Regio- and stereoselective methods for the conversion of (2*S*,3*R*)-β-phenylglycidic acid esters to taxoids and other enantiopure (2*R*,3*S*)-phenylisoserine esters

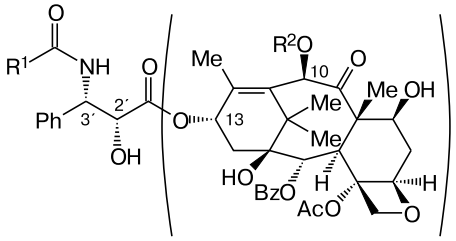
A. A. Afon´kin,[a,b] L. M. Kostrikin,[a] A. E. Shumeiko,[a] A. F. Popov,[a] A. A. Matveev,[a,b]†*
V. N. Matvienko,[b] and A. F. Zabudkin[b]

[a]*L. M. Litvinenko Institute of Physicoorganic Chemistry and Coal Chemistry, National Academy of Sciences of Ukraine, 70 ul. R. Lyuksemburg, 83114 Donetsk, Ukraine. E-mail: AAAfonkin@newmail.ru*
[b]*Co. Ltd "Sinbias Farma," 181 ul. Krepil´shchikov, 83085 Donetsk, Ukraine*

A novel efficient method was proposed for the synthesis of enantiopure precursors of taxane-containing cytostatics, *i.e.*, methyl esters of (2*R*,3*S*)- and (2*S*,3*R*)-*N*-benzoylphenylisoserine and similar taxoid esters. The method is based on the regio- and stereoselective hydrobromolysis of the corresponding *trans*-β-phenyl glycidate enatiomers, consecutive reactions of O-acylcarbamoylation of the obtained 3-bromohydrins, intramolecular cyclization to 4-phenyloxazolidin-2-one-5-carboxylic acid derivatives, and oxazolidinone ring opening.

Key words: taxane cytostatic agents, *trans*-β-phenylglycidic acid, phenylisoserine, 4-phenyloxazolidin-2-one-5-carboxylic acid esters, enantioselective synthesis.

In the modern anticancer chemotherapy, taxanes **1** and anthracycline derivatives are characterized by the most versatility of application, unlike many other oncological drugs acting according to the principle "one drug—one type of cancer."[1—3] The formation of cytotoxic activity of taxanes is substantially affected by both the diterpene baccatin core (the right part of the molecule) and the *N*-acylphenylisoserine moiety (the left part of the molecule **1b**) in the rigid (2*R*,3*S*)-configuration.[4]



1a: R^1 = Ph, R^2 = Ac (Paclitaxel (Taxol™));
1b: R^1 = Bu^tO, R^2 = H (Docetaxel (Taxotere™))

A biogenetic precursor of taxanes, 10-deacetylbaccatin III (the right part of the structure of **1b**), has recently become accessible,[5] since it was found in considerable amounts in needles of the European yew-tree. Therefore, the development of synthesis of the (2*R*,3*S*)-*N*-acylphenylisoserine moiety of taxanes became urgent. Numerous synthesis methods[3,6—25] of phenylisoserine (PIS) and any isomers of its esters and amides, including the target isomer with the *syn*-configuration, are known to date. These methods differ in the choice of a chirality source (substrate, reactant, or catalyst) and the type of chemical transformations.

However, difficulties of baccatin III acylation with phenylisoserine and high pharmacopeia requirements[26] imposed on optical purity of the final products **1** substantially restrict the choice of the method for construction of the (2*R*,3*S*)-*N*-acylphenylisoserine unit. It is known that the spatial structure of the baccatin core resembles in shape a basket with the C(13)-hydroxy group on the bottom forming a strong hydrogen bond with the C(4)-acetyl group.[27] As a result, O-acylation at the C(13)OH fragment is difficult and is often accompanied by epimerization at the C(2´) atom of the side chain due to the possible transformation of the acylating agent into a ketene derivative. The content of an epimer admixture is the highest in the case of acylation by the *N*,*O*-diprotected PIS itself.[28] That is why, only the methods, where less prone to epimerization crypto forms of PIS (*trans*-cinnamic,[29] β-phenylglycidic,[9] oxazolinic,[30] and oxazolidinic[31] acids and β-lactams[32]) are used for acylation and the target fragment of *N*-acylphenylisoserine is formed by the subsequent transformations of the residue of the introduced acid or directly at the moment of ester bond formation (as for β-lactam), have practical value as appropriate semisynthetic methods towards taxane **1**. Each of these methods has draw-

† Deceased.

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backs.[9,28,33,34] In spite of the evidently optimum β-lactam method, the potential of the method through transformations of phenylglycidic esters is far from exhaustion because of easy accessibility of all isomers of β-phenylglycidic acid and its stability and ability to react quantitatively with the baccatin III derivatives.

This work is aimed at developing a novel practical method for the synthesis of taxanes **1** and other taxoids from enantiopure β-phenylglycidic acid and the corresponding 10-deacetylbaccatin III derivative.

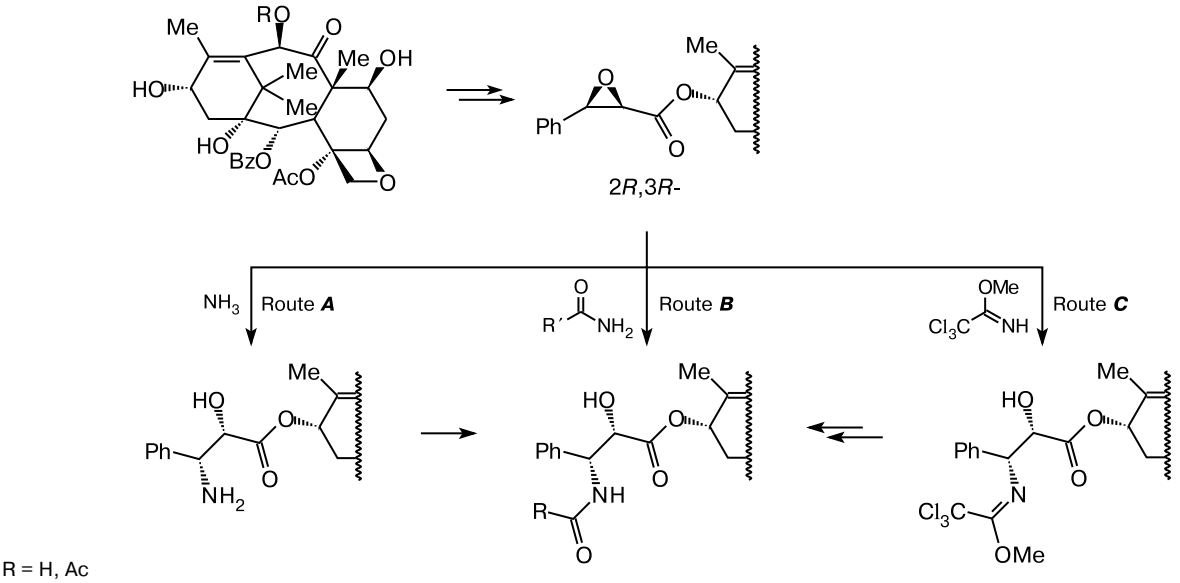
The strategy based on the transformations of baccatin esters of (2*R*,3*R*)-phenylglycidic acid (Scheme 1) seems to be most promising.

In this case, the one-step stereoselective opening of the oxirane ring by an *N*-nucleophile provides the target *syn*-configuration of the amino and hydroxy substituents of the side chain. However, the range of nucleophiles suitable for this purpose is small. The ammonolysis of β-phenyl glycidate under standard conditions (see Scheme 1, route ***A***) results in the cleavage of the ester bond to form PIS amide and is accompanied, in any case, by inappropriate levels of regio- and stereoselectivity.[8] Aminolysis is resultant only for the reaction of sterically non-hindered β-phenylglycidic acid esters with anilines, which react, most likely, not *via* the classical S_N2 mechanism.[35] Therefore, unlike the reaction of aliphatic amines, this reaction is efficiently catalyzed by transition metal salts.[7] Unlike the known examples of satisfactory intermolecular benzamidolysis of alicyclic epoxides,[36a] trifluoroacetamidolysis of terminal epoxides,[36b] and successful intramolecular acylamidolysis of oxiranes of different structure,[37] acylamidolysis by primary amides (see Scheme 1, route ***B***, R = Ph, CF_3, Bu^tO) is inapplicable in the case of phenylglycidates. Our attempts to open the oxirane ring of β-phenylglycidate with methyl trichloroacetimidate (see Scheme 1, route ***C***), which readily enters the intramolecular reaction with oxiranes of different structure[38] and then easily forms the amino group under mild conditions,[39] were also unsuccessful. Only the interaction of azide[9,40] and halide anions[8,20a] with esters (including baccatin esters) of β-phenylglycidic acid provides high yields of the products of oxirane ring opening. The stereoselectivity of azidolysis of baccatin esters of (2*R*,3*R*)-phenylglycidic acid is satisfactory only in the presence of fairly toxic crown ethers[9b] as catalysts. In the case of halide ions, stereo- and regioselectivities[20a,41] of the process depend substantially on the conditions. In addition, oxirane ring opening by halide anions as a way to *syn*-amino alcohols requires the inversion of the formed chiral center C—Hal and, hence, is applicable to the *trans*-isomer of enantiopure β-phenylglycidic acid ester only.

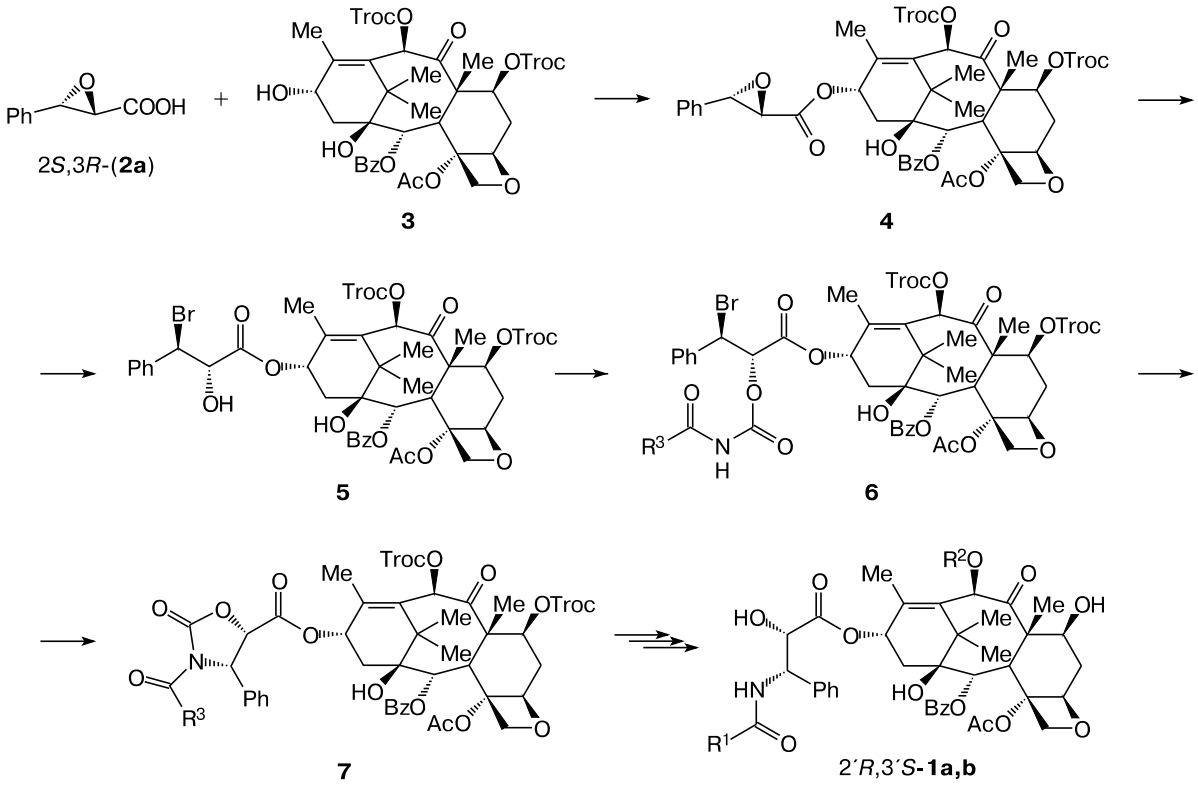
Based on the above presented results and taking into account restrictions known for the chemistry of taxanes,[3,5] we accomplished the method of synthesis of taxoids (Scheme 2), including the reaction of (2*S*,3*R*)-β-phenylglycidic acid **2a** and diprotected 10-deacylbaccatin **3** to give ester **4**, the regio- and stereoselective transformation of the latter into the corresponding enantiomer of bromohydrin **5**, and the reaction of **5** with acyl isocyanate followed by the intramolecular stereospecific transformation of intermediate **6** into oxazolidinone detivative **7**, whose conversion potentially leads to taxanes of the type **1**.

Reaction of *trans*-β-phenylglycidic acid with diprotected baccatin III. 7,10-Bis-*O*,*O*´-(2,2,2-trichloroethoxycarbonyl)-10-*O*-deacetylbaccatin (**3**) was synthesized by the reaction of 10-deacetylbaccatin III with 2,2,2-trichloroethyl

Scheme 1



Scheme 2

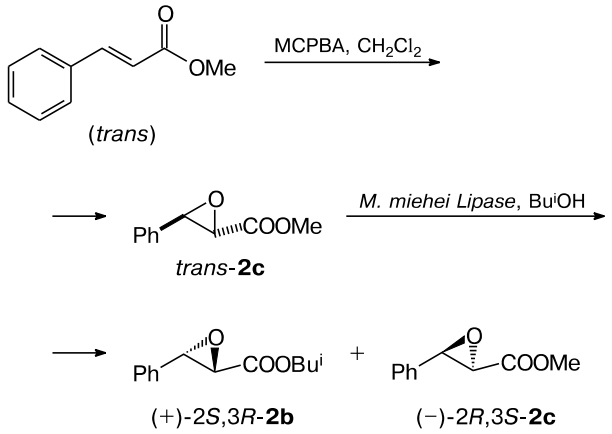


1a: R^1 = Ph, R^2 = Ac; **1b:** R^1 = Bu^tO, R^2 = H; **6,7:** R^3 = Ph, CCl_3
Troc = Cl_3CCH_2OCO

chloroformate in pyridine.[42] The desired enantiomer of (2*S*,3*R*)-β-phenylglycidic acid was obtained (Scheme 3) as isobutyl ester **2b** by the chemoenzymatic transesterification of racemic methyl *trans*-β-phenyl glycidate,[9a] which was synthesized by the epoxidation of methyl *trans*-cinnamate.[43]

(2*S*,3*R*)-β-Phenylglycidate **2b** was hydrolyzed by the treatment with 0.1 *M* NaOH in THF. Acidic form **2a** obtained after neutralization was extracted with toluene and used as a toluene solution for the acylation of baccatin derivative **3**. Esterification* of **3** with 2.0 equiv. of acid **2a** in the presence of 2.1 equiv. of DCC and 0.5 equiv. of DMAP** in toluene at ambient temperature gives the 13-*O*-acylation product **4** in 97% yield. If the process is carried out thoroughly, an admixture of C(2′)-epimer of the side chain does not exceed 10%.

Scheme 3



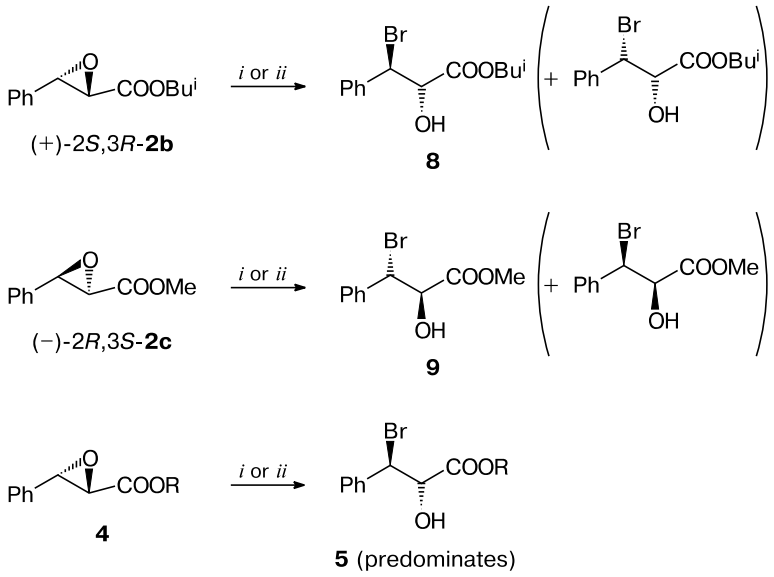
Synthesis of bromohydrins of esters of phenylpropionic acid

Optimization of the reaction conditions of the subsequent transformations of ester **4** (see Scheme 2) was per-

* An attempt to synthesize the 13-*epi*-*O*-phenylglycidyl derivative of diprotected baccatin by the Mitsunobu acylation[44] was unsuccessful. Esterification with acid **2a** in the presence of activators of different structure, *viz.*, DCC/1-hydroxybenztriazole, propanephosphonic cycloanhydride, BOP/diisopropylethylamine, and others with a low epimerization level in peptide and ester formation processes,[45] did not either yield the target product **4**.

** Comparable results were obtained using 2-methylpyridine *N*-oxide instead of DMAP.

Scheme 4



R = di-Troc-deacylbaccatin

Reagents and conditions: *i*. $TiBr_4$, CH_2Cl_2—HMPA (10 : 1), −75—+5 °C; *ii*. $MgBr_2 \cdot 2Et_2O$, −75—+5 °C.

formed on similar model reactions involving simpler analogs **2b**,**c**. It was found that the regioselective interaction of the bromide anion with esters of the type **2b**,**c** occurs successfully only in the presence of Lewis acids and the required level of stereoselectivity is provided by low temperatures of the process. We found that the use of $TiBr_4$ in a dichloromethane—HMPA (10 : 1 vol/vol) mixture or magnesium dibromide etherate $MgBr_2 \cdot 2Et_2O$ in diethyl ether gives predominantly compounds **8** or **9** (Scheme 4) in high yields (98 and 96%, respectively) of two possible regioisomers. Their structures are indicated by the characteristic signals from the C(2)H and C(3)H protons (δ_H 4.5—4.7 and δ_H 5.3—5.4, respectively), while in the case of 2-bromo regioisomers, these protons should give doublet signals in a stronger field: δ_H 4.3—4.4 and δ_H 5.0—5.1 (see Refs 46, 9a, 9b, and 20a). The ^{1}H NMR spectral data for the unpurified reaction products show that the content of 2-bromo-3-hydroxy isomers PhCH(OH)CH(Br)COOR does not exceed 1%.

The reactions in the temperature range from −75—−55 °C (onset of the process) to −10—+5 °C (completion of the process) involving both $MgBr_2 \cdot 2Et_2O$ and $TiBr_4$ (with a HMPA additive)[9b] afford predominantly *anti*-stereoisomers of bromohydrins **8** and **9** with the content of *syn*-isomers not higher than 2% (see Scheme 4).

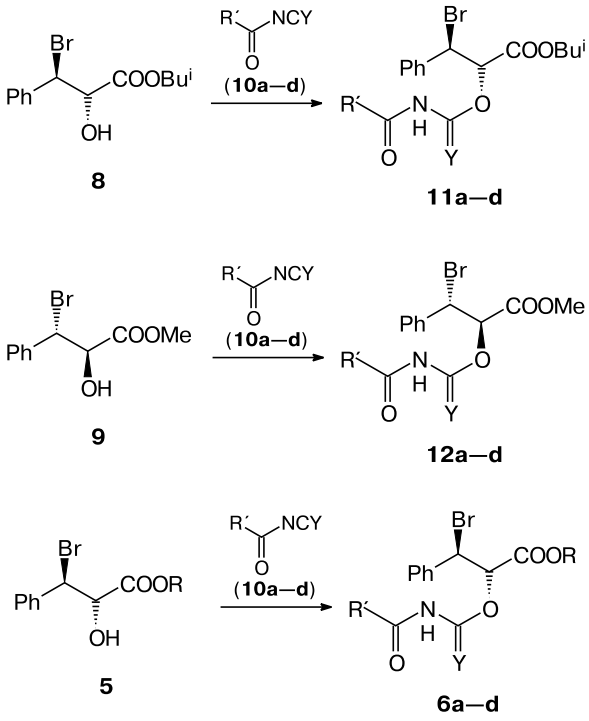
An insignificant content of the *syn*-isomers is indicated by the absence of satellite signals in the characteristic[4b,9a,9b,20a] ^{1}H NMR spectral ranges of the isolated products and by the results of direct determination of an enantiomeric excess in the case of bromolysis of active *trans*-phenyl glycidate with magnesium dibromide etherate.[20a] We found that products **8** and **9**, as expected, were right- and left-rotating enantiomers, respectively, and their $[\alpha]_D$ values corresponded to the literature data.[9a,9b,20a]

When using $TiBr_4$ and $MgBr_2 \cdot 2Et_2O$, the indicated yields of products **8** and **9** are attained with reaction durations of 3.5 and 6.5 h, respectively (see Scheme 4). In all cases, freshly prepared[47a] magnesium dibromide etherate is 20—30% more active than the commercially available reagent. The both brominating agents are also efficient for baccatin ester **4**. However, the rates of reactions (see Scheme 4) with this substrate are significantly lower for both reagents: under comparable concentration and temperature conditions, the 95% conversion is attained within ~30 h for $TiBr_4$ and within ~120 h for $MgBr_2 \cdot 2Et_2O$. As in the case of simpler esters **2b**,**c**, oxirane ring opening in the side chain of compound **4** yields 3-bromo-2-hydroxy derivative **5** with the signals characteristic of this regioisomer at δ_H 4.5 and 5.3.[9b]

Reactions of 3-bromo-2-hydroxy-3-phenylpropionic acid esters with acyl iso(thio)cyanates. To convert the bromoalkyl moiety of compounds **8**, **9**, and **5** to the target amino function, we used the method based on the intramolecular S_N2 substitution for halogen by the *N*-acyl carbamate anion formed by the acylation of the vicinal OH group with acyl isocyanate followed by the NH-deprotonation with a strong base[48,49] (alternative but less efficient method for the solution of this problems were described[50—54]). Both stages of this route were studied for model bromohydrins **8** and **9**.

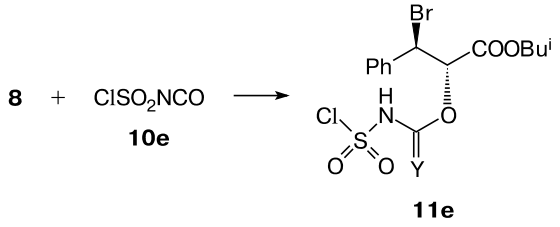
The reaction (Scheme 5) of compounds **8** and **9** with benzoyl isocyanate **10a** in THF occurs readily at low temperature and in 3 h completes by the formation of *O*-(*N*-benzoyl carbamate) derivatives **11a** and **12a**, respectively, in 94% yield.

Scheme 5



R = di-Troc-deacetylbaccatin

R´ = Ph, Y = O (**a**); R´ = CCl_3, Y = O (**b**)
R´ = EtO, Y = S (**c**); R´ = CCl_3, Y = S (**d**)



As initial bromohydrins **8** and **9**, products of their O-carbamoylation **11a** and **12a** differ in signs of specific rotation $[\alpha]_D$ +14.2 and −23.1°, respectively.

One of the key stages of the synthesis shown in Scheme 2 is oxazolidinone ring opening in compound **7** to form the target amino alcohol derivative and, hence, the corresponding functionalization of this fragment is important. Therefore, the O-carbamoylation of bromohydrins with the labile[55] *N*-acyl group **10b**,**e** and isothiocyanate derivatives **10c**—**d** with the readily modified C=S function was studied.[56] It was found that the result of interaction (see Scheme 5) of compounds **8** and **9** depends substantially on the structure of acyl iso(thio)cyanate **10** (Table 1). Reactants **10b** and **10e** interact with bromohydrins with the same high rate as **10a** but give lower or comparable chromatographic purity of the products formed.

Unlike primary alcohols, bromohydrins **8** and **9** react with ethoxycarbonyl isothiocyanate **10c** and trichloroacetyl isothiocyanate **10d** very slowly (see Table 1). Satisfactory yields were not attained by either replacement of THF by more polar MeCN, or the use of basic catalysts, or increasing temperature to 50 °C.

In the reactions with acyl isocyanates **10a,b**, baccatin derivative of bromohydrin **5** is ~8—10 times less active than esters **8** and **9**. So, the 90% conversion of bromohydrin **5** in the reaction with reactant **10a** was achieved within 28 h in THF and within 3 h in acetonitrile.

Cyclization of *O*-acyl carbamate derivatives of bromohydrins. Conversion (Scheme 6) of benzoyl carbamate derivatives **11** and **12** to oxazolidinones **13** and **14** is achieved by the treatment with sodium hydride in THF at low temperatures. The structures of the isolated products of intramolecular cyclization are determined by both the elemental analysis results (the absence of halogen) and the characteristic changes in the spectra. The ^{1}H NMR spectrum contains no signals from the NH-imide fragment, while the doublet signals from the C(2)H and C(3)H protons undergo a slight downfield shift to δ_H 4.9 and 5.6, respectively. In the IR spectra, the bands of stretching vibrations of the NH group disappear and the bands of three C=O groups (1801, 1761, and 1688 cm^{-1}) become more intense. The values of specific rotation decrease for compounds **13** and **14** to $[\alpha]_D^{20}$ +1.5 and −13.7°, respectively, whereas the signs of optical rotation remain still opposite.

Scheme 6

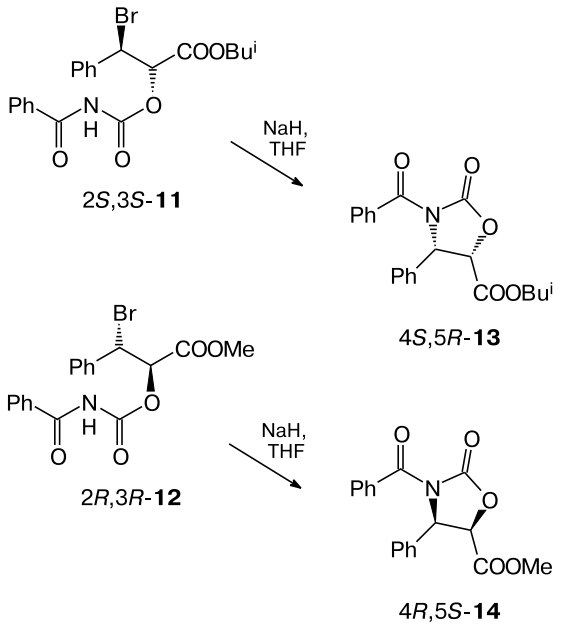


Table 1. Conditions[a] and the results of the actions of bromohydrins **8**, **9**, and **5** with acyl iso(thio)cyanates **10**

Bromo-hydrin	Acyl iso(thio)-cyanate **10**	Product	Solvent	*T*/°C	*t*/h	Conver-sion (%)	Chromatographic purity[b] (%)	Yield[c] (%)
8	**10a**	**11a**	THF	−4—+25	3	98	78	94
8	**10b**	**11b**	THF	25	2.5	98	88	90
8	**10c**	**11c**	THF	25	3	40[d]	—	—
8	**10c**	**11c**	MeCN	25	4	40	—	—
8	**10c**	**11c**	MeCN	25	23	73[d]		—
8	**10c**	**11c**	$MeCN—CH_2Cl_2$ (1 : 1)	25	118	50	—	—
8	**10d**	**11d**	THF	25	23	4[d]		—
8	**10e**	**11e**	Et_2O	25	3.5	22[d]	—	—
8	**10e**	**11e**	CH_2Cl_2	25	0.5	92	82	—
8	**10e**	**11e**	CH_2Cl_2	25	2	99	80	92
9	**10a**	**12a**	THF	−4—+25	2.5	96	82	92
9	**10b**	**12b**	THF	−4—+25	2	93	84	88
5	**10a**	**6a**	THF	0—25	5	58	78	—
5	**10a**	**6a**	THF	0—25	28	90	72	—
5	**10a**	**6a**	CH_2Cl_2	0—25	24	90	73	—
5	**10a**	**6a**	MeCN	0—25	3	91	85	—
5	**10b**	**6b**	MeCN	0—25	4.5	95	82	74
5	**10a**	**6a**	MeCN	0—25	5.5	96	87	83

[a] In the most cases, the bromohydrin : reactant **10** ratio is 1 : 1.25.
[b] Chromatographic purity of the product at the maximum conversion.
[c] Yield of the isolated product.
[d] The use of additional amounts of reactant **10** does not result in a substantial increase in the conversion of bromohydrin.

The best yields of products **13** and **14** (88 and 86%, respectively) are attained by the following prerequisites: the temperature of the process from −15 to 25 °C, using not more than a threefold excess of the deprotonating agent, portionwise addition of the deprotonating agent to the reaction mixture, and, principally, the use of a solvent with a residual water content at most 0.03%. Otherwise, products of ester group hydrolysis are predominantly formed instead of the target oxazolidinones, since baccatin derivatives **6** are especially susceptible to hydrolysis.

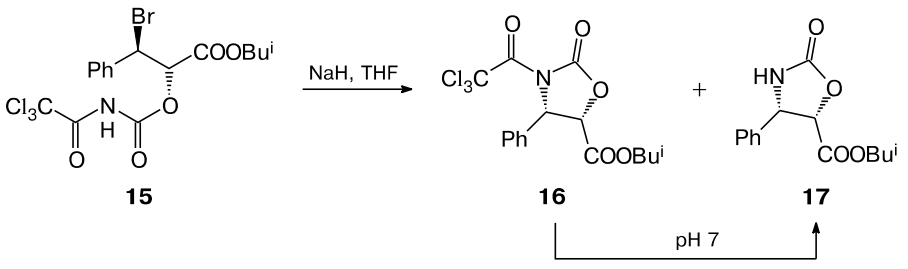
In the case of trichloroacetyl carbamate derivative **15**, intramolecular cyclization is complicated by the lability of the *N*-acyl group in addition to the factors listed above (Scheme 7). Both in the course of the reaction and during the isolation of product **16**, the trichloroacetamide group is readily hydrolyzed even at pH 7 to form deacylated oxazolidinone **17**. In our opinion, the route with preliminary deacylation of the initial substrate followed by the cyclization of the formed carbamate to oxazolidinone is less probable.

If the conditions are fulfilled thoroughly, the reaction can be stopped at the stage of formation of compound **16** as the major product (see Scheme 7). However, the further manipulations spontaneously transform compound **16** into final product **17** (HPLC data). The preparative yield of compound **17** is 71%.

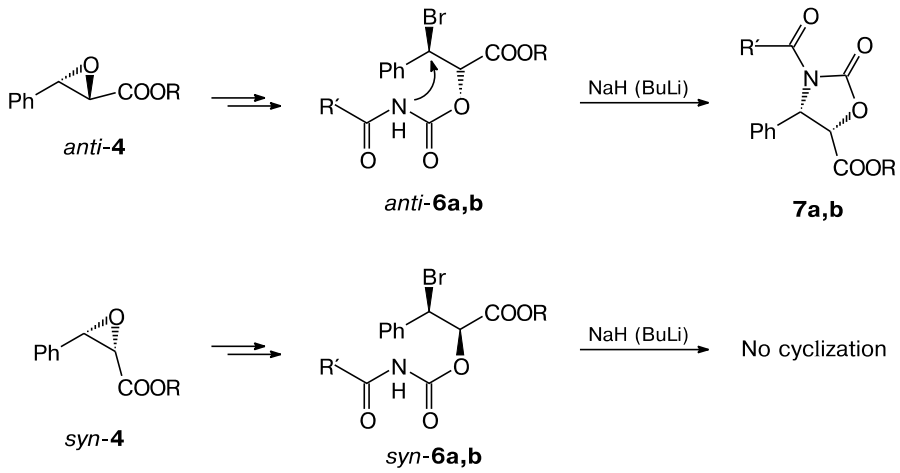
Attempts of cyclization of *O*-(*N*-chlorosulfonylcarbamate) derivatives of bromohydrin of the type **11e** by the action of sodium hydride in THF were unsuccessful: an inseparable multicomponent mixture was obtained.

Intramolecular cyclization (Scheme 8) of baccatin acyl carbamate derivatives **6** under the action of deprotonating

Scheme7



Scheme 8



R is di-Troc-deacetylbaccatin.
R´ = Ph (**a**), CCl_3 (**b**)

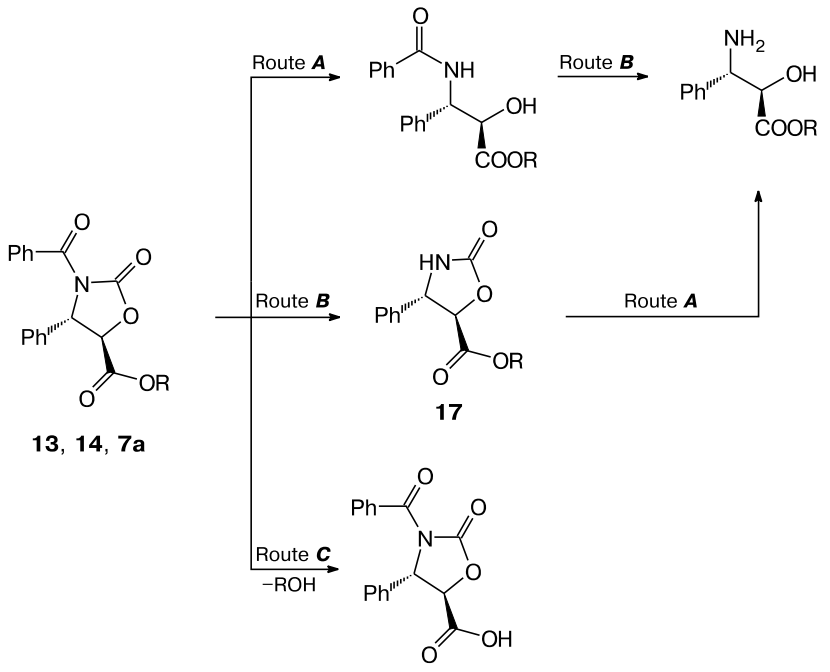
agents has additional singularities along with high sensitivity to the water content in the reaction medium.

Acylation of diprotected baccatin III **3** with *trans*-β-phenylglycidic acid **2a** affords some amount of an admixture fairly similar in structure to that of expected product **4** (see Scheme 2), which appears as a characteristic shoulder on the chromatographic peaks of this product. According to patented information and our experience in taxane chemistry, the observed admixture (inseparable by purification) was interpreted as C(2´)-epimer *syn*-**4** (see Scheme 8). At the next synthesis stages, this epimer undergoes the same transformations as major epimer *anti*-**4** and the corresponding admixtures follow the major products up to the cyclization stage. However, at this stage the back intramolecular attack is hindered for intermediate *syn*-**6**. Indeed, neither an increase in the sodium hydride concentration to 5—8 equiv., nor the use of catalytic and stoichiometric amounts of 18-crown-6, nor the transition to another deprotonating agent (BuLi), nor the variation of the structure of acyl fragment R´, nor an increase in the temperature reaction time result in the expected cyclization of admixture *syn*-**6**. When 97% conversion the completion of transformation of isomer *anti*-**6** to compound **7** is achieved (2 h, 3 equiv. NaH in THF, low temperature), the further increase in the reaction time results only in hydrolysis of all baccatin esters to the initial substrate **3**. Such a pronounced difference in chemical behavior of *anti*-**6** and *syn*-**6** indicates stereospecificity of the intramolecular cyclization of the studied *O*-carbamate derivatives of bromohydrins. The transformation of the imide fragment of the side chain, which is present in structure **6a** (R´ = Ph), is indicated by characteristic changes in the ^{1}H NMR spectrum of the cyclization product: the absence of the signal from the NH proton (δ_H 8.6) can unambiguously be established against the background of numerous signals from the aliphatic protons, and the ratio of integral intensities of signals from the aromatic and aliphatic protons corresponds to the expected structure of compound **7a**.

The structure of compound **7a** synthesized by us was proved by the independent synthesis. Baccatin (4*S*,5*R*)-3-benzoyl-4-phenyloxazolidin-2-one-5-carboxylates were described in the patent.[57] They are obtained in the 31% yield by the DCC/DMAP-activated acylation of the corresponding baccatin derivative with the indicated acid, which was synthesized by the cyclization of the phenylisoserine derivative. The corresponding acid synthesized by us using acidic hydrolysis of ester **13** was introduced into the esterification reaction with 7,10-*O*,*O*´-bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin **3** under the earlier described conditions.[57] Contrary to expectation, acylation proceeds very slowly and the esterification product is formed only in insignificant amounts (up to 4—5%). Nevertheless, its retention time under various HPLC analysis conditions (isocratic and gradient reverse- and direct-phase variants) is identical to the retention time of compound **7a** obtained by us.

Oxazolidinone cycle cleavage to amino alcohol fragment. The key stage of the method described in Scheme 2 is the conversion of the oxazolidinone fragment of compound **7a** to the target amino alcohol fragment of phenylisoserine. This process requires endocyclic heterocycle opening (Scheme 9, route ***A***), which for oxazolidinones of different structure can be attained by acidic[58] or alkaline (more frequently) hydrolysis.[58,59] In addition, for esters of phenyloxazolidinone acids **13**, **14**, and **7a**, exocyclic hydrolysis with

Scheme 9



R = Bu^i (**13**), Me (**14**); di-Troc-deacetylbaccatin (**7a**)

N-deacylation of the cycle (Scheme 9, route ***B***) is possible and also potentially leads to PIS ester. A very undesirable hydrolysis of the ester bond (Scheme 9, route ***C***), which is weaker than the imide bond, is also possible.

Among many acidic and basic hydrolytic agents successfully used[59,60] for oxazolidinones of different structure, we failed to find a universal agent providing selective endocyclic hydrolysis (see Scheme 9, route ***A***) that does not involve the ester group. In the case of compound **14**, alkali carbonates in an anhydrous* MeOH—THF medium resulting in *N*-benzoylphenylisoserine methyl ester 2*R*,3*S*-**18** is efficient. With an increase in the reaction time, the latter undergoes a more complete transformation and forms (Scheme 10) methyl ester of PIS **19**.

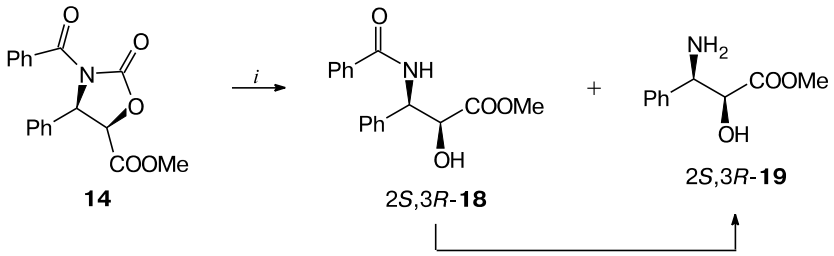
Cesium carbonate is most active in the series of studied carbonates. In the presence of 0.2 equiv. Cs_2CO_3, the conversion of compound **14** to *N*-benzoylphenylisoserine methyl ester 2*S*,3*R*-**18** in an anhydrous MeOH—THF (2 : 1) mixture achieves 99% within 1.5 h. The rate and selectivity of the process can be controlled by the fraction of THF in the reaction mixture.

* It is known[57] that in aqueous media alkali carbonates efficiently hydrolyze esters of the types **13** and **14** to form free acids. We found that the acidic hydrolysis of these esters in the presence of hydrochloric acid in a THF—water (1 : 1) mixture is characterized by almost the same efficiency. For example, for the hydrolysis of compound **13** the 90% yield of (4*S*,5*R*)-3-benzoyl-4-phenyloxazolin-2-one-5-carboxylic acid is achieved after reflux for 1 h.

However, as it was revealed, in the case of esters **13** and **7a**, oxazolidinone cycle opening is always preceded (Scheme 11) by transesterification with the formation of intermediate 4*S*,5*R*-**14**, and the product of its further transformations is methyl ester 2*R*,3*S*-**18**. The physicochemical characteristics of enantiomers **18** completely correspond to the literature data.[6,9a,20a,20b,61]

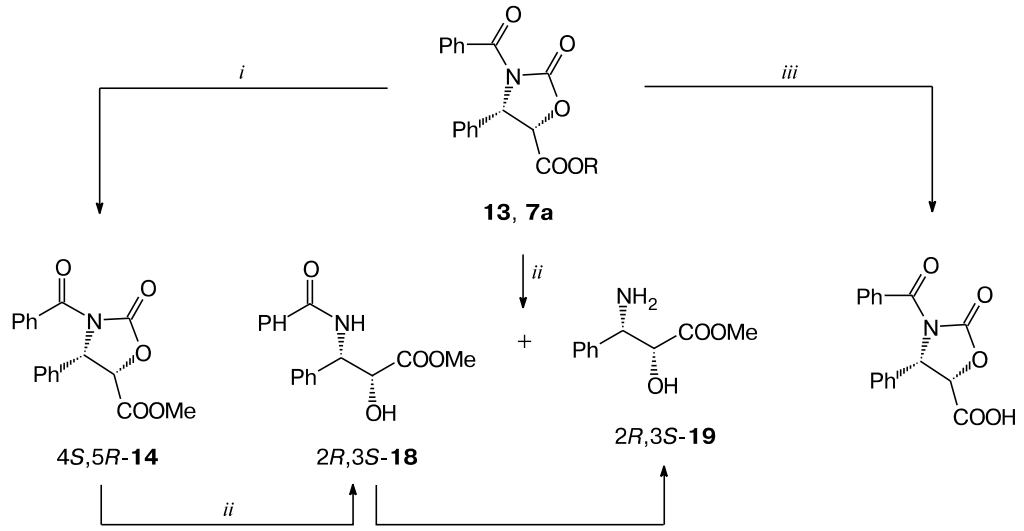
Conversion of compound **13** was ceased at the stage of formation of transesterificated intermediate 4*S*,5*R*-**14**, using less reactive lithium carbonate as a reagent. Most likely, the methoxide ion generated by the carborate anion acts as a reacting species (see Schemes 10 and 11) in all cases. In fact, on going from methanol to isopropyl alcohol, the carbonate-promoted hydrolysis of substrate **13** affords isopropyl (4*S*,5*R*)-3-benzoyl-4-phenyloxazolidin-2-one-5-carboxylate. At the same time, under similar conditions, 2,2,2-trifluoroethanol and isobutyl alcohol are not involved in either transesterification or oxazolidinone cycle opening with the formation of the PIS derivative, and *tert*-butyl alcohol causes racemization of enantiomer **13** in the presence of potassium *tert*-butoxide, which generally indicates significance of the basicity (nucleophilicity) and steric factor when choosing the alkoxide reagent. We found that, in the series of methoxides, the nature of the counterion exerts a substantial effect on the selectivity of hydrolysis. The treatment of compound **13** with magnesium methoxide[62] (Scheme 12) resulted in the inversion of the order of bond cleavage: in a MeOH—THF mixture in the presence of 20 equiv. $Mg(OMe)_2$, the imide bond of

Scheme 10



Reagents and conditions: *i*. M_2CO_3 (M = Li, K, Cs), MeOH—THF.

Scheme 11



R = Bu^i (**13**), di-Troc-deacetylbaccatin (**7a**)

Reagents and conditions: *i*. Li_2CO_3, MeOH—THF; *ii*. Cs_2CO_3, MeOH—THF; *iii*. HCl, THF—H_2O.

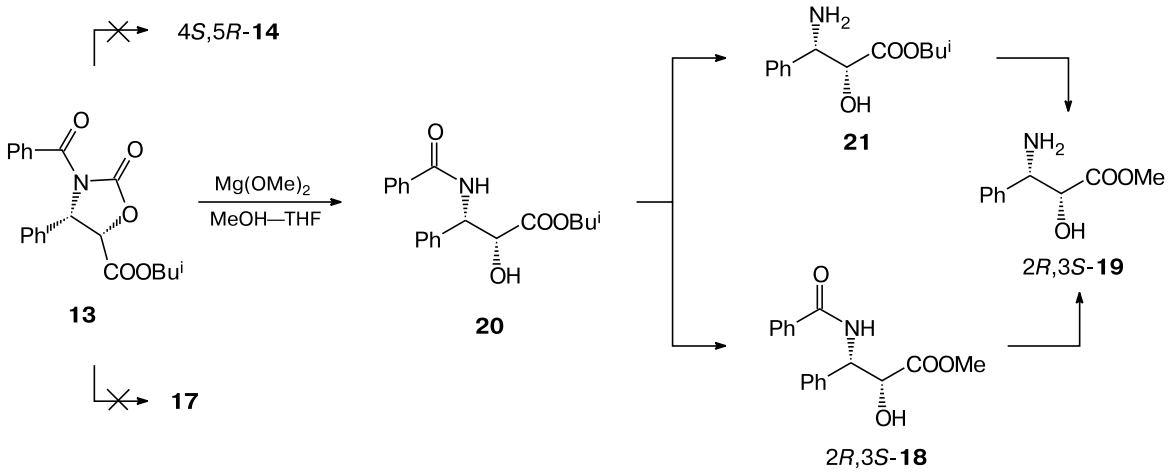
the heterocycle undergoes cleavage first to form the target product **20**, which further either undergoes *N*-debenzoylation or transesterification with the formation of by-products **21** and 2*R*,3*S*-**18**, respectively. Finally, these products are transformed into PIS methyl ester 2*R*,3*S*-**19**. According to the chromatographic composition of the reaction mixture, none of the variants of exocyclic hydrolysis with the formation of products 4*S*,5*R*-**14** and **17** occurs.

Under the indicated conditions, the maximum yield of product **20** is 51% at the 80% conversion of the starting substrate **13**, which is achieved in 45—50 min at 20 °C. The fraction of product 2*R*,3*S*-**19** reaches 75% with an increase in the duration time to 22 h.

Baccatin esters are more sensitive to bases, and their stability under the "hydrolysis" conditions depends on the structure of the acyl fragment[62]: under alkaline conditions, the ester bond of the *N*-acyl form of PIS sometimes is more stable than the *N*,*O*-diprotected forms (or the crypro form) of PIS. We found that substrate **7a**, being treated with 0.2 equiv. cesium carbonate in anhydrous methanol for 30 min at lowered temperature, undergoes (see Scheme 11) transesterification to the methyl derivative of oxazolidinic acid with the recovery of the initial baccatin alcohol **3**, which further converts to 10-deacetylbaccatin III. The search for selective procedures aimed at the required transforming baccatin ester **7a** among numerous traditional method was unsuccessful. However, we succeeded to find a practical method for selective heterocycle cleavage in compound **7a** to give the corresponding PIS derivatives, which will be discussed elsewhere.

To conclude, the novel method for the synthesis of practically significant compounds, *viz.*, enantiopure (2*R*,3*S*)-(−)-*N*-benzoyl-3-phenylisoserine methyl ester (2*R*,3*S*-**18**) and taxoids of the type **7**, from β-(2*S*,3*R*)-phenylglycidic acid has appropriate preparative yields and achieved levels of regio- and stereoselectivity at each individual stage.

Scheme 12



Experimental

^{1}H NMR spectra (200 and 400 MHz) were measured on Bruker AM-200 and Bruker AM-400 spectrometers using Me_4Si as an internal standard. IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer in KBr pellets. The optical rotation was determined as an arithmetical mean of five measurements on an ATAGO AP-100 automated polarimeter. The completeness of reactions and chromatographic purity of the obtained products were monitored on an HPLC Shimadzu instrument equipped with a UV detector (232 and 254 nm) and columns Zorbax SB-C18 5.0 μ/150 mm/4.6 mm (mobile phases: a gradient (water (pH 7.0; $AcONH_4$/AcOH)—MeCN mixture from 70 : 30 to 10 : 90) and an isocratic (water (pH 5.5; $AcONH_4$/AcOH)—MeCN (57 : 43) mixture) and Hypersil-Silica 5.0 μ/150 mm/4.6 mm (mobile phase: an isocratic *n*-hexane—ethyl acetate—acetonitrile (72 : 17 : 11) mixture). Melting points were determined on a Boetius heating stage. Solvents were purified and dried using standard methods.[63] The residual water content in dried solvents was monitored by the Fischer non-aqueous titration on a Metrohm 787 KF Titrino/703 Ti Stand instrument.

Trifluoroacetamide was synthesized by the reaction of trifluoroacetic anhydride with an ammonia excess in anhydrous methanol. *N*-Trimethylsilylbenzamide was obtained by the reaction of benzamide with trimethylsilyl chloride in benzene in the presence of triethylamine.[64] *tert*-Butoxycarbonylacetimide was synthesized by the reaction of *tert*-butoxycarbonylacetamide (Aldrich) with sodium hydride in anhydrous THF followed by the reaction with acetyl chloride. Methyl trichloroacetimidate was obtained by the dehydration of trichloroacetamide with P_2O_5 to form trichloroacetonitrile[65] followed by the reaction of the latter with methanol in CH_2Cl_2 in the presence of DBN.[66] The physicochemical characteristics of the indicated target products correspond to literature data.

10-Deacetylbaccatin III (Shanghai Synnad Chemical Co. Ltd) was used. Commerically available benzoyl isocyanate **10a**, trichloroacetyl isocyanate **10b**, and chlorosulfonyl isocyanate **10e** (Aldrich) were used without additional purification. Ethoxycarbonyl isothiocyanate **10c** and trichloroacetyl isothiocyanate **10d** were synthesized by the reaction of potassium thiocyanate with ethyl chloroformate and trichloroacetyl chloride, respectively, using the published method.[47b]

7,10-*O*,*O*´-Bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin (3) was synthesized using the known procedure.[42] A mixture of 2,2,2-trichloroethyl chloroformate (7 mL, 10.77 g, 50.8 mmol) and dichloromethane (21 mL) was added to a precooled to −20 °C solution of 10-deacetylbaccatin III (10 g, 18.8 mmol) in anhydrous pyridine (100 mL) by portions maintaining the reaction temperature below 0 °C. The reaction mixture was kept at 0 °C for 35 min and treated with water and dichloromethane. The organic phase containing the target product of ~90% purity was separated and multiply washed with water. Compound **3** with 99.9% chromatographic purity was obtained by preparative chromatography on Silicagel Si60 (eluent dichloromethane—hexane, 98 : 2) followed by crystallization from methanol in a yield of 15 g (91%). The physicochemical characteristics of the synthesized product correspond to the literature data.[42]

Methyl *trans*-β-phenylglycidate (2), racemate. *m*-Chloroperoxybenzoic acid (70%, 124 g, 0.50 mol) was added to a solution of freshly distilled methyl *trans*-cinnamate (65 g, 0.40 mol) in dichloromethane (500 mL). The reaction mixture was refluxed for 50 h to 85% conversion, the residue of *m*-chlorobenzoic acid formed was filtered off through a layer of neutral Al_2O_3, the solvent was removed on a rotary evaporator under reduced pressure, and the viscous residue was distilled *in vacuo*. Product **2** with 96% chromatographic purity was obtained in a yield of 51 g (71%), b.p. 114—116 °C (0.30—0.35 Torr). ^{1}H NMR ($CDCl_3$), δ: 7.25—7.40 (m, 5 H, Ar); 4.08—4.12 (d, 1 H, CH); 3.70 (s, 3 H, CH_3); 3.52—3.55 (d, 1 H, CH).

Enantioselective transesterification of racemic ester 2 was carried out using the known method.[9a] A suspension containing 300 g of lipase PS-C *M. miehei* (Amano International Enzyme Co.), 100 g (0.56 mol) of methyl *rac-trans*-β-phenyl glycidate **2**, 400 mL of isobutyl alcohol, and 400 mL of *n*-hexane was shaken for 55 h at 30 °C. The solid phase was filtered off, the solvent was evaporated, and the residue was fractionated twice *in vacuo*.

(+)-Isobutyl (2*S*,3*R*)-3-phenylglycidate (2b). The yield was 60 g (48%), b.p. 105—107 °C (0.10 Torr) (*cf.* Ref. 9a: b.p. 117—119 °C (0.1 Torr)). Chromatographic purity was 96%; $[\alpha]_D^{20}$ +127° (*c* 1.5, $CHCl_3$), *cf.* Ref. 9a: $[\alpha]_D^{20}$ +129° (*c* 1.5, $CHCl_3$)). ^{1}H NMR ($CDCl_3$), δ: 7.25—7.40 (m, 5 H, Ar):

4.08—4.12 (d, 1 H, CH, J = 4.5 Hz); 3.95—4.06 (m, 2 H, CH_2 Bu^iO); 3.52—3.55 (d, 1 H, CH, J = 4.5 Hz); 1.90—2.10 (m, 1 H, CH, Bu^iO); 0.95, 1.00 (both s, 6 H, 2 CH_3 Bu^iO).

(−)-Methyl (2*R*,3*S*)-3-phenylglycidate (2c). The yield was 18 g (18%), b.p. 88—95 °C (0.12 Torr) (*cf.* Ref. 9a: b.p. 85—95 °C (0.1—0.05 Torr)). Chromatographic purity was 95%; $[\alpha]_D^{20}$ −160° (*c* 1.5, $CHCl_3$) (*cf.* Ref. 9a: $[\alpha]_D^{20}$ −163 ° (*c* 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ: 7.25—7.40 (m, 5 H, Ar); 4.08—4.12 (d, 1 H, CH, J = 6.0 Hz); 3.67 (s, 3 H, CH_3); 3.52—3.55 (d, 1 H, CH, J = 5.5 Hz).

13-*O*-((2*S*,3*R*)-3-Phenylglycidoyl)-7,10-*O*,*O*′-bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin (4). Aqueous 1.0 *M* NaOH (22 mL) was added dropwise with stirring to a solution of compound **2b** (2.43 g, 11 mmol) in THF (60 mL) cooled to 0 °C. The mixture was stirred for 40 min at ambient temperature, and then H_2O (75 mL) and diethyl ether (80 mL) were added. The aqueous phase was separated, and toluene (100 mL) was added. The obtained mixture was cooled to 0—2 °C and acidified with 1.0 *M* HCl to pH 3—4. The organic phase was separated, the aqueous phase was repeatedly extracted with toluene (100 mL), and combined organic extracts were dried over Na_2SO_4. A solution of acid **2a** in toluene was concentrated to a volume of 20 mL. Anhydrous toluene (85 mL), substrate **3** (4.9 g, 5.56 mmol), DCC (2.38 g, 11.5 mmol), and DMAP (0.34 g, 2.78 mmol) were added to the residue with stirring, the mixture was stirred at ambient temperature to the reaction completion (~10 min). Dichloromethane (200 mL) was added to the reaction mixture, which was washed with a dilute aqueous solution of $NaHCO_3$ and water, and the organic phase was dried over Na_2SO_4. An amorphous residue (7.3 g) obtained after distilling off the solvent on a rotary evaporator was dissolved in an acetone—dichloromethane (1.5 : 98.5 vol/vol) mixture, and the non-separated part was filtered off. Compound **4** was isolated by preparative chromatography on Silicagel Si60 (column 3.5×60 cm, eluent acetone—dichloromethane (1.5 : 98.5% vol/vol), detection at λ = 254 nm) in a yield of 5.54 g (97%), white solid, $[\alpha]_D^{20}$ −45.8° (*c* 0.5, EtOH). ^{1}H NMR ($CDCl_3$), δ: 8.00—8.10 (m, 2 H, Ar); 7.30—7.70 (m, 8 H, Ar); 6.25—6.30 (m, 2 H); 5.60—5.70 (m, 2 H); 4.9 (m, 2 H); 4.60—4.80 (m, 3 H); 4.20—4.30 (m, 2 H); 2.60—2.70 (m, 1 H); 2.3—2.4 (m, 2 H); 2.10, 2.20 (both s, 6 H, 2 CH_3); 2.00—2.05 (m, 1 H); 1.85 (s, 3 H, CH_3); 1.60—1.75 (br.s, 1 H, in exchange); 1.20, 1.30 (both s, 6 H, 2 CH_3). The ^{1}H NMR spectrum is consistent with that described earlier.[9b] Found (%): C, 50.35; H, 4.02; Cl, 20.78. $C_{43}H_{42}Cl_6O_{16}$. Calculated (%): C, 50.26; H, 4.12; Cl, 20.70.

Hydrobromolysis of *trans*-phenylglycidates 2b, 2c, and 4 (general procedure). ***A.*** A mixture of $MgBr_2 \cdot 2Et_2O_2$ (Aldrich) (15 mmol) was added to diethyl ether (50 mL) with a residual water content of 0.02% and cooled to −55 °C (−18 °C in the case of substrate **4**). A solution of *trans*-phenylglycidic acid ester (10 mmol) in diethyl ether (10 mL) was added by portions with stirring. The reaction mixture was stirred maintaining the temperature in the range from −18 to 3 °C. The reaction course was visually monitored by the formation of a milk-white finely dispersed suspension of the magnesium derivative of bromohydrin **5**, **8**, or **9** and using HPLC by the disappearance of the starting substrate. After the completion of the reaction, water (70 mL) containing 5% NaCl was added, and the mixture was stirred to suspension dissolution. The organic phase was separated, and the aqueous phase was repeatedly extracted with diethyl ether (50 mL). Combined organics were dried over Na_2SO_4. The subsequent evaporation of the solvent gives bromohydrins **5**, **8**, or **9** fairly pure for further work.

B. A solution of *trans*-phenylglycidic acid ester (30 mmol) in a mixture of CH_2Cl_2 (160 mL) and hexamethylphosphoramide (16 mL) with the total content of residual water at most 0.15% was cooled to −75 °C (0 °C in the case of substrate **4**), and $TiBr_4$ (33 mmol) was added by portions with stirring. The reaction mixture was stirred, gradually increasing the temperature to −8 °C (5 °C in the case of substrate **4**). The reaction course was monitored by the consumption of substrate **2a**, **2b**, and **4**. After the completion of the reaction, H_2O (140 mL) containing 5% NaCl was added to the reaction mixture, which was stirred to decoloration of the solution. The organic phase was separated, washed with water, and dried over Na_2SO_4. The subsequent distilling off the solvent gives bromohydrins **5**, **8**, or **9** with appropriate chromatographic purity, and an HMPA admixture in the product exerts no effect on the occurrence of the next stage.

Both methods of hydrobromolysis give identical results.

Isobutyl (2*S*,3*S*)-(+)-3-bromo-2-hydroxy-3-phenylpropionate (8). The yield of the unpurified product was 96—98%; chromatographic purity was 96% (by method ***A***) and 95% (by method ***B***); $[\alpha]_D^{20}$ +97° (*c* 0.7, $CHCl_3$). ^{1}H NMF ($CDCl_3$), δ: 7.25—7.40 (m, 5 H, Ar); 5.3 (d, 1 H, C(3)H, J = 6.0 Hz); 4.70 (dd, 1 H, 2 CH, J = 3.0 Hz, J = 5.8 Hz); 3.9—4.0 (m, 2 H, CH_2 Bu^iO); 3.00 (br.s, 1 H, C(2)OH, in exchange); 1.90—2.10 (m, 1 H, CH of Bu^iO); 0.95, 1.00 (both s, 6 H, 2 CH_3, Bu^iO).

Methyl (2*R*,3*R*)-(−)-3-bromo-2-hydroxy-3-phenylpropionate (9). The yield of the unpurified product was 96—98%; chromatographic purity was 97% (by method ***A***) and 98% (by method ***B***); $[\alpha]_D^{22}$ −134° (*c* 1.2, $CHCl_3$) (*cf.* Ref. 20a: $[\alpha]_D^{20}$ −134° (*c* 1.1, $CHCl_3$)), −138° (*c* 1.5, $CHCl_3$)). ^{1}H NMR ($CDCl_3$), δ: 7.30—7.50 (m, 5 H, Ar); 5.30 (d, 1 H, C(3)H, J = 4.5 Hz); 4.70 (dd, 1 H, C(2)H, J = 4.8 Hz, J = 6.8 Hz); 3.70 (s, 3 H, CH_3); 3.00 (br.s, 1 H, C(2)OH, in exchange).

13-*O*-((2*S*,3*S*)-3-Bromo-2-hydroxy-3-phenylpropionyl)-7,10-*O*,*O*′-bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin (5). The yield of the unpurified product was 96%; chromatographic purity was 96% (by method ***A***) and 92% (by method ***B***). ^{1}H NMR ($CDCl_3$), δ: 8.00—8.10 (m, 2 H, Ar); 7.30—7.50 (m, 8 H, Ar); 6.15—6.30 (m, 2 H); 5.50—5.70 (m, 2 H); 5.27 (d, 1 H, CHBr, J = 6.2 Hz); 4.90 (m, 2 H); 4.60—4.80 (m, 3 H); 4.50 (m, C<u>H</u>OH); 4.00—4.30 (m, 3 H); 3.00 (br.s, 1 H, CHO<u>H</u>); 2.60—2.70 (m, 1 H); 2.40 (s, 3 H); 2.00—2.30 (s, 3 H); 1.80—1.90 (m, 6 H); 1.60—1.75 (m, 4 H, in exchange); 1.20, 1.30 (both s, 6 H, 2 CH_3). The spectrum of compound **5** is consistent with that described previously.[9b] Found (%): C, 46.67; H, 4.10; Br, 7.15; Cl, 20.08. $C_{43}H_{43}BrCl_6O_{16}$. Calculated (%): C, 46.60; H, 3.91; Br, 7.21; Cl, 19.19.

Reaction of acyl iso(thio)cyanates 10 with bromohydrins 8 and 9 (general procedure). A solution of benzoyl isocyanate (5.4 g, 37 mmol) in THF (15 mL) was added by portions with stirring to a cooled to −4 °C solution of isobutyl (2*S*,3*S*)-(+)-3-bromo-2-hydroxy-3-phenylpropionate **8** (obtained by method ***B***) (8.9 g, 29.6 mmol) in THF (50 mL) with a residual water content at most 0.02%. The mixture was stirred for 3 h at −4—20 °C to the completion of the reaction. An excess of the reactant was decomposed by the addition of water (1 mL). The solvent was removed under reduced pressure, a viscous residue was dissolved in an acetone—toluene mixture, and the solvent was evaporated to dryness. The product was isolated by preparative chromatography on Silicagel Si60 (column 3.5×60 cm, eluent dichloromethane, detection at λ = 254 nm).

Isobutyl (2*S*,3*S*)-(+)-2-[*N*-benzoyl(carbamoyloxy)]-3-bromo-3-phenylpropionate (11a). The yield was 12.47 g (94%), m.p.

123—124 °C; $[\alpha]_D^{20}$ +14.2° (*c* 0.5, EtOH). ^{1}H NMR ($CDCl_3$), δ: 8.20 (s, 1 H, NH); 7.20—7.80 (both m, 10 H, Ar); 5.75 (d, 1 H, C(3)H, *J* = 5.0 Hz); 5.40 (d, 1 H, C(2)H, *J* = 5.5 Hz); 3.90—4.00 (m, 2 H, CH_2, Bu^{i}O); 1.90—2.00 (m, 1 H, CH, Bu^{i}O); 0.90, 0.95 (both s, 6 H, 2 CH_3, Bu^{i}O). IR, ν/cm^{-1}: 3250, 2964 (m); 1772 (s); 1759 (s); 1749 (s); 1689 (m); 1524 (s); 1493 (m); 1217 (m); 1192 (s); 1059 (m); 698 (m). Found (%): C, 56.34; H, 4.85; Br, 17.69; N, 3.33. $C_{21}H_{22}BrNO_5$. Calculated (%): C, 56.26; H, 4.95; Br, 17.82; N, 3.12.

Isobutyl (2*S*,3*S*)-(+)-3-bromo-2-[*N*-(2,2,2-trichloroacetyl)-carbamoyloxy]-3-phenylpropionate (11b). $[\alpha]_D^{20}$ +16° (*c* 0.5, EtOH). ^{1}H NMR ($CDCl_3$), δ: 8.30 (s, 1 H, NH); 7.20—7.60 (m, 5 H, Ar); 5.75 (d, 1 H, C(3)H, *J* = 5.1 Hz); 5.50 (d, 1 H, C(2)H, *J* = 5.0 Hz); 3.90—4.00 (m, 2 H, CH_2, Bu^{i}O); 1.90—2.00 (m, 1 H, CH, Bu^{i}O); 0.90, 0.95 (both s, 6 H, 2 CH_3, Bu^{i}O).

Isobutyl (2*S*,3*S*)-(+)-3-bromo-2-[*N*-(chlorosulfonyl)carbamoyloxy]-3-phenylpropionate (11e). ^{1}H NMR ($CDCl_3$), δ: 8.40 (s, 1 H, NH); 7.20—7.65 (m, 5 H, Ar); 5.75 (d, 1 H, C(3)H, *J* = 5.2 Hz); 5.50 (d, 1 H, C(2)H, *J* = 5.1 Hz); 3.90—4.00 (m, 2 H, CH_2, Bu^{i}O); 1.90—2.00 (m, 1 H, CH, Bu^{i}O); 0.90, 0.95 (both s, 6 H, 2 CH_3, Bu^{i}O).

Methyl (2*R*,3*R*)-(−)-2-benzoylcarbamoyloxy-3-bromo-3-phenylpropionate (12a). $[\alpha]_D^{20}$ −23.1° (*c* 0.5, EtOH). ^{1}H NMR ($CDCl_3$), δ: 8.20 (s, 1 H, NH); 7.20—7.80 (m, 10 H, Ar); 5.75 (d, 1 H, C(3)H, *J* = 4.8 Hz); 5.40 (d, 1 H, C(2)H, *J* = 5.0 Hz); 3.70 (s, 3 H, CH_3). Found (%): C, 53.44; H, 4.00; Br, 19.39; N, 3.36. $C_{18}H_{16}BrNO_5$. Calculated (%): C, 53.22; H, 3.97; Br, 19.67; N, 3.45.

13-*O*-[(2*S*,3*S*)-2-[*N*-Benzoyl(carbamoyloxy)-3-bromo-3-phenylpropionyl]-7,10-*O*,*O*´-bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin (6a). A solution of benzoyl isocyanate (0.24 g, 1.62 mmol) in acetonitrile (3 mL) was added by portions with stirring at 20 °C to a solution of compound **5** (1.45 g, 1.3 mmol) in acetonitrile (15 mL) with the residual water content at most 0.01%. The mixture was stirred for 8 h at ambient temperature until the 95—97% conversion of the starting bromohydrin was achieved. A 3% aqueous solution of NH_4Cl (30 mL) was added to the reaction mixture, and organics were extracted with diethyl ether (2×40 mL). The organic phase was washed with water (50 mL) and dried over Na_2SO_4. The solvent was evaporated. Compound **6a** was isolated by preparative chromatography of the amorphous residue on Silicagel Si60 (column 3.5×60 cm, eluent acetone—dichloromethane (1.5 : 98.5 vol/vol), detection at λ = 254 nm) in a yield of 1.4 g (83% at the 92% conversion of the substrate). ^{1}H NMR ($CDCl_3$), δ: 8.6 (s, 1 H, NH); 8.00—8.10 (m, 2 H, Ar); 7.30—7.80 (m, 15 H, Ar); 6.20—6.35 (m, 2 H); 5.50—5.80 (m, 2 H); 5.30 (d, 1 H, CHBr, *J* = 6.0 Hz), 4.90 (m, 2 H); 4.60—4.80 (m, 3 H); 4.35 (m, C(2´)H); 4.10—4.30 (m, 3 H); 2.60—2.70 (m, 1 H); 2.40 (s, 3H); 2.00—2.30 (m, 3 H); 1.80—1.90 (m, 6 H); 1.60—1.80 (m, 4 H); 1.20, 1.30 (both s, 6 H, 2 CH_3). Found (%): C, 48.72; H, 3.92; Br, 6.24; Cl, 17.05; N, 1.13. $C_{51}H_{48}BrCl_6NO_{18}$. Calculated (%): C, 48.79; H, 3.85; Br, 6.36; Cl, 16.94; N, 1.12.

Intramolecular cyclization of compounds 6, 11, and 12 (general procedure). Sodium hydride (1.5—3.0 equiv., 60% dispersion in mineral oil) was added under an inert gas atmosphere in portions for 1 h with stirring to a solution cooled to −15 °C of 3-bromo-2-acylcarbamoyloxy-3-phenylpropionic acid ester (1 mmol) in THF (10 mL) with the residual water content at most 0.03%. The mixture was kept for 2 h under the indicated conditions, and 18-crown-6 (0.05 equiv.) was added. Stirring was continued, gradually raising the temperature of the mixture to ambient one within 3—6 h and monitoring the reaction course by HPLC. After the reaction completion, dichloromethane (15 mL) was added to the reaction mixture. An excess of NaH was decomposed with 5% HCl, maintaining pH not higher than 7.5. The organic phase was separated, washed with a 5% aqueous solution of NaCl, and dried over Na_2SO_4. The solvent was evaporated. Products **13**, **14**, and **17** were crystallized from EtOH, and product **7** was isolated by chromatography on Silicagel Si60 (column 3.5×60 cm, eluent dichloromethane—acetone, 98 : 2).

Isobutyl (4*S*,5*R*)-3-benzoyl-4-phenyloxazolidin-2-one-5-carboxylate (13). The yield was 88%, m.p. 143 °C (EtOH), $[\alpha]_D^{20}$ +1.5° (*c* 0.5, CH_2Cl_2). ^{1}H NMR ($CDCl_3$), δ: 7.30—7.70 (m, 10 H, Ar); 5.60—5.70 (d, 1 H, C(3)H, *J* = 5.5 Hz), 4.85—4.95 (d, 1 H, C(2)H, *J* = 5.2 Hz); 4.05—4.15 (d, 2 H, CH_2, Bu^{i}O); 1.95—2.10 (m, 1 H, CH, Bu^{i}O); 0.95, 1.05 (both s, 6 H, 2 CH_3, Bu^{i}O). IR, ν/cm^{-1}: 2962 (m); 1801 (s); 1761 (s); 1688 (s); 1323 (s); 1308 (s); 1294 (s); 1221 (s); 1182 (s); 1111 (s); 696 (m). Found (%): C, 68.64; H, 5.85; N, 3.73. $C_{21}H_{21}NO_5$. Calculated (%): C, 68.65; H, 5.76; N, 3.81.

Methyl (4*R*,5*S*)-3-benzoyl-4-phenyloxazolidin-2-one-5-carboxylate (14). The yield was 86%; $[\alpha]_D^{20}$ −13.7° (*c* 0.5, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 7.35—7.70 (m, 10 H, Ar); 5.65—5.70 (d, 1 H, C(3)H, *J* = 5.2 Hz); 4.90 (d, 1 H, C(2)H, *J* = 5.0 Hz); 3.90 (s, 3 H, CH_3). Found (%): C, 66.34; H, 4.52; N, 4.42. $C_{18}H_{15}NO_5$. Calculated (%): C, 66.46; H, 4.65; N, 4.31.

7,10-*O*´,*O*-Bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin-13*O*-yl (4*S*,5*R*)-3-benzoyl-4-phenyloxazolidin-2-one-5-carboxylate (7). The conversion of the target substrate was 97%. ^{1}H NMR ($CDCl_3$), δ: 8.00—8.10 (m, 2 H, Ar); 7.30—7.80 (m, 15 H, Ar); 6.15—6.35 (m, 2 H); 5.50—5.70 (m, 2 H); 5.30 (d, 1 H, CHPh, *J* = 6.0 Hz); 4.90 (m, 2 H); 4.60—4.90 (m, 3 H); 4.30—4.40 (m, C(O)C<u>H</u>CHPh); 4.10—4.30 (m, 3 H); 2.60—2.70 (m, 1 H); 2.40 (s, 3 H); 2.00—2.30 (m, 3 H); 1.80—1.90 (m, 6 H); 1.60—1.80 (m, 4 H); 1.20, 1.30 (both s, 6 H, 2 CH_3). Found (%): C, 52.22; H, 3.96; Cl, 18.20; N, 1.14. $C_{51}H_{47}Cl_6NO_{18}$. Calculated (%): C, 52.15; H, 4.03; Cl, 18.11; N, 1.19.

Isobutyl (4*S*,5*R*)-4-phenyloxazolidin-2-one-5-carboxylate (17) was synthesized similarly from compound **15**. The yield was 71%; $[\alpha]_D^{20}$ +1.1° (*c* 0.1, EtOH). ^{1}H NMR ($CDCl_3$), δ: 7.35—7.45 (m, 5 H, Ar); 5.70—5.80 (br.s, 1 H, NH); 5.00 (d, 1 H, C(3)H, *J* = 5.2 Hz); 4.80 (d, 2 H, C(2)H, *J* = 5.3 Hz); 4.00 (d, 2 H, CH_2, Bu^{i}O, *J* = 5.2); 1.95—2.05 (m, 1 H, CH, Bu^{i}O); 0.95, 1.05 (both s, 6 H, 2 CH_3, Bu^{i}O). IR, ν/cm^{-1}: 3240 (m); 3146 (m); 2980 (m); 1761 (s); 1753 (s); 1452 (m); 1385 (m); 1230 (m); 1205 (s); 1078 (s); 930 (m). Found (%): C, 63.84; H, 6.45; N, 5.23. $C_{14}H_{17}NO_4$. Calculated (%): C, 63.87; H, 6.51; N, 5.32.

Cleavage of 4-phenyloxazolidin-2-one-5-carboxylates under the action of alkali carbonates (general procedure). Anhydrous MeOH (4 mL) was added to a solution of 4-phenyloxazolidin-2-one-5-carboxylate **13**, **14**, or **7a** (0.25 mmol) in anhydrous THF (2 mL), and then Li_2CO_3 or K_2CO_3 (0.25 mmol) or Cs_2CO_3 (0.05 mmol) was added with stirring. The mixture was stirred at ambient temperature until the starting substrate disappeared, monitoring the reaction course by HPLC. Unreacted carbonate was filtered off (in the case of Cs_2CO_3, its residue was neutralized with dilute HCl), and the organic solvent was evaporated on a rotary evaporator.

(2*S*,3*R*)-(+)-*N*-Benzoyl-3-phenylisoserine methyl ester (2*S*,3*R*-18) was synthesized from compound **14** in the presence of 0.2 equiv. cesium carbonate (Aldrich). The reaction time was 1.5 h. The yield was 54%, m.p. 180—182 °C (*cf.* Ref. 9a:

181—183 °C). ^{1}H NMR ($CDCl_3$), δ: 7.30—7.80 (m, 10 H, Ar); 7.20 (d, 1 H, NH); 5.70 (dd, 1 H, J = 2.0 Hz, J = 8.5 Hz); 4.65 (d, 1 H, J = 2.0 Hz); 3.80 (s, 3 H, CH_3); 2.90 (br.s, 1 H, OH).

(2*R*,3*S*)-(−)-*N*-Benzoyl-3-phenylisoserine methyl ester (2*R*,3*S*-18) was synthesized from isobutyl ester **13** similarly to compound 2*S*,3*R*-**18**. The yield was 51%, m.p. 180—182 °C (*cf.* Ref. 9a: 181—183 °C); $[\alpha]_D^{20}$ −44° (*c* 0.9, EtOH) (*cf.* Ref. 9a: $[\alpha]_D^{20}$ −49° (*c* 1.0, MeOH)). ^{1}H NMR ($CDCl_3$), δ: 7.30—7.80 (m, 10 H, Ar); 7.20 (br.s, 1 H, NH); 5.70 (dd, 1 H, J = 2.0 Hz, J = 8.5 Hz); 4.75 (d,1 H, J = 3.0 Hz); 3.80 (s, 3 H, CH_3); 3.00 (br.s, 1 H).

Methyl (4*S*,5*R*)-3-benzoyl-4-phenyloxazolidin-2-one-5-carboxylate (4*S*,5*R*-14) was synthesized from isobutyl ester **13** in the presence of lithium carbonate (1.0 equiv.). The reaction time was 3 h. The yield was 95%. ^{1}H NMR ($CDCl_3$), δ: 7.40—7.80 (m, 10 H, Ar); 5.60—5.70 (d, 1 H, C(3)H, J = 5.0 Hz); 4.85—4.95 (d, 1 H, C(2)H, J = 5.0 Hz); 3.90 (s, 3 H, CH_3). Found (%): C, 66.57; H, 4.50; N, 4.38. $C_{18}H_{15}NO_5$. Calculated (%): C, 66.46; H, 4.65; N, 4.31.

(2*R*,3*S*)-(−)-3-Phenylisoserine methyl ester (2*R*,3*S*-19). Methanolysis of isobutyl ester **13** under the action of magnesium methoxide was carried out according to a described procedure.[62a] Anhydrous MeOH (9 mL) was added to a solution of compound **13** (0.27 g, 0.73 mmol, 1 equiv.) in anhydrous THF (6 mL). Then a freshly prepared methanolic solution of magnesium methoxide was added at ambient temperature with stirring in such a way that its content would be 20 equiv. The mixture was stirred, monitoring the reaction course by HPLC. When the required conversion of the substrate was achieved, the reaction mixture was neutralized with an acetate buffer to pH 7. Brine (15 mL) was added, and the product was extracted with dichloromethane (2×40 mL). The organic phase was separated and dried over sodium sulfate. Exhaustive methanolysis (25 h) gives compound 2*R*,3*S*-**19** in 75% yield (after a series of additional purifications). ^{1}H NMR ($CDCl_3$), δ: 7.35—7.45 (m, 5 H, Ar); 5.55 (m, 1 H); 5.00 (d, 1 H, J = 3.0 Hz); 4.75 (d, 1 H, J = 3.0 Hz); 3.85 (s, 3 H, CH_3); 1.60—1.90 (m, 2 H). Found (%): C, 61.57; H, 6.64; N, 7.08. $C_{10}H_{13}NO_3$. Calculated (%): C, 61.53; H, 6.71; N, 7.17.

The treatment of compound 2*R*,2*S*-**19** with benzoyl chloride in the presence of Et_3N gives (2*R*,3*S*)-(−)-*N*-benzoyl-3-phenylisoserine methyl ester (2*R*,3*S*-**18**), whose characteristics are identical to those described above.

3-Benzoyl-4-phenyloxazolidin-2-one-5-carboxylic acid. Concentrated hydrochloric acid (1 mL) was added to a solution of compound **13** (0.09 g, 0.25 mmol) in THF (3 mL), and the mixture was refluxed for 1 h. 3-*N*-Benzoyl-4-phenyloxazolidin-2-one-5-carboxylic acid that formed was isolated as described above for the enantiomer of *trans*-phenylglycidic acid (see synthesis of compound **4**).

Acylation of 7,10-*O*,*O*´-bis(2,2,2-trichloroethoxycarbonyl)-10-deacetylbaccatin (**3**) with a toluene solution of (4*S*,5*R*)-3-*N*-benzoyl-4-phenyloxazolidin-2-one-5-carboxylic acid was carried out as described in the patent.[57]

References

1. S. Neidl, *Cancer Drug Design and Discovery*, Acad. Press, New York—Burlington—San Diego—London, 2008, 473 pp.
2. *Wilson and Gisvold´s Textbook of Organic Medicinal and Pharmaceutical Chemistry*, 10th ed., Eds J. N. Delgado, W. A. Remers, Lippincott—Raven Publ., Philadelphia, 2008, 974 pp.
3. *Taxol: Science and Application*, Ed. M. Suffness, CRS Press, Boca Raton—London—New York—Washington (DC), 1995, 426 pp.
4. (a) M. Hepperle, G. Georg, *Drugs Future*, 1994, **19**, 573; (b) F. Guéritte-Voegelein, D. Guénard, F. Lavelle, M.-T. Le Goff, L. Mangatal, P. Potier, *J. Med. Chem.*, 1991, **34**, 992; (c) D. G. Kingston, G. Samaranayaka, C. A. Ivey, *J. Nat. Prod.*, 1990, **53**, 1.
5. D. G. Kingston, *J. Nat. Prod.*, 2000, **63**, 726.
6. H. Hónig P. Seufer-Wasserthal, H. Weber, *Tetrahedron*, 1990, **46**, 3841.
7. (a) B. Bhatia, S. Jain, A. De, I. Bagchi, J. Iqbal, *Tetrahedron Lett.*, **37**, 1996, 7311; (b) J. M. Chong, K. B. Sharpless, *J. Org. Chem.*, 1985, **50**, 1560.
8. (a) K. Harada, Y. Nakajima, *Bull. Chem. Soc. Jpn.*, 1974, **47**, 2911; (b) E. Kaji, A. Igarashi, S. Zen, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 3181.
9. (a) D.-M. Gou, Y.-C. Liu, C.-S. Chen, *J. Org. Chem.*, 1993, **58**, 1287; (b) T. Yamaguchi, N. Harada, K. Ozaki, M. Hayashi, H. Arakawa, T. Hashiyama, *Tetrahedron*, 1999, **55**, 1005; (c) J. N. Denis, A. Correa, A. E. Greene, *J. Org. Chem.*, 1990, **55**, 1957; (d) T. Yamaguchi, N. Harada, K. Ozaki, M. Hayashi, T. Hashiyama, *Tetrahedron Lett.*, 1998, **39**, 5575; (e) US Pat. 5677470; http://patft.uspto.gov.
10. (a) R. N. Patel, A. Banerjee, J. M. Howell, C. G. McNamee, D. Brozozowski, D. Mirfakhrae, V. Nanduri, J. K. Thottathil, L. J. Szarka, *Tetrahedron: Asymmetry*, 1993, **4**, 2069; (b) H. Hamamoto, V. A. Mamedov, M. Kitamoto, H. Hayashi, S. Tsuboi, *Tetrahedron: Asymmetry*, 2000, **11**, 4485.
11. (a) J. N. Denis, A. Correa, A. E. Greene, *J. Org. Chem.*, 1991, **56**, 6939; (b) A. M. Kanazawa, A. Correa, J. N. Denis, M. J. Luche, A. E. Greene, *J. Org. Chem.*, 1993, **58**, 255.
12. K. Hattori, H. Yamamoto, *Tetrahedron*, 1994, **50**, 2785.
13. C. S. Swindell, M. Tao, *J. Org. Chem.*, 1993, **58**, 5889.
14. C. Mukai, I. J. Kim, M. Hanaoka, *Tetrahedron: Asymmetry*, 1992, **3**, 1007.
15. (a) F. A. Davis, R. T. Reddy, R. E. Reddy, *J. Org. Chem.*, 1992, **57**, 6387; (b) M. E. Bunnage, S. G. Davies, C. J. Goodwin, *J. Chem. Soc., Perkin Trans.1*, 1993, 1375.
16. C. Palomo, A. Arrieta, F. P. Cossio, J. M. Aizpurua, A. Mielgo, N. Aurrekoetxea, *Tetrahedron Lett.*, 1990, **31**, 6429.
17. (a) US Pat. 5175315, http://patfl.uspto.gov/netahtml/PTO/srchnum.htm; (b) R. A. Holton, J. H. Lin, *Bioorg. Med. Chem. Lett.*, 1993, **3**, 2475.
18. (a) I. Ojima, I. Habus, M. Zhao, G. I. Georg, L. R. Jayasingha, *J. Org. Chem.*, 1991, **56**, 1681; (b) I. Ojima, I. Habus, *Tetrahedron Lett.*, 1990, **31**, 4289.
19. (a) P. G. M. Wuts, A. M. Anderson, M. P. Goble, S. F. Mancini, R. VanderRest, *Org. Lett.*, 2000, **2**, 2267; (b) L. Mangatal, M.-T. Adeline, D. Guénard, F. Guéritte-Voegelein, P. Potier, *Tetrahedron*, 1989, **45**, 4177.
20. (a) G. Righi, G. Rumboldt, C. Bonini, *J. Org. Chem.*, 1996, **61**, 3557; (b) B. N. Saha, J. Nandy, S. Shukla, I. Siddiqui, J. Iqbal, *J. Org. Chem.*, 2002, **67**, 7858; (c) Y. S. Rho Kim, W. J. Yoo, D. J. Ang, S. R. Chung, *Bull. Korean Chem. Soc.*, 2001, **22**, 963; (d) O. N. Zefirova, E. V. Selyunina, N. V. Zyk, N. S. Zefirov, *Zh. Org. Khim.*, 2003, **39**, 880 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2003, **39**, 831].
21. J. L. García Ruano, C. García Paredes, *Tetrahedron. Lett.*, 2000, **41**, 5357.

22. M. V. Voronkov, A. V. Goncharov, Z.-M. Wang, *Tetrahedron Lett.*, 2003, **44**, 407.
23. (a) G. Cardillo, L. Gantilucci, A. Tolomelli, C. Tomasini, *J. Org. Chem.*, 1998, **63**, 2351; (b) S.-H. Lee, J. Yoon, K. Nakamura, Y.-S. Lee, *Org. Lett.*, 2000 **2**, 1243.
24. (a) E. Baloglu, D. G. Kingston, *J. Nat. Prod.*, 1999, **62**, 1068; (b) Y. Hayashi, M. Skwarzynski, Y. Hamada, Y. Sohma, T. Kimura, Y. Kiso, *J. Med. Chem.*, 2003, **46**, 3782; (c) E. Didier, E. Fouque, A. Commersen, *Tetrahedron Lett.*, 1994, **35**, 3063.
25. A. Dondoni, D. Perrone, T. Semola, *Synthesis*, 1995, 181.
26. *United States Pharmacopoeia 30-National Formulary 25 (USP30-NF25)*, United States Pharmacopeial, Rockville, 2007, p. 2844.
27. (a) K. C. Nicolaou, W. M. Dai, R. K. Guy, *Angew. Chem., Int. Ed.*, 1994, **33**, 15.
28. (a) J. N. Denis, A. M. Kanazawa, A. E. Greene, *Tetrahedron Lett.*, 1994, **35**, 105; (b) C. Gennari, M. Carcano, M. Donghi, N. Mongelli, E. Vanotti, A. Vulpetti, *J. Org. Chem.*, 1997, **62**, 4746.
29. EP Pat. 0253738 (A1); http://wordwide.espacenet.com/?locate=en_EP.
30. US Pat. 6090951; http://patfl.uspto.gov/netahtml/PTO/srchnum.htm.
31. (a) US Pat. 6365750; http://patft.uspto.gov/netahtml/PTO/srchnum.htm; (b) US Pat. 5677462; http://patft.uspto.gov/netahtml/PTO/srchnum.htm.
32. (a) US Pat. 6210660 (B2); http://www.patentlens.net; (b) Eur. Pat. EP0582469 (A2); http://worldwide.espacenet.com/numberSearch?locale=en_EP.
33. D. G. I. Kingston, A. G. Chaudhary, A. A. L. Gunatilaka, M. L. Middleton, *Tetrahedron Lett.*, 1994 **35**, 4483.
34. I. Brackenridge, S. G. Davies, D. R. Fenwick, O. Ichihara, M. E. Polywka, *Tetrahedron*, 1999, **55**, 533.
35. L. I. Kas´yan, S. I. Okovityi, A. O. Kas´yan, *Zh. Org. Khim.*, 2004, **40**, 11 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2004, **40**, 1].
36. (a) W. N. Chan, J. M. Evans, M. S. Hadley, H. J. Herdon, J. C. Jerman, H. K. Morgan, T. O. Stean, M. Thompson, N. Upton, A. K. Vong, *J. Med. Chem.*, 1996, **39**, 4537; (b) D. Albanese, D. Landini, M. Penso, *Tetrahedron*, 1997, **53**, 4787.
37. (a) W. H. Staas, L. A. Spurlock, *J. Org. Chem.*, 1974, **39**, 3822; (b) W. R. Roush, M. A. Adam, *J. Org. Chem.*, 1985, **50**, 3752; (c) D. Tanner, A. Almario, Th. Högberg, *Tetrahedron*, 1995, **51**, 6061.
38. (a) U. Schmidt, M. Respondek, A. Lieberknecht, J. Werner, P. Fisher, *Synthesis*, 1989, 256; (b) S. Hatakeyama, H. Matsumoto, Y. Mukugi, H. Irie, *J. Org. Chem.*, 1997, **62**, 2275; (c) B. Bernet, A. Vassela, *Tetrahedron Lett.*, 1983, **24**, 5491.
39. (a) *Comprehensive Organic Chemistry*, Vol. **3**, Eds D. Barton, W. D. Ollis, Pergamon Press, Oxford, 1979, 1323 pp.; (b) M. B. Smith, H. N. Shroff, *Tetrahedron Lett.*, 1983, **24**, 2091.
40. F. Fringuelli, F. Pizzo, L. Vaccaro, *J. Org. Chem.*, 2001, **66**, 3554.
41. (a) D. Amantini, F. Fringuelli, F. Pizzo, L. Vaccaro, *J. Org. Chem.*, 2001, 446; (b) C. Bonini, G. Riggi, *Synthesis*, 1994, 225.
42. F. Guéritte-Voegelein, V. Sénilh, B. David, D. Guénard, P. Potier, *Tetrahedron*, 1986, **42**, 4451.
43. G. Moina, H. J. Williams, A. I. Scott, *Synth. Commun.*, 1996, **26**, 2235.
44. M. Varasi, K. A. M. Walker, M. L. Maddox, *J. Org. Chem.*, 1987, **52**, 4235.
45. R. Escher, P. Büning, *Angew. Chem., Int. Ed.*, 1986, 108.
46. E. J. Corey, S. Choi, *Tetrahedron Lett.*, 1991, **32**, 2857.
47. (a) L. Fieser, M. Fieser, *Reagents for Ordanic Synthesis*, J. Willey and Sons, New York—London—Sidney, 1970, Vol. **2**; (b) *Ibid.*, Vol. **1**.
48. R. Larsen, P. Davis, E. Corley, P. Reider, T. Lamanec, E. Grabowski, *J. Org. Chem.*, 1990, **55**, 299.
49. (a) S. Knapp, P. Kukkola, S. Sharma, S. Pietranico, *Tetrahedron Lett.*, 1987, **28**, 5399; (b) S. Knapp, *Chem. Soc. Rev.*, 1999, **28**, 61; (c) T. H. Al-Tel, R. A. Al-Qawasmeh, C. Schröder, W. Voelter, *Tetrahedron*, 1995, **51**, 3141.
50. (a) A. Hassner, M. E. Lorber, C. Heathcock, *J. Chem. Soc.*, 1967, **32**, 540; (b) S. Rajesh, M. Madhava Reddy, J. Iqbal, *Tetrahedron Lett.*, 1996, **37**, 7315.
51. A. Baba, K. Seki, H. Matsuda, *J. Org. Chem.*, 1991, **56**, 2684.
52. C. Tomasini, A. Vecchione, *Org. Lett.*, 1999, **1**, 2153.
53. J. N. Park, S. Y. Ko, H. Y. Koh, *Tetrahedron Lett.*, 2000, **41**, 5553.
54. F. Coelho, R. C. Rossi, *Tetrahedron Lett.*, 2002, **43**, 2797.
55. (a) J. De Blas, J. C. Carretero, E. Dominguez, *Tetrahedron Lett.*, 1994, **35**, 4603; (b) C. Battistini, C. Scarafile, M. Foglio, G. F. Franceschi, *Tetrahedron Lett.*, 1984, **25**, 2395; (c) H. Hirama, H. Hioki, S. Ito, *Tetrahedron Lett.*, 1988, **29**, 3125; (d) G. Dewynter, M. Abdaoui, L. Toupet, J.-L. Montero, *Tetrahedron Lett.*, 1997, **38**, 8691.
56. (a) R. Esmail, F. Kurzer, *Synthesis*, 1975, 301; (b) J. Rasmussen, A. Hassner, *Chem. Rev.*, 1976, **76**, 389; (c) D. N. Dhar, K. S. Keshava Murthy, *Synthesis*, 1986, 437.
57. US Pat. Apl. 20020068833 (A1); http://appft.uspto.gov/netahtml/PTO/srchnum.html.
58. M. E. Dyen, D. Swern, *Chem. Rev.*, 1967, **67**, 197.
59. D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.*, 1996, **96**, 835.
60. (a) N. Kanomato, S. Maruyama, K. Tomono, Sh. Anada, *Tetrahedron Lett.*, 2003, **44**, 3599; (b) S.-i. Fukuzawa, H. Matsuzawa, S.-i. Yoshimitsu, *J. Org. Chem.*, 2000, **65**, 1702; (c) D. A. Evans, T. C. Britton, J. A. Ellman, *Tetrahedron Lett.*, 1987, **28**, 6141; (d) R. E. Damon, G. M. Coppola, *Tetrahedron Lett.*, 1990, **31**, 2849; (e) S.-i. Fukuzawa, Yu. Hongo, *Tetrahedron Lett.*, 1998, **39**, 3521; (f) M. Hirama, H. Hioki, Sh. Ito, *Tetrahedron Lett.*, 1988, **29**, 3125; (g) A. J. Pearson, P. Zhang, *J. Org. Chem.*, 1996, **61**, 9603.
61. J. N. Denis, A. E. Greene, A. Serra, M. J. Luche, *J. Org. Chem.*, 1986, **51**, 46.
62. (a) P. G. Jagtap, D. G. I. Kingston, *Tetrahedron Lett.*, 1999, **40**, 189; (b) Q. Y. Zheng, L. G. Darbie, X. Cheng, C. Murray, *Tetrahedron Lett.*, 1995, **36**, 2001.
63. A. J. Gordon, R. A. Ford, *The Chemist´s Companion: A Handbook for Practical Data, Techniques, and References*, Wiley, New York, 1972, 537 pp.
64. W. Ried, E. Suarez-Rivero, *Chem. Ber.*, 1963, **96**, 1475.
65. M. Gudlitskii, *Khimiya organicheskikh soedinenii ftora* [*The Chemistry of Fluorine-Containing Organic Compounds*], GosNTI, Moscow, 1961, 372 pp. (in Russian).
66. Weygand-Hilgetag, *Organisch-chemische Experimentierkunst*, Johann Ambrosius Barth, 1964, 1142 S.

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