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Synthesis and Antifeedant Properties of *N*-Acylphenylisoserinates of *Lactarius* Sesquiterpenoid Alcohols

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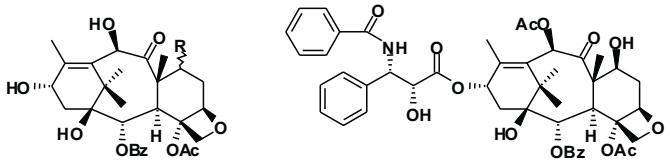
The esterification of various sesquiterpenoid alcohols of *Lactarius* origin with N-benzoyl-[2*R*,3*S*]-phenylisoserine (side chain of Taxol®), N-acetyl-[2*R*,3*S*]-phenylisoserine and *N*-*tert*-butoxy-[2*R*,3*S*]-phenylisoserine (side chain of Taxotere®) produced compounds whose antifeedant properties against storage pests *Tribolium confusum*, *Trogoderma granarium*, *Sitophylus granarius* and *Rhizoperta dominica* were measured. The introduction of the ester moiety in these molecules, in comparison to original compounds, moderately enhanced their antifeedant activities, as well as changed their selectivity of activity towards the test insects.

Key words: sesquiterpenoid alcohols isolated from mushrooms of *Lactarius* genus, *N*-benzoylphenylisoserinates, N-*tert*-butoxyphenylisoserinates, N-acetylphenylisoserinates, *Lactarius* sesquiterpenoid, Taxol®, Taxotere®, antifeedant activity, storage pests, *Tribolium confusum*, *Trogoderma granarium*, *Sitophilus granarius*, *Rhizopertha dominica*

In our recent paper we have identified a group of compounds responsible for the resistance of *Taxus baccata* to the attack of insects. It appeared that the taxanes 10-deacetylbaccatin III **(1)** and its 7α isomer **(2)** (Fig. 1), contained in the needles of *Taxus baccata*, possessing a very strong antifeedant activity, protect them from the attack of insects.



1 R = β-OH (10-deacetylbaccatin III)
2 R = α-OH (7-*epi*-10-deacetylbaccatin III)

3 (Taxol®)

Figure 1

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This fact prompted us to investigate the antifeedant activity against the storage pests, of Taxol® **(3)**, the very important anticancer compound isolated from *Taxus brevifolia*. The antifeedant activity tests of Taxol® revealed its very potent activity, and perhaps, its role in the bark of *Taxus brevifolia* in defence against insects. In our previous papers [2,3] we studied the antifeedant properties of sesquiterpenoid alcohols from *Lactarius* species. The sesquiterpenes, as in the case of 10-deacetylbaccatin III **(1)** or Taxol® **(3)**, are responsible for chemical defence of the mushrooms against several predators. Since Taxol® **(3)** is the 10-acetyl-13-*N*-benzoylphenylisoserine ester of 10-deacetylbaccatin III, we decided to attach the Taxol® side chain to a series of sesquiterpenoid alcohols to produce *N*-benzoylphenylisoserine esters and to investigate their antifeedant properties. The results of this investigation were published and showed that the introduction of the taxol side chain in these molecules, in comparison to original compounds moderately enhanced their antifeedant activities, as well as changed their selectivity of activity towards the test insects. Since the synthesis of Taxotere®, a compound with the modified taxol side chain, gave also a very potent anticancer drug it seemed very reasonable to us to produce a series of sesquiterpenoid analogues of Taxotere® (N-Boc-phenylisoserinates), and N-acetylphenylisoserinates and to check their antifeedant properties and to study structure antifeedant activity relationship.

RESULTS AND DISCUSSION

Synthesis. The synthesis of N-benzoylphenylisoserinates and antifeedant properties of various sesquiterpenoid alcohols of mushroom origin are described in our previous paper [4]. But, in order to facilitate the observation of structure activity relationship, structures of all the sesquiterpenoid esters of N-acyl-(2R,3S)-phenylisoserine are included in the Table 1 presenting their antifeedant properties against test insects.

The sesquiterpenoid alcohols of *Lactarius* origin were isolated from ethanolic extracts of two kinds of mushrooms *Lactarius rufus* and *Lactarius vellereus* according to [5]. They are presented in Fig. 2. The sesquiterpenes included three skeletons: marasmane (**a**), isolactarane (**b, c, d**) and lactarane (**e–s**). Some of them were modified chemically regarding their stereochemistry at C-8 (**g, j ,m**) and the ring junction between the seven and five membered rings (**h, j, n**).

The sesquiterpenoid analogues of Taxol® and Taxotere® and N-acetyl phenylisoserinates were prepared by three methods A, B and C. Method A was published [4,6] with detailed description and it is shown in Scheme 1. Oxazoline **(5)** was prepared from phenylisoserine **(4)** with natural configuration by the reaction with trimethyl orthobenzoate. Subsequently the acid **6** was obtained by alkaline hydrolysis followed by acidification. Sesquiterpenoid alcohols (**a–s**) were esterified with acid **6** in presence of DCC and DMAP. The esters (**7a–7s**) thus formed were hydrolyzed in mild acidic conditions and gave required N-benzoyl-(2R,3S)-phenylisoserinates (**8a–8s**) in good yields.

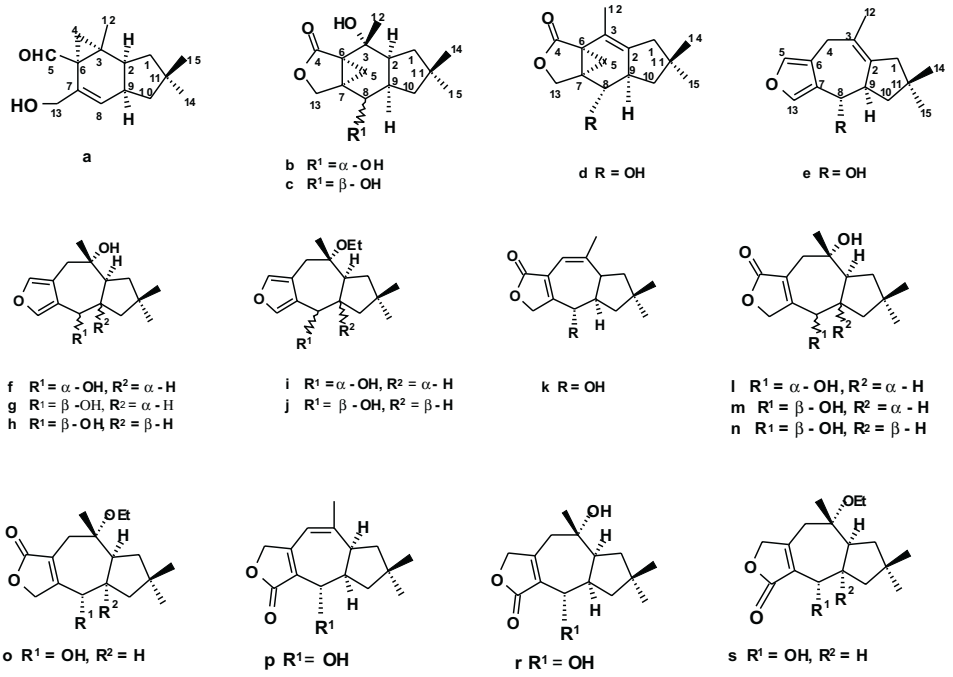
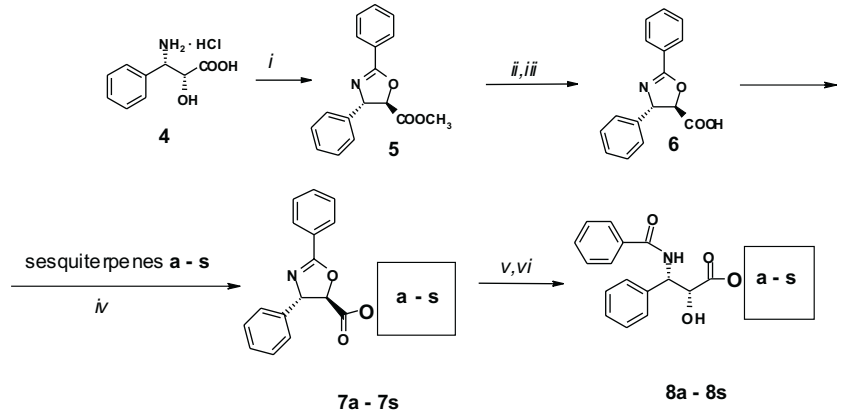


Figure 2

Scheme 1

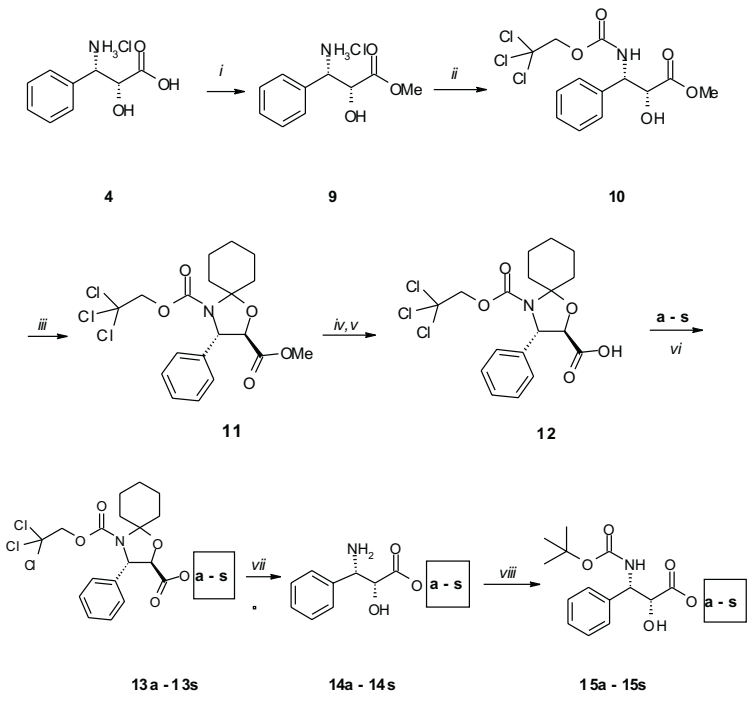


i - $Ph(OMe)_3$, *ii* - $NaOH/H_2O$, *iii* - HCl/H_2O, *iv* - DCC, DMAP, CH_2Cl_2 rt. *v* - HCl/H_2O-MeOH, *vii* - $NaHCO_3/H_2O$.

Although method A gave satisfactory results for the synthesis of analogues of Taxol® it could not be applied for the preparation of analogues of Taxotere® and N-acetyl derivatives. The syntheses of N-Boc- and N-acetyl-phenylisoserinates required more complicated methods and these are described in details [7,8].

Method B is shown in Scheme 2. The (2R,3S) phenylisoserine hydrochloride **(1)** was transformed into its methyl ester **(9)** in quantitative yield. Then, the ester was acylated with TrocCl to give the amide derivative **(10)**. The hydroxyl group was protected simultaneously with the NH amide group by treatment with cyclohexanone dimethyl acetal yielding the oxazolidine **(11)**. Alkaline hydrolysis of the ester group and then acidification gave the acid **(12)**, which was used for esterification with various sesquiterpenoic alcohols in presence of DCC and DMAP. Esters **(13a–13s)** were deprotected by reduction with zinc in acetic acid to give amines **(14a–14s)**. After acylation with (*tert*-BuOCO)$_2$O, the required N-Boc-phenylisoserinates **(15a–15s)** of various sesquiterpenoic alcohols were obtained (Scheme 2).

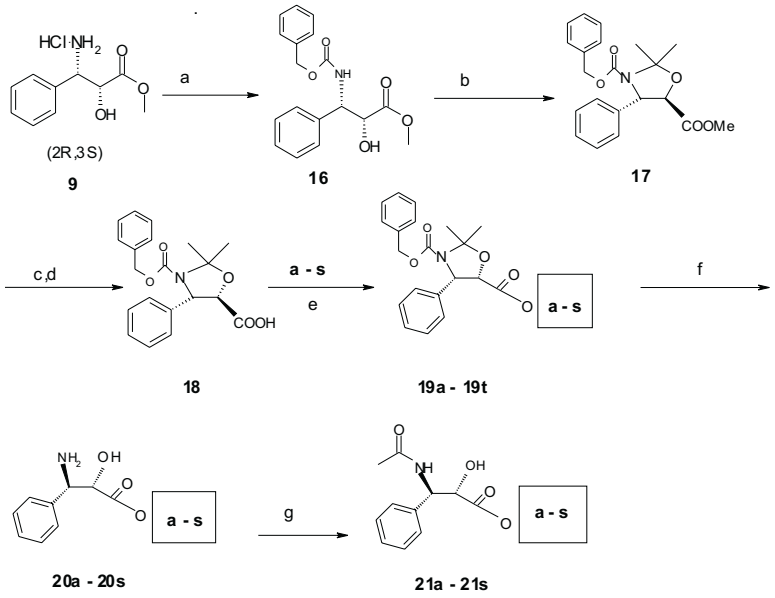
Scheme 2



i - $SOCl_2$, MeOH, 0^{0}C, *ii* - Cl_3CH_2OCOCl, $NaHCO_3$, CH_2Cl_2; *iii* - 1,1-dimethoxycyclohexane, p-TsOH, toluene, 110 ^{0}C; *iv* - LiOH, CH_3OH; *v* - HCl; *vi* - DCC, DMAP, toluene; *vii* - Zn, CH_3CO_2H - CH_3OH; *viii* - (^{t}BuOCO)$_2$O, Et_2O

Method C is shown in Scheme 3. The (2*R*,3*S*)-3-phenylisoserine hydrochloride **(4)** was transformed into its methyl ester **(9)** in quantitative yield. Subsequently the amide derivative **(16)** was prepared by the reaction of the ester with benzyl chloroformate in presence of sodium hydrogen carbonate. The hydroxyl group of the amide **(16)** was protected with 2-methoxypropene with the formation of oxazolidine **(17)**. Alkaline hydrolysis of the ester group in **17** followed by acidification gave the acid **18** ready for esterification with various sesquiterpenoid alcohols **(a–s)** in presence of DCC and DMAP. Esters **19a–19s** were deprotected by hydrogenolysis using 10% palladium catalyst and gave the phenylisoserine esters **20a–20s**. The deprotection step reaction conditions must be mild enough to prevent the decomposition of the sesquiterpenoid part of the molecule. Esters **20a–20s** were ready for acylation, when acetic anhydride was used the required N-acetylphenylisoserinates **21a–21s** were prepared.

Scheme 3



a - $C_6H_5CH_2OCOCl$, $NaHCO_3$; b - 2-methoxypropene, pyridinium 4-toluenesulfonate;

c - LiOH/MeOH; d - HCl aq: e - DCC, DMAP, CH_2Cl_2; f - H_2, 10%Pd/C, MeOH;

g - Ac_2O, $NaHCO_3/CH_2Cl_2$

Antifeedant properties. Using these methods, to enable a better understanding of the structure activity relationship a series of new N-acylphenylisoserinates of various sesquiterpenoid alcohols was prepared, their antifeedant activities were measured and are included in Table 1. At the top of the table structures of the acid part of the ester are presented (R = A, B, C). Esters are numbered with arabic numerals (showing position on particular scheme) in connection with small letters **(a–s)** referring to the structures of sesquiterpenes shown in Fig. 2.

Table 1.

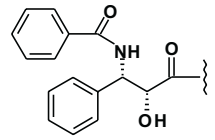
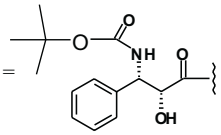
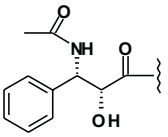
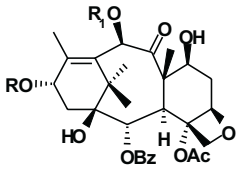
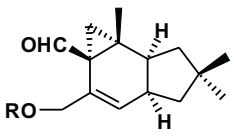
ANTIFEEDANT ACTIVITY OF N-ACYL-PHENYLISOSERINATES OF SESQUITERPENOIC ALCOHOLS OF *LACTARIUS* ORIGIN						
ANALOGUES OF TAXOL R = A		ANALOGUES OF TAXOTERE R = B		N-ACETYL DERIVATIVES R = C		
A = 		**B** = 		**C** = 		
Method A		Method B		Method C		
COMPOUND (ESTER)		Test insects				
		Trogoderma granarium (larvae)	*Tribolium confusum* (larvae)	*Sitophilus granarius* (adults)	*Rhizopertha dominica* (adults)	Mean Coef. T (deterrent class)
R-OMe	R = A **9**	83.4	59.1	59.4	–12.1	47.5 (I)
	R=H R^1=H **1**	180.2	149.4	115.5	185.0	157.5 (IV)
	R=A R_1=Ac Taxol **3**	178.9	122.6	190.8	131.5	156.0 (IV)
	R=H **a**	200.0	161.9	176.0	–	179.3 (IV)
	R=A **8a**	99.2	95.1	165.5	132.7	123.1 (II)
	R=B **15a**	93.5	101.0	64.8	9.4	67.2 (II)

Table 1 (continuation)

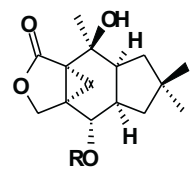
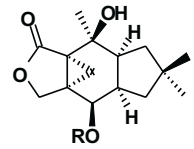
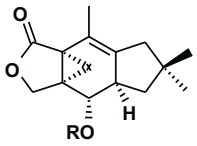
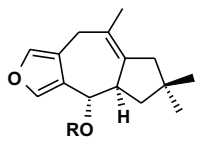
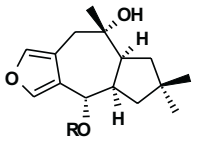
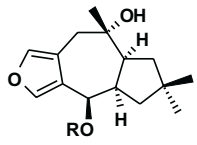
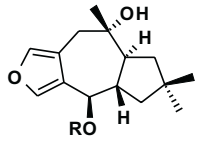
	R=H **b**	–50.4	15.3	–7.0	–	–42.1 (atr.)
	R=A **8b**	70.1	164.9	122.4	70.0	106.9 (II)
	R=B **15b**	89.6	104.9	–47.1	139.1	71.6 (II)
	R=C **21b**	25.0	77.6	118.4	–40.7	45.1 (I)
	R=H **c**	42.6	–22.8	35.3	–	18.4 (I)
	R=A **8c**	92.9	67.9	111.1	–23.0	62.2 (II)
	R=B **15c**	66.4	36.5	106.5	144.7	88.5 (II)
	R=H **d**	5.0	57.0	12.0	–	24.7 (I)
	R=B **15d**	109.4	115.0	12.2	128.6	91.3 (II)
	R=C **21d**	121.6	51.9	73.6	82.3	82.4 (II)
	R=H **e**	21.0	152.7	137.0	–	103.6 (III)
	R=A **8e**	43.5	103.6	102.3	141.2	97.7 (II)
	R=B **15e**	–17.1	101.4	92.9	114.4	72.9 (II)
	R=H **f**	9.2	95.7	60.0	–	55.0 (II)
	R=A **8f**	78.1	84.1	118.5	125.1	101.5 (III)
	R=B **15f**	62.9	89.4	115.0	94.6	90.5 (II)
	R=H **g**	22.6	97.5	97.9	–	82.9 (II)
	R=B **15g**	79.5	100.9	83.1	49.5	78.3 (II)
	R=H **h**	102.7	23.6	0.0	–	49.6 (I)
	R=B **15h**	90.2	96.7	95.8	122.8	101.4 (III)
	R=C **21h**	85.2	42.6	113.1	85.8	81.6 (II)

Table 1 (continuation)

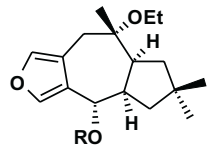
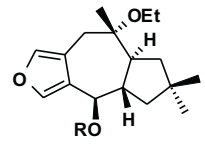
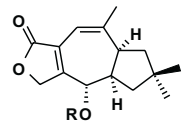
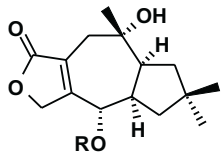
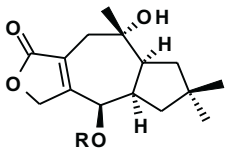
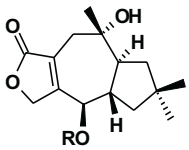
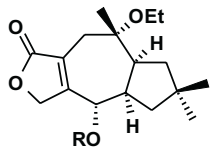
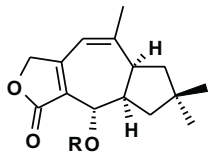
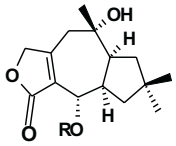
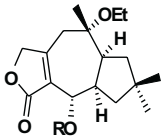
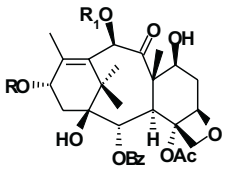
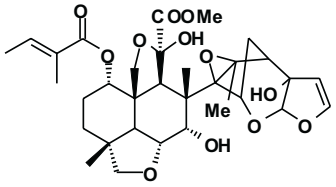
	R=H **i**	41.6	163.8	173.7	–	126.4 (III)
	R=A **8i**	119.6	91.0	115.9	172.3	124.7 (III)
	R=B **15i**	77.4	120.2	–11.0	89.7	69.1 (II)
	R=C **21i**	81.9	114.1	108.3	64.8	92.3 (II)
	R=H **j**	60.5	97.3	46.2	–	68.0 (II)
	R=B **15j**	95.8	41.2	81.2	70.9	72.3 (II)
	R=B **15k**	128.9	63.7	124.0	108.2	106.2 (III)
	R=C **21k**	127.5	87.7	79.9	113.8	102.2 (III)
	R=H **l**	148.6	144.9	88.6	–	127.4 (III)
	R=A **8l**	118.9	11.7	162.9	51.2	86.2 (II)
	R=B **15l**	78.9	122.9	16.9	109.8	82.1 (II)
	R=C **21l**	131.5	105.6	76.9	108.6	105.6 (III)
	R=H **m**	–17.4	59.3	–11.9	–	10.0 (I)
	R=A **8m**	79.9	42.7	94.6	–46.6	42.7 (I)
	R=B **15m**	52.7	55.9	89.9	96.2	73.7 (II)
	R=C **21m**	61.0	86.8	109.9	–	85.9 (II)
	R=B **13n**	113.95	60.9	90.8	71.56	84.31 (II)
	R=H **o**	52.3	150.2	69.0	–	90.5 (II)
	R=B **15o**	118.0	115.9	135.5	87.9	114.3 (III)
	R=C **21o**	112.6	80.5	72.5	–	98.5 (II)

Table 1 (continuation)

	R=B **15p**	76.2	86.9	74.9	73.5	77.9 (II)
	R=H **r**	93.3	150	73.4	–	10.0 (I)
	R=A **8r**	123.0	66.4	129.3	133.8	113.1 (III)
	R=B **15r**	70.4	108.9	82.16	67.5	82.24 (II)
	R=H **s**	65.2	46.7	94.9	–	68.9 (II)
	R=B **15s**	47.0	103.8	103.6	100.0	88.6 (II)
	R=B R_1=H Taxotere **22**	115.5	149.4	185.0	–	150.0 (III)
	R=B R_1=Ac **23**	145.7	151.6	164.5	128.4	147.6 (III)
 Azadirachtin		190.0	185.0	170.0	–	181.7 (IV)

As it was already mentioned in the introduction, we wanted to check the antifeedant properties of the synthesized compounds in order to find the influence of introduction of Taxol® side chain into their molecules. First we checked Taxol® **(3)** (R = A, R′ = Ac) that has a very potent antifeedant activity to the storage pests mentioned in Table 1. Therefore, one can assume that its role in *Taxus brevifolia* is to protect the plant against insects. 10-Deacetylbaccatin III **(1)** (R = H, R′ = H), which is a good antifeedant, demonstrated lower activity than Taxol®, especially against *Trogoderma granarium* and *Sitophylus granarius*. We checked the antifeedant activity of Taxotere® and its acetyl derivative to observe the influence of the modification of the side chain on the activity. Taxotere® is still a good antifeedant, however its activity towards *Trogoderma granarium* is much decreased. The acetyl derivative of Taxotere® showed all around better activity, however slightly smaller than Taxol®. The

attachment of Taxol® side chain to the molecule of isovellerol **(8a)** decreased its activity. Introduction of Taxol® side chain into the molecule of isolactarorufin **(b)** (R = H) (which is an attractant) enhanced its antifeedant properties (compound **8b**). The change of the N-acyl substituents from N-benzoyl to N-*tert*-butoxycarbonyl and N-acetyl decreased activity. The change of stereochemistry at C-8 **(8c, 15c)** had very little effect on activity. Introduction of 2,3-double bond followed by esterification improved activities **(15d, 21d)**. Esterification of furanol **(e)** did not have important effect on antifeedant activity. In case of furandiol **(f)**, the esterification gave a compounds **8f** and **15f** with twice as high activity. The change of configuration at C-8 in furandiol gave an ester **15g**, which had similar activity as **15f**. The change of the stereochemistry of the 5- and 7-membered ring junction into *trans* in furandiol **(h)** had very little effect on the activity. Introduction of the Taxol® side chain into "artifact" **(i)** as well as into lactarorufin A **(l)** influenced only the selectivities of antifeedant activity, Taxol® analogues showed best activity. Esterification of 8-*epi*-lactarorufin A **(m)**, which is inactive, caused some activity. Introduction of the side chain into 5-deoxy-lactarolid B (Item 10) did not increase its activity but changed its selectivity towards storage pests. Removal of the 3-hydroxyl group in lactarorufin A **(l)** with the formation of 3,4-double bond followed by esterification gave compounds with slightly improved antifeedant activity. As in the case of compounds **15h**, **21h**, **15j** the change of stereochemistry of the 6–7-membered ring junction in **15n** did not increase its activity. Esterification of the 3-hydroxyl group caused slight improvement in activity the analogue of Taxotere® was the best. Compounds with lactonic carbonyl group at carbon 13 **(15p, 8r, 15r, 15s)** exhibited moderate activity, the analogue of Taxol® was the best. To complete the structure activity investigation, antifeedant activity of Taxotere® **(22)** and its acetyl derivative **(23)** were measured and showed that all three **3**, **22** and **23** were very good antifeedants. Our procedure of measuring antifeedant activity was verified with azadirachtin test, which is presented at the bottom of Table 1.

EXPERIMENTAL

General: All melting points were measured on a Koffler hot plate and are uncorrected. ^{1}H and ^{13}C NMR spectra were run at 500 and 125 MHz respectively (Bruker 500 MHz spectrometer) in $CDCl_3$ as otherwise noted, using TMS as internal standard. All signals of carbons were identified by DEPT, 2D ^{1}H and ^{13}C correlation, and ^{1}H and ^{13}C long range correlation. IR spectra were recorded on Perkin-Elmer 1680 FT spectrometer. Mass spectra were obtained on AMD 604 mass spectrometer. Column chromatography (CC) was carried out using silica gel, and the TLC were conducted on silica gel or RP-18 TLC plates.

The phenylisoserinates were prepared from sesquiterpenoid alcohols isolated from mushrooms (*Lactarius rufus*, *Lactarius vellereus*, voucher numbers 33550, and 32260 respectively, specimen deposited at the Department of Systematics and Geography of Plants of the University of Warsaw) or synthesized by transformation of natural products. The references of the procedures of isolation or preparation of all the sesquiterpenes **(a–t)** used for the preparation of esters can be found in the recent review [5]. At the top of the table structures of the acid part of the ester are presented (R = A, B, C). Esters are numbered with arabic numerals (showing position on particular scheme) in connection with small letters **(a–s)** referring to the structures of sesquiterpenes shown in Fig. 2. Compounds: **8a**, **8b**, **8c**, **8e**, **8f**, **8i**, **8l**, **8m** were prepared by the method A and their data were published [4]. Compounds: **15b**, **15d**, **15g**, **15h**, **15p** were prepa-

red by the method B and their data were published [7]. Compounds: **21h**, **21o** were prepared by the method C and their data were published [8].

General procedure for the synthesis of analogues of Taxotere® (Method B). The sesquiterpenoid alcohols (**a–s**, 1 mmole) and the acid **12** (1.2 mmole) were dissolved in toluene (25 ml) and DCC (1.4 mmole) and DMAP (0.15 mmole) were added. The reaction was carried out at r.t. and was monitored by TLC. When the reaction was completed (5–20 hrs) the contents of the flask were filtered, the solution evaporated and the residue purified by chromatography to give the desired esters **(13a–13s)**. The esters (**13a–13s**, 200 mg) dissolved in MeOH (3 ml) were treated with powdered zinc (1 g) and concentrated AcOH (0.5 ml). The reaction was carried out at r.t. until ester disappeared (TLC, CH_2Cl_2:iPrOH, 98:2), what took place in about 0.5 h. Subsequently, the excess of zinc was filtered off and the filtrate was diluted with water, extracted with methylene chloride and the extract was washed with aqueous $NaHCO_3$ solution. The aqueous phase was made alkaline with $NaHCO_3$ solution and extracted with methylene chloride. Combined methylene chloride extracts were dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography (CH_2Cl_2:iPrOH gradient) to give pure amines **(14a–14s)**, which were immediately acylated. Amine (1 mmole) dissolved in diethyl ether (5 ml) was treated with Boc_2O (5 mmoles). Reaction was carried out at r.t. until the amine disappeared (TLC, CH_2Cl_2:iPrOH 98:2), which took place within 5–20 hrs. Subsequently, the reaction mixture was evaporated and the residue was purified by column chromatography to give pure **15a–15s**.

General procedure for preparation of N-acetylphenylisoserinates (Method C). Sesquiterpenoid alcohol **(a–s)** (2 mmol), the acid **18** (0.852 g, 2.40 mmol), DMAP (0.035 g, 0.28 mmol) and DCC (0.650 g, 3.60 mmol) was dissolved in methylene chloride (50 ml). The reaction mixture was stirred during 15 min, and the N,N-dicyclohexyl urea formed during the reaction was filtered off. The filtrate was concentrated *in vacuo*, and the product **(19a–19s)** was isolated by filtration through silica-gel in dichloromethane/diethyl ether 93:7. An ester **(19a–19s)** (0.65 mmole) was dissolved in methanol (10 ml), and the resulting solution was treated with palladium 10% charcoal catalyst (30 mg). The ester was deprotected with stoichiometric amount of hydrogen at atmospheric pressure and room temperature. The reaction was followed by TLC. The catalyst was filtered off and the filtrate evaporated on rot.vap. leaving a residue which was dissolved in dichloromethane (25 ml). To the resulting solution, ground sodium hydrogencarbonate was added to form a thick suspension and subsequently to the reaction mixture acetic anhydride was added (0.105 ml, 0.85 mmol) while stirring. After 10 min the reaction mixture was treated with water (50 ml) and the product was extracted with dichloromethane (3×50 ml). The extract was dried over anhydrous $MgSO_4$, which was filtered off, and the filtrate evaporated *in vacuo* leaving a residue, from which the N-acetylphenylisoserinates **(21a–21s)** were isolated by column chromatography in solvents indicated separately for each compound.

2-(13-Isovellerolyl) 4-(2,2,2-trichloroethyl)-(2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13a). Compound **(13a)** was prepared from isovellerol **(a)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/Et_2O (93:7) solvent system. Yield 36%; Oil. $[\alpha]_D^{20}$ –4.9 (*c* 1.05, $CHCl_3$). IR (film): ν_{max} = 3432, 2935, 2865, 1723 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3H), 1.02 (s, 3H), 1.26 (s, 3H), 1.27–1.40 (m, 4H), 1.55–1.85 (m, 9H), 1.95 (br d, *J* = 11.1 Hz, 1H), 2.35–2.49 (m, 2H), 2.49–2.55 (m, 2H, H), 4.45–4.80 (m, 3H), 4.85 (d, *J* = 12.1 Hz, 1H), 5.18 (d, *J* = 12.1 Hz, 1H), 5.33 (d, *J* = 3.9 Hz, 1H), 5.40 (s, 1H), 7.30–7.40 (m, 5H), 9.52 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.81, 23.24, 24.52, 30.69, 31.53, 31.68, 32.94, 34.75, 35.59, 37.08, 37.38, 38.26, 42.39, 44.83, 47.57, 63.36, 67.85, 74.56, 81.66, 94.97, 99.06, 126.28, 127.77, 128.62, 130.20, 131.44, 140.35, 150.27, 170.06, 199.99. HRMS (ESI): calcd. for $C_{33}H_{40}NO_6Cl_3Na$ $[M+Na]^+$ 674.1813, found 674.1829.

Isovellerol 13-[N-(*tert*-butoxycarbonyl)-(2*R*,3*S*)-3-phenylisoserinate] (15a). Compound **15a** was prepared by the general method B. The reduction of **13a** gave the amine **14a** which was not isolated and upon acylation gave **15a** which was purified by chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (45:45:10) solvent system. Yield 40%; Oil. $[\alpha]_D^{20}$ +12.7 (*c* 0.90, EtOH). IR (film): ν_{max} = 3440, 3387, 2866, 2953, 1708, 1497 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.01 (s, 3H), 1.02 (s, 3H), 1.20–1.27 (m, 1H), 1.29 (s, 3H), 1.41 (br s, 9H), 1.36–1.43 (m, 2H), 1.65 (m, 1H), 1.81 (dd, *J* = 13.2, 8.0 Hz, 1H), 1.87 (d, *J* = 4.4 Hz, 1H), 2.50–2.57 (m, 2H), 4.41 (br s, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 5.11 (d, *J* = 8.4 Hz, 1H), 5.30 (d, *J* = 12.0 Hz, 1H), 5.39 (s, 1H), 5.40–5.45 (m, 1H), 7.26–7.35 (m, 5H), 9.47 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.97, 28.25, 30.86, 31.55, 31.69, 35.49, 36.98, 37.38, 38.29, 42.50,

44.85, 47.56, 55.98, 68.36, 73.44, 79.76, 126.65, 127.63, 128.49, 130.10, 131.42, 39.23, 155.02, 172.45, 200.38. HRMS (ESI): calcd. for $C_{29}H_{39}NO_6Na$ $[M+Na]^+$ 520.2670, found 520.2680.

3-Benzyl 5-(8-isolactarorufinyl) (4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5R-dicarboxylate (19b). Compound **(19b)** was prepared from isolactarorufin **(b)** by esterification with the acid **18** using the general method C. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/ethyl acetate (7:3) solvent system. Yield 96%; TLC: R_f= 0.24 (hexane/ethyl acetate – 7:3); Oil. $[\alpha]_D^{20}$ –45.3 (*c* 1.02, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 3607, 2956, 1757, 1704, 1655 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (s, 3H), 1.06–1.07 (m, 4H), 1.28 (m, 1H), 1.48 (dd, *J* = 12.2, 5.8 Hz, 1H), 1.59–1.61 (m, 5H), 1.66–1.72 (m, 4H), 1.80 (s, 3H), 2.01–2.10 (m, 3H), 4.09 (d, *J* = 9.4 Hz, 1H), 4.36 (d, *J* = 9.4 Hz, 1H), 4.55 (d, *J* = 4.9 Hz, 1H), 4.90 (br s, 1H), 4.99 (br s, 1H), 5.18 (d, *J* = 4.9 Hz, 1H), 5.60 (d, *J* = 7.6 Hz, 1H), 7.23–7.31 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.22, 24.53, 26.01, 26.52, 26.83, 28.72, 31.51, 38.32, 38.93, 39.94, 45.82, 47.13, 63.63, 66.92, 70.94, 71.41, 79.22, 81.31, 97.22, 126.51, 127.61, 127.94, 128.23, 128.72, 135.81, 152.21, 170.35, 175.02. HRMS (LSIMS): calcd. for $C_{35}H_{41}NO_8Na$ $[M+Na]^+$ 626.27299, found 626.27561.

Isolactarorufin-8 [(2R,3S)-N-(acetyl)-phenylisoserinate] (21b). Compound **19b** was prepared by the method C. The hydrogenolysis of **19b** gave the amine **20b** which was not isolated, and upon acylation gave **21b** which was purified by chromatography on Si-gel using methylene chloride/isopropanol – 49:1. Yield 54%; TLC: R_f= 0.18 (methylene chloride/isopropanol – 24:1); m.p. 242–245°C. $[\alpha]_D^{20}$ +33.1 (*c* 1.12, C_5H_5N). IR (KBr): ν_{max} = 3539, 3354, 1775, 1711, 1642 cm^{-1}. ^1H NMR (500 MHz, $DMSO_{d\text{-}6}$) δ = 0.85 (s, 3 H), 0.95 (m, 1H), 0.99 (s, 3H), 1.06 (d, *J* = 6.2 Hz, 1H), 1.34 (m, 2H), 1.42 (s, 3H), 1.59 (m, 1H), 1.86 (s, 3H), 1.87 (d, *J* = 6.2 Hz, 1H), 2.00 (m, 1H), 2.11 (m, 1H), 4.01 (d, *J* = 9.2 Hz, 1H), 4.03 (d, *J* = 9.2 Hz, 1H), 4.35 (dd, *J* = 4.2, 6.4 Hz, 1H), 4.88 (s, 1H), 5.23 (dd, *J* = 4.2, 9.2 Hz, 1H), 5.46 (d, *J* = 9.0 Hz, 1H), 5.68 (d, *J* = 6.4 Hz, 1H), 7.22–7.34 (m, 5H), 8.30 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (125 MHz, $DMSO_{d\text{-}6}$): δ = 17.44, 22.61, 23.52, 26.51, 28.83, 31.02, 37.81, 38.02, 39.34, 39.71, 45.75, 46.42, 54.91, 69.83, 70.32, 73.62, 77.81, 126.92, 127.21, 128.04, 140.31, 168.73, 172.02, 174.72. HRMS (LSIMS): calcd. for $C_{26}H_{33}NO_7Na$ $[M+Na]^+$ 494.21547, found 494.21785.

2-(8-*Epi*-isolactarorufinyl) 4-(2,2,2-trichloroethyl)-(2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13c). Compound **(13c)** was prepared from 8-*epi*-isolactarorufin **(c)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (67.5:22.5:10) solvent system. Yield 80%; Oil. $[\alpha]_D^{20}$ +45.8 (*c* 1.70, CH_2Cl_2). IR ($CHCl_3$): ν_{max} = 3552, 2956, 1771, 1717 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.95 (s, 3H), 1.07 (s, 3H), 1.15 (d, *J* = 6.4 Hz, 1H), 1.21 (t, *J* = 11.8 Hz, 1H), 1.24–1.30 (m, 2H), 1.47–1.55 (m, 2H), 1.60 (d, *J* = 6.4 Hz, 1H), 1.61 (s, 3H), 1.68–1.78 (m, 6H), 2.00–2.11 (m, 2H), 2.28–2.37 (m, 2H), 2.58–2.70 (m, 1H), 3.96 (d, *J* = 9.2 Hz, 1H), 4.12 (d, *J* = 9.2 Hz, 1H), 4.35–4.77 (m, 3H), 5.19 (d, *J* = 7.2 Hz, 1H), 5.79 (d, *J* = 4.6 Hz, 1H), 7.26–7.36 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.36, 22.80, 23.27, 24.47, 24.91, 26.46, 28.82, 31.96, 33.65, 33.91, 35.03, 37.75, 37.87, 39.85, 42.31, 44.33, 63.93, 67.99, 69.23, 70.63, 74.71, 81.22, 93.45, 99.06, 126.37, 128.25, 128.93, 150.44, 168.35, 173.64. HRMS (ESI): calcd. for $C_{33}H_{40}NO_8Cl_3Na$ $[M+Na]^+$ 706.1712, found 706.1728.

8-*Epi*-isolactarorufin-8 [(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15c). Compound **15c** was prepared by the method B. The reduction of **13c** gave the amine **14c** which was not isolated, and upon acylation gave **15c** which was purified by chromatography on Si-gel using CH_2Cl_2-iPrOH (49:1). Yield 66%; Oil. $[\alpha]_D^{20}$ +56.2 (*c* 1.0, EtOH). IR ($CHCl_3$): ν_{max} = 3453, 3340, 2959, 1771, 1736, 1714 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.92 (s, 3H), 1.07 (d, *J* = 6.3 Hz, 1H), 1.14 (s, 3H), 1.17 (t, *J* = 12.0 Hz, 1H), 1.26 (s, 3H), 1.26–1.42 (m, 2H), 1.42 (s, 9H), 1.48 (d, *J* = 6.3 Hz, 1H), 1.60 (t, *J* = 12.3 Hz, 1H), 1.94 (dt, *J* = 11.7, 7.6 Hz, 1H), 2.20–2.26 (m, 1H), 3.77 (d, *J* = 9.4 Hz, 1H), 3.99 (d, *J* = 9.4 Hz, 1H), 4.69 (br s, 1H), 5.26 (d, *J* = 9.3 Hz, 1H), 5.63 (d, *J* = 4.1 Hz, 1H), 6.36 (d, *J* = 9.3 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.31–7.40 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.29, 25.23, 26.51, 28.34, 29.30, 32.10, 34.51, 37.85, 37.69, 39.86, 42.03, 44.34, 55.76, 68.13, 70.06, 70.47, 74.20, 79.64, 126.66, 127.57, 128.46, 139.15, 155.21, 172.27, 174.23. HRMS (ESI): calcd. for $C_{29}H_{39}NO_8Na$ $[M+Na]^+$ 552.2568, found 552.2574.

3-Benzyl 8-(2,3-*anhydro*-isolactarorufin)-5-[(4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5-dicarboxylate] (19d). Compound **(19d)** was prepared from 2,3-anhydro-isolactarorufin **(d)** by esterification with the acid **18** using the general method C. Final purification of the compound was

achieved by column chromatography on Si-gel using hexane/ethyl acetate (9:1) solvent system. Yield 90%; TLC: R_f = 0.35 (hexane/ethyl acetate – 7:3); Oil. $[\alpha]_D^{20}$ –31.2 (*c* 1.08, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 2958, 1769, 1704 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96 (s, 3H), 1.06 (s, 3H), 1.23 (t, *J* = 11.3 Hz, 1H), 1.30 (d, *J* = 5.1 Hz, 1H), 1.62–1.69 (m, 3H), 1.73 (s, 3H), 1.77 (d, *J* = 5.1 Hz, 1H), 1.81 (s, 3H), 2.01 (br s, 3H), 2.49 (m, 1H), 4.16 (d, *J* = 9.7 Hz, 1H), 4.38 (d, *J* = 9.7 Hz, 1H), 4.59 (d, *J* = 4.8 Hz, 1H), 4.92 (br s, 1H), 5.00 (br s, 1H), 5.09 (d, *J* = 9.2 Hz, 1H), 5.21 (d, *J* = 4.8 Hz, 1H), 7.23–7.32 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.31, 23.92, 26.14, 26.62, 28.41, 29.52, 33.63, 34.42, 37.51, 41.92, 43.91, 45.94, 63.72, 67.01, 71.42, 77.81, 81.22, 97.23, 120.93, 126.52, 127.71, 127.92, 128.31, 128.72, 134.21, 135.84, 152.21, 170.70, 173.41. HRMS (LSIMS): calcd. for $C_{35}H_{39}NO_7Na$ $[M+Na]^+$ 608.26242, found 608.26182.

2,3-Anhydro-isolactarorufin-8-[(2R,3S)-N-(acetyl)-phenylisoserinate] (21d). Compound **21d** was prepared by the method C. The hydrogenolysis of **19d** gave the amine **20d** which was not isolated, and upon acylation gave **21d** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH – 49:1. Yield 54%; TLC: R_f = 0.33 (CH_2Cl_2/iPrOH – 24:1); m.p. 216–218°C. $[\alpha]_D^{20}$ +22.7 (*c* 1.02, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 3435, 1770, 1734, 1680 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3H), 1.07 (s, 3H), 1.25 (dd, *J* = 12.0, 11.6 Hz, 1H), 1.35 (d, *J* = 5.1 Hz, 1H), 1.72 (dd, *J* = 12.0 7.2 Hz, 1H), 1.87 (d, *J* = 5.1 Hz, 1H), 2.01 (s, 3H), 2.02 (br s, 3H), 2.08 (m, 2H), 2.57 (m, 1H), 3.38 (br s, 1H), 4.14 (d, *J* = 9.6 Hz, 1H), 4.32 (d, *J* = 9.6 Hz, 1H), 4.58 (d, *J* = 2.6 Hz, 1H), 5.10 (d, *J* = 9.3 Hz, 1H), 5.52 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.32 (d, *J* = 9.0 Hz, 1H), 7.29–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.36, 23.32, 24.01, 28.43, 29.63, 33.62, 34.41, 37.56, 42.12, 44.01, 45.52, 54.73, 71.42, 73.53, 78.81, 120.73, 127.03, 128.14, 128.85, 134.62, 138.61, 169.42, 173.13, 173.51. HRMS (LSIMS): calcd. for $C_{26}H_{31}NO_6Na$ $[M+Na]^+$ 476.20491, found 476.20315.

3-Benzyl 5-(furanoyl)-8 (4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5-dicarboxylate (19e). Compound **19e** was prepared from **(e)** according to the general procedure (Method C). The reaction product was purified by chromatography on Si-gel using hexane/ethyl acetate – (9:1) solvent system. Yield 83%; TLC: R_f = 0.44 (hexane/ethyl acetate – 7:3); oil; $[\alpha]_D^{20}$ –20.4 (*c* 1.08, $CHCl_3$). IR ($CHCl_3$) ν/cm^{-1}: 2956, 1740, 1704. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 0.90 s, 3H (H-15); 1.08 s, 3H (H-14); 1.23 dd, 1H, *J*(10β,10α) = 13.0, *J*(10β,9α) = 9.0 (H-10β); 1.74 br s, 6H (H-12, H-5′); 1.79 s, 3H (H-6′); 1.88 dd, 1H, *J*(10α,10β) = 13.0, *J*(10α,9α) = 7.5 (H-10α); 2.01 d, 1H, *J*(1a,1b) = 14.8 (H-1a); 2.17 d, 1H, *J*(1b,1a) = 14.8 (H-1b); 2.92 d, 1H, *J*(4a,4b) = 16.3 (H-4a); 3.18 m, 1H (H-9α); 3.41 d, 1H, *J*(4b,4a) = 16.3 (H-4b); 4.62 d, 1H, *J*(2′,3′) = 5.0 (H-2′); 4.90 br s, 1H (PhC$\underline{H}_2$O-); 4.99 br s, 1H (PhC$\underline{H}_2$O–); 5.22 br s, 1H (H-3′); 5.73 d, 1H, *J*(8β,9α) = 9.9 (H-8β); 7.12 br s, 1H (H-5); 7.22 br s, 1H (H-13); 7.24–7.33 m, 10H (Ar). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C: 22.4 (C-12), 26.2 (C-5′), 26.4 (C-6′), 27.5 (C-15), 28.2 (C-14), 28.9 (C-4), 37.5 (C-11), 44.2 (C-9), 45.5 (C-10), 46.0 (C-1), 63.8 (C-3′), 66.9 (Ph$\underline{C}H_2$O–), 75.0 (C-8), 81.0 (C-2′), 97.3 (C-4′),121.2 (C-6), 124.6 (C-7), 126.6, 127.8, 127.9, 128.1, 128.8 (Ar), 130.9, 135.9 (C-2, C-3), 137.5 (Ar), 138.1 (C-5), 142.1 (C-13), 152.1 (C-7′), 169.5 (C-1′); MS (LSIMS, HR) *m/z*: $[M+Na]^+$ calc. for $C_{35}H_{39}NO_6Na$ 592.26751, found 592.26696.

Furanol-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15e). Compound **15e** was prepared by the method C. The reduction of **19e** gave the amine **20e** which was not isolated, and upon acylation gave **15e** which was purified by chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (9:9:1). Yield 44%; Oil. $[\alpha]_D^{20}$ +21.8 (*c* 1.04, EtOH). IR (film): ν_{max} = 3438, 2953, 1722 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (s, 3H), 1.10 (s, 3H), 1.35–1.40 (m, 1H), 1.42 (br s, 9H), 1.76 (s, 3H), 1.91–1.99 (m, 1H), 2.05 (d, *J* = 15.0 Hz, 1H), 2.19 (d, *J* = 15.0 Hz, 1H), 2.90 (d, *J* = 15.9 Hz, 1H), 3.32 (dt, *J* = 10.1, 8.3 Hz, 1H), 3.44 (d. *J* = 15.9 Hz, 1H), 4.43 (br s, 1H), 5.21 (d, *J* = 8.6 Hz, 1H), 5.49 (d, *J* = 8.6 Hz, 1H), 5.79 (d, *J* = 11.0 Hz, 1H), 7.14 (br s, 1H), 7.26 (br s, 1H), 7.28 (tt, *J* = 7.1, 1.5 Hz, 1H), 7.32–7.39 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.52, 27.45, 28.38, 28.73, 29.40, 37.74, 44.40, 45.90, 45.97, 55.88, 74.11, 74.73, 79.82, 121.64, 123.99, 126.59, 127.64, 128.57, 130.33, 136.05, 137.71, 139.69, 142.17, 155.03, 172.75. HRMS (ESI): calcd. for $C_{29}H_{37}NO_6Na$ $[M+Na]^+$ 518.2513, found 518.2525.

3-Benzyl 5-(8-furandiolyl) (4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5-dicarboxylate (19f). Compound **(19f)** was prepared from furandiol **(f)** by esterification with the acid **18** using the general method C. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/acetone (7:3) solvent system. Yield 87%; TLC: R_f = 0.48 (hexane/acetone – 7:3); Oil. $[\alpha]_D^{20}$ –39.2 (*c* 1.06, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 3567, 2956, 1751, 1703 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 3H), 1.08 (s, 3H), 1.26 (s, 3H), 1.36 (dd, *J* = 13.5, 4.0 Hz, 1H), 1.47 (dd, *J* = 13.5, 6.9 Hz, 1H), 1.58

(m, 2H), 1.66 (s, 3H), 1.79 (s, 3H), 2.38 (m, 1H), 2.49 (m, 1H), 2.59 (d, J = 15.3 Hz, 1H), 2.83 (dd, J = 15.3, 1.1 Hz, 1H), 4.60 (d, J = 5.0 Hz, 1H), 4.90 (br s, 1H), 4.98 (br s, 1H), 5.27 (br s, 1H), 6.01 (d, J = 6.9 Hz, 1H), 7.17 (s, 1H), 7.22 (s, 1H), 7.24–7.32 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.84, 26.43, 30.65, 31.22, 31.11, 32.54, 35.53, 43.22, 43.81, 44.52, 53.31, 63.33, 66.81, 70.72, 71.71, 81.32, 97.42, 118.35, 124.33, 126.41, 127.8, 128.23, 128.72, 135.84, 140.01, 141.73, 152.24, 168.81. HRMS (LSIMS): calcd. for $C_{35}H_{41}NO_7Na$ $[M+Na]^+$ 610.27807, found 610.27664.

2-(8-Furandiol) 4-(2,2,2-trichloroethyl) (2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4-dicarboxylate (13f). Compound **13f** was prepared from **(f)** according to the general procedure (Method B). The reaction product was purified by chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (47.5:47.5:5). Yield 77%. $[\alpha]_D^{20}$ –13.3 (c 0.65, EtOH). UV (EtOH) λ_{max} 209 nm; ε_{max} 14988. IR (film) ν_{max}: 2936, 2868, 1758, 1722 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.06 (s, 3H); 1.10 (s, 3H); 1.28 (s, 3H); 1.22–1.30 (m, 1H)5); 1.44 (dd, J = 13.5, 3.2 Hz, 1H); 1.53 (dd, J = 13.5, 6.6 Hz, 1H); 1.57–1.65 (m, 2H); 1.65–1.80 (m, 6H); 1.98 (br d, J = 12.9 Hz); 2.35–2.42 (m, 1H); 2.42–2.49 (m, 2H); 2.52 (m, 1H); 2.60 (d, J = 15.2 Hz, 1H); 2.84 (dd, J = 15.2, 1.4 Hz, 1H); 4.35–4.72 (m, 3H); 5.40 (d, J = 4.3 Hz, 1H); 6.03 (d, J = 9.9 Hz, 1H); 7.15 (s, 1H); 7.25 (s, 1H); 7.26–7.40 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.13, 23.29, 24.56, 30.64, 31.54, 32.58, 33.14, 34.76, 35.50, 43.01, 43.89, 44.66, 53.52, 63.52, 70.70, 71.65, 74.80, 81.77, 95.09, (C$(CH_2)_5$); 99.36 (CCl_3); 118.32 and 124.58 (C6 and C7); 126.34, 128.02, 128.80, 139.58, 140.35, 141.90, 150.49, 169.10. ESI (MeOH) m/z: 690 $(M+Na)^+$; HR-MS 690.1763 calc. for $C_{33}H_{40}NO_7NaCl_3$, found: 690.1804.

Furandiol-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (13f). Compound **15f** was prepared by the method B. The reduction of **13f** gave the amine **14f** which was not isolated, and upon acylation with $(BOC)_2$ gave **15f** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (49:1) solvent system. Yield 42%. Oil. $[\alpha]_D^{20}$ +12.4 (c 0.91, EtOH). IR (film): ν_{max} = 3437, 2955, 2871, 1721 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 3H), 1.10 (s, 3H), 1.30 (s, 3H), 1.42 (br s, 9H), 1.52 (dd, J = 12.8, 6.7 Hz, 1H), 1.53–1.59 (m, 2H), 1.64 (dd, J = 12.6, 7.0 Hz, 1H), 2.40–2.50 (m, 1H), 2.55–2.63 (m, 1H), 2.63 (d, J = 15.4 Hz, 1H), 2.85 (dd, J = 15.4, 1.4 Hz, 1H), 4.52 (br s, 1H), 5.25 (d, J = 8.6 Hz, 1H), 5.54 (d, J = 8.6 Hz, 1H), 6.05 (dd, J = 9.4, 0.7 Hz, 1H), 7.13 (br s, 1H), 7.25 (br s, 1H), 7.29 (tt, J = 7.2, 1.3 Hz, 1H), 7.33–7.41 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.38, 30.83, 31.07, 31.28, 32.54, 35.54, 43.49, 43.64, 44.31, 53.09, 55.94, 71.80, 71.89, 73.87, 80.01, 118.61, 124.26, 126.70, 127.77, 128.62, 139.38, 140.11, 141.85, 155.18, 171.80. HRMS (ESI): calcd. for $C_{29}H_{39}NO_7Na$ $[M+Na]^+$ 536.2619, found 536.2634.

2-(8-*O*-Ethylfurandiolyl) 4-(2,2,2-trichloroethyl)-(2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13i). Compound **(13i)** was prepared from 3-*O*-ethylfurandiol **(i)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (78.4:19.6:2) solvent system. Yield 84%; Oil; $[\alpha]_D^{20}$ –20.9 (c 1.00, EtOH). IR (film): ν_{max} = 2936, 2868, 1759, 1723 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, J = 6.9 Hz, 3H), 1.07 (s, 3H), 1.12 (s, 3H), 1.20 (s, 3H), 1.24–1.35 (m, 1H), 1.42–1.53 (m, 2H), 1.58 (dd, J = 12.4, 6.5 Hz, 1H), 1.67 (m, 1H), 1.68–1.87 (m, 6H), 1.99 (br d, J = 12.4 Hz, 1H), 2.38 (dt, J = 12.8, 6.1 Hz, 1H), 2.46 (m, 2H), 2.58 (dd, J = 15.3, 1.1 Hz, 1H), 2.55–2.61 (m, 1H), 2.76 (d, J = 15.3 Hz, 1H), 3.30 (dq, J = 8.5, 6.9 Hz, 1H), 3.38 (dq, J = 8.5, 6.9 Hz, 1H), 4.39 (d, J = 11.3 Hz, 1H), 4.63 (br s, 1H), 4.72 (d, J = 11.3 Hz, 1H), 5.42 (d, J = 4.2 Hz, 1H), 6.00 (d, J = 11.2 Hz, 1H), 7.02 (s, J = 1H), 7.14 (t, J = 1.2 Hz, 1H), 7.26–7.40 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.74, 23.19, 23.33, 24.57, 25.48, 29.00, 32.07, 32.61, 33.16, 34.86, 34.92, 41.70, 43.58, 44.52, 52.47, 55.67, 63.72, 71.15, 74.64, 75.51, 81.89, 95.13, 99.45, 119.35, 125.56, 126.28, 127.95, 128.79, 137.80, 140.31, 140.52, 150.52, 169.43. HRMS (ESI): calcd for $C_{35}H_{44}NO_7Cl_3Na$ $[M+Na]^+$ 718.2076, found 718.2064.

3-O-Ethylfurandiol-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15i). Compound **15i** was prepared by the method B. The reduction of **13i** gave the amine **14i** which was not isolated, and upon acylation gave **15i** which was purified by chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (45:45:10). Yield 34%. Oil. $[\alpha]_D^{20}$ +8.2 (c 0.97, EtOH). IR (film): ν_{max} = 3440, 2953, 1722 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, J = 6.9 Hz, 3H), 1.06 (s, 3H), 1.13 (s, 3H), 1.21 (s, 3H), 1.42 (br s, 9H), 1.47–1.68 (m, 4H), 2.37–2.45 (m, 1H), 2.60 (dd, J = 15.4, 1.4 Hz, 1H), 2.60–2.66 (m, 1H), 2.77 (d, J = 15.4 Hz, 1H), 3.30 (dq, J = 8.5, 7.0 Hz, 1H), 3.40 (dq, J = 8.5, 7.0 Hz, 1H), 4.53 (br s, 1H), 5.25 (d, J = 8.6 Hz, 1H), 5.58 (d, J = 8.6 Hz, 1H), 6.04 (dd, J = 11.0, 1.0 Hz, 1H), 6.97 (t, J = 1.4 Hz, 1H), 7.15 (br s, 1H), 7.29 (tt, J = 7.2, 1.3 Hz, 1H), 7.34–7.42 (m,4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.70, 25.54, 28.40, 29.00,

31.93, 32.34, 34.94, 42.05, 43.03, 44.31, 52.14, 55.70, 55.95, 72.25, 73.89, 75.53, 79.80, 119.42, 125.38, 126.66, 127.68, 128.58, 138.13, 139.65, 140.38, 154.98, 171.97. HRMS (ESI): calcd for $C_{31}H_{43}NO_7Na$ $[M+Na]^+$ 564.2932, found 564.2917.

3-Benzyl 5-(8-*O*-ethylfurandiolyl) (4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5-dicarboxylate (19i). Compound **(19i)** was prepared from 3-*O*-ethylfurandiol **(i)** by esterification with the acid **18** using the general method C. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/acetone (7:3) solvent system. Yield 88%. TLC: R_f = 0.45 (hexane/ethyl acetate 4:1). Oil. $[\alpha]_D^{20}$ –30.5 (*c* 1.09, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 2951, 1756, 1709 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 6.9 Hz, 3H), 1.04 (s, 3H), 1.10 (s, 3H), 1.19 (s, 3H), 1.39 (d, *J* = 13.6 Hz, 1H), 1.47 (dd, *J* = 13.6, 6.4 Hz, 1H), 1.55 (dd, *J* = 12.4, 6.4 Hz, 1H), 1.66 (t, *J* = 12.4 Hz, 1H,), 1.76 (s, 3H), 1.80 (s,1H), 2.35 (m, 1H), 2.54 (m, 1H), 2.57 (dd, *J* = 15.4, 1.4 Hz, 1H), 2.74 (d,*J* = 15.4 Hz, 1H), 3.28 (m, 1H), 3.35 (m, 1H), 4.62 (d,*J* = 5.3 Hz, 1H), 4.91 (br s, 1H), 4.99 (br s, 1H), 5.30 (br s, 1H), 5.99 (dd, *J* = 11.4, 1.4 Hz, 1H), 7.02 (s, 1H), 7.12 (t, *J* = 1.4 Hz, 1H), 7.25–7.32 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.72, 25.53, 26.22, 26.51, 29.01, 32.01, 32.62, 34.92, 41.73, 43.42, 44.42, 52.41, 55.63, 63.52, 66.91, 71.23, 75.44, 81.62 , 97.11, 119.32, 125.83, 126.42, 127.81, 127.92, 128.01, 128.21, 128.72, 135.91, 137.92, 140.21, 152.31, 169.12. HRMS (LSIMS): calcd. for $C_{37}H_{45}NO_7Na$ $[M+Na]^+$ 638.30937, found 638.56392.

3-O-Ethylfurandiol-8-[(2R,3S)-N-acetyl-phenylisoserinate] (21i). Compound **21i** was prepared by the method C. The hydrogenolysis of **19i** gave the amine **20i** which was not isolated, and upon acetylation gave **21i** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (99:1). Yield 25%. TLC: R_f = 0.41 (CH_2Cl_2/iPrOH, 24:1). Oil $[\alpha]_D^{20}$ –3.2 (*c* 0.96, $CHCl_3$). IR ($CHCl_3$):ν_{max} = 2956, 1732, 1682 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 0.91 (t,*J* = 6.9 Hz, 3H), 1.04 (s, 3H), 1.08 (s, 3H), 1.19 (s, 3H), 1.35 (dd,*J* = 13.9, 2.8 Hz, 1H), 1.48 (dd,*J* = 13.9, 6.8 Hz, 1H), 1.60 (m, 2H), 1.95 (s, 3H), 2.40 (m, 1H), 2.58 (m, 2H), 2.76 (d,*J* = 15.5Hz, 1H), 3.29 (m, 1H), 3.37 (m, 1H), 3.66 (br s, 1H), 4.53 (d, *J* = 2.5 Hz, 1H), 5.53 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.00 (d, *J* = 10.7 Hz, 1H), 6.75 (br s, 1H), 6.96 (br s, 1H), 7.13 (br s, 1H), 7.26–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.62, 23.18, 25.46, 28.91, 31.72, 32.16, 34.92, 42.04, 43.03, 44.15, 52.03, 54.64, 55.71, 72.02, 73.63, 75.71, 119.42, 125.21, 126.92, 127.71, 128.54, 138.31, 138.8, 140.32, 169.41, 171.93. HRMS (LSIMS): calcd. for $C_{28}H_{37}NO_6Na$ $[M+Na]^+$ 506.25186, found 506.25301.

2-(3-*O*-Ethyl-8-*epi*-9-*epi*-furandiolyl)-8 4-(2,2,2-trichloroethyl)-(2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13j). Compound **(13j)** was prepared from 8-*epi*-9-*epi*-3-O-ethylfurandiol **(j)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (78.4:19.6:2) solvent system. Yield 97%. Oil. $[\alpha]_D^{20}$ +0.7 (*c* 1.04, EtOH). IR (film) ν_{max} = 2939, 2866, 1723 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.97 (s, 3H), 0.98 (s, 3H), 1.05 (s, 3H), 1.16 (t, *J* = 6.9 Hz, 3H), 1.20–1.30 (m, 1H), 1.37 (dd,*J* = 12.5, 10.6 Hz, 1H), 1.50 (dd, *J* = 13.4, 10.9 Hz, 1H), 1.66 (dd, *J*= 12.5, 7.1 Hz, 1H), 1.73 (dd,*J* = 13.4, 8.3 Hz, 1H), 1.68–1.85 (m, 6H), 1.99 (br d, *J* = 13.3 Hz, 1H), 2.12 (dq, *J* = 10.6, 7.1 Hz, 1H), 2.31 (td,*J* = 10.9, 8.3 Hz, 1H), 2.36–2.53 (m, 2H), 2.68 (s, 2H), 3.47 (m, 2H), 4.42–4.82 (m, 3H), 5.39 (d,*J* = 4.3 Hz, 1H), 5.82 (d, *J* = 10.3 Hz, 1H), 7.06 (s, 1H), 7.18 (s, 1H), 7.28–7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.09, 18.56, 23.26, 24.52, 30.98, 31.15, 33.10, 34.58, 34.73, 34.75, 43.19, 46.22, 46.24, 52.05, 55.91, 63.68, 74.58, 75.94, 76.83, 81.66, 94.99, 99.36, 119.38, 125.02, 126.43, 128.02, 128.76, 138.15, 139.36, 140.67, 169.50, 170.82. HRMS (ESI): calcd. for $C_{35}H_{44}NO_7Cl_3Na$ $[M+Na]^+$ 718.2076, found 718.2081.

3-O-Ethyl-8-*epi*-9-*epi*-furandiol-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15j). Compound **15j** was prepared by the method B. The reduction of **13j** gave the amine **14j** which was not isolated, and upon acylation gave **15j** which was purified by chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (47.5:47.5:6). Yield 72%. Oil. $[\alpha]_D^{20}$ +27.3 (*c* 0.89, EtOH). IR (film): ν_{max} = 3442, 2952, 2868, 1716 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.97 (s, 3H), 1.01 (s, 3H, H), 1.06 (s, 3H), 1.16 (t, *J* = 6.9 Hz, 3H), 1.27–1.34 (m, 1H), 1.42 (br s, 9H), 1.54 (dd,*J* = 13.5, 11.0 Hz, 1H), 1.67 (dd, *J* = 12.3, 6.6 Hz, 1H), 1.76 (dd,*J* = 13.5, 8.3 Hz, 1H), 2.19 (dq,*J* = 10.8, 6.6 Hz, 1H), 2.31 (m, 1H), 2.66 (d,*J* = 13.8 Hz, 1H), 2.73 (d,*J* = 13.8 Hz, 1H), 3.48 (m, 2H), 4.52 (br s, 1H), 5.33 (d,*J* = 8.8 Hz, 1H), 5.52 (d, *J* = 8.8 Hz, 1H), 5.81 (d, *J* = 10.2 Hz, 1H), 7.17 (s, 1H), 7.25 (s, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.40–7.44 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.13, 18.33, 28.27, 31.14, 31.44, 34.28, 35.04, 43.39, 46.34, 46.51, 52.31, 55.67, 55.89, 73.79, 76.84, 77.28, 80.26, 119.01, 124.23, 126.68, 127.77,

128.65, 138.84, 140.64, 155.18, 172.24. HRMS (ESI): calcd. for $C_{31}H_{43}NO_7Na$ $[M+Na]^+$ 564.2932, found 564.2922.

2-(3,4-Anhydro-lactarorufinyl A)-8 4-(2,2,2-trichloroethyl) (2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13k). Compound **(13k)** was prepared from 3,4-anhydrolactarorufin A **(k)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (72:18:10) solvent system. Yield 65%. Oil. $[\alpha]_D^{20}$ –93.0 (*c* 1.22, CH_2Cl_2). IR (film): ν_{max} = 2938, 2867, 1762, 1721 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 3H), 1.08 (s, 3H), 1.20–1.37 (m, 1H), 1.47 (dd, *J* = 13.6, 4.8 Hz, 1H), 1.55 (t, *J* = 12.1 Hz, 1H), 1.65–1.80 (m, 7H), 1.94 (s, 3H), 1.96–1.99 (m, 2H), 2.38–2.55 (m, 2H), 2.61 (m, 1H), 2.84 (dt, *J* = 12.3, 6.7 Hz, 1H), 4.55–4.87 (m, 5H), 5.33 (d, *J* = 4.7 Hz, 1H), 5.70 (d, *J* = 8.8 Hz, 1H), 6.01 (s, 1H), 7.28–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.28, 24.49, 26.36, 30.86, 31.50, 33.30, 34.62, 37.22, 43.87, 45.25, 48.08, 48.33, 63.65, 69.36, 71.24, 74.58, 81.54, 95.01, 99.74, 112.89, 123.67, 126.25, 128.18, 128.87, 135.55, 148.56, 150.48, 153.88, 169.73, 172.90. HRMS (ESI): calcd. for $C_{33}H_{38}NO_7Cl_3Na$ $[M+Na]^+$ 688.1606, found 688.1627.

3,4-Anhydro-lactarorufin A-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15k). Compound **15k** was prepared by the method B. The reduction of **13k** gave the amine **14k** which was not isolated, and upon acylation gave **15k** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (49:1). Yield 63%. Oil. $[\alpha]_D^{20}$ –43.0 (*c* 0.73, EtOH). UV (EtOH) λ_{max} 208 nm; λ_2 273 nm; ε_{max} 24698. IR (film) ν_{max}: 3436, 2955, 1751, 1497 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.05 (s, 3H, H-14 lub H-15); 1.06 (s, 3H, H-14 lub H-15); 1.42 (br s, 9H, *t*-Bu); 1.47–1.52 (m, 1H, H-10); 1.54 (t, *J* = 11.8 Hz, 1H, H-1); 1.68 (dd, *J* = 13.7, 7.2 Hz, 1H, H-10); 1.97 (s, 3H, H-12); 2.01 (dd, *J* = 11.8, 6.8 Hz, 1H, H-1); 2.66 (m, 1H, H-9); 2.89 (m, 1H, H-2); 4.52 (br s, 1H, H-2′); 4.59 (d, *J* = 18.0 Hz, 1H, H-13); 4.75 (d, *J* = 18.0 Hz, 1H, H-13); 5.19 (d, *J* = 8.6 Hz, 1H, H-3′); 5.43 (d, *J* = 8.6 Hz, 1H, NH); 5.68 (d, *J* = 8.2 Hz, 1H, H-8); 6.02 (s, 1H, H-4); 7.28–7.38 (m, 5H, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 26.38 (C12); 28.29 ($C(\underline{C}H_3)_3$); 30.72 and 31.35 (C14 and C15); 34.56 (C11); 43.37 (C10); 44.97 (C9); 48.14 (C1); 48.22 (C2); 56.22 (C3′); 69.38 (C13); 71.93 (C8); 73.90 (2′); 80.23 ($\underline{C}(CH_3)_3$); 112.73 (C4); 126.63, 127.99, 128.73 and 138.91 (Ph); 135.84, 148.97 and 153.46 (C3, C6 and C7); 155.21, 172.07 and 172.99 (3 CO). LSIMS (NBA) *m/z* 534 $(M+Na)^+$; HR-MS 534.24677 calcd. for $C_{29}H_{37}NO_7Na$, found 534.24746.

3-Benzyl 5-(3,4-anhydro-lactarorufinyl A)-8 [(4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5-dicarboxylate] (19k). Compound **(19k)** was prepared from 2,3-anhydro-lactarorufin A **(k)** by esterification with the acid **18** using the general method C. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/ethyl acetate (9:1) solvent system. Yield 87%. TLC: R_f = 0.31 (hexane/ethyl acetate – 7:3). Oil. $[\alpha]_D^{20}$ –98.7 (*c* 1.10, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 2958, 1757, 1704 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 3H), 1.05 (s, 3H), 1.42 (dd, *J* = 13.6, 4.6 Hz, 1H), 1.51 (t, *J* = 12.2 Hz, 1H), 1.65 (dd, *J* = 13.6, 7.0 Hz, 1H), 1.73 (s, 3H), 1.79 (s, 3H), 1.92 (s, 3H), 1.99 (dd, *J* = 12.2, 6.7 Hz, 1H), 2.57 (m, 1H), 2.79 (m, 1H), 4.58 (d, *J* = 5.5 Hz, 1H), 4.66 (ABq, *J* = 18.1 Hz, 2H), 4.91 (br s, 1H), 4.99 (br s, 1H), 5.20 (br s, 1H), 5.67 (d, *J* = 9.6 Hz, 1H), 5.99 (s, 1H), 7.24–7.33 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.31, 26.63, 26.82, 30.81, 31.43, 34.53, 43.81, 45.22, 48.14, 48.23, 63.71, 67.01, 69.33, 71.22, 81.14, 97.32, 112.81, 123.54, 126.42, 127.72, 127.83, 128.01, 128.21, 128.83, 135.73, 148.52, 152.12, 154.13, 169.52, 172.91. HRMS (LSIMS): calcd. for $C_{35}H_{39}NO_7Na$ $[M+Na]^+$ 608.26242, found 608.26246.

3,4-Anhydro-lactarorufin A-8-[(2R,3S)-N-acetyl-3-phenylisoserinate] (21k). Compound **21k** was prepared by the method C. The hydrogenolysis of **19k** gave the amine **20k** which was not isolated, and upon acylation gave **21k** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (197:3). Yield 55%. TLC: R_f = 0.30 (CH_2Cl_2/iPrOH, 24:1). Oil. $[\alpha]_D^{20}$ –60.5 (*c* 1.06, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 3352, 1751, 1655cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 3H), 1.05 (s, 3H), 1.39 (dd, *J* = 13.8, 5.1 Hz, 1H), 1.55 (m, 1H), 1.66 (dd, *J* = 13.8, 7.3 Hz, 1H), 1.96 (br s, 3H), 1.98 (s, 3H), 1.99 (m, 1H), 2.59 (m, 1H), 2.86 (m, 1H), 4.54 (m, 2H), 4.72 (d, *J* = 18.0 Hz, 1H), 5.47 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.64 (d, *J* = 9.5 Hz, 1H), 5.98 (s, 3H), 6.61 (d, *J* = 8.8 Hz, 1H), 7.29–7.34 (m, 5H). ^{13}C NMR (125 MHz, CDC_{l3}): δ = 23.22, 26.41, 30.63, 31.22, 34.51, 43.33, 45.02, 48.13, 54.92, 69.41, 71.84, 73.61, 112.61, 123.52, 126.91, 127.83, 128.72, 138.5, 149.01, 153.91, 169.82, 172.01, 173.12. HRMS (LSIMS): calcd. for $C_{26}H_{31}NO_6Na$ $[M+Na]^+$ 476.20491, found 476.20360.

3-Benzyl 5-(lactarorufinyl A)-8 [(4S,5R)-2,2-dimethyl-4-phenyl-1,3oxazolane-3,5-dicarboxylate] (19l). Compound **(19l)** was prepared from lactarorufin A **(l)** by esterification with the acid **18** using the general method C. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/acetone (9:1) solvent system. Yield 94%. TLC: R_f = 0.43 (hexane/acetone 4:1). Oil $[\alpha]_D^{20}$ –51.9 (*c* 0.98, $CHCl_3$). IR ($CHCl_3$): ν_{max} = 3486, 2951, 1757, 1707 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3H), 1.07 (s, 3H), 1.22 (dd, *J* = 13.0, 6.9 Hz, 1H), 1.25 (s, 3H), 1.47 (t, *J* = 12.7 Hz, 1H), 1.53 (dd, *J* = 13.0, 7.1 Hz, 1H), 1.67 (dd, *J* = 12.7, 6.9 Hz, 1H), 1.71 (s, 3H), 1.78 (s, 3H), 2.35 (br s, 1H), 2.47 (m, 1H), 2.57 (d, *J* = 17.3 Hz, 1H), 2.63–2.70 (m, 2H), 4.52 (d, *J* = 17.5 Hz, 1H), 4.58 (d, *J* = 5.5 Hz, 1H), 4.66 (d, *J* = 17.5 Hz, 1H), 4.90 (br s, 1H), 4.98 (br s, 1H), 5.18 (br s, 1H), 5.86 (d, *J* = 9.4 Hz, 1H), 7.27–7.34 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.14, 26.32, 28.81, 29.01, 30.33, 35.72, 42.61, 43.14, 44.73, 51.72, 63.51, 67.01, 69.82, 71.64, 72.01, 81.01, 97.45, 126.16, 126.42, 127.72, 127.83, 128.01, 128.22, 128.81, 135.63, 152.12, 156.53, 169.21, 173.93. HRMS (LSIMS): calcd. for $C_{35}H_{41}NO_8Na$ $[M+Na]^+$ 626.27299, found 626.27407.

Lactarorufin A-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15l). Compound **15l** was prepared by the method C. The hydrogenolysis of **19l** gave the amine **20l** which was not isolated, and upon acylation with BOC_2O gave **15l** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (49:1). Yield 47%. Oil. $[\alpha]_D^{20}$ +14.3 (*c* 0.78, EtOH). IR (film): ν_{max} = 3435, 2955, 1746 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3H), 1.07 (s, 3H), 1.15–1.21 (m, 1H), 1.28 (s, 3H), 1.30–1.37 (m, 1H), 1.43 (br s, 9H), 1.60 (dd, *J* = 12.3, 7.0 Hz, 1H), 1.67 (dd, *J* = 12.0, 7.5 Hz, 1H), 2.55–2.66 (m, 3H), 2.79 (m, 1H), 4.47–4.55 (m, 2H), 4.70 (dt, *J* = 17.3, 2.5 Hz, 1H), 5.22 (d, *J* = 9.1 Hz, 1H), 5.59 (d, *J* = 9.1 Hz, 1H), 5.66 (d, *J* = 5.2 Hz, 1H), 7.28 (tt, *J* = 7.0, 1.6 Hz, 1H), 7.32–7.38 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.61, 29.77, 28.34, 30.62, 34.94, 36.20, 42.42, 44.78, 45.13, 50.59, 56.00, 70.66, 71.69, 72.45, 73.74, 80.43, 126.71, 127.92, 128.71, 138.73, 154.04, 155.62, 172.12, 174.27. HRMS (ESI): calcd. for $C_{29}H_{39}NO_8Na$ $[M+Na]^+$ 552.2568, found 552.2556.

Lactarorufin A-8-[(2R,3S)-N-acetyl-3-phenylisoserinate] (21l). Compound **21l** was prepared by the method C. The hydrogenolysis of **19l** gave the amine **20l** which was not isolated, and upon acylation gave **21l**, which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (49:1). Yield 40%. TLC: R_f = 0.10 (CH_2Cl_2/iPrOH, 24:1); m.p. 222–224°C. $[\alpha]_D^{20}$ +9.6 (*c* 0.92, CH_3OH). IR ($CHCl_3$): ν_{max} = 2955, 2931, 1755, 1677 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ = 1.01 (s, 3H), 1.06 (s, 3H), 1.21 (dd, *J* = 7.2, 13.5 Hz, 1H), 1.23 (s, 3H), 1.47 (dd, *J* = 5.5, 13.5 Hz, 1H), 1.60 (dd, *J* = 12.5, 10.7 Hz, 1H), 1.65 (dd, *J* = 12.5, 6.7 Hz, 1H), 2.00 (s, 3H), 2.49 (m, 2H (H-2α), 2.65 (m, 2H), 4.53 (d, *J* = 17.3 Hz, 1H), 4.55 (d, *J* = 3.7 Hz, 1H), 4.80 (d, *J* = 17.3 Hz, 1H), 5.38 (d, *J* = 3.7 Hz, 1H), 5.95 (d, *J* = 10.9 Hz, 1H), 7.27–7.39 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD): δ = 22.81, 28.13, 30.12, 31.21, 36.63, 43.64, 43.71, 45.31, 56.82, 71.13, 72.41, 73.42, 74.81, 125.82, 128.33, 128.71, 129.52, 140.62, 160.71, 172.73, 173.13, 176.4. HRMS (ESI): calcd. for $C_{26}H_{33}NO_7Na$ $[M+Na]^+$ 494.2149, found 494. 2194.

2-(8-*Epi*-lactarorufinyl A)-8 4-(2,2,2-trichloroethyl) (2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13m). Compound **(13m)** was prepared from 8-*epi*-lactarorufin A **(m)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/acetone (48.5:48.5:3) solvent system. Yield 92%. Oil. $[\alpha]_D^{20}$ –28.2 (*c* 0.81, EtOH). IR (film): ν_{max} = 3475, 2935, 2862, 1757, 1727 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.95 (s, 3H), 1.03 (s, 3H), 1.08 (t, *J* = 11.9 Hz, 1H), 1.19 (dd, *J* = 12.6, 12.2 Hz, 1H), 1.49–1.53 (m, 1H), 1.56–1.62 (m, 2H), 1.65–1.83 (m, 6H), 1.97 (br d, *J* = 12.6 Hz, 1H), 2.40–2.52 (m, 2H), 2.58–2.70 (m, 2H), 2.95 (m, 1H), 4.40–4.85 (m, 5H), 5.29 (d, *J* = 3.1 Hz, 1H), 6.97 (br s, 1H), 7.28–7.40 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.32, 23.51, 24.51, 26.32, 29.06, 32.56, 33.18, 34.75, 34.94, 37.84, 42.38, 44.00, 44.68, 49.18, 63.56, 70.32, 74.05, 74.65, 81.63, 94.98, 99.37, 122.58, 126.50, 128.28, 128.91, 158.01, 169.38, 174.25. HRMS (ESI): calcd. for $C_{33}H_{40}NO_8Cl_3Na$ $[M+Na]^+$ 706.1712, found 706.1675.

8-*Epi*-lactarorufin A-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15m). Compound **15m** was prepared by the method B. The reduction of **13m** gave the amine **14m** which was not isolated, and upon acylation gave **15m** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (44:1). Yield 66%. Oil. $[\alpha]_D^{20}$ –1.9 (*c* 1.0, EtOH). IR (film): ν_{max} = 3437, 2956, 2935, 1742 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96 (s, 3H), 1.05 (s, 3H), 1.10 (t, *J* = 11.9 Hz, 1H), 1.24–1.28 (m, 1H), 1.31 (s, 3H), 1.40 (br s, 9H), 1.50–1.65 (m, 2H), 2.49 (dt, *J* = 19.2, 1.3 Hz, 1H), 2.63 (m, 1H), 2,69 (dq, *J* = 19.2, 2.9 Hz, 1H), 2.93 (m, 1H), 4.48 (br s, 1H, H), 4.81 (ABq, *J* = 17.8 Hz, 2H), 5.15 (d, *J* = 9.0 Hz, 1H), 5.38 (d, *J* =

9.0 Hz, 1H), 6.94 (br s, 1H), 7.28–7.40 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.36, 29.04, 28.25, 32.63, 35.08, 37.86, 42.49, 44.10, 44.7, 49.09, 56.02, 70.67, 73.61, 74.01, 74.83, 80.42, 122.16, 126.73, 127.98, 128.76, 138.96. HRMS (ESI): calcd for $C_{29}H_{39}NO_8Na$ $[M+Na]^+$ 552.2568, found 552.2614.

2-(3-O-Ethyllactarorufinyl A)-8 4-(2,2,2-trichloroethyl)-(2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13o). Compound **(13o)** was prepared from 3-*O*-ethyllactarorufin A **(o)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/ Et_2O (72:18:10) solvent system. Yield 79%. Oil. $[\alpha]_D^{20}$ –19.4 (*c* 0.53, EtOH). IR (film): ν_{max} = 2938, 2868, 1760, 1723 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 6.9 Hz, 3H), 1.06 (s, 3H), 1.11 (s, 3H), 1.20 (s, 3H), 1.32 (dd, *J* = 13.7, 3.5 Hz, 1H), 1.53–1.67 (m, 4H), 1.68–1.82 (m, 6H), 1.99 (br d, *J* = 12.8 Hz, 1H), 2.40–2.55 (m, 4H), 2.64–2.75 (m, 2H), 3.27 (dq, *J* = 8.6, 7.0 Hz, 1H), 3.89 (dq, *J* = 8.6, 7.0 Hz, 1H), 4.51 (dt, *J* = 17.4 Hz, 1H), 4.58 (br s, 1H), 4.65 (d, *J* = 17.4 Hz, 1H), 4.70 (d, *J* = 11.9 Hz, 2H), 5.31 (d, *J* = 4.8 Hz, 1H), 6.02 (d, *J* = 11.1 Hz, 1H), 7.28–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.91, 23.30, 24.32, 24.50, 29.76, 31.07, 31.49, 33.35, 34.71, 35.33, 41.92, 41.98, 44.11, 51.62, 56.25, 63.73, 69.11, 72.64, 74.65, 75.12, 81.55, 95.04, 99.63, 124.60, 126.29, 128.22, 128.90, 140.00, 150.41, 158.70, 169.78, 173.85. HRMS (LSIMS): calcd. for $C_{35}H_{44}NO_8Cl_3Na$ $[M+Na]^+$ 734.2025, found 734.2035.

3-*O*-Ethyl-lactarorufin A-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15o). Compound **15o** was prepared by the method B. The reduction of **13o** gave the amine **14o** which was not isolated, and upon acylation gave **15o** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (49:1). Yield 90%. Oil. $[\alpha]_D^{20}$ +16.5 (*c* 0.48, EtOH). IR (film): ν_{max} = 3439, 2955, 2871, 1755, 1723 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 3H), 1.05 (t, *J* = 6.9 Hz, 3H), 1.10 (s, 3H), 1.20 (s, 3H), 1.25–1.35 (m, 1H), 1.42 (br s, 9H), 1.53 (dd, *J* = 13.7, 6.9 Hz, 1H), 1.55–1.62 (m, 1H), 1.64 (dd, *J* = 12.5, 6.7 Hz, 1H), 2.48–2.55 (m, 2H), 2.69–2.77 (m, 2H,), 3.26 (dq, *J* = 8.6, 7.0 Hz, 1H), 3.42 (dq, *J* = 8.6, 7.0 Hz, 1H), 4.43 (d, *J* = 17.5 Hz, 1H), 4.52 (br s, 1H), 4.69 (d, *J* = 17.5 Hz, 1H), 5.18 (d, *J* = 8.5 Hz, 1H), 5.45 (d, *J* = 8.5 Hz, 1H), 5.97 (d, *J* = 9.6 Hz, 1H), 7.28–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.95, 24.52, 28.34, 29.70, 30.83, 31.33, 35.30, 41.87, 42.31, 43.60, 51.20, 56.19, 56.24, 69.37, 73.19, 73.99, 74.88), 80.24, 124.83, 126.66, 128.01, 128.75, 138.95, 155.19, 158.23, 172.15, 174.01. HRMS (ESI): calcd. for $C_{31}H_{43}NO_8Na$ $[M+Na]^+$ 580.2881, found 580.2876.

2-(5-Deoxylactarolidyl B)-8 4-(2,2,2-trichloroethyl) (2R,3S)-3-phenyl-1-oxa-4-azaspiro[4,5]decane-2,4dicarboxylate (13r). Compound **(13r)** was prepared from 5-deoxylactarolid B **(r)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (45:45:10) solvent system. Yield 45%. Oil $[\alpha]_D^{20}$ –33.9 (*c* 0.97, EtOH). IR ($CHCl_3$): ν_{max} = 3553, 2941, 1766, 1719 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.98 (s, 3H), 1.05 (s, 3H), 1.08 (t, *J* = 12.4 Hz, 1H), 1.18 (t, *J* = 12.1 Hz, 1H), 1.22 (s, 3H), 1.20–1.28 (m, 1H), 1.45–1.75 (m, 8H), 1.92 (br d, *J* = 13.7 Hz, 1H), 2.28–2.52 (m, 2H), 2.59 (d, *J* = 19.0 Hz, 1H), 2.57–2.65 (m, 1H), 2.79–2.86 (m, 1H), 2.88 (d, *J* = 19.0 Hz, 1H), 4.50–4.63 (m, 3H), 4.63 (d, *J* = 17.5 Hz, 1H), 4.72 (d, *J* = 17.5 Hz, 1H), 5.48 (d, *J* = 3.1 Hz, 1H), 6.00 (d, *J* = 3.7 Hz, 1H), 7.23–7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.93, 23.23, 24.62, 26.43, 29.24, 30.23, 32.54, 34.79, 36.73, 38.27, 42.56, 45.16, 46.10, 50.15, 62.79, 69.10, 72.19, 73.65, 74.59, 81.64, 95.00, 99.14, 122.89, 126.57, 127.91, 128.67, 140.42, 150.41, 164.05, 168.96, 172.84. HRMS (ESI): calcd. for $C_{33}H_{40}NO_8Cl_3Na$ $[M+Na]^+$ 706.1712, found 706.1729.

5-Deoxy-lactarolide B-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15r). Compound **15r** was prepared by the method B. The reduction of **13r** gave the amine **14r** which was not isolated, and upon acylation gave **15r** which was purified by chromatography on Si-gel using CH_2Cl_2/iPrOH (49:1). Yield 52%. Oil. $[\alpha]_D^{20}$ –8.1 (*c* 0.58, EtOH). IR ($CHCl_3$): ν_{max} = 3435, 2960, 1758, 1695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (s, 3H), 1.04 (s, 3H), 1.08 (t, *J* = 12.0 Hz, 1H), 1.13–1.20 (m, 1H), 1.28 (s, 3H), 1.45 (br s, 9H), 1.66 (dd, *J* = 11.9, 8.2 Hz, 1H), 1.72 (dd, *J* = 12.0, 7.4 Hz, 1H), 2.58 (d, *J* = 19.1 Hz, 1H), 2.69 (m, 1H), 2.79 (d, *J* = 19.1 Hz, 1H), 2.84–2.91 (m, 1H), 4.55 (br s, 1H), 4.70 (s, 2H), 5.27 (d, *J* = 10.4 Hz, 1H), 5.55 (d, *J* = 10.4 Hz, 1H), 5.81 (d, *J* = 2.0 Hz, 1H), 7.23–7.39 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.13, 28.41, 29.18, 32.20, 36.45, 37.10, 42.14, 45.83, 46.46, 49.33, 55.21, 69.99, 72.21, 72.87, 73.09, 80.40, 122.80, 126.72, 127.63, 128.51, 139.12, 156.06, 164.00, 172.38, 173.90. HRMS (ESI): calcd. for $C_{29}H_{39}NO_8Na$ $[M+Na]^+$ 552.2568, found 552.2585.

2-(3-*O*-Ethyl-5-deoxylactarolidyl B)-8 4-(2,2,2-trichloroethyl) (2R,3S)-3-phenyl-1-oxa-4-aza-spiro[4,5]decane-2,4dicarboxylate (13s). Compound **(13s)** was prepared from 3-*O*-ethyl-5-deoxy-lactarolid B **(s)** by esterification with the acid **12** using the general method B. Final purification of the compound was achieved by column chromatography on Si-gel using hexane/CH_2Cl_2/Et_2O (48.5:48.5:3) solvent system. Yield 45%. Oil. $[\alpha]_D^{20}$ –28.6 (c 0.93, EtOH). IR (film): ν_{max} = 2937, 2868, 1758, 1720 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 3H), 1.07 (s, 3H), 1.15 (t, *J* = 6.9 Hz, 3H), 1.18 (s, 3H), 1.22–1.35 (m, 2H), 1.37 (t, *J* = 11.7 Hz, 1H), 1.55–1.75 (m, 8H), 1.92 (br d, *J* = 12.6 Hz, 1H), 2.27–2.37 (m, 1H), 2.40–2.52 (m, 1H), 2.57 (d, *J* = 17.7 Hz, 1H), 2.62–2.74 (m, 3H), 3.33 (m, 1H), 3.39 (m, 1H), 4.45–4.80 (m, 5H), 5.58 (br s, 1H), 5.82 (d, *J* = 6.3 Hz, 1H), 7.22–7.44 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.78, 22.99, 23.25, 24.66, 24.82, 28.54, 30.30, 32.55, 35.09, 35.56, 35.92, 42.57, 43.92, 45.37, 47.65, 56.50, 62.87, 69.47, 71.71, 74.48, 76.46, 81.94, 95.22, 99.02, 124.00, 126.50, 127.62, 128.54, 141.16, 150.48, 161.30, 170.77, 172.25. HRMS (ESI): calcd. for $C_{35}H_{44}NO_8Cl_3Na$ $[M+Na]^+$ 734.2025, found 734.2011.

3-O-Ethyl-5-deoxy-lactarolide B-8-[(2R,3S)-N-(*tert*-butoxycarbonyl)-phenylisoserinate] (15s). Compound **15s** was prepared by the method B. The reduction of **13s** gave the amine **14s** which was not isolated, and upon acylation gave **15s** which was purified by chromatography on Si-gel using hexane/CH_2Cl_2/acetone (47.5:47.5:5). Yield 62%. Oil. $[\alpha]_D$ –4.4 (*c* 0.86, EtOH). IR (film): ν_{max} = 3442, 2934, 1753, 1715 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 3H), 1.11 (s, 3H), 1.11 (t, *J* = 6.9 Hz, 3H), 1.18 (s, 3H), 1.41 (br s, 9H), 1.38–1.50 (m, 2H), 1.57–1.67 (m, 2H), 2.58 (d, *J* = 16.8 Hz, 1H), 2.64–2.74 (m, 3H), 3.34 (dq, *J* = 8.2, 7.0 Hz, 1H), 3.48 (dq, *J* = 8.2, 7.0 Hz, 1H), 4.57 (dd, *J* = 17.5, 2.1 Hz, 1H), 4.65 (dd, *J* = 17.5, 1.3 Hz, 1H), 4.65 (br s, 1H), 5.24 (d, *J* = 8.4 Hz, 1H), 5.55 (d, *J* = 8.4 Hz, 1H), 5.90 (d, *J* = 7.4 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.36–7.40 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.05, 24.15, 28.37, 29.72, 30.89, 35.50, 35.72, 42.90, 43.20, 43.92, 48.27, 55.30, 56.43, 70.17, 71.73, 73.43, 76.34, 79.48, 124.32, 126.56, 127.39, 128.40, 139.87, 155.03, 161.07, 171.74, 172.71. HRMS (ESI): calcd. for $C_{31}H_{43}NO_8Na$ $[M+Na]^+$ 580.2881, found 580.2861.

Taxotere® (22) and 10-acetyl-Taxotere (23). Compounds **22** and **23** were prepared by combination of preparative methods described in the following references: [9], [10] and [11].

Antifeedant activity test. The test is described in detail [12]. Insects (adults and larvae) used for the test were reared under laboratory conditions at temp. of 26°C and 75% humidity. All compounds investigated were dissolved in EtOH at concentration of 10 $mg \cdot ml^{-1}$. Air dry wheat wafer discs were used as test food. The discs (1 cm in diameter) were saturated with EtOH solutions of pure compounds to produce 0.5% (by weight) contamination of the wafer in every test. Feeding of insects was recorded under three conditions: (1) on pure food (control); (2) on food with possibility of choice (choice test); on food with the compounds tested (no choice test). The wafer discs were weighed after saturation and drying in air for 30 min before the experiments and again after 7 days of feeding by beetles or larvae. On the basis of eaten food, the index of activity of the compounds tested was calculated in the following way: three values of the food eaten were obtained in the control KK, in the no-choice test EE, and in the choice test K, E. Thus:

The absolute coefficient of antifeedancy:

$$A = \frac{KK - EE}{KK + EE} \times 100$$

The relative coefficient of antifeedancy:

$$R = \frac{K - E}{K + E} \times 100$$

The total coefficient of antifeedancy is equal to T = A + R, and the maximum value of the coefficient can reach 200 for a perfect antifeedant.

REFERENCES

1. Daniewski W.M., Gumułka M., Anczewski W., Masnyk M., Błoszyk E. and Gupta K.K., *Phytochem*., **49**, 1279 (1998).
2. Daniewski W.M., Gumułka M., Ptaszyńska K., Skibicki P., Błoszyk E., Drożdż B., Stromberg S., Norin T. and Holub M., *Eur. J. Entomol*., **90**, 65 (1993).
3. Daniewski W.M., Gumułka M., Przesmycka D., Ptaszyńska K., Błoszyk E. and Drożdż B., *Phytochem*., **38**, 1161 (1995).
4. Kopczacki P., Gumułka M., Masnyk M., Grabarczyk H., Nowak G. and Daniewski W.M., *Phytochem*., **58**, 775 (2001).
5. Daniewski W.M. and Vidari G., *Progress in the Chemistry of Organic Natural Products*, **77**, 69 (1999).
6. Daniewski W.M., Gumułka M., Kopczacki P. and Masnyk M., *Polish J. Chem.*, **75**, 1287 (2001).
7. Sarosiek A., Masnyk M., Gumułka M., Daniewski W.M., Kobus M., Krawczyk E. and Łuczak M., *Polish J. Chem*., **76**, 73 (2002).
8. Barycki R., Gumułka M., Masnyk M., Daniewski W.M., Kobus M. and Łuczak M., *Collect. Czech. Chem. Commun.*, **67**, 75 (2002).
9. Mangatal L., Adeline M.-T., Guenard D., Guerite-Vogelein F. and Potier P., *Tetrahedron*, **45**, 4177 (1989).
10. Bourzat J.D. and Commercon A., *Tetraherdon Lett.*, **34**, 6049 (1993).
11. Didier E., Fouque E., Taillepied I. and Commercon A., *Tetrahedron Lett*., **35**, 2349 (1994).
12. Błoszyk E., Szafrański F., Drożdż B. and Al-Shameri K., *Journal of Herbs*, *Spices & Medicinal Plants*, **3**, 25 (1995).