi, 1987).

Table 7 Depsidones found in Usneaceae

					
		R	R'		
Salazinic acid	21	H	OH		
Stictic acid	22	CH ₃	H		
Norstictic acid	23	H	H		
					
		R	R'	R''	R'''
Protocetraric acid	24	OH	H	COOH	CH ₃
Psoromic acid	25	H	CH ₃	H	COOH

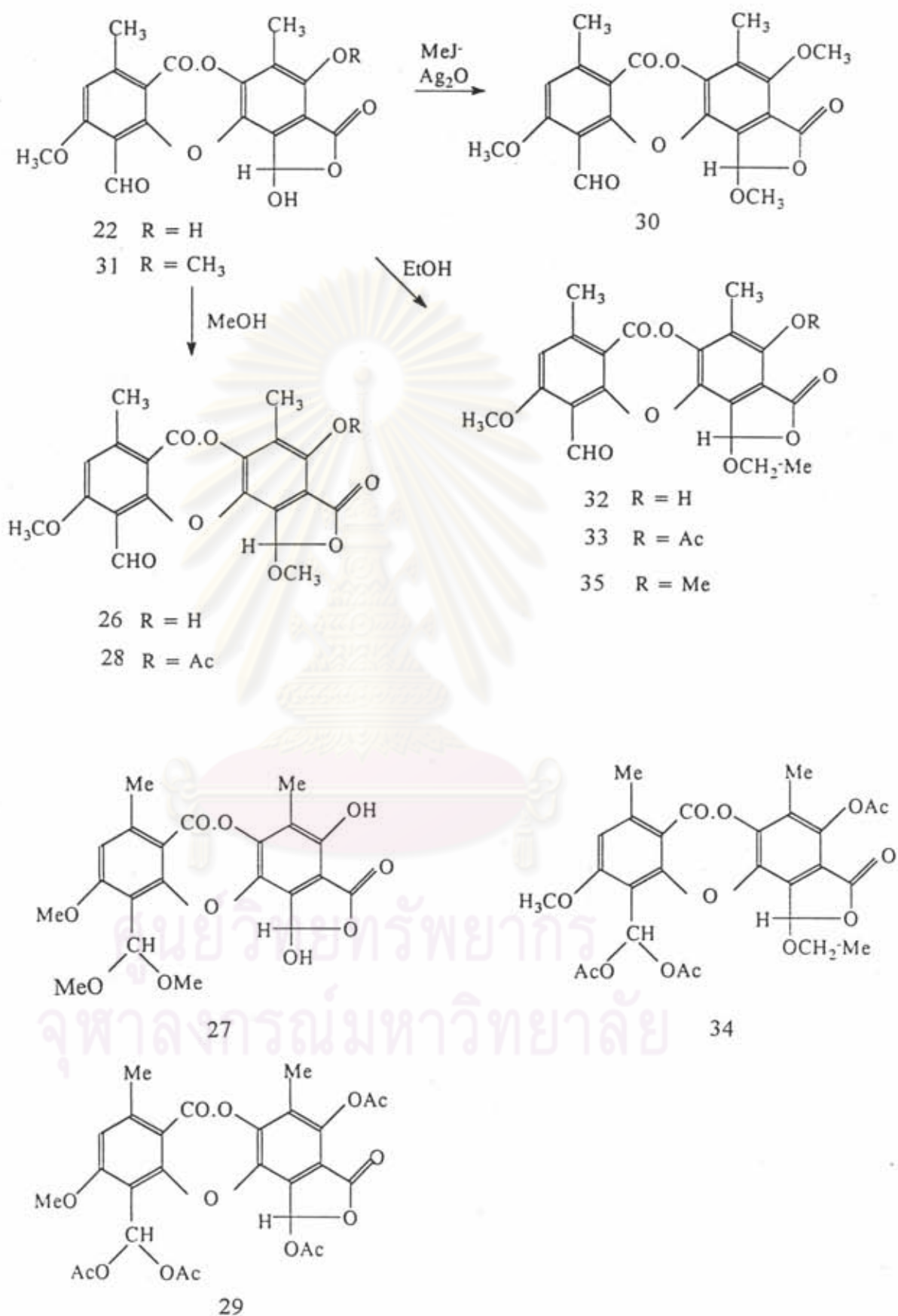
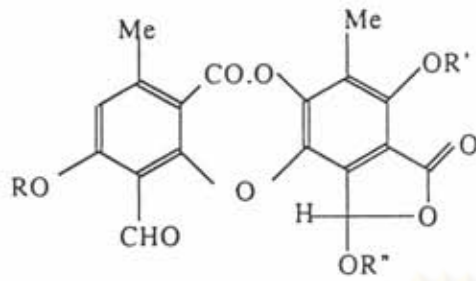


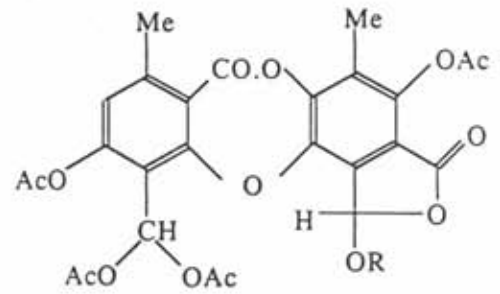
Figure 11 Alcoholysis of depsidones



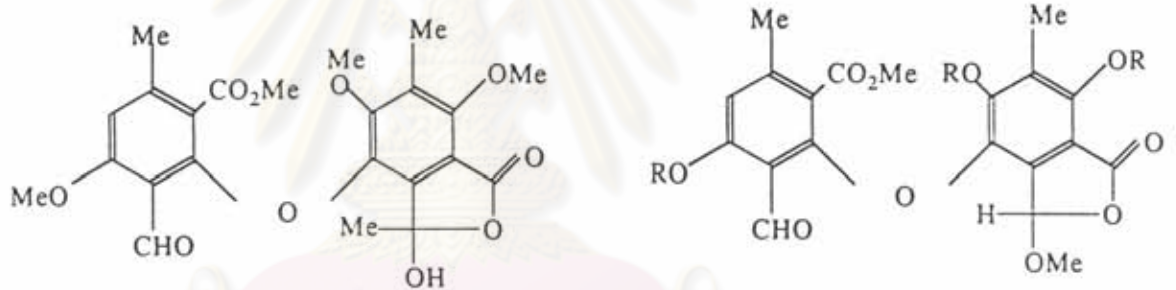
36 $R = R' = R'' = H$

37 $R = R' = H, R'' = Me$

38 $R = R' = Ac, R'' = Me$



39 $R = Me$



42

40 $R = H$

41 $R = Ac$

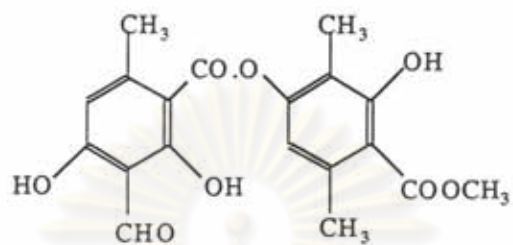
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Figure 11 : (continued)

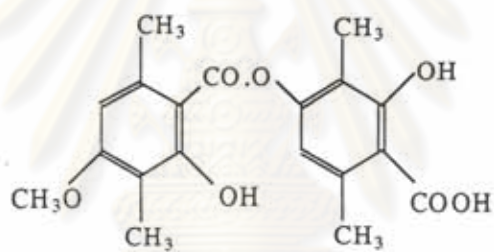
ORCINOL-SERIES
PARA-DEPSIDES
EVERNIC ACID 43
DEPSIDONES
DIPLOICIN 44
PHYSODIC ACID 45

β -ORCINOL SERIES

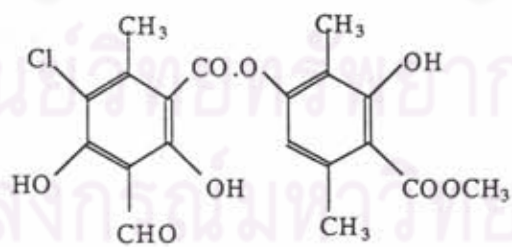
PARA-DEPSIDES



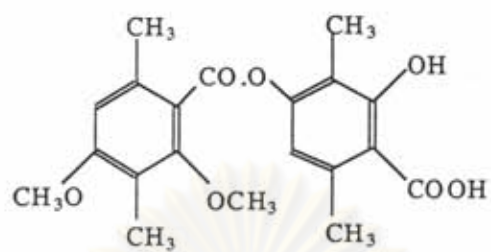
ATRANORIN 5



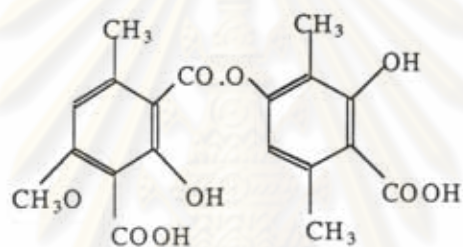
BARBATIC ACID 2



CHLOROATRANORIN 9

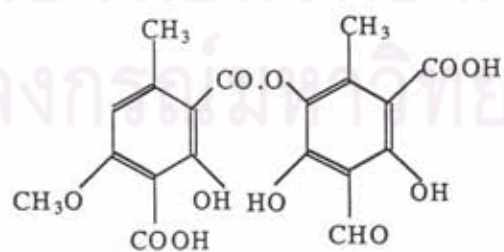


DIFFRACTAIC ACID 6



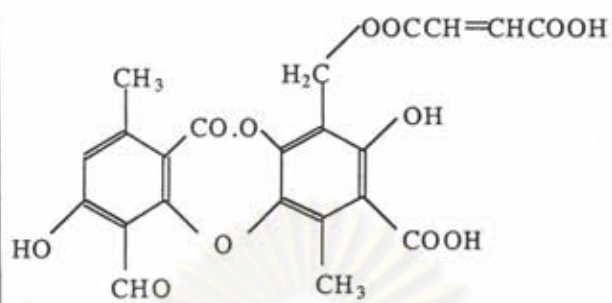
SQUAMATIC ACID 46

META-DEPSIDES

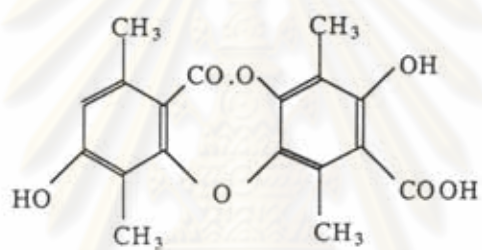


THAMNOLIC ACID 7

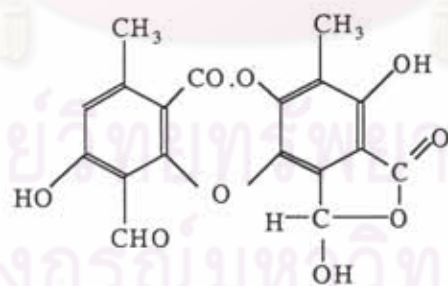
DEPSIDONES



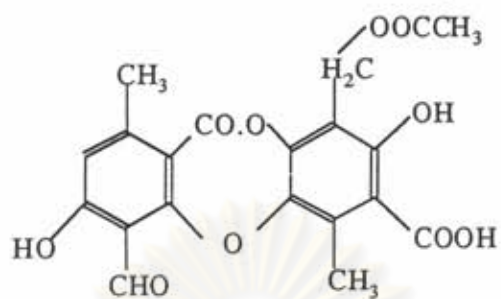
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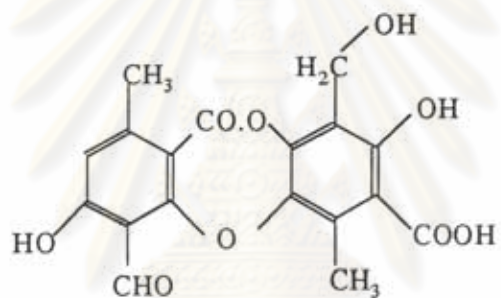
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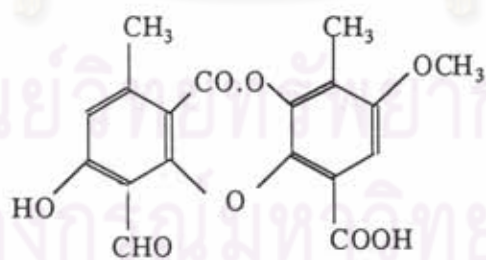
NORSTICTIC ACID 23



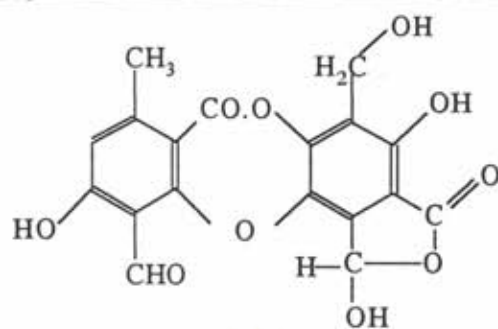
PHYSODALIC ACID 49



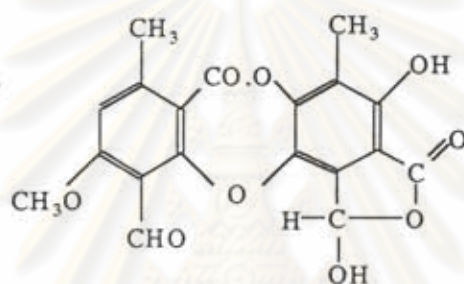
PROTOCETRATIC ACID 24



PSROMIC ACID 25

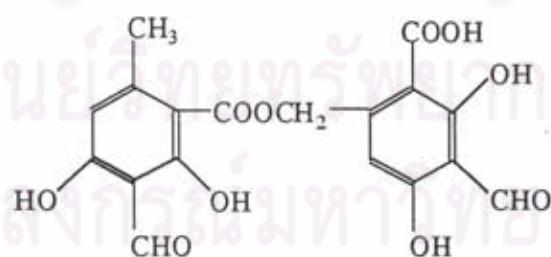


SALAZINIC ACID 21



STICTIC ACID 22

BENZYL ESTER



BARBATOLIC ACID 50