Synthesis G. Varró et al. Paper

Highly Stereoselective Synthesis of *trans*-Dihydronarciclasine Analogues

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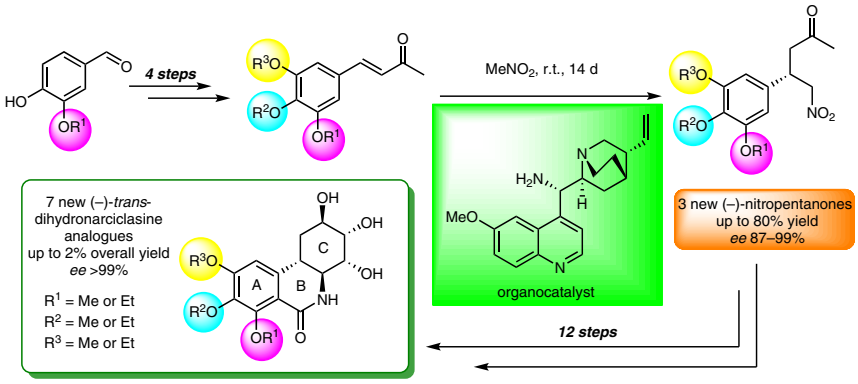

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Abstract Several new *trans*-dihydronarciclasine analogues were stereoselectively synthesised by applying our feasible and efficient process developed recently. These new phenanthridone alkaloid derivatives were obtained in both racemic and optically active forms. During their enantioselective syntheses, high selectivities (up to 99% ee) were achieved by using (8*S*,9*S*)-9-amino(9-deoxy)epiquinine as an organocatalyst. The modifications, the introduction of ethoxy or methoxy groups, were made in ring A of the phenanthridone scaffold.

Key words alkaloids, *trans*-dihydronarciclasine analogues, phenanthridone scaffold, stereoselective synthesis, organocatalysis

Previously we reported an efficient stereoselective total synthesis of racemic *trans*-dihydronarciclasine [(±)-**1**][1] and an enantioselective process for that of (–)-*trans*-dihydronarciclasine [(–)-**1**],[2] the *ent*-form of naturally occurring (+)-*trans*-dihydronarciclasine [(+)-**1**], a highly potent cytostatic alkaloid (Figure 1).

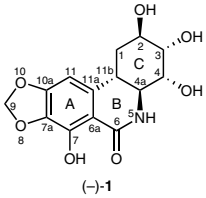


Figure 1 Structure of (–)-*trans*-dihydronarciclasine [(–)-**1**]

Beside compound (+)-**1**, pancratistatin (**2**), narciclasine (**3**), 7-deoxypancratistatin (**4**), lycoricidine (**5**) and 7-deoxy-*trans*-dihydronarciclasine (**6**) possessing a phenanthridone scaffold also belong to a subclass of the *Amaryllidaceae* alkaloid family (Figure 2). Compound (+)-**1** was first isolated by Pettit and co-workers from the bulbs of *Zephyranthes candida* in 1990.[3] Earlier this alkaloid was known as an unnatural derivative of narciclasine, because compound **1** was first prepared by the catalytic hydrogenation of **3**.[4] However, no uniform product was obtained in this reduction; namely, *cis*-dihydronarciclasine (**7**) and isonarciclasine (**8**) were also formed in considerable amounts (Scheme 1). Compound (+)-**1** is also known as the most potent anticancerous agent (GI_{50} = 12.6 nM) among these alkaloids, while *cis*-dihydronarciclasine (GI_{50} = 3800 nM) and isonarciclasine proved to be practically ineffective.[4a]

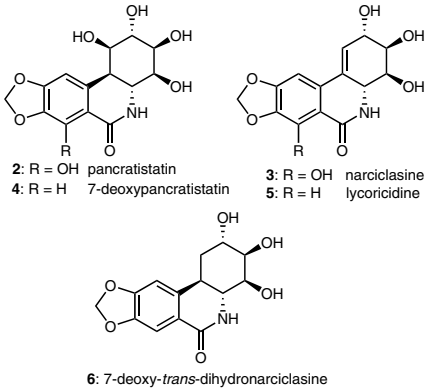
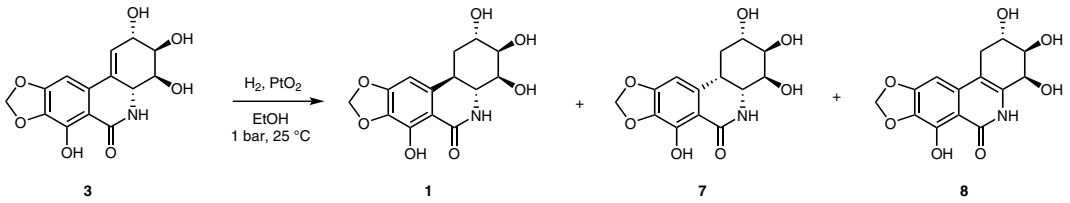


Figure 2 Further members **2**–**6** of the narciclasine subclass of the natural phenanthridone alkaloids

Furthermore, *Amaryllidaceae* alkaloids also have significant antiviral activities. Lycorine (**9**), the first alkaloid isolated from the *Amaryllidaceae* family, is one of the most screened compounds in this alkaloid family (Figure 3). It was found to have strong activity in the treatment of herpes simplex 1 and varicella zoster DNA viruses[5] and against several RNA viruses, such as avian influenza virus (H5N1)[6] or



3 1 7 8

Scheme 1 Phenanthridone alkaloids **1**, **7** and **8** obtained by catalytic hydrogenation of narciclasine (**3**)

SARS coronavirus.[7] Besides, lycorine showed inhibition against reverse transcriptase enzyme in the HIV-1 virus.[8] Amongst the phenanthridone alkaloids, compounds **2**, **3** and **5** also show strong antiviral activity against RNA viruses like the *Flaviviridae* (Japanese encephalitis, yellow fever or dengue).[9] More recently, significant anti-Zika virus activity of (+)-**1** has also been recorded.[10]

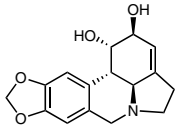


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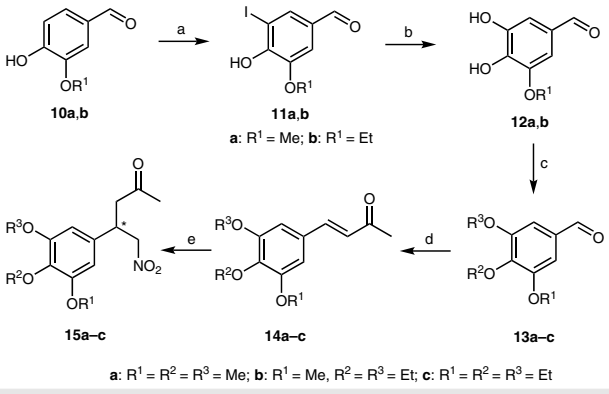
Figure 3 Structure of lycorine (**9**)

In the last two decades there have been intensive research efforts to clarify the structure–activity relationships of this alkaloid subgroup.[11] Thus, several modifications were made in the phenanthridone skeleton and the biological activity of these derivatives was determined. Whereas these changes were mainly concerned with the C ring of the phenanthridone scaffold,[12] so far only a few total syntheses have been reported where the aromatic ring (A) or its substituents were modified.[13] Moreover, the aim of these total syntheses was to obtain (+)-pancratistatin; i.e., *Amaryllidaceae* alkaloid derivatives without the dioxolane ring, but having phenolic oxygens at positions A-7, A-8 and A-9, have not been prepared up to now.

In this work, we describe the stereoselective synthesis of some new *trans*-dihydronarciclasine analogues possessing small alkyloxy substituents (ethoxy and/or methoxy) at positions A-8 and A-9, as well as A-7, A-8 and A-9, of the aromatic ring.

The synthesis of these new phenanthridone alkaloids was based on our previous total syntheses of the racemic[1] and (–)-*trans*-dihydronarciclasine,[2] and its 7-deoxy derivative.[14] As seen in Scheme 2, the synthesis started from vanillin (**10a**) or ethylvanillin (**10b**) which were selectively iodinated at position 5 of the aromatic ring, using a known method,[15] in excellent yields (96–99%). Then, the 5-iodo derivatives **11a** and **11b** were hydrolysed with 20% aqueous NaOH solution, in the presence of $CuSO_4$,[16] but some dehalogenation was observed in both cases. Therefore, after two recrystallisations of the crude products from toluene, the pure dihydroxy compounds **12a** and **12b** were obtained in moderate yields (62–64%). These dihydroxybenzaldehydes were reacted with ethyl bromide, in the presence of K_2CO_3 and a catalytic amount of KI, in DMF using the method of Miao and co-workers.[17] In both cases, the products were purified by distillation in vacuo to obtain the pure trialkyloxybenzaldehydes **13b** and **13c** in 90% yield. In the next step, these benzaldehydes along with the purchased 3,4,5-trimethoxybenzaldehyde (**13a**) were condensed with acetone, in the presence of NaOH, in an aqueous suspension. All three (trialkyloxyphenyl)butenone derivatives **14a**, **14b** and **14c** were purified by distillation in vacuo; compounds **14b** and **14c** were prepared in very good yields (86–92%), while the trimethoxy derivative **14a** was obtained in moderate yield (57%). The difference in the isolated yields can be attributed to a lower stability of the trimethoxy derivative **14a** under the distillation conditions.



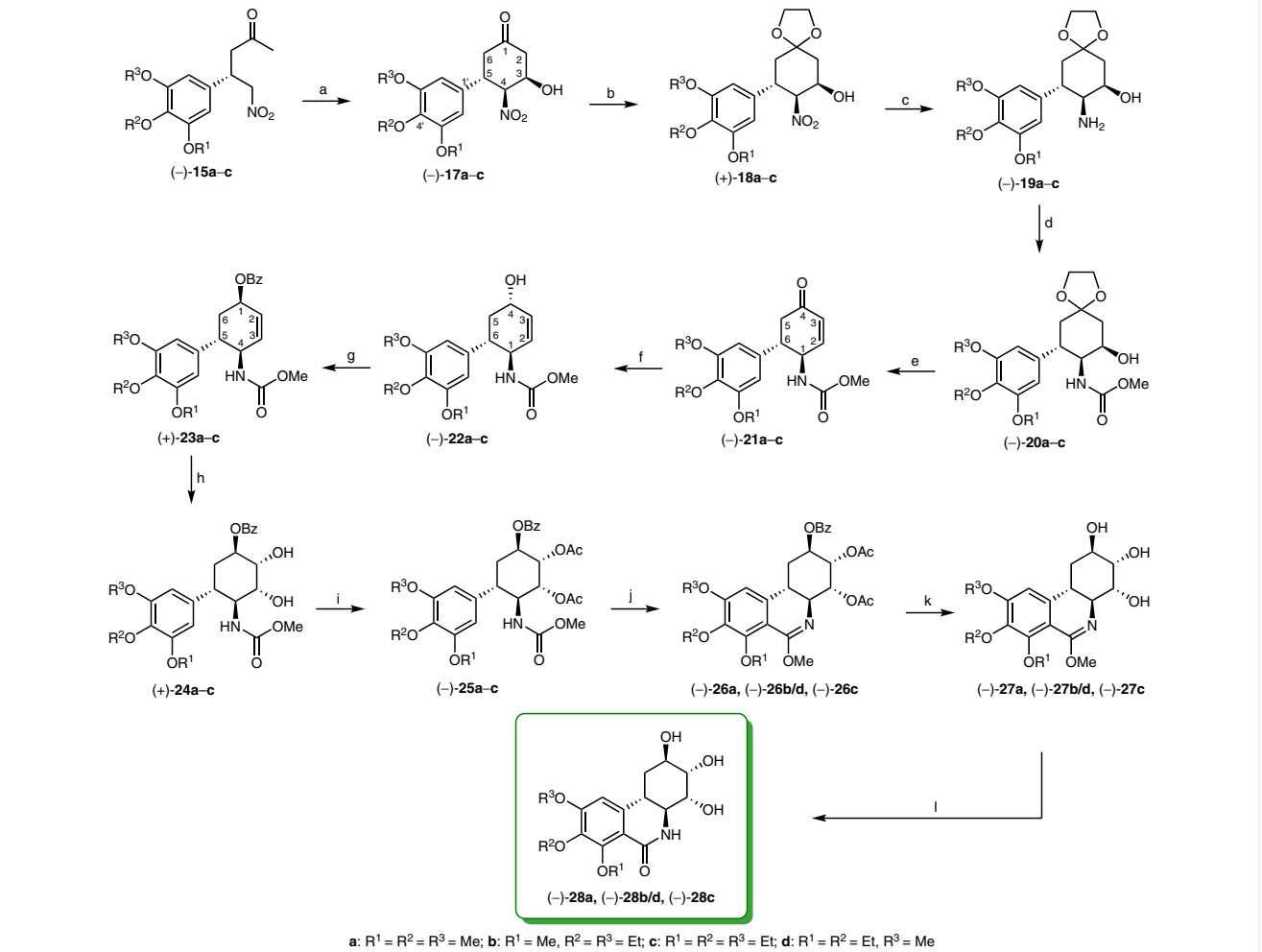
Scheme 2 Synthesis of racemic (trialkyloxyphenyl)nitropentanone derivatives **15a–c**. *Reagents and conditions*: a) I_2, KI, $NaHCO_3$, H_2O, r.t., 3 h; b) 20% aq NaOH, $CuSO_4$, reflux, 20 h; c) EtBr, K_2CO_3, KI, DMF, r.t., 20 h; d) acetone, NaOH, H_2O, r.t., 20 h; e) **15a**: $MeNO_2$, NaOMe, MeOH, reflux, 4 h, **15b**,**c**: $MeNO_2$, K_2CO_3, EtOH, reflux, 5 h.

In the next step, racemic nitropentanones (±)-**15a–c** were prepared by Michael addition of nitromethane to the (trialkyloxyphenyl)butenones **14a–c**. When Walker's method[18] ($MeNO_2$, NaOMe, MeOH) was used for this purpose, however, the trimethoxy derivative (±)-**15a** was obtained in moderate yield (53%). Therefore, the milder method of

Peseke and co-workers[19] ($MeNO_2$, K_2CO_3, EtOH) was applied, which gave the nitropentanones (±)-**15b** and (±)-**15c** with good or excellent yield (99% and 65%, respectively). This reaction also provides an opportunity to construct the first asymmetric centre of these compounds.

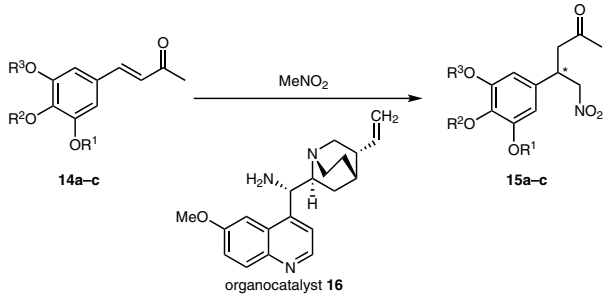
The results of the enantioselective Michael addition are summarised in Table 1. As seen, based on our previous experience[2] and using (8*S*,9*S*)-9-amino(9-deoxy)epiquinine (**16**) organocatalyst,[20] the optically active nitropentanones (–)-**15a**, (–)-**15b** and (–)-**15c** were prepared in good yield (59–80%) and very high enantioselectivity (87–99% ee) after 14 days. Our previous results[2] and the negative optical rotation values indicate that these new intermediates are suitable for obtaining (–)-*trans*-dihydronarciclasine analogues.

Hereinafter, only the syntheses of the optically active compounds are described, but the racemic derivatives can be prepared in the same way. The isolated yields and enantiomeric purities of all intermediates and products are summarised in Table 2. As shown in Scheme 3, ring C was closed by the Claisen–Henry reaction with ethyl formate and dry NaOMe in anhydrous Et_2O to give nitrocyclohexanolones (–)-**17a**, (–)-**17b** and (–)-**17c** in moderate yields (25–46%) after column chromatography or recrystallisation from EtOAc or Et_2O. This step was fully stereoselective, which was determined by the formation of a hydrogen bond between the C-3 hydroxy and C-4 nitro groups, as described by Walker[18] and observed by us during the enantioselective synthesis of (–)-**1**.[2] Prior to the catalytic hydrogenation of the nitro group, the carbonyl group of (–)-**17a**, (–)-**17b** or (–)-**17c** was converted into a cyclic ketal with ethylene glycol to give compounds (+)-**18a**, (+)-**18b** and



Scheme 3 Synthesis of trialkyloxy (–)-*trans*-dihydronarciclasine analogues (–)-**28a–d**. *Reagents and conditions*: a) HCOOEt, NaOMe, Et_2O, r.t., 20 h; b) $(CH_2OH)_2$, $(COOH)_2$, MeCN, r.t., 3 d; c) H_2, 10% Pd/C, MeOH, 60–65 °C, 6 h; d) ClCOOMe, aq NaOH, THF, r.t., 2 h; e) *p*-TsOH, acetone, reflux, 1 h; f) $NaBH_4$, $CaCl_2$, MeOH, 0 °C, 30 min; g) PhCOOH, DEAD, Ph_3P, THF, 45–50 °C, 5 h; h) OsO_4, NMO, H_2O, THF, argon atm, r.t., 24 h; i) AcCl, r.t., 24 h; j) Tf_2O, DMAP, CH_2Cl_2, 0 °C to r.t., 22 h; k) NaOMe, MeOH, anhyd THF, r.t., 2 h; l) 2 M aq HCl, THF, r.t., 24 h.

Table 1 Asymmetric Michael Addition of Nitromethane Using Organocatalyst **16** in the Synthesis of **15a–c**[a]

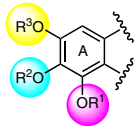


R^1	R^2	R^3	Product	Yield (%)[b]	ee (%)[c]
Me	Me	Me	(–)-**15a**	59	99
Me	Et	Et	(–)-**15b**	80	94
Et	Et	Et	(–)-**15c**	78	87

[a] Reaction conditions: compound **14a–c** (29 mmol), organocatalyst **16** (20 mol%), $MeNO_2$ (39 mL), r.t., 14 d.
[b] Isolated yield.
[c] Determined by chiral HPLC.

(+)-**18c** in good yields (62–76%), to avoid side reactions (e.g., formation of imines). Nitro ketal (+)-**18a**, (+)-**18b** or (+)-**18c** was reduced quantitatively to the corresponding amino derivatives (–)-**19a**, (–)-**19b** and (–)-**19c** over 10% Pd/C (Selcat Q-6[21]), in MeOH, at 12 bar and 60–65 °C, similarly to our previous results.[22] Amine (–)-**19a**, (–)-**19b** or (–)-**19c** was reacted with methyl chloroformate in a biphasic solvent mixture (THF–H_2O) to give urethanes (–)-**20a**, (–)-**20b** and (–)-**20c** in excellent yields (90–100%). The carbonyl group in compound (–)-**20a**, (–)-**20b** or (–)-**20c** was deprotected with *p*-TsOH in acetone, which was accompanied with dehydration, to obtain enones (–)-**21a**, (–)-**21b** and (–)-**21c** also in excellent yields (80–98%). Subsequent stereoselective reduction of compound (–)-**21a**, (–)-**21b** or (–)-**21c** with $NaBH_4$ in the presence of $CaCl_2$ (Utimoto's method[23]) provided the corresponding allyl alcohols (–)-**22a**, (–)-**22b** and (–)-**22c** in good yields (62–90%) and with excellent enantiomeric purity (>99% ee) after recrystallisation from hexane–EtOAc (2:1). This was due to an axial attack of the small hydride ion derived from $NaBH_4$ enhanced by the coordination with Ca^{2+}, resulting in an equatorial position of the formed hydroxy group. As its position in the final product is axial, its inversion in compound (–)-**22a**, (–)-**22b** or (–)-**22c** was realised by the Mitsunobu reaction[24] (DEAD, Ph_3P, THF), in the presence of benzoic acid, resulting in benzoates (+)-**23a**, (+)-**23b** and (+)-**23c** in moderate yields (40–57%) after column chromatography.

Table 2 Summary of All New Optically Active Intermediates and Products in the Synthesis of (–)-*trans*-Dihydronarciclasine Analogues



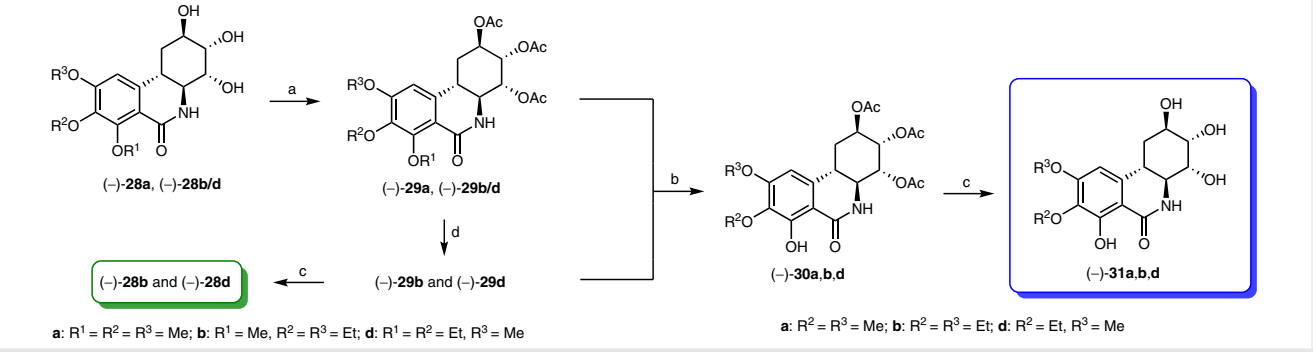
R^1	R^2	R^3	Product	Yield (%)[a]	ee (%)[b]
Me	Me	Me	(–)-**17a**	46	99
Me	Et	Et	(–)-**17b**	42	97
Et	Et	Et	(–)-**17c**	25	92
Me	Me	Me	(+)-**18a**	62	99
Me	Et	Et	(+)-**18b**	76	97
Et	Et	Et	(+)-**18c**	74	92
Me	Me	Me	(–)-**19a**	98	99
Me	Et	Et	(–)-**19b**	100	97
Et	Et	Et	(–)-**19c**	97	92
Me	Me	Me	(–)-**20a**	98	99
Me	Et	Et	(–)-**20b**	90	97
Et	Et	Et	(–)-**20c**	100	92
Me	Me	Me	(–)-**21a**	98	99
Me	Et	Et	(–)-**21b**	80	96
Et	Et	Et	(–)-**21c**	82	91
Me	Me	Me	(–)-**22a**	90	>99
Me	Et	Et	(–)-**22b**	62	>99
Et	Et	Et	(–)-**22c**	80	>99
Me	Me	Me	(+)-**23a**	57	>99
Me	Et	Et	(+)-**23b**	40	>99
Et	Et	Et	(+)-**23c**	57	>99
Me	Me	Me	(+)-**24a**	100	>99
Me	Et	Et	(+)-**24b**	99	>99
Et	Et	Et	(+)-**24c**	59	>99
Me	Me	Me	(–)-**25a**	99	>99
Me	Et	Et	(–)-**25b**	100	>99
Et	Et	Et	(–)-**25c**	100	>99
Me	Me	Me	(–)-**26a**	80	>99
Me	Et	Et	(–)-**26b**	75[c]	>99
Et	Et	Et	(–)-**26c**	82	>99
Et	Et	Me	(–)-**26d**	75[c]	>99
Me	Me	Me	(–)-**27a**	77	>99
Me	Et	Et	(–)-**27b**	100[d]	>99
Et	Et	Et	(–)-**27c**	85	>99
Et	Et	Me	(–)-**27d**	100[d]	>99
Me	Me	Me	(–)-**28a**	26	>99
Me	Et	Et	(–)-**28b**	73[e]	>99
Et	Et	Et	(–)-**28c**	76	>99

R^1	R^2	R^3	Product	Yield (%)[a]	ee (%)[b]
Et	Et	Me	(–)-**28d**	49[f]	>99
Me	Me	Me	(–)-**29a**	42	>99
Me	Et	Et	(–)-**29b**	20	>99
Et	Et	Me	(–)-**29d**	38	>99
H	Me	Me	(–)-**30a**	76	>99
H	Et	Et	(–)-**30b**	77	>99
H	Et	Me	(–)-**30d**	58	>99
H	Me	Me	(–)-**31a**	79	>99
H	Et	Et	(–)-**31b**	80	>99
H	Et	Me	(–)-**31d**	78	>99

[a] Isolated yield.
[b] Determined by chiral HPLC.
[c] 1:1 mixture of **26b**/**d**.
[d] 1:1 mixture of **27b**/**d**.
[e] From **29b**.
[f] From **29d**.

Using the Sharpless–Upjohn method,[25] *cis*-dihydroxylation of compound (+)-**23a**, (+)-**23b** or (+)-**23c** gave the *cis*-diols (+)-**24a**, (+)-**24b** and (+)-**24c** in very good yields (59–100%), using NMO and OsO_4 catalyst in THF–H_2O. In this step, the stereoselectivity was provided by the steric hindrance of the bulky, axial benzoyl group. Before ring B was closed, the hydroxy groups in compound (+)-**24a**, (+)-**24b** or (+)-**24c** were protected with acetyl chloride, resulting in the diacetoxy derivatives (–)-**25a**, (–)-**25b** and (–)-**25c** in quantitative yields. Although uniform methoxyphenanthridines were obtained in the case of the trimethoxy and triethoxy derivatives (–)-**26a** and (–)-**26c** after the Bischler–Napieralski ring-closure reaction modified by Banwell[26] in very good yield (80–82%), the 3,4-diethoxy-5-methoxy derivative contained two regioisomers (–)-**26b** and (–)-**26d** in a ratio of 1:1. Moreover, the regioisomers proved to be inseparable in this step. This phenomenon has also been observed in several total syntheses of pancratistatin[27] and *trans*-dihydronarciclasine[1,2,28] when Banwell's method was applied. At this stage we had to modify our synthetic strategy, because during the formation of the lactam ring by cleaving the methoxy group in ring B, two regioisomers were lost due to dealkylation of the methyl or ethyl group in ring A. Furthermore, there was another problem in this step; namely, the trimethoxy derivative cannot be obtained using our method[1,2] described earlier because of insolubility of the target molecule. To avoid these problems, the protected methoxyphenanthridine (–)-**26a**, (–)-**26b**/**d** or (–)-**26c** was deacetylated using Zemplén's method[29] (NaOMe, MeOH) in THF, giving the methoxyphenanthridinetriols (–)-**27a**, (–)-**27b**/**d** and (–)-**27c** in very good yields (77–100%). They were subsequently converted into lactams (–)-**28a**, (–)-**28b**/**d** and (–)-**28c**, respectively, in moderate yields (26–76%), in the presence of HCl in THF. It should also be noted that trace amounts of acids induce the transformation of methoxyphenanthridines to lactams. We also observed this conversion of the methoxyphenanthridinetriols after they were left standing for a few days.

During the cleavage of the A-7 alkyloxy moiety to obtain a hydroxy group, which potentially enhances the biological activity, another selectivity problem can arise; namely, ring A contains a further two alkyloxy groups. Further transformation of the triethoxy derivative (–)-**28c** was not considered, because its A-7 dealkylation results in the same diethoxy product [i.e., (–)-**31b**] as can be obtained from compound (–)-**28b**. Since our object was to prepare compounds possessing a hydroxy group only at position 7, the three hydroxy groups in ring C had to be protected (Scheme 4). Therefore, compound (–)-**28a** or (–)-**28b**/**d** was acetylated with acetyl chloride, giving triacetoxyphenanthridones (–)-**29a** and (–)-**29b**/**d**; surprisingly, we were able to separate the regioisomers (–)-**29b** and (–)-**29d** by preparative TLC (hexane–EtOAc, 1:1). Then, the pure triacetoxyphenanthridones were reacted with TMSCl in MeCN to obtain the 7-hydroxy derivatives (–)-**30a**, (–)-**30b** and (–)-**30d** in good yields (58–77%). According to the analytical results, only the alkyloxy group at position 7 was cleaved; no byproducts were detected. Finally, the repeated Zemplén deacetylation provided the target compounds (–)-**31a**, (–)-



Scheme 4 Synthesis of dialkyloxy (–)-*trans*-dihydronarciclasine analogues (–)-**31a**, (–)-**31b** and (–)-**31d**. *Reagents and conditions*: a) AcCl, r.t., 20–24 h; b) TMSCl, KI, anhyd MeCN, 50–60 °C, 3–5 h; c) NaOMe, MeOH, anhyd THF, r.t., 2 h; d) preparative TLC (hexane–EtOAc, 1:1).

31b and (–)-**31d** in very good yields (78–80%); as well, the isolated triacetoxyphenanthridones (–)-**29b** and (–)-**29d** were converted into the lactams (–)-**28b** and (–)-**28d**, respectively, in good yields (49–73%).

In conclusion, four trialkyloxy [(–)-**28a–d**] and three dialkyloxy-7-hydroxy [(–)-**31a**, (–)-**31b** and (–)-**31d**] (–)-*trans*-dihydronarciclasine analogues, substituted in ring A, were prepared by using stereo- and enantioselective synthetic steps. These new, optically active derivatives were obtained with excellent enantiomeric purity (>99% ee). According to their negative optical rotation values, these compounds appear to be new analogues of (–)-*trans*-dihydronarciclasine. After the modified Bischler–Napieralski step was applied, the 3,4-diethoxy-5-methoxy regioisomers were successfully separated in a simple way (preparative TLC). Biological evaluation of these new, potentially antitumoral and antiviral molecules is in progress.

Compounds **11a**, **12a** and **16** were prepared as described previously,[2] while 3,4,5-trimethoxybenzaldehyde (**13a**) was purchased from Alfa Aesar. All other reagents are commercially available (Merck). Melting points were measured on a Büchi 510 apparatus using a certified mercury thermometer (ASTM 2C). Optical rotations were measured on a Perkin Elmer 241 polarimeter. IR spectra were obtained on a Perkin Elmer 1600 FT-IR instrument. NMR spectra were recorded on a Bruker AV-300 instrument. HPLC analyses were carried out with a Jasco PU-1580 apparatus equipped with a Jasco UV-1575 detector (λ = 256 nm) using a Daicel Chiralpack® AS-H (250 × 4.6 mm × 5 µm) column (eluent: hexane–*i*-PrOH, 8:2; flow rate: 2.0 mL·min^{-1}; 20 °C). Elemental analyses were performed on a vario EL III instrument (Elementar Analysensysteme). Precoated silica gel plates (Merck 60 F_{254}) were used for analytical TLC and Kieselgel 60 for column cromatography.

5-Iodoethylvanillin (11b)

To a solution of $NaHCO_3$ (22.50 g, 0.27 mol) and KI (45.00 g, 0.27 mol) in water (900 mL) was added ethylvanillin (36.55 g, 0.22 mol) under rigorous stirring. Then, I_2 (56.70 g, 0.22 mmol) was added in four portions in 30 min. The reaction mixture was stirred for 3 h at r.t., then was allowed to stand overnight. The crude product was collected by filtration, then washed with dilute $Na_2S_2O_3$ solution and water to give compound **11b** as a light brown powder, which was used without further purification.

Yield: 61.68 g (96%); mp 129–130 °C; R_f = 0.68 (hexane–EtOAc, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.75 (s, 1 H, CHO), 7.80 (s, 1 H, 6-H_{Ar}), 7.35 (s, 1 H, 2-H_{Ar}), 6.80 (br s, 1 H, OH), 4.20 (q, *J* = 6.9 Hz, 2 H, OCH_2CH$_3$), 1.48 (t, *J* = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.6 (CHO), 151.5 (4-C_{Ar}), 145.7 (3-C_{Ar}), 136.0 (6-C_{Ar}), 131.0 (1-C_{Ar}), 109.3 (2-C_{Ar}), 80.3 (5-C_{Ar}), 65.3 (OCH_2CH$_3$), 14.6 (OCH$_2$$CH_3$).

5-Hydroxyethylvanillin (12b)

A mixture of 5-iodoethylvanillin (**11b**; 93.46 g, 0.32 mol), $CuSO_4$·5H_2O (16.24 g, 65.10 mmol) and 20% aqueous NaOH solution (1500 mL) was heated to reflux and stirred for 20 h. Then, it was cooled below 10 °C and acidified with concd HCl to pH 2. The mixture was filtered and the aqueous phase was extracted with EtOAc (4 × 900 mL). The combined organic phase was dried over $MgSO_4$ and concentrated to give the dark grey, crude product. After recrystallisation from toluene, compound **12b** was obtained as light grey crystals.

Yield: 36.14 g (62%); mp 105–108 °C (Lit.[30] 117–118 °C); R_f = 0.44 (hexane–EtOAc, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.78 (s, 1 H, CHO), 7.15 (d, *J* = 1.5 Hz, 1 H, 2-H_{Ar}), 7.07 (d, *J* = 1.2 Hz, 1 H, 6-H_{Ar}), 6.22 (br s, 1 H, OH), 5.75 (br s, 1 H, OH), 4.20 (q, *J* = 6.9 Hz, 2 H, OCH_2CH$_3$), 1.48 (t, *J* = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.2 (CHO), 146.5 (3-C_{Ar}), 144.0 (5-C_{Ar}), 138.6 (4-C_{Ar}), 128.9 (1-C_{Ar}), 112.8 (6-C_{Ar}), 103.7 (2-C_{Ar}), 65.0 (OCH_2CH$_3$), 14.7 (OCH$_2$$CH_3$).

Trialkyloxybenzaldehydes 13b and 13c; General Procedure

To a solution of compound **12a** or **12b** (89.2 mmol) in DMF (134 mL) were added anhydrous K_2CO_3 (24.65 g, 0.18 mol), KI (1.48 g, 8.92 mmol) and EtBr (20 mL, 29.22 g, 0.27 mol), and the reaction mixture was stirred at r.t. for 20 h. Then, CH_2Cl_2 (178 mL) was added, and the inorganic solid was removed by filtration. The filtrate was washed with brine (3 × 268 mL), then the aqueous layer was extracted with CH_2Cl_2 (2 × 71 mL). The combined organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by distillation in vacuo to give trialkyloxybenzaldehyde **13b** or **13c**.

3,4-Diethoxy-5-methoxybenzaldehyde (13b)

Yield: 18.01 g (90%); white solid; mp 25–26 °C (Lit.[31] ~20 °C); bp 92–95 °C/0.4 mbar (Lit.[31] 95–110 °C/0.4 mbar); R_f = 0.76 (hexane–EtOAc, 1:1).

IR (KBr): 2980, 2937, 1694, 1586, 1498, 1432, 1387, 1328, 1231, 1126, 1029, 843, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.85 (s, 1 H, CHO), 7.11 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.17 (q, *J* = 7.2 Hz, 2 H, OCH_2CH$_3$), 4.14 (q, *J* = 6.9 Hz, 2 H, OCH_2CH$_3$), 3.91 (s, 3 H, OCH$_3$), 1.46 (t, *J* = 6.9 Hz, 3 H, OCH$_2$$CH_3$), 1.38 (t, *J* = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.1 (CHO), 154.1 (3-C_{Ar}), 153.2 (5-C_{Ar}), 143.1 (4-C_{Ar}), 131.6 (1-C_{Ar}), 108.2 (2-C_{Ar}), 106.4 (6-C_{Ar}), 69.2 (OCH_2CH$_3$), 64.8 (OCH_2CH$_3$), 56.3 (OCH$_3$), 15.6 (OCH$_2$$CH_3$), 14.8 (OCH$_2$$CH_3$).

3,4,5-Triethoxybenzaldehyde (13c)

Yield: 19.08 g (90%); white solid; mp 48 °C (Lit.[32] 68 °C); bp 109 °C/0.3 mbar; R_f = 0.70 (hexane–EtOAc, 1:1).

IR (KBr): 3062, 2977, 2930, 2882, 1689, 1587, 1499, 1444, 1393, 1329, 1234, 1123, 829, 736 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.83 (s, 1 H, CHO), 7.09 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.16 (q, *J* = 6.9 Hz, 2 H, OCH_2CH$_3$), 4.13 (q, *J* = 6.9 Hz, 4 H, 2 × OCH_2CH$_3$), 1.46 (t, *J* = 6.9 Hz, 6 H, 2 × OCH$_2$$CH_3$), 1.37 (t, *J* = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.2 (CHO), 153.3 (3-C_{Ar} and 5-C_{Ar}), 143.6 (4-C_{Ar}), 131.5 (1-C_{Ar}), 108.0 (2-C_{Ar} and 6-C_{Ar}), 69.1 (OCH_2CH$_3$), 64.8 (2 × OCH_2CH$_3$), 15.6 (OCH$_2$$CH_3$), 14.8 (2 × OCH$_2$$CH_3$).

(Trialkyloxyphenyl)butenones 14a, 14b and 14c; General Procedure

A solution of the benzaldehyde derivative **13a**, **13b** or **13c** (80.7 mmol) in acetone (74 mL) was added to water (34 mL); then, the starting material precipitated in a fine crystal form. Aqueous NaOH solution [from NaOH (1.21 g, 30.3 mmol) and water (5.5 mL)] and finally water (303 mL) were also added, and the yellow mixture was

stirred intensively at r.t. for 20 h. The crude product was collected by filtration, washed with water and dried. Finally, it was purified by distillation in vacuo to give (trialkyloxyphenyl)butenone **14a**, **14b** or **14c**.

4-(3,4,5-Trimethoxyphenyl)but-3-en-2-one (14a)

Yield: 10.87 g (57%); yellow solid; mp 87–89 °C (Lit. 87–89 °C,[33a] 86 °C,[33b] 84–86 °C[33c]); bp 136–140 °C/0.3 mbar; R_f = 0.49 (hexane–EtOAc, 1:1).

IR (KBr): 2997, 2940, 1670, 1645, 1580, 1504, 1465, 1339, 1251, 1127, 997, 981, 811 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 16.2 Hz, 1 H, Ar–*CH*=CH), 6.77 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.65 (d, *J* = 16.2 Hz, 1 H, CH=*CH*CO), 3.89 (s, 9 H, 3 × OCH_3), 2.37 (s, 3 H, $COCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.2 (CO), 153.4 (3-C_{Ar} and 5-C_{Ar}), 143.4 (Ar–*CH*=CH), 140.3 (4-C_{Ar}), 129.8 (1-C_{Ar}), 126.5 (CH=*CH*CO), 105.4 (2-C_{Ar} and 6-C_{Ar}), 61.0 (OCH_3), 56.1 (2 × OCH_3), 27.4 ($COCH_3$).

4-(3,4-Diethoxy-5-methoxyphenyl)but-3-en-2-one (14b)

Yield: 18.34 g (86%); white solid; mp 86–89 °C; bp 148–152 °C/0.3 mbar; R_f = 0.60 (hexane–EtOAc, 1:1).

IR (KBr): 2980, 2939, 1666, 1643, 1578, 1504, 1449, 1386, 1339, 1251, 1124, 993, 900, 827 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 16.5 Hz, 1 H, Ar–*CH*=CH), 6.76 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.61 (d, *J* = 16.5 Hz, 1 H, CH=*CH*CO), 4.11 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 4.09 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 3.87 (s, 3 H, OCH_3), 2.37 (s, 3 H, $COCH_3$), 1.45 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.36 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.2 (CO), 153.9 (3-C_{Ar}), 153.1 (5-C_{Ar}), 143.7 (Ar–*CH*=CH), 139.9 (4-C_{Ar}), 129.6 (1-C_{Ar}), 126.3 (CH=*CH*CO), 107.0 (2-C_{Ar}), 105.4 (6-C_{Ar}), 69.1 (OCH_2CH_3), 64.7 (OCH_2CH_3), 56.2 (OCH_3), 27.4 ($COCH_3$), 15.6 (OCH_2CH_3), 14.9 (OCH_2CH_3).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.16; H, 7.62.

4-(3,4,5-Triethoxyphenyl)but-3-en-2-one (14c)

Yield: 20.77 g (92%); white solid; mp 114–115 °C; bp 150–151 °C/0.4 mbar; R_f = 0.64 (hexane–EtOAc, 1:1).

IR (KBr): 2985, 2938, 2891, 1667, 1644, 1579, 1504, 1436, 1392, 1337, 1250, 1123, 993, 819 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 16.2 Hz, 1 H, Ar–*CH*=CH), 6.75 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.59 (d, *J* = 16.2 Hz, 1 H, CH=*CH*CO), 4.10 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.09 (q, *J* = 6.9 Hz, 4 H, 2 × OCH_2CH_3), 2.37 (s, 3 H, $COCH_3$), 1.44 (t, *J* = 6.9 Hz, 6 H, 2 × OCH_2CH_3), 1.36 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.3 (CO), 153.2 (3-C_{Ar} and 5-C_{Ar}), 143.7 (Ar–*CH*=CH), 140.4 (4-C_{Ar}), 129.5 (1-C_{Ar}), 126.2 (CH=*CH*CO), 107.0 (2-C_{Ar} and 6-C_{Ar}), 69.0 (OCH_2CH_3), 64.8 (2 × OCH_2CH_3), 27.4 ($COCH_3$), 15.6 (OCH_2CH_3), 14.9 (2 × OCH_2CH_3).

Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.03; H, 7.98.

Racemic (Trialkyloxyphenyl)nitropentanones (±)-15b and (±)-15c; General Procedure

To a solution of compound **14b** or **14c** (28.4 mmol) in a mixture of anhydrous EtOH (11.3 mL) and $MeNO_2$ (7.68 mL, 8.66 g, 0.14 mol) was added anhydrous K_2CO_3 (0.08 g, 0.58 mmol) and the reaction mixture was refluxed for 5 h. Then, it was cooled to r.t. and water (14.3 mL) was added. After extraction with CH_2Cl_2 (3 × 50 mL), the organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was recrystallised from MeOH to give racemic (trialkyloxyphenyl)nitropentanone (±)-**15c** or used without further purification [(±)-**15b**].

(±)-4-(3,4-Diethoxy-5-methoxyphenyl)-5-nitropentan-2-one [(±)-15b]

Yield: 9.14 g (99%); orange oil; R_f = 0.44 (hexane–EtOAc, 1:1).

IR (KBr): 2980, 2938, 1717, 1553, 1507, 1456, 1378, 1333, 1235, 1125, 819 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.38 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.69–4.54 (m, 2 H, CH_2NO_2), 4.04 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.01 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 3.92 (quint, *J* = 6.9 Hz, 1 H, Ar–CH), 3.82 (s, 3 H, OCH_3), 2.88 (d, *J* = 6.9 Hz, 2 H, CH_2CO), 2.13 (s, 3 H, $COCH_3$), 1.41 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.33 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.4 (CO), 153.9 (3-C_{Ar}), 153.1 (5-C_{Ar}), 137.1 (1-C_{Ar}), 134.1 (4-C_{Ar}), 106.0 (2-C_{Ar}), 104.5 (6-C_{Ar}), 79.4 (CH_2NO_2), 68.8 (OCH_2CH_3), 64.7 (OCH_2CH_3), 56.2 (OCH_3), 46.3 (CH_2CO), 39.3 (Ar–CH), 30.4 ($COCH_3$), 15.5 (OCH_2CH_3), 14.9 (OCH_2CH_3).

Anal. Calcd for $C_{16}H_{23}NO_6$: C, 59.06; H, 7.13; N, 4.31. Found: C, 59.05; H, 7.14; N, 4.30.

(±)-5-Nitro-4-(3,4,5-triethoxyphenyl)pentan-2-one [(±)-15c]

Yield: 6.26 g (65%); white solid; mp 57–58 °C; R_f = 0.50 (hexane–EtOAc, 1:1).

IR (KBr): 2982, 2938, 2883, 1719, 1550, 1507, 1445, 1382, 1317, 1253, 1232, 1118, 819, 669 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.37 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.66–4.54 (m, 2 H, CH_2NO_2), 4.04 (q, *J* = 7.0 Hz, 4 H, 2 × OCH_2CH_3), 4.02 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 3.90 (quint, *J* = 7.0 Hz, 1 H, Ar–CH), 2.87 (d, *J* = 7.0 Hz, 2 H, CH_2CO), 2.12 (s, 3 H, $COCH_3$), 1.40 (t, *J* = 6.9 Hz, 6 H, 2 × OCH_2CH_3), 1.32 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.5 (CO), 153.2 (3-C_{Ar} and 5-C_{Ar}), 137.7 (1-C_{Ar}), 133.9 (4-C_{Ar}), 106.2 (2-C_{Ar} and 6-C_{Ar}), 79.4 (CH_2NO_2), 68.8 (OCH_2CH_3), 64.8 (2 × OCH_2CH_3), 46.3 (CH_2CO), 39.3 (Ar–CH), 30.4 ($COCH_3$), 15.6 (OCH_2CH_3), 14.9 (2 × OCH_2CH_3).

Anal. Calcd for $C_{17}H_{25}NO_6$: C, 60.16; H, 7.42; N, 4.13. Found: C, 60.15; H, 7.43; N, 4.14.

(±)-5-Nitro-4-(3,4,5-trimethoxyphenyl)pentan-2-one [(±)-15a]

A solution of compound **14a** (7.2 g, 30.5 mmol) in anhydrous MeOH (30 mL) and $MeNO_2$ (4.4 mL, 5.0 g, 81.2 mmol) was stirred under reflux. Freshly prepared NaOMe [from Na (0.15 g, 6.5 mmol) and anhydrous MeOH (10 mL)] was added dropwise for an hour, then the reaction mixture was further stirred for 4 h under reflux. The solvent was evaporated and the residue was dissolved in $CHCl_3$ (50 mL), then washed with 20% AcOH solution (100 mL) and water (4 × 50 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. After recrystallisation from MeOH, compound (±)-**15a** was obtained as a white solid.

Yield: 5.16 g (53%); mp 93 °C; R_f = 0.29 (hexane–EtOAc, 1:1).

IR (KBr): 2960, 2840, 1721, 1544, 1509, 1465, 1372, 1362, 1254, 1126, 842, 775 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.40 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.71–4.56 (m, 2 H, CH_2NO_2), 3.95 (quint, *J* = 7.2 Hz, 1 H, Ar–CH), 3.85 (s, 6 H, 2 × OCH_3), 3.81 (s, 3 H, OCH_3), 2.89 (d, *J* = 6.9 Hz, 2 H, CH_2CO), 2.14 (s, 3 H, $COCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.3 (CO), 153.6 (3-C_{Ar} and 5-C_{Ar}), 137.6 (1-C_{Ar}), 134.5 (4-C_{Ar}), 104.5 (2-C_{Ar} and 6-C_{Ar}), 79.4 (CH_2NO_2), 60.8 (OCH_3), 56.2 (2 × OCH_3), 46.3 (CH_2CO), 39.3 (Ar–CH), 30.4 ($COCH_3$).

Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.56; H, 6.43; N, 4.72.

Asymmetric Michael Addition of Nitromethane; General Procedure

Compound **14a**, **14b** or **14c** (29.3 mmol) and (8*S*,9*S*)-9-amino(9-deoxy)epiquinine (**16**; 20 mol%) were dissolved in anhydrous $MeNO_2$ (39 mL). The reaction mixture was stirred at r.t. for 14 d, and then the solvent was evaporated in vacuo. The residue was recrystallised from MeOH to give optically active (trialkyloxyphenyl)nitropentanone (–)-**15a** or purified by column chromatography (hexane–EtOAc, 2:1) to obtain compound (–)-**15b** or (–)-**15c**. Spectroscopic data and elemental analysis for these compounds matched those for the racemates as given above.

(–)-5-Nitro-4-(3,4,5-trimethoxyphenyl)pentan-2-one [(–)-15a]

Yield: 5.14 g (59%); white solid; mp 73–75 °C; $[\alpha]_D^{22}$ –16.8 (*c* 1.5, acetone); R_f = 0.29 (hexane–EtOAc, 1:1).

(–)-4-(3,4-Diethoxy-5-methoxyphenyl)-5-nitropentan-2-one [(–)-15b]

Yield: 7.63 g (80%); pale yellow oil; $[\alpha]_D^{22}$ –11.5 (*c* 1.5, acetone); R_f = 0.44 (hexane–EtOAc, 1:1).

(–)-5-Nitro-4-(3,4,5-triethoxyphenyl)pentan-2-one [(–)-15c]

Yield: 7.76 g (78%); yellow oil; $[\alpha]_D^{22}$ –13.5 (*c* 1.5, acetone); R_f = 0.50 (hexane–EtOAc, 1:1).

(Trialkyloxyphenyl)nitrocyclohexanolones (–)-17a, (–)-17b and (–)-17c; General Procedure

Dry and freshly prepared NaOMe powder (3.36 g, 0.06 mol) was suspended in anhydrous Et_2O (70 mL). Then, HCOOEt (7.16 mL, 6.61 g, 89.16 mmol) and (trialkyloxyphenyl)nitropentanone (–)-**15a**, (–)-**15b** or (–)-**15c** (15.06 mmol) were added, and the reaction mixture was stirred at r.t. for 20 h. Then, it was cooled to 0 °C and H_2O (33 mL) was added dropwise. After the phases were separated, the aqueous layer was acidified with AcOH to pH 4 at 0 °C. The precipitated crystals were collected by filtration, washed with H_2O and dried. The crude product was purified as specified.

(–)-3-Hydroxy-4-nitro-5-(3,4,5-trimethoxyphenyl)cyclohexanone [(–)-17a]

Purified by column chromatography ($CHCl_3$–acetone, 5:1) to afford a white solid.

Yield: 2.45 g (46%); mp 170–174 °C; $[\alpha]_D^{22}$ –41.5 (*c* 0.5, THF); R_f = 0.17 (hexane–EtOAc, 1:1).

IR (KBr): 3353, 2941, 2841, 1709, 1592, 1551, 1514, 1464, 1372, 1249, 1129, 821 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.76 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.01 (d, *J* = 4.5 Hz, 1 H, OH), 5.79 (dd, *J* = 11.7, 2.1 Hz, 1 H, 4-H), 4.70–4.67 (m, 1 H, 3-H), 3.90 (td, *J* = 12.9, 4.2 Hz, 1 H, 5-H), 3.76 (s, 6 H, 2 × OCH_3), 3.62 (s, 3 H, OCH_3), 3.03 (dd, *J* = 14.4, 2.4 Hz, 1 H, 2-H_β), 2.72 (t, *J* = 14.1 Hz, 1 H, 6-H_β), 2.42 (td, *J* = 14.4, 2.4 Hz, 1 H, 2-H_α), 2.36 (ddd, *J* = 14.7, 4.5, 1.8 Hz, 1 H, 6-H_α).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 206.0 (CO), 152.8 (3-C_{Ar} and 5-C_{Ar}), 136.4 (4-C_{Ar}), 130.7 (1-C_{Ar}), 104.6 (2-C_{Ar} and 6-C_{Ar}), 89.1 (4-C), 69.7 (3-C), 59.8 (OCH_3), 55.9 (2 × OCH_3), 47.3 (6-C), 46.3 (2-C), 39.8 (5-C).

Anal. Calcd for $C_{15}H_{19}NO_7$: C, 55.38; H, 5.89; N, 4.31. Found: C, 55.39; H, 5.88; N, 4.30.

(–)-5-(3,4-Diethoxy-5-methoxyphenyl)-3-hydroxy-4-nitrocyclohexanone [(–)-17b]

Recrystallisation from EtOAc gave white crystals.

Yield: 2.24 g (42%); mp 151–154 °C; $[\alpha]_D^{22}$ –28.0 (*c* 0.5, THF); R_f = 0.26 (hexane–EtOAc, 1:1).

IR (KBr): 3366, 2983, 2940, 1733, 1593, 1552, 1510, 1457, 1375, 1242, 1123, 828 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.73 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.01 (d, *J* = 4.5 Hz, 1 H, OH), 5.77 (dd, *J* = 11.7, 1.5 Hz, 1 H, 4-H), 4.69–4.66 (m, 1 H, 3-H), 4.01 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 3.90-3.83 [m (overlapped with OCH_2CH_3), 1 H, 5-H], 3.86 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 3.74 (s, 3 H, OCH_3), 3.02 (dd, *J* = 14.4, 2.1 Hz, 1 H, 2-H_β), 2.71 (t, *J* = 14.1 Hz, 1 H, 6-H_β), 2.42 (td, *J* = 14.7, 2.7 Hz, 1 H, 2-H_α), 2.37 (ddd, *J* = 15.3, 5.1, 1.5 Hz, 1 H, 6-H_α), 1.30 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.20 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 207.3 (CO), 153.6 (3-C_{Ar}), 152.7 (5-C_{Ar}), 136.4 (4-C_{Ar}), 135.9 (1-C_{Ar}), 106.1 (2-C_{Ar}), 104.9 (6-C_{Ar}), 89.6 (4-C), 70.1 (3-C), 68.4 (OCH_2CH_3), 64.5 (OCH_2CH_3), 56.3 (OCH_3), 47.7 (6-C), 46.7 (2-C), 40.4 (5-C), 15.8 (OCH_2CH_3), 15.1 (OCH_2CH_3).

Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.79; H, 6.57; N, 3.95.

(–)-3-Hydroxy-4-nitro-5-(3,4,5-triethoxyphenyl)cyclohexanone [(–)-17c]

Recrystallised from Et_2O to afford a white solid.

Yield: 1.38 g (25%); mp 154 °C; $[\alpha]_D^{22}$ –21.0 (*c* 0.5, THF); R_f = 0.29 (hexane–EtOAc, 1:1).

IR (KBr): 3431, 2981, 2932, 1715, 1588, 1556, 1508, 1475, 1443, 1389, 1374, 1334, 1245, 1124, 816, 656 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.72 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.99 (d, *J* = 4.5 Hz, 1 H, OH), 5.75 (dd, *J* = 12.0, 2.1 Hz, 1 H, 4-H), 4.68–4.65 (m, 1 H, 3-H), 4.01 (q, *J* = 6.9 Hz, 4 H, 2 × OCH_2CH_3), 3.91-3.81 [m (overlapped with OCH_2CH_3), 1 H, 5-H], 3.88 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 3.02 (dd, *J* = 14.1, 2.1 Hz, 1 H, 2-H_β), 2.70 (t, *J* = 14.1 Hz, 1 H, 6-H_β), 2.41 (td, *J* = 14.7, 2.4 Hz, 1 H, 2-H_α), 2.35 (ddd, *J* = 14.4, 4.8, 1.8 Hz, 1 H, 6-H_α), 1.31 (t, *J* = 6.9 Hz, 6 H, 2 × OCH_2CH_3), 1.21 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 206.0 (CO), 152.2 (3-C_{Ar} and 5-C_{Ar}), 135.9 (4-C_{Ar}), 133.6 (1-C_{Ar}), 105.8 (2-C_{Ar} and 6-C_{Ar}), 89.2 (4-C), 69.6 (3-C), 67.7 (OCH_2CH_3), 63.9 (2 × OCH_2CH_3), 47.3 (6-C), 46.3 (2-C), 42.6 (5-C), 15.5 (OCH_2CH_3), 14.7 (2 × OCH_2CH_3).

Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 6.86; N, 3.81. Found: C, 58.85; H, 6.87; N, 3.80.

(Trialkyloxyphenyl)nitrocyclohexanolone Ketals (+)-18a, (+)-18b and (+)-18c; General Procedure

To a solution of anhydrous oxalic acid (3.43 g, 0.038 mol) in anhydrous MeCN (58 mL) were added ethylene glycol (9.79 mL, 10.85 g, 0.17 mol) and (trialkyloxyphenyl)nitrocyclohexanolone (–)-**17a**, (–)-**17b** or (–)-**17c** (4.08 mmol). The mixture was stirred at r.t. for 3 d.

Then, it was poured into a cooled saturated $NaHCO_3$ solution (163 mL). The precipitated solid was collected by filtration, washed with H_2O and dried to give acetal (+)-**18a**, (+)-**18b** or (+)-**18c**.

(+)-3-Hydroxy-4-nitro-5-(3,4,5-trimethoxyphenyl)cyclohexanone Ethylene Acetal [(+)-18a]

Yield: 0.93 g (62%); white solid; mp 153–156 °C; $[\alpha]_D^{22}$ +13.9 (*c* 1, THF); R_f = 0.86 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3481, 2941, 2839, 1592, 1551, 1510, 1463, 1382, 1327, 1245, 1125, 831, 740 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.45 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.76 (dd, *J* = 12.0, 3.0 Hz, 1 H, 4-H), 4.64 (dq, *J* = 10.0, 3.0 Hz, 1 H, 3-H), 4.09–3.94 (m, 5 H, OCH_2CH_2O, OH), 3.84 (s, 6 H, 2 × OCH_3), 3.80 (s, 3 H, OCH_3), 3.78 (td, *J* = 12.0, 4.5 Hz, 1 H, 5-H), 2.20 (dt, *J* = 14.0, 3.0 Hz, 1 H, 2-$H_α$), 2.07 (dd, *J* = 14.5, 3.0 Hz, 1 H, 2-$H_β$), 2.04 (dt, *J* = 14.0, 3.5 Hz, 1 H, 6-$H_α$), 1.84 (t, *J* = 13.5 Hz, 1 H, 6-$H_β$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.4 (3-C_{Ar} and 5-C_{Ar}), 135.1 (1-C_{Ar}), 133.9 (4-C_{Ar}), 107.6 (1-C), 104.5 (2-C_{Ar} and 6-C_{Ar}), 91.0 (4-C), 69.7 (3-C), 65.2 (OCH_2CH_2O), 64.5 (OCH_2CH_2O), 60.8 (OCH_3), 56.2 (2 × OCH_3), 41.4 (6-C), 38.7 (5-C), 38.5 (2-C).

Anal. Calcd for $C_{17}H_{23}NO_8$: C, 55.28; H, 6.28; N, 3.79. Found: C, 55.28; H, 6.27; N, 3.78.

(+)-5-(3,4-Diethoxy-5-methoxyphenyl)-3-hydroxy-4-nitrocyclohexanone Ethylene Acetal [(+)-18b]

Yield: 1.00 g (76%); white solid; mp 120–122 °C; $[\alpha]_D^{22}$ +13.0 (*c* 1, THF); R_f = 0.86 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3523, 2979, 2939, 1591, 1553, 1508, 1456, 1387, 1327, 1248, 1121, 822, 654 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.44 (s, 1 H, 2/6-H_{Ar}), 6.43 (s, 1 H, 2/6-H_{Ar}), 4.74 (dd, *J* = 12.0, 3.0 Hz, 1 H, 4-H), 4.63 (dq, *J* = 10.0, 3.0 Hz, 1 H, 3-H), 4.08–3.94 (m, 9 H, 2 × OCH_2CH_3, OCH_2CH_2O, OH), 3.82 (s, 3 H, OCH_3), 3.77 (td, *J* = 12.5, 4.5 Hz, 1 H, 5-H), 2.19 (dt, *J* = 14.5, 3.0 Hz, 1 H, 2-$H_α$), 2.06 (dd, *J* = 14.5, 3.5 Hz, 1 H, 2-$H_β$), 2.04 (dt, *J* = 14.0, 3.5 Hz, 1 H, 6-$H_α$), 1.84 (t, *J* = 13.5 Hz, 1 H, 6-$H_β$), 1.40 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.32 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.7 (5-C_{Ar}), 152.9 (3-C_{Ar}), 136.9 (1-C_{Ar}), 134.7 (4-C_{Ar}), 107.6 (1-C), 106.2 (2-C_{Ar}), 104.6 (6-C_{Ar}), 91.1 (4-C), 69.7 (3-C), 68.8 (OCH_2CH_3), 65.1 (OCH_2CH_3), 64.7 (OCH_2CH_2O), 64.4 (OCH_2CH_2O), 56.2 (OCH_3), 41.4 (6-C), 38.7 (5-C), 38.5 (2-C), 15.6 (OCH_2CH_3), 14.9 (OCH_2CH_3).

Anal. Calcd for $C_{19}H_{27}NO_8$: C, 57.42; H, 6.85; N, 3.52. Found: C, 57.41; H, 6.86; N, 3.51.

(+)-3-Hydroxy-4-nitro-5-(3,4,5-triethoxyphenyl)cyclohexanone Ethylene Acetal [(+)-18c]

Yield: 1.24 g (74%); white solid; mp 118 °C; $[\alpha]_D^{22}$ +22.4 (*c* 1, THF); R_f = 0.86 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3523, 2979, 2939, 1591, 1553, 1508, 1456, 1387, 1327, 1248, 1121, 822, 654 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.43 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.72 (dd, *J* = 12.0, 3.0 Hz, 1 H, 4-H), 4.62 (dq, *J* = 9.9, 2.7 Hz, 1 H, 3-H), 4.09–3.92 (m, 11 H, 3 × OCH_2CH_3, OCH_2CH_2O, OH), 3.75 (td, *J* = 12.6, 4.2 Hz, 1 H, 5-H), 2.19 (dt, *J* = 14.4, 3.0 Hz, 1 H, 2-$H_α$), 2.05 (dd, *J* = 14.4, 3.3 Hz, 1 H, 2-$H_β$), 2.03 (dt, *J* = 14.0, 3.5 Hz, 1 H, 6-$H_α$), 1.81 (t, *J* = 13.5 Hz, 1 H, 6-$H_β$), 1.40 (t, *J* = 6.9 Hz, 6 H, 2 × OCH_2CH_3), 1.32 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.0 (3-C_{Ar} and 5-C_{Ar}), 137.4 (1-C_{Ar}), 134.5 (4-C_{Ar}), 107.6 (1-C), 106.3 (2-C_{Ar} and 6-C_{Ar}), 91.1 (4-C), 69.6 (3-C), 68.8 (OCH_2CH_3), 65.1 (OCH_2CH_2O), 64.8 (2 × OCH_2CH_3), 64.4 (OCH_2CH_2O), 41.4 (6-C), 38.6 (5-C), 38.5 (2-C), 15.6 (OCH_2CH_3), 14.9 (2 × OCH_2CH_3).

Anal. Calcd for $C_{20}H_{29}NO_8$: C, 58.38; H, 7.10; N, 3.40. Found: C, 58.39; H, 7.09; N, 3.39.

(Trialkyloxyphenyl)aminocyclohexanolone Ketals (–)-19a, (–)-19b and (–)-19c; General Procedure

Over 10% Pd/C catalyst (Selcat Q-6, 0.89 g) compound (+)-**18a**, (+)-**18b** or (+)-**18c** (7.50 mmol) was hydrogenated in MeOH (60 mL), in a 250-mL stainless steel autoclave equipped with a magnetic stirrer (stirring speed: 1100 rpm). The reduction was carried out at 12 bar and 60–65 °C for 6 h. After the hydrogen uptake was finished, the catalyst was removed by filtration and the filtrate was concentrated in vacuo to afford aminoketal (–)-**19a**, (–)-**19b** or (–)-**19c**.

(–)-4-Amino-3-hydroxy-5-(3,4,5-trimethoxyphenyl)cyclohexanone Ethylene Acetal [(–)-19a]

Yield: 2.49 g (98%); dark green oil; $[\alpha]_D^{22}$ –10.3 (*c* 1, MeOH); R_f = 0.36 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3483, 2940, 2840, 1591, 1509, 1461, 1247, 1125, 1007, 837, 670 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.45 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.13–4.11 (m, 1 H, 3-H), 4.07–3.86 (m, 5 H, OH, OCH_2CH_2O), 3.86 (s, 6 H, 2 × OCH_3), 3.83 (s, 3 H, OCH_3), 2.87–2.85 (m, 2 H, 4-H, 5-H), 2.57 (br s, 2 H, NH_2), 2.13 (dt, *J* = 14.5, 3.0 Hz, 1 H, 2-$H_α$), 1.97 (dd, *J* = 14.5, 3.5 Hz, 1 H, 2-$H_β$), 1.87 (dt, *J* = 13.0, 3.0 Hz, 1 H, 6-$H_α$), 1.83 (t, *J* = 13.0 Hz, 1 H, 6-$H_β$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.5 (3-C_{Ar} and 5-C_{Ar}), 137.6 (1-C_{Ar}), 136.9 (4-C_{Ar}), 108.8 (1-C), 104.7 (2-C_{Ar} and 6-C_{Ar}), 70.1 (3-C), 64.9 (OCH_2CH_2O), 64.1 (OCH_2CH_2O), 60.8 (OCH_3), 57.3 (4-C), 56.1 (2 × OCH_3), 44.4 (5-C), 41.5 (6-C), 39.1 (2-C).

Anal. Calcd for $C_{17}H_{25}NO_6$: C, 60.16; H, 7.42; N, 4.13. Found: C, 60.17; H, 7.43; N, 4.12.

(–)-4-Amino-5-(3,4-diethoxy-5-methoxyphenyl)-3-hydroxycyclohexanone Ethylene Acetal [(–)-19b]

Yield: 2.75 g (100%); dark green oil; $[\alpha]_D^{22}$ –16.0 (*c* 1, MeOH); R_f = 0.31 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3503, 2978, 2889, 1589, 1507, 1456, 1387, 1246, 1124, 1033, 803, 670 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.42 (s, 1 H, 2/6-H_{Ar}), 6.41 (s, 1 H, 2/6-H_{Ar}), 4.08–3.90 (m, 10 H, OH, 3-H, 2 × OCH_2CH_3, OCH_2CH_2O), 3.84 (s, 3 H, OCH_3), 2.81–2.79 (m, 2 H, 4-H, 5-H), 2.33 (br s, 2 H, NH_2), 2.13 (dt, *J* = 14.4, 3.0 Hz, 1 H, 2-$H_α$), 1.96 (dd, *J* = 14.4, 3.0 Hz, 1 H, 2-$H_β$), 1.86 (dt, *J* = 13.5, 2.7 Hz, 1 H, 6-$H_α$), 1.81 (t, *J* = 12.9 Hz, 1 H, 6-$H_β$), 1.42 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 1.35 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8 (3-C_{Ar}), 153.1 (5-C_{Ar}), 137.4 (1-C_{Ar}), 136.3 (4-C_{Ar}), 108.9 (1-C), 106.2 (2-C_{Ar}), 104.8 (6-C_{Ar}), 70.3 (3-C), 68.8 (OCH_2CH_3), 64.9 (OCH_2CH_2O), 64.6 (OCH_2CH_3), 64.4 (OCH_2CH_2O), 57.4 (4-C), 56.2 (OCH_3), 44.7 (5-C), 41.6 (6-C), 39.2 (2-C), 15.6 (OCH_2CH_3), 15.0 (OCH_2CH_3).

Anal. Calcd for $C_{19}H_{29}NO_6$: C, 62.11; H, 7.96; N, 3.81. Found: C, 62.10; H, 7.97; N, 3.81.

(–)-4-Amino-3-hydroxy-5-(3,4,5-triethoxyphenyl)cyclohexanone Ethylene Acetal [(–)-19c]

Yield: 2.77 g (97%); dark green oil; $[\alpha]_D^{22}$ –0.8 (*c* 1, MeOH); R_f = 0.33 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3446, 2979, 2930, 2885, 1588, 1507, 1443, 1388, 1247, 1124, 1034, 802 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.41 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.09–3.90 (m, 12 H, 3-H, 3 × O*C*H_2CH$_3$, OCH$_2$C*H*$_2$O, OH), 2.80–2.77 (m, 2 H, 4-H, 5-H), 2.34 (br s, 2 H, NH_2), 2.13 (dt, *J* = 14.4, 2.7 Hz, 1 H, 2-H_α), 1.95 (dd, *J* = 14.4, 3.0 Hz, 1 H, 2-H_β), 1.85 (dt, *J* = 14.4, 3.3 Hz, 1 H, 6-H_α), 1.80 (t, *J* = 12.9 Hz, 1 H, 6-H_β), 1.41 (t, *J* = 7.2 Hz, 6 H, 2 × OCH$_2$*C*H_3), 1.34 (t, *J* = 7.2 Hz, 3 H, OCH$_2$*C*H_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1 (3-C_{Ar} and 5-C_{Ar}), 139.2 (1-C_{Ar}), 137.1 (4-C_{Ar}), 108.9 (1-C), 106.4 (2-C_{Ar} and 6-C_{Ar}), 70.2 (3-C), 68.8 (O*C*H_2CH$_3$), 64.9 (OCH$_2$*C*H_2O), 64.7 (2 × O*C*H_2CH$_3$), 64.1 (O*C*H_2CH$_2$O), 57.3 (4-C), 44.5 (5-C), 41.5 (6-C), 39.2 (2-C), 15.6 (OCH$_2$*C*H_3), 15.0 (2 × OCH$_2$*C*H_3).

Anal. Calcd for $C_{20}H_{31}NO_6$: C, 62.97; H, 8.19; N, 3.67. Found: C, 62.96; H, 8.18; N, 3.68.

(Trialkyloxyphenyl)cyclohexylcarbamates (–)-20a, (–)-20b and (–)-20c; General Procedure

To a solution of compound (–)-**19a**, (–)-**19b** or (–)-**19c** (7.50 mmol) in THF (46 mL) were added half of the required ClCOOMe (0.58 mL, 0.73 g, 7.68 mmol) and 3% aqueous NaOH solution (18 mL), followed by the other half of the ClCOOMe (0.58 mL, 0.73 g, 7.68 mmol). The reaction mixture was stirred rigorously at r.t. for 2 h, then poured into H_2O (102 mL) and extracted with EtOAc (4 × 60 mL). The combined organic layer was washed with brine and dried over Na_2SO_4, and the solvent was evaporated in vacuo to give carbamate (–)-**20a**, (–)-**20b** or (–)-**20c**.

(–)-3-Hydroxy-4-(methoxycarbonylamino)-5-(3,4,5-trimethoxyphenyl)cyclohexanone Ethylene Acetal [(–)-20a]

Yield: 2.92 g (98%); white solid (fluffy); mp 40–43 °C; $[\alpha]_D^{22}$ –4.0 (*c* 1, $CHCl_3$); R_f = 0.39 (CH_2Cl_2–acetone, 4:1).

IR (KBr): 3503, 2937, 2841, 1717, 1592, 1510, 1459, 1246, 1125, 1078, 825, 646 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.45 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.97 (d, *J* = 9.5 Hz, 1 H, NH), 4.13–4.11 (m, 1 H, 3-H), 4.07–3.90 (m, 5 H, OCH$_2$CH$_2$O, 4-H), 3.85 (s, 6 H, 2 × OCH$_3$), 3.82 (s, 3 H, OCH$_3$), 3.58 (d, *J* = 9.5 Hz, 1 H, OH), 3.50 (s, 3 H, NHCOO*C*H_3), 2.98 (td, *J* = 12.5, 3.0 Hz, 1 H, 5-H), 2.11 (dt, *J* = 14.0, 3.0 Hz, 1 H, 2-H_α), 2.03 (dd, *J* = 14.5, 2.5 Hz, 1 H, 2-H_β), 1.96 (dt, *J* = 13.0, 3.0 Hz, 1 H, 6-H_α), 1.86 (t, *J* = 13.0 Hz, 1 H, 6-H_β).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0 (NH*C*OOCH$_3$), 153.1 (3-C_{Ar} and 5-C_{Ar}), 137.0 (1-C_{Ar}), 136.7 (4-C_{Ar}), 108.5 (1-C), 104.6 (2-C_{Ar} and 6-C_{Ar}), 69.9 (3-C), 64.9 (OCH$_2$*C*H_2O), 64.1 (O*C*H_2CH$_2$O), 60.8 (OCH$_3$), 56.1 (2 × OCH$_3$), 55.8 (4-C), 51.9 (NHCOO*C*H_3), 43.0 (6-C), 41.8 (5-C), 38.7 (2-C).

Anal. Calcd for $C_{19}H_{27}NO_8$: C, 57.42; H, 6.85; N, 3.52. Found: C, 57.43; H, 6.84; N, 3.53.

(–)-5-(3,4-Diethoxy-5-methoxyphenyl)-3-hydroxy-4-(methoxycarbonylamino)cyclohexanone Ethylene Acetal [(–)-20b]

Yield: 2.87 g (90%); light brown oil; $[\alpha]_D^{22}$ –7.7 (*c* 0.5, $CHCl_3$); R_f = 0.44 (CH_2Cl_2–acetone, 4:1).

IR (KBr): 3342, 2977, 2894, 1713, 1591, 1509, 1456, 1391, 1251, 1124, 1084, 639 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.42 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.95 (d, *J* = 9.6 Hz, 1 H, NH), 4.13–4.11 (m, 1 H, 3-H), 4.09–3.88 (m, 9 H, 2 × O*C*H_2CH$_3$, OCH$_2$CH$_2$O, 4-H), 3.82 (s, 3 H, OCH$_3$), 3.57 (d, *J* = 9.6 Hz, 1 H, OH), 3.48 (s, 3 H, NHCOO*C*H_3), 2.94 (td, *J* = 12.0, 3.3 Hz, 1 H, 5-H), 2.10 (dt, *J* = 14.1, 2.7 Hz, 1 H, 2-H_α), 2.02 (dd, *J* = 14.7, 2.7 Hz, 1 H, 2-H_β), 1.95 (dt, *J* = 13.2, 3.0 Hz, 1 H, 6-H_α), 1.85 (t, *J* = 12.9 Hz, 1 H, 6-H_β), 1.41 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*C*H_3), 1.33 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*C*H_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0 (NH*C*OOCH$_3$), 153.4 (3-C_{Ar}), 152.7 (5-C_{Ar}), 136.5 (1-C_{Ar}), 136.0 (4-C_{Ar}), 108.5 (1-C), 106.2 (2-C_{Ar}), 104.7 (6-C_{Ar}), 69.8 (3-C), 68.7 (O*C*H_2CH$_3$), 64.9 (OCH$_2$*C*H_2O), 64.5 (O*C*H_2CH$_3$), 64.2 (O*C*H_2CH$_2$O), 56.1 (OCH$_3$), 55.9 (4-C), 51.9 (NHCOO*C*H_3), 42.8 (6-C), 41.7 (5-C), 38.7 (2-C), 15.5 (OCH$_2$*C*H_3), 14.9 (OCH$_2$*C*H_3).

Anal. Calcd for $C_{21}H_{31}NO_8$: C, 59.28; H, 7.34; N, 3.29. Found: C, 59.30; H, 7.33; N, 3.28.

(–)-3-Hydroxy-4-(methoxycarbonylamino)-5-(3,4,5-triethoxyphenyl)cyclohexanone Ethylene Acetal [(–)-20c]

Yield: 3.29 g (100%); light brown solid; mp 94–98 °C; $[\alpha]_D^{22}$ –4.0 (*c* 1, $CHCl_3$); R_f = 0.49 (CH_2Cl_2–acetone, 4:1).

IR (KBr): 3530, 3345, 2981, 2937, 2883, 1720, 1588, 1509, 1474, 1440, 1374, 1235, 1126, 1077, 814, 669 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.41 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 4.92 (d, *J* = 9.6 Hz, 1 H, NH), 4.13–3.82 (m, 12 H, 3 × O*C*H_2CH$_3$, OCH$_2$CH$_2$O, 3-H, 4-H), 3.56 (d, *J* = 9.6 Hz, 1 H, OH), 3.48 (s, 3 H, NHCOO*C*H_3), 2.92 (td, *J* = 12.0, 3.3 Hz, 1 H, 5-H), 2.09 (dt, *J* = 14.5, 3.0 Hz, 1 H, 2-H_α), 2.01 (dd, *J* = 14.4, 2.4 Hz, 1 H, 2-H_β), 1.95 (dt, *J* = 13.2, 3.0 Hz, 1 H, 6-H_α), 1.84 (t, *J* = 12.9 Hz, 1 H, 6-H_β), 1.40 (t, *J* = 6.9 Hz, 6 H, 2 × OCH$_2$*C*H_3), 1.33 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*C*H_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9 (NH*C*OOCH$_3$), 152.8 (3-C_{Ar} and 5-C_{Ar}), 137.6 (1-C_{Ar}), 136.4 (4-C_{Ar}), 108.5 (1-C), 106.4 (2-C_{Ar} and 6-C_{Ar}), 69.8 (3-C), 68.7 (O*C*H_2CH$_3$), 64.9 (OCH$_2$*C*H_2O), 64.6 (2 × O*C*H_2CH$_3$), 64.2 (O*C*H_2CH$_2$O), 56.0 (4-C), 51.9 (NHCOO*C*H_3), 42.7 (6-C), 41.7 (5-C), 38.7 (2-C), 15.6 (OCH$_2$*C*H_3), 15.0 (2 × OCH$_2$*C*H_3).

Anal. Calcd for $C_{22}H_{33}NO_8$: C, 60.12; H, 7.57; N, 3.19. Found: C, 60.11; H, 7.57; N, 3.18.

(Trialkyloxyphenyl)cyclohexenones (–)-21a, (–)-21b and (–)-21c; General Procedure

Compound (–)-**20a**, (–)-**20b** or (–)-**20c** (12.56 mmol) and *p*-TsOH (4.27 g, 22.46 mmol) were dissolved in acetone (298 mL). The solution was heated to reflux and stirred for 1 h. After cooling to r.t., it was poured into a saturated $NaHCO_3$ solution (584 mL) and extracted with EtOAc (4 × 200 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to afford enone (–)-**21a**, (–)-**21b** or (–)-**21c**.

(–)-Methyl [4-Oxo-6-(3,4,5-trimethoxyphenyl)cyclohex-2-enyl]-carbamate [(–)-21a]

Yield: 4.13 g (98%); light brown solid (fluffy); mp 55–58 °C; $[\alpha]_D^{22}$ –123.8 (*c* 1, $CHCl_3$); R_f = 0.77 (CH_2Cl_2–acetone, 4:1).

IR (KBr): 3358, 2955, 2838, 1685, 1592, 1534, 1459, 1384, 1247, 1127, 1084, 1025, 723 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.94 (d, *J* = 10.2 Hz, 1 H, 2-H), 6.44 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.09 (dd, *J* = 10.2, 2.4 Hz, 1 H, 3-H), 4.83–4.78 (m, 1 H, NH), 4.74–4.70 (m, 1 H, 1-H), 3.84 (s, 6 H, 2 × OCH$_3$), 3.83 (s, 3 H, OCH$_3$), 3.61 (s, 3 H, NHCOO*C*H_3), 3.24–3.20 (m, 1 H, 6-H), 2.71–2.67 (m, 2 H, 5-H_α and 5-H_β).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.4 (CO), 156.5 (NH*C*OOCH$_3$), 153.6 (3-C$_{Ar}$ and 5-C$_{Ar}$), 151.8 (2-C), 136.7 (1-C$_{Ar}$), 135.4 (4-C$_{Ar}$), 129.5 (3-C), 104.3 (2-C$_{Ar}$ and 6-C$_{Ar}$), 60.9 (OCH$_3$), 56.2 (2 × OCH$_3$), 52.9 (1-C), 52.5 (NHCOO*C*H$_3$), 48.3 (6-C), 45.2 (5-C).

Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.89; H, 6.31; N, 4.18. Found: C, 60.90; H, 6.32; N, 4.18.

(–)-Methyl [6-(3,4-Diethoxy-5-methoxyphenyl)-4-oxocyclohex-2-enyl]carbamate [(–)-21b]

Yield: 3.65 g (80%); light brown oil; $[\alpha]_D^{22}$ –123.6 (*c* 1, acetone); R_f = 0.74 (CH_2Cl_2–acetone, 4:1).

IR (KBr): 3202, 2979, 2897, 1698, 1590, 1544, 1456, 1384, 1248, 1128, 1033, 772 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.94 (d, *J* = 10.2 Hz, 1 H, 2-H), 6.42 (s, 2 H, 2-H$_{Ar}$ and 6-H$_{Ar}$), 6.09 (dd, *J* = 9.9, 1.8 Hz, 1 H, 3-H), 4.75–4.71 (m, 1 H, NH), 4.70–4.66 (m, 1 H, 1-H), 4.05 (q, *J* = 6.9 Hz, 4 H, 2 × OC*H*$_2$CH$_3$), 3.83 (s, 3 H, OCH$_3$), 3.60 (s, 3 H, NHCOOC*H*$_3$), 3.21–3.18 (m, 1 H, 6-H), 2.71–2.67 (m, 2 H, 5-H$_\alpha$ and 5-H$_\beta$), 1.44 (t, *J* = 6.9 Hz, 3 H, OCH$_2$C*H*$_3$), 1.35 (t, *J* = 7.2 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.4 (CO), 156.4 (NH*C*OOCH$_3$), 153.8 (3-C$_{Ar}$), 153.1 (5-C$_{Ar}$), 139.2 (2-C), 134.9 (1-C$_{Ar}$), 132.7 (4-C$_{Ar}$), 129.3 (3-C), 105.8 (2-C$_{Ar}$), 104.3 (6-C$_{Ar}$), 68.8 (O*C*H$_2$CH$_3$), 64.7 (O*C*H$_2$CH$_3$), 56.2 (OCH$_3$), 53.0 (1-C), 52.3 (NHCOO*C*H$_3$), 48.0 (6-C), 45.0 (5-C), 15.6 (OCH$_2$*C*H$_3$), 14.9 (OCH$_2$*C*H$_3$).

Anal. Calcd for $C_{19}H_{25}NO_6$: C, 62.80; H, 6.93; N, 3.85. Found: C, 62.80; H, 6.94; N, 3.84.

(–)-Methyl [4-Oxo-6-(3,4,5-triethoxyphenyl)cyclohex-2-enyl]carbamate [(–)-21c]

Yield: 3.89 g (82%); light brown oil; $[\alpha]_D^{22}$ –118.7 (*c* 1, acetone); R_f = 0.60 (CH_2Cl_2–acetone, 4:1).

IR (KBr): 3393, 2980, 2897, 1718, 1683, 1523, 1475, 1443, 1387, 1324, 1244, 1124, 1102, 1031, 820, 655 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.93 (d, *J* = 9.9 Hz, 1 H, 2-H), 6.41 (s, 2 H, 2-H$_{Ar}$ and 6-H$_{Ar}$), 6.07 (dd, *J* = 10.2, 2.1 Hz, 1 H, 3-H), 4.77–4.73 (m, 1 H, NH), 4.69–4.65 (m, 1 H, 1-H), 4.04 (q, *J* = 6.9 Hz, 6 H, 3 × OC*H*$_2$CH$_3$), 3.59 (s, 3 H, NHCOOC*H*$_3$), 3.21–3.18 (m, 1 H, 6-H), 2.70–2.66 (m, 2 H, 5-H$_\alpha$ and 5-H$_\beta$), 1.41 (t, *J* = 6.9 Hz, 6 H, 2 × OCH$_2$C*H*$_3$), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.5 (CO), 156.4 (NH*C*OOCH$_3$), 153.1 (3-C$_{Ar}$ and 5-C$_{Ar}$), 151.7 (2-C), 134.9 (1-C$_{Ar}$), 134.8 (4-C$_{Ar}$), 129.3 (3-C), 105.9 (2-C$_{Ar}$ and 6-C$_{Ar}$), 68.8 (O*C*H$_2$CH$_3$), 64.7 (2 × O*C*H$_2$CH$_3$), 53.1 (1-C), 52.3 (NHCOO*C*H$_3$), 48.0 (6-C), 45.1 (5-C), 15.6 (OCH$_2$*C*H$_3$), 14.9 (2 × OCH$_2$*C*H$_3$).

Anal. Calcd for $C_{20}H_{27}NO_6$: C, 63.64; H, 7.21; N, 3.71. Found: C, 63.65; H, 7.22; N, 3.70.

(Trialkyloxyphenyl)cyclohexenols (–)-22a, (–)-22b and (–)-22c; General Procedure

A solution of compound (–)-**21a**, (–)-**21b** or (–)-**21c** (7.93 mmol) and anhydrous $CaCl_2$ (1.80 g, 16.18 mmol) in MeOH (220 mL) was stirred at r.t. for 30 min. Then, it was cooled to 0 °C and $NaBH_4$ (0.45 g, 11.89 mmol) was added. It was further stirred at 0 °C for 30 min, then poured into H_2O (337 mL) and extracted with EtOAc (4 × 218 mL). The combined organic layer was washed with brine and dried over Na_2SO_4, and the solvent was evaporated in vacuo. The residue was recrystallised from hexane–EtOAc (2:1) to afford allyl alcohol (–)-**22a**, (–)-**22b** or (–)-**22c**.

(–)-Methyl [4-Hydroxy-6-(3,4,5-trimethoxyphenyl)cyclohex-2-enyl]carbamate [(–)-22a]

Yield: 2.41 g (90%); white solid; mp 151–156 °C; $[\alpha]_D^{22}$ –103.5 (*c* 1, acetone); R_f = 0.51 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3349, 2929, 2844, 1681, 1588, 1538, 1513, 1458, 1278, 1242, 1124, 824, 659 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.44 (s, 2 H, 2-H$_{Ar}$ and 6-H$_{Ar}$), 5.83 (dd, *J* = 9.9, 1.2 Hz, 1 H, 3-H), 5.75 (d, *J* = 10.2 Hz, 1 H, 2-H), 4.57 (br s, 1 H, NH), 4.48–4.45 (m, 1 H, 4-H), 4.41–4.38 (m, 1 H, 1-H), 3.84 (s, 6 H, 2 × OCH$_3$), 3.83 (s, 3 H, OCH$_3$), 3.55 (s, 3 H, NHCOOC*H*$_3$), 2.70–2.67 (m, 1 H, 6-H), 2.29 (dd, *J* = 11.1, 4.5 Hz, 1 H, 5-H$_\beta$), 1.83 (td, *J* = 12.6, 10.2 Hz, 1 H, 5-H$_\alpha$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.4 (NH*C*OOCH$_3$), 153.2 (3-C$_{Ar}$ and 5-C$_{Ar}$), 137.5 (4-C$_{Ar}$), 136.8 (1-C$_{Ar}$), 132.5 (3-C), 131.1 (2-C), 104.3 (2-C$_{Ar}$ and 6-C$_{Ar}$), 67.7 (4-C), 60.8 (OCH$_3$), 56.1 (2 × OCH$_3$), 53.1 (1-C), 52.1 (NHCOO*C*H$_3$), 46.6 (6-C), 40.7 (5-C).

Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.52; H, 6.88; N, 4.14.

(–)-Methyl [6-(3,4-Diethoxy-5-methoxyphenyl)-4-hydroxycyclohex-2-enyl]carbamate [(–)-22b]

Yield: 1.80 g (62%); white solid; mp 96–104 °C; $[\alpha]_D^{22}$ –121.2 (*c* 1, acetone); R_f = 0.51 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3325, 2979, 2940, 1686, 1590, 1542, 1509, 1457, 1394, 1246, 1128, 1049, 658 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.41 (s, 2 H, 2-H$_{Ar}$ and 6-H$_{Ar}$), 5.81 (d, *J* = 9.9 Hz, 1 H, 3-H), 5.74 (d, *J* = 10.5 Hz, 1 H, 2-H), 4.58–4.54 (m, 1 H, NH), 4.46–4.43 (m, 1 H, 4-H), 4.36–4.33 (m, 1 H, 1-H), 4.04 (q, *J* = 6.6 Hz, 2 H, OC*H*$_2$CH$_3$), 4.03 (q, *J* = 6.9 Hz, 2 H, OC*H*$_2$CH$_3$), 3.82 (s, 3 H, OCH$_3$), 3.53 (s, 3 H, NHCOOC*H*$_3$), 2.66–2.63 (m, 1 H, 6-H), 2.28 (dd, *J* = 12.0, 4.5 Hz, 1 H, 5-H$_\beta$), 1.81 (td, *J* = 12.6, 10.2 Hz, 1 H, 5-H$_\alpha$), 1.41 (t, *J* = 6.9 Hz, 3 H, OCH$_2$C*H*$_3$), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.4 (NH*C*OOCH$_3$), 153.6 (3-C$_{Ar}$), 152.8 (5-C$_{Ar}$), 137.4 (4-C$_{Ar}$), 137.1 (1-C$_{Ar}$), 132.6 (3-C), 131.1 (2-C), 105.9 (2-C$_{Ar}$), 104.4 (6-C$_{Ar}$), 68.8 (O*C*H$_2$CH$_3$), 67.7 (4-C), 64.6 (O*C*H$_2$CH$_3$), 56.1 (OCH$_3$), 52.9 (1-C), 52.0 (NHCOO*C*H$_3$), 44.5 (6-C), 40.8 (5-C), 15.6 (OCH$_2$*C*H$_3$), 14.9 (OCH$_2$*C*H$_3$).

Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.44; H, 7.45; N, 3.82.

(–)-Methyl [4-Hydroxy-6-(3,4,5-triethoxyphenyl)cyclohex-2-enyl]carbamate [(–)-22c]

Yield: 2.41 g (80%); white solid; mp 142–144 °C; $[\alpha]_D^{22}$ –94.7 (*c* 1, acetone); R_f = 0.51 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3327, 2977, 2930, 2875, 1688, 1540, 1510, 1475, 1441, 1391, 1246, 1130, 1054, 809, 642 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.40 (s, 2 H, 2-H$_{Ar}$ and 6-H$_{Ar}$), 5.81 (dd, *J* = 10.2, 1.2 Hz, 1 H, 3-H), 5.75 (d, *J* = 10.2 Hz, 1 H, 2-H), 4.55–4.51 (m, 1 H, NH), 4.46–4.43 (m, 1 H, 4-H), 4.34–4.30 (m, 1 H, 1-H), 4.04 (q, *J* = 6.9 Hz, 4 H, 2 × OC*H*$_2$CH$_3$), 4.03 (q, *J* = 6.9 Hz, 2 H, OC*H*$_2$CH$_3$), 3.53 (s, 3 H, NHCOOC*H*$_3$), 2.64–2.61 (m, 1 H, 6-H), 2.27 (ddd, *J* = 12.0, 4.5, 1.8 Hz, 1 H, 5-H$_\beta$), 1.81 (td, *J* = 12.6, 9.9 Hz, 1 H, 5-H$_\alpha$), 1.40 (t, *J* = 6.9 Hz, 6 H, 2 × OCH$_2$C*H*$_3$), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.4 (NH*C*OOCH$_3$), 152.9 (3-C$_{Ar}$ and 5-C$_{Ar}$), 137.0 (4-C$_{Ar}$), 135.4 (1-C$_{Ar}$), 132.4 (3-C), 131.2 (2-C), 106.2 (2-C$_{Ar}$ and 6-C$_{Ar}$), 68.8 (O*C*H$_2$CH$_3$), 67.8 (4-C), 64.7 (2 × O*C*H$_2$CH$_3$), 53.0 (1-C), 52.0 (NHCOO*C*H$_3$), 46.6 (6-C), 40.8 (5-C), 15.6 (OCH$_2$*C*H$_3$), 15.0 (2 × OCH$_2$*C*H$_3$).

Anal. Calcd for $C_{20}H_{29}NO_6$: C, 63.31; H, 7.70; N, 3.69. Found: C, 63.32; H, 7.71; N, 3.68.

(Trialkyloxyphenyl)cyclohexenyl Benzoates (+)-23a, (+)-23b and (+)-23c by the Mitsunobu Reaction; General Procedure

Compound (–)-**22a**, (–)-**22b** or (–)-**22c** (1.21 mmol) and Ph_3P (0.39 g, 1.49 mmol) were dissolved in anhydrous THF (19 mL) and cooled to 0 °C. Diethyl azodicarboxylate (0.25 mL, 0.28 g, 1.59 mmol) in anhydrous THF (0.9 mL) was added dropwise at 0 °C and the mixture was stirred for 10 min. Benzoic acid (0.16 g, 1.31 mmol) was also added, and the reaction mixture was stirred at 0 °C for 2 h, then heated to 45–50 °C and further stirred for 5 h. The solvent was removed in vacuo. The residue was purified as specified.

(+)-4-(Methoxycarbonylamino)-5-(3,4,5-trimethoxyphenyl)cyclohex-2-enyl Benzoate [(+)-23a]

Purified by column chromatography ($CHCl_3$–acetone, 20:1) to afford a white solid (fluffy).

Yield: 0.30 g (57%); mp 56–61 °C; $[\alpha]_D^{22}$ +74.7 (*c* 1, $CHCl_3$); R_f = 0.81 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3314, 2938, 2837, 1713, 1684, 1590, 1509, 1451, 1363, 1270, 1216, 1130, 1105, 1027, 841, 654 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.2 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.58 (t, *J* = 7.2 Hz, 1 H, 4-H_{Bz}), 7.46 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.46 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.07–6.03 (m, 2 H, 2-H, 3-H), 5.55–5.52 (m, 1 H, 1-H), 4.66–4.62 (m, 1 H, NH), 4.44–4.41 (m, 1 H, 4-H), 3.86 (s, 6 H, 2 × OCH_3), 3.83 (s, 3 H, OCH_3), 3.57 (s, 3 H, NHCOO*CH*$_3$), 2.93 (td, *J* = 10.2, 4.8 Hz, 1 H, 5-H), 2.24–2.20 (m, 2 H, 6-$H_α$ and 6-$H_β$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (Ph–CO), 156.5 (NH*CO*OCH$_3$), 153.3 (3-C_{Ar} and 5-C_{Ar}), 137.5 (4-C_{Ar}), 137.0 (1-C_{Ar}), 135.8 (3-C), 133.0 (4-C_{Bz}), 130.3 (1-C_{Bz}), 129.6 (2-C_{Bz} and 6-C_{Bz}), 128.4 (3-C_{Bz} and 5-C_{Bz}), 125.7 (2-C), 104.6 (2-C_{Ar} and 6-C_{Ar}), 66.7 (1-C), 60.8 (OCH_3), 56.2 (2 × OCH_3), 52.7 (4-C), 52.1 (NHCOO*CH*$_3$), 42.5 (5-C), 35.9 (6-C).

Anal. Calcd for $C_{24}H_{27}NO_7$: C, 65.29; H, 6.16; N, 3.17. Found: C, 65.30; H, 6.15; N, 3.18.

(+)-5-(3,4-Diethoxy-5-methoxyphenyl)-4-(methoxycarbonylamino)cyclohex-2-enyl Benzoate [(+)-23b]

Isolated by column chromatography ($CHCl_3$–acetone, 20:1) to give a yellow oil.

Yield: 0.23 g (40%); $[\alpha]_D^{22}$ +33.9 (*c* 1, $CHCl_3$); R_f = 0.83 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3356, 2979, 2938, 1717, 1654, 1589, 1509, 1455, 1363, 1271, 1126, 1108, 1026, 714 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.5 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.58 (t, *J* = 7.2 Hz, 1 H, 4-H_{Bz}), 7.46 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.44 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.06–6.03 (m, 2 H, 2-H, 3-H), 5.55–5.52 (m, 1 H, 1-H), 4.64 (d, *J* = 7.8 Hz, 1 H, NH), 4.41–4.38 (m, 1 H, 4-H), 4.06 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 4.04 (q, *J* = 7.2 Hz, 2 H, O*CH*$_2$CH$_3$), 3.83 (s, 3 H, OCH_3), 3.56 (s, 3 H, NHCOO*CH*$_3$), 2.92–2.89 (m, 1 H, 5-H), 2.23–2.18 (m, 2 H, 6-$H_α$ and 6-$H_β$), 1.41 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.34 (t, *J* = 7.2 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (Ph–CO), 156.4 (NH*CO*OCH$_3$), 153.6 (5-C_{Ar}), 152.8 (3-C_{Ar}), 137.1 (4-C_{Ar}), 136.5 (1-C_{Ar}), 135.8 (3-C), 133.0 (4-C_{Bz}), 130.3 (1-C_{Bz}), 129.6 (2-C_{Bz} and 6-C_{Bz}), 128.4 (3-C_{Bz} and 5-C_{Bz}), 125.6 (2-C), 106.2 (2-C_{Ar}), 104.7 (6-C_{Ar}), 68.8 (O*CH*$_2$CH$_3$), 66.7 (1-C), 64.7 (O*CH*$_2$CH$_3$), 56.1 (OCH_3), 52.8 (4-C), 52.1 (NHCOO*CH*$_3$), 41.3 (5-C), 33.9 (6-C), 15.5 (OCH$_2$*CH*$_3$), 14.9 (OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{26}H_{31}NO_7$: C, 66.51; H, 6.65; N, 2.98. Found: C, 66.50; H, 6.65; N, 2.99.

(+)-4-(Methoxycarbonylamino)-5-(3,4,5-triethoxyphenyl)cyclohex-2-enyl Benzoate [(+)-23c]

Purified by column chromatography ($CHCl_3$–acetone, 100:1) to afford a semi-solid.

Yield: 0.28 g (57%); $[\alpha]_D^{22}$ +60.7 (*c* 1, $CHCl_3$); R_f = 0.85 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3343, 2981, 1717, 1653, 1587, 1508, 1441, 1387, 1271, 1110, 715 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.5 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.59 (t, *J* = 7.5 Hz, 1 H, 4-H_{Bz}), 7.47 (t, *J* = 7.2 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.45 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 6.07–6.03 (m, 2 H, 2-H, 3-H), 5.56–5.53 (m, 1 H, 1-H), 4.66 (d, *J* = 8.1 Hz, 1 H, NH), 4.40–4.37 (m, 1 H, 4-H), 4.06 (q, *J* = 7.2 Hz, 4 H, 2 × O*CH*$_2$CH$_3$), 4.04 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 3.57 (s, 3 H, NHCOO*CH*$_3$), 2.90 (td, *J* = 9.6, 3.9 Hz, 1 H, 5-H), 2.22–2.19 (m, 2 H, 6-$H_α$ and 6-$H_β$), 1.41 (t, *J* = 6.9 Hz, 6 H, 2 × OCH$_2$*CH*$_3$), 1.35 (t, *J* = 7.2 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (Ph–CO), 156.0 (NH*CO*OCH$_3$), 153.0 (3-C_{Ar} and 5-C_{Ar}), 137.2 (4-C_{Ar}), 136.9 (1-C_{Ar}), 133.5 (3-C), 133.0 (4-C_{Bz}), 130.3 (1-C_{Bz}), 129.6 (2-C_{Bz} and 6-C_{Bz}), 128.4 (3-C_{Bz} and 5-C_{Bz}), 125.5 (2-C), 106.5 (2-C_{Ar} and 6-C_{Ar}), 68.7 (O*CH*$_2$CH$_3$), 66.7 (1-C), 64.8 (2 × O*CH*$_2$CH$_3$), 52.8 (4-C), 51.9 (NHCOO*CH*$_3$), 42.4 (5-C), 36.1 (6-C), 15.6 (OCH$_2$*CH*$_3$), 15.0 (2 × OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{27}H_{33}NO_7$: C, 67.06; H, 6.88; N, 2.90. Found: C, 67.07; H, 6.86; N, 2.91.

cis-(Trialkyloxyphenyl)cyclohexanediols (+)-24a, (+)-24b and (+)-24c; General Procedure

To a solution of compound (+)-**23a**, (+)-**23b** or (+)-**23c** (1.28 mmol) in a mixture of THF (7.8 mL) and H_2O (1.3 mL) were added *N*-methylmorpholine *N*-oxide (0.32 g, 2.75 mmol) and subsequently 4% aqueous OsO_4 solution (0.56 mL, 22.30 mg, 0.09 mmol) under an argon atmosphere. The mixture was stirred at r.t. for 24 h, then poured into a saturated $Na_2S_2O_3$ solution (51 mL) and extracted with EtOAc (4 × 44 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to give *cis*-diol (+)-**24a**, (+)-**24b** or (+)-**24c**.

(+)-2,3-Dihydroxy-4-(methoxycarbonylamino)-5-(3,4,5-trimethoxyphenyl)cyclohexyl Benzoate [(+)-24a]

Yield: 0.61 g (100%); white solid (fluffy); mp 59–81 °C; $[\alpha]_D^{22}$ +45.1 (*c* 1, $CHCl_3$); R_f = 0.48 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3487, 3395, 3290, 2932, 1708, 1590, 1556, 1508, 1455, 1360, 1274, 1128, 1074, 719 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (dd, *J* = 8.5, 1.0 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.61 (tt, *J* = 7.5, 1.0 Hz, 1 H, 4-H_{Bz}), 7.49 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.42 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.44 (q, *J* = 3.0 Hz, 1 H, 1-H), 4.62 (d, *J* = 6.5 Hz, 1 H, NH), 4.32 (br s, 1 H, OH), 4.23–4.20 (m, 1 H, 2-H), 4.07–4.04 (m, 1 H, 4-H), 4.01–3.98 (m, 1 H, 3-H), 3.84 (s, 6 H, 2 × OCH_3), 3.83 (s, 3 H, OCH_3), 3.58 (s, 3 H, NHCOO*CH*$_3$), 3.42 (br s, 1 H, OH), 2.86 (td, *J* = 12.5, 3.5 Hz, 1 H, 5-H), 2.33 (ddd, *J* = 15.0, 13.0, 2.5 Hz, 1 H, 6-$H_β$), 2.07 (dt, *J* = 15.0, 2.5 Hz, 1 H, 6-$H_α$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2 (Ph–CO), 160.4 (NHCOOCH$_3$), 153.5 (3-C_{Ar} and 5-C_{Ar}), 137.1 (1-C_{Ar}), 136.4 (4-C_{Ar}), 133.4 (4-C_{Bz}), 129.9 (1-C_{Bz}), 129.7 (2-C_{Bz} and 6-C_{Bz}), 128.6 (3-C_{Bz} and 5-C_{Bz}), 104.5 (2-C_{Ar} and 6-C_{Ar}), 79.3 (3-C), 71.3 (1-C), 70.2 (2-C), 60.8 (OCH_3), 56.2 (2 × OCH_3), 55.4 (4-C), 52.6 (NHCOO*CH*$_3$), 43.1 (5-C), 33.0 (6-C).

Anal. Calcd for $C_{24}H_{29}NO_9$: C, 60.62; H, 6.15; N, 2.95. Found: C, 60.61; H, 6.16; N, 2.94.

(+)-5-(3,4-Diethoxy-5-methoxyphenyl)-2,3-dihydroxy-4-(methoxycarbonylamino)cyclohexyl Benzoate [(+)-24b]

Yield: 0.64 g (99%); white solid (fluffy); mp 76–83 °C; $[\alpha]_D^{22}$ +66.1 (*c* 1, $CHCl_3$); R_f = 0.46 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3481, 3411, 3302, 2978, 1708, 1587, 1556, 1508, 1456, 1363, 1274, 1118, 1074, 719 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.2 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.61 (t, *J* = 7.2 Hz, 1 H, 4-H_{Bz}), 7.49 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.40 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.44 (q, *J* = 3.0 Hz, 1 H, 1-H), 4.62 (d, *J* = 6.3 Hz, 1 H, NH), 4.44 (br s, 1 H, OH), 4.22–4.19 (m, 1 H, 2-H), 4.05 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.04 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.02–3.99 (m, 1 H, 4-H), 3.98–3.95 (m, 1 H, 3-H), 3.82 (s, 3 H, OCH_3), 3.56 (s, 3 H, $NHCOOCH_3$), 3.32 (br s, 1 H, OH), 2.83 (ddd, *J* = 12.9, 10.8, 3.0 Hz, 1 H, 5-H), 2.33 (ddd, *J* = 14.7, 12.9, 2.4 Hz, 1 H, 6-H_β), 2.07 (dt, *J* = 14.7, 2.7 Hz, 1 H, 6-H_α), 1.41 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.1 (Ph–CO), 158.9 ($NHCOOCH_3$), 153.9 (3-C_{Ar}), 153.1 (5-C_{Ar}), 136.6 (1-C_{Ar}), 135.8 (4-C_{Ar}), 133.3 (4-C_{Bz}), 130.0 (1-C_{Bz}), 129.7 (2-C_{Bz} and 6-C_{Bz}), 128.6 (3-C_{Bz} and 5-C_{Bz}), 106.1 (2-C_{Ar}), 104.6 (6-C_{Ar}), 74.0 (3-C), 71.3 (1-C), 70.2 (2-C), 68.8 (OCH_2CH_3), 64.7 (OCH_2CH_3), 56.3 (OCH_3), 55.6 (4-C), 52.6 ($NHCOOCH_3$), 43.0 (5-C), 32.8 (6-C), 15.5 (OCH_2CH_3), 14.9 (OCH_2CH_3).

Anal. Calcd for $C_{26}H_{33}NO_9$: C, 62.02; H, 6.61; N, 2.78. Found: C, 62.01; H, 6.61; N, 2.77.

(+)-2,3-Dihydroxy-4-(methoxycarbonylamino)-5-(3,4,5-triethoxyphenyl)cyclohexyl Benzoate [(+)-24c]

Yield: 0.39 g (59%); white solid (fluffy); mp 76–80 °C; $[\alpha]_D^{22}$ +62.4 (*c* 1, $CHCl_3$); R_f = 0.46 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3483, 3422, 2984, 2929, 2878, 1710, 1587, 1551, 1507, 1440, 1388, 1273, 1232, 1124, 1072, 810, 669 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.2 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.62 (t, *J* = 7.2 Hz, 1 H, 4-H_{Bz}), 7.49 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.39 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.44 (q, *J* = 3.0 Hz, 1 H, 1-H), 4.60 (d, *J* = 6.0 Hz, 1 H, NH), 4.46 (br s, 1 H, OH), 4.22–4.19 (m, 1 H, 2-H), 4.04 (q, *J* = 6.9 Hz, 6 H, 3 × OCH_2CH_3), 4.02–3.99 (m, 1 H, 4-H), 3.98–3.95 (m, 1 H, 3-H), 3.57 (s, 3 H, $NHCOOCH_3$), 3.32 (br s, 1 H, OH), 2.80 (ddd, *J* = 12.6, 10.5, 3.0 Hz, 1 H, 5-H), 2.32 (ddd, *J* = 14.7, 12.9, 2.4 Hz, 1 H, 6-H_β), 2.07 (dt, *J* = 14.7, 2.7 Hz, 1 H, 6-H_α), 1.40 (t, *J* = 6.9 Hz, 6 H, 2 × OCH_2CH_3), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.1 (Ph–CO), 158.9 ($NHCOOCH_3$), 153.2 (3-C_{Ar} and 5-C_{Ar}), 137.2 (1-C_{Ar}), 135.7 (4-C_{Ar}), 133.3 (4-C_{Bz}), 130.0 (1-C_{Bz}), 129.7 (2-C_{Bz} and 6-C_{Bz}), 128.5 (3-C_{Bz} and 5-C_{Bz}), 106.3 (2-C_{Ar} and 6-C_{Ar}), 74.1 (3-C), 71.3 (1-C), 70.2 (2-C), 68.8 (OCH_2CH_3), 64.8 (2 × OCH_2CH_3), 55.7 (4-C), 52.6 ($NHCOOCH_3$), 42.9 (5-C), 32.8 (6-C), 15.6 (OCH_2CH_3), 15.0 (2 × OCH_2CH_3).

Anal. Calcd for $C_{27}H_{35}NO_9$: C, 62.66; H, 6.82; N, 2.71. Found: C, 62.65; H, 6.81; N, 2.72.

(Trialkyloxyphenyl)cyclohexanediyl Diacetates (–)-25a, (–)-25b and (–)-25c; General Procedure

Compound (+)-**24a**, (+)-**24b** or (+)-**24c** (1.30 mmol) was dissolved in acetyl chloride (4.86 mL, 5.37 g, 0.07 mol) and the solution was stirred at r.t. for 20–24 h. Then, it was poured into a saturated $NaHCO_3$ solution (424 mL) at 0 °C and extracted with EtOAc (4 × 90 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to afford diacetate (–)-**25a**, (–)-**25b** or (–)-**25c**.

(–)-2,3-Diacetoxy-4-(methoxycarbonylamino)-5-(3,4,5-trimethoxyphenyl)cyclohexyl Benzoate [(–)-25a]

Yield: 0.72 g (99%); white solid (fluffy); mp 81–89 °C; $[\alpha]_D^{22}$ –12.9 (*c* 1, $CHCl_3$); R_f = 0.76 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3380, 2945, 2842, 1751, 1725, 1592, 1538, 1510, 1457, 1369, 1274, 1244, 1127, 1054, 715 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.5 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.63 (t, *J* = 7.5 Hz, 1 H, 4-H_{Bz}), 7.51 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.44 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.50 (t, *J* = 3.0 Hz, 1 H, 1-H/2-H), 5.38 (dd, *J* = 10.5, 3.0 Hz, 1 H, 3-H), 5.31–5.28 (m, 1 H, 1-H/2-H), 4.46 (d, *J* = 9.5 Hz, 1 H, NH), 4.34–4.30 (m, 1 H, 4-H), 3.85 (s, 6 H, 2 × OCH_3), 3.82 (s, 3 H, OCH_3), 3.51 (s, 3 H, $NHCOOCH_3$), 3.00 (td, *J* = 11.0, 3.0 Hz, 1 H, 5-H), 2.25 (s, 3 H, CH_3CO), 2.21–2.16 (m, 2 H, 6-H_α and 6-H_β), 2.03 (s, 3 H, CH_3CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.1 (CH_3CO), 169.5 (CH_3CO), 164.9 (Ph–CO), 156.6 ($NHCOOCH_3$), 153.3 (3-C_{Ar} and 5-C_{Ar}), 136.6 (1-C_{Ar}), 135.9 (4-C_{Ar}), 133.6 (4-C_{Bz}), 129.9 (2-C_{Bz} and 6-C_{Bz}), 129.4 (1-C_{Bz}), 128.7 (3-C_{Bz} and 5-C_{Bz}), 104.9 (2-C_{Ar} and 6-C_{Ar}), 71.4 (3-C), 69.5 (1-C), 69.3 (2-C), 60.8 (OCH_3), 56.3 (2 × OCH_3), 54.1 (4-C), 52.1 ($NHCOOCH_3$), 43.9 (5-C), 33.0 (6-C), 21.0 (CH_3CO), 20.7 (CH_3CO).

Anal. Calcd for $C_{28}H_{33}NO_{11}$: C, 60.10; H, 5.94; N, 2.50. Found: C, 60.09; H, 5.93; N, 2.50.

(–)-2,3-Diacetoxy-5-(3,4-diethoxy-5-methoxyphenyl)-4-(methoxycarbonylamino)cyclohexyl Benzoate [(–)-25b]

Yield: 0.76 g (100%); white solid (fluffy); mp 71–78 °C; $[\alpha]_D^{22}$ –13.2 (*c* 1, $CHCl_3$); R_f = 0.80 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3376, 2979, 1752, 1726, 1589, 1540, 1508, 1455, 1370, 1273, 1244, 1124, 1053, 715 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.2 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.64 (t, *J* = 7.5 Hz, 1 H, 4-H_{Bz}), 7.52 (t, *J* = 7.2 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.43 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.51 (t, *J* = 3.0 Hz, 1 H, 1-H/2-H), 5.38 (dd, *J* = 10.5, 3.0 Hz, 1 H, 3-H), 5.32–5.29 (m, 1 H, 1-H/2-H), 4.43 (d, *J* = 9.9 Hz, 1 H, NH), 4.34–4.31 (m, 1 H, 4-H), 4.06 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.04 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 3.84 (s, 3 H, OCH_3), 3.49 (s, 3 H, $NHCOOCH_3$), 2.97 (td, *J* = 11.1, 5.1 Hz, 1 H, 5-H), 2.25 (s, 3 H, CH_3CO), 2.21–2.17 (m, 2 H, 6-H_α and 6-H_β), 2.04 (s, 3 H, CH_3CO), 1.42 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.34 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7 (CH_3CO), 169.4 (CH_3CO), 164.9 (Ph–CO), 156.5 ($NHCOOCH_3$), 153.6 (3-C_{Ar}), 152.8 (5-C_{Ar}), 136.6 (1-C_{Ar}), 135.5 (4-C_{Ar}), 133.6 (4-C_{Bz}), 129.8 (2-C_{Bz} and 6-C_{Bz}), 129.4 (1-C_{Bz}), 128.6 (3-C_{Bz} and 5-C_{Bz}), 106.5 (2-C_{Ar}), 105.0 (6-C_{Ar}), 71.3 (3-C), 69.5 (1-C), 69.3 (2-C), 68.7 (OCH_2CH_3), 64.8 (OCH_2CH_3), 56.3 (OCH_3), 52.9 (4-C), 52.1 ($NHCOOCH_3$), 43.8 (5-C), 33.9 (6-C), 21.1 (CH_3CO), 20.7 (CH_3CO), 15.5 (OCH_2CH_3), 14.9 (OCH_2CH_3).

Anal. Calcd for $C_{30}H_{37}NO_{11}$: C, 61.32; H, 6.35; N, 2.38. Found: C, 61.33; H, 6.34; N, 2.37.

(–)-2,3-Diacetoxy-4-(methoxycarbonylamino)-5-(3,4,5-triethoxyphenyl)cyclohexyl Benzoate [(–)-25c]

Yield: 0.78 g (100%); white solid (fluffy); mp 69–74 °C; $[\alpha]_D^{22}$ –10.3 (*c* 1, $CHCl_3$); R_f = 0.86 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3399, 2974, 2933, 2886, 1751, 1722, 1587, 1524, 1509, 1480, 1444, 1369, 1270, 1250, 1121, 1030, 722 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 6.9 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.63 (tt, *J* = 7.2, 1.2 Hz, 1 H, 4-H_{Bz}), 7.51 (t, *J* = 7.2 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.41 (s, 2 H, 2-H_{Ar} and 6-H_{Ar}), 5.49 (t, *J* = 3.0 Hz, 1 H, 1-H/2-H), 5.37 (dd, *J* = 10.5, 3.0 Hz, 1 H, 3-H), 5.30–5.27 (m, 1 H, 1-H/2-H), 4.41 (d, *J* = 9.9 Hz, 1 H, NH), 4.30–4.27 (m, 1 H, 4-H), 4.05 (q, *J* = 6.9 Hz, 4 H, 2 × O*CH*$_2$CH$_3$), 4.03 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 3.48 (s, 3 H, NHCOO*CH*$_3$), 2.94 (td, *J* = 10.8, 5.7 Hz, 1 H, 5-H), 2.24 (s, 3 H, CH_3CO), 2.19–2.15 (m, 2 H, 6-$H_α$ and 6-$H_β$), 2.02 (s, 3 H, CH_3CO), 1.40 (t, *J* = 6.9 Hz, 6 H, 2 × OCH$_2$*CH*$_3$), 1.33 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6 (CH_3*CO*), 169.5 (CH_3*CO*), 164.9 (Ph–CO), 156.5 (NH*CO*OCH$_3$), 152.9 (3-C_{Ar} and 5-C_{Ar}), 137.3 (1-C_{Ar}), 135.3 (4-C_{Ar}), 133.6 (4-C_{Bz}), 129.8 (2-C_{Bz} and 6-C_{Bz}), 129.4 (1-C_{Bz}), 128.6 (3-C_{Bz} and 5-C_{Bz}), 106.8 (2-C_{Ar} and 6-C_{Ar}), 71.4 (3-C), 69.5 (1-C), 69.3 (2-C), 68.7 (O*CH*$_2$CH$_3$), 64.9 (2 × O*CH*$_2$CH$_3$), 52.9 (4-C), 52.1 (NHCOO*CH*$_3$), 43.8 (5-C), 33.8 (6-C), 21.1 (*CH*$_3$CO), 20.8 (*CH*$_3$CO), 15.6 (OCH$_2$*CH*$_3$), 15.0 (2 × OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{31}H_{39}NO_{11}$: C, 61.89; H, 6.53; N, 2.33. Found: C, 61.88; H, 6.54; N, 2.32.

Trialkyloxy(methoxy)phenanthridines (–)-26a, (–)-26b/d and (–)-26c by the Modified Bischler–Napieralski Reaction; General Procedure

Compound (–)-**25a**, (–)-**25b** or (–)-**25c** (1.21 mmol) and 4-(dimethylamino)pyridine (0.45 g, 3.67 mmol) were dissolved in anhydrous CH_2Cl_2 (31.6 mL) and the solution was cooled to 0 °C. A solution of triflic anhydride (1.07 mL, 1.80 g, 6.39 mmol) in anhydrous CH_2Cl_2 (5.4 mL) was added dropwise. The reaction mixture was stirred for 20–24 h while being allowed to warm to r.t. Then, it was diluted with CH_2Cl_2 (23 mL) and subsequently washed with saturated $NaHCO_3$ solution (305 mL), 20% aqueous AcOH (305 mL) and again with saturated $NaHCO_3$ solution (305 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified as specified.

(–)-3,4-Diacetoxy-6,7,8,9-tetramethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-2-yl Benzoate [(–)-26a]

Isolated by column chromatography ($CHCl_3$–acetone, 20:1) to afford a white solid (fluffy).

Yield: 0.52 g (80%); mp 84–92 °C; $[\alpha]_D^{22}$ –116.6 (*c* 1, $CHCl_3$); R_f = 0.61 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2942, 1753, 1726, 1638, 1594, 1492, 1456, 1370, 1268, 1240, 1115, 1035, 712 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (dd, *J* = 8.5, 1.5 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.59 (tt, *J* = 7.5, 1.5 Hz, 1 H, 4-H_{Bz}), 7.46 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.57 (s, 1 H, 10-H), 5.57–5.54 (m, 1 H, 3-H), 5.53 (dd, *J* = 11.0, 3.5 Hz, 1 H, 4-H), 5.45 (q, *J* = 3.0 Hz, 1 H, 2-H), 3.90 (s, 3 H, OCH_3), 3.85 (s, 9 H, 2 × OCH_3, $CNOCH_3$), 3.43 (dd, *J* = 14.0, 11.0 Hz, 1 H, 4a-H), 2.80 (td, *J* = 13.0, 4.0 Hz, 1 H, 10b-H), 2.67 (dt, *J* = 14.0, 3.0 Hz, 1 H, 1-$H_α$), 2.14 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), 2.03 (ddd, *J* = 14.5, 12.5, 2.5 Hz, 1 H, 1-$H_β$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 (CH_3*CO*), 169.4 (CH_3*CO*), 165.3 (Ph–CO), 160.3 (6-C), 155.6 (7-C), 152.4 (9-C), 141.8 (10a-C), 135.8 (8-C), 133.5 (4-C_{Bz}), 129.8 (1-C_{Bz}), 129.3 (2-C_{Bz} and 6-C_{Bz}), 128.6 (3-C_{Bz} and 5-C_{Bz}), 112.8 (6a-C), 103.0 (10-C), 72.5 (4-C), 69.6 (2-C), 69.3 (3-C), 61.9 (OCH_3), 61.1 (OCH_3), 56.8 (4a-C), 56.1 (OCH_3), 52.7 ($CNOCH_3$), 33.9 (10b-C), 27.6 (1-C), 21.0 (CH_3CO), 20.8 (CH_3CO).

Anal. Calcd for $C_{28}H_{31}NO_{10}$: C, 62.10; H, 5.77; N, 2.59. Found: C, 62.11; H, 5.76; N, 2.60.

(–)-3,4-Diacetoxy-8,9-diethoxy-6,7-dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-2-yl Benzoate/(–)-3,4-Diacetoxy-7,8-diethoxy-6,9-dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-2-yl Benzoate [(–)-26b/d]

Purified by column chromatography ($CHCl_3$–acetone, 40:1) to afford a white solid (fluffy) containing two regioisomers (1:1).

Yield: 0.52 g (75%); mp 83–86 °C; $[\alpha]_D^{22}$ –124.6 (*c* 1, $CHCl_3$); R_f = 0.67 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2978, 2943, 1752, 1725, 1643, 1593, 1490, 1438, 1362, 1270, 1238, 1110, 719 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.2 Hz, 4 H, 2 × 2-H_{Bz} and 6-H_{Bz}), 7.59 (tt, *J* = 7.5, 1.5 Hz, 2 H, 2 × 4-H_{Bz}), 7.46 (t, *J* = 7.5 Hz, 4 H, 2 × 3-H_{Bz} and 5-H_{Bz}), 6.56 (s, 2 H, 2 × 10-H), 5.58–5.54 (m, 2 H, 2 × 3-H), 5.53 (dd, *J* = 12.3, 2.7 Hz, 2 H, 2 × 4-H), 5.46–5.41 (m, 2 H, 2 × 2-H), 4.13–3.99 (q, *J* = 6.9 Hz, 8 H, 4 × O*CH*$_2$CH$_3$), 3.88 (s, 3 H, OCH_3), 3.85 (s, 9 H, OCH_3, 2 × $CNOCH_3$), 3.43 (dd, *J* = 13.5, 10.5 Hz, 2 H, 2 × 4a-H), 2.80 (td, *J* = 12.9, 3.9 Hz, 2 H, 2 × 10b-H), 2.69–2.62 (m, 2 H, 2 × 1-$H_α$), 2.14 (s, 6 H, 2 × CH_3CO), 2.10 (s, 6 H, 2 × CH_3CO), 2.03–1.98 (m, 2 H, 2 × 1-$H_β$), 1.46 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.37 (t, *J* = 6.9 Hz, 9 H, 3 × OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 (2 × CH_3*CO*), 169.4 (2 × CH_3*CO*), 165.3 (Ph–CO), 165.2 (Ph–CO), 160.4 (2 × 6-C), 155.8 (7-C), 155.3 (7-C), 152.7 (9-C), 151.7 (9-C), 141.0 (2 × 10a-C), 138.3 (8-C), 138.2 (8-C), 133.5 (2 × 4-C_{Bz}), 129.8 (2 × 2-C_{Bz} and 6-C_{Bz}), 129.3 (2 × 1-C_{Bz}), 128.6 (2 × 3-C_{Bz} and 5-C_{Bz}), 113.1 (6a-C), 112.6 (6a-C), 103.9 (10-C), 102.8 (10-C), 72.6 (4-C), 72.5 (4-C), 70.3 (O*CH*$_2$CH$_3$), 69.7 (2 × 2-C), 69.4 (2 × 3-C), 69.3 (2 × O*CH*$_2$CH$_3$), 64.5 (O*CH*$_2$CH$_3$), 61.8 (OCH_3), 56.8 (2 × 4a-C), 56.0 (OCH_3), 52.6 ($CNOCH_3$), 52.5 ($CNOCH_3$), 33.8 (2 × 10b-C), 27.6 (2 × 1-C), 21.0 (2 × *CH*$_3$CO), 20.9 (2 × *CH*$_3$CO), 15.7 (2 × OCH$_2$*CH*$_3$), 15.6 (OCH$_2$*CH*$_3$), 14.8 (OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{30}H_{35}NO_{10}$: C, 63.26; H, 6.19; N, 2.46. Found: C, 63.28; H, 6.20; N, 2.44.

(–)-3,4-Diacetoxy-7,8,9-triethoxy-6-methoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-2-yl Benzoate [(–)-26c]

Isolated by column chromatography ($CHCl_3$–acetone, 100:1) to afford a white solid (fluffy).

Yield: 0.58 g (82%); mp 74–78 °C; $[\alpha]_D^{22}$ –110.0 (*c* 1, $CHCl_3$); R_f = 0.76 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2982, 2944, 2886, 1753, 1731, 1642, 1596, 1492, 1439, 1373, 1239, 1111, 1041, 749 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (dd, *J* = 7.2, 1.2 Hz, 2 H, 2-H_{Bz} and 6-H_{Bz}), 7.58 (tt, *J* = 7.5, 1.2 Hz, 1 H, 4-H_{Bz}), 7.46 (t, *J* = 7.5 Hz, 2 H, 3-H_{Bz} and 5-H_{Bz}), 6.55 (s, 1 H, 10-H), 5.57–5.54 (m, 1 H, 3-H), 5.52 (dd, *J* = 10.8, 3.0 Hz, 1 H, 4-H), 5.44 (q, *J* = 3.0 Hz, 1 H, 2-H), 4.14–3.99 (q, *J* = 6.9 Hz, 6 H, 3 × O*CH*$_2$CH$_3$), 3.83 (s, 3 H, OCH_3), 3.42 (dd, *J* = 13.8, 10.8 Hz, 1 H, 4a-H), 2.79 (td, *J* = 12.9, 3.9 Hz, 1 H, 10b-H), 2.64 (dt, *J* = 14.4, 3.0 Hz, 1 H, 1-$H_α$), 2.13 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), 2.01 (ddd, *J* = 14.4, 12.6, 2.7 Hz, 1 H, 1-$H_β$), 1.46 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.37 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.36 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 (CH_3*CO*), 169.4 (CH_3*CO*), 165.2 (Ph–CO), 160.4 (6-C), 155.3 (7-C), 151.8 (9-C), 141.2 (10a-C), 138.1 (8-C), 133.0 (4-C_{Bz}), 129.8 (2-C_{Bz} and 6-C_{Bz}), 129.3 (1-C_{Bz}), 128.6 (3-C_{Bz} and 5-C_{Bz}), 112.9 (6a-C), 103.8 (10-C), 72.6 (4-C), 70.3 (O*CH*$_2$CH$_3$), 69.7 (2-C), 69.3 (3-C), 69.2 (O*CH*$_2$CH$_3$), 64.4 (O*CH*$_2$CH$_3$), 56.8 (4a-C), 52.4 ($CNOCH_3$), 33.8 (10b-C), 27.6 (1-C), 21.0 (CH_3CO), 20.9 (CH_3CO), 15.7 (2 × OCH$_2$*CH*$_3$), 14.8 (OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{31}H_{37}NO_{10}$: C, 63.80; H, 6.39; N, 2.40. Found: C, 63.80; H, 6.40; N, 2.39.

Trialkyloxy(methoxy)phenanthridinetriols (–)-27a, (–)-27b/d and (–)-27c by Zemplén Deacetylation; General Procedure

To a solution of compound (–)-**26a**, (–)-**26b**/**d** or (–)-**26c** (0.65 mmol) in anhydrous THF (47 mL) was added dropwise a 0.5 M methanolic solution of NaOMe (26 mL) at r.t. and the mixture was stirred for 2 h. The reaction mixture was poured into H_2O (75 mL) and extracted with EtOAc (2 × 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified as specified.

(–)-6,7,8,9-Tetramethoxy-1,2,3,4,4a,10b-hexahydrophenanthridine-2,3,4-triol [(–)-27a]

Isolated by column chromatography (EtOAc–MeOH, 20:1) to afford a white solid.

Yield: 0.18 g (77%); mp 121–123 °C; $[\alpha]_D^{22}$ –50.2 (*c* 1, $CHCl_3$); R_f = 0.30 (EtOAc–MeOH, 10:1).

IR (KBr): 3461, 2940, 1636, 1594, 1490, 1458, 1403, 1260, 1115, 1032, 718 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.71 (s, 1 H, 10-H), 4.87 (d, *J* = 3.3 Hz, 1 H, OH), 4.55 (d, *J* = 3.3 Hz, 1 H, OH), 4.21 (d, *J* = 4.8 Hz, 1 H, OH), 3.91–3.88 (m, 1 H, 2-H), 3.86 (s, 3 H, OCH_3), 3.77 (s, 4 H, OCH_3, 3-H/4-H), 3.72–3.71 (s, 7 H, OCH_3, $CNOCH_3$, 3-H/4-H), 2.90 (dd, *J* = 13.8, 10.2 Hz, 1 H, 4a-H), 2.45 (td, *J* = 13.2, 3.3 Hz, 1 H, 10b-H), 2.18 (dt, *J* = 12.9, 3.0 Hz, 1 H, 1-H_α), 1.71 (ddd, *J* = 14.7, 10.8, 1.5 Hz, 1 H, 1-H_β).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.1 (6-C), 155.0 (7-C), 151.3 (9-C), 140.7 (10a-C), 140.5 (8-C), 112.0 (6a-C), 103.5 (10-C), 71.8 (3-C), 71.2 (4-C), 68.6 (2-C), 61.3 (OCH_3), 60.4 (OCH_3), 58.8 (4a-C), 55.8 (OCH_3), 52.1 ($CNOCH_3$), 32.8 (10b-C), 28.9 (1-C).

Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.79; H, 6.55; N, 3.95.

(–)-8,9-Diethoxy-6,7-dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridine-2,3,4-triol/(–)-7,8-Diethoxy-6,9-dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridine-2,3,4-triol [(–)-27b/d]

Purified by column chromatography (EtOAc–MeOH, 15:1) to give a white solid containing two regioisomers (1:1).

Yield: 0.25 g (100%); mp 98–100 °C; $[\alpha]_D^{22}$ –43.3 (*c* 0.5, MeOH); R_f = 0.32 (EtOAc–MeOH, 10:1).

IR (KBr): 3420, 2979, 2937, 1635, 1594, 1561, 1491, 1438, 1386, 1239, 1117, 712 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.69 (s, 1 H, 10-H), 6.68 (s, 1 H, 10-H), 4.86 (d, *J* = 3.3 Hz, 2 H, 2 × OH), 4.55 (d, *J* = 3.3 Hz, 2 H, 2 × OH), 4.19 (d, *J* = 4.5 Hz, 2 H, 2 × OH), 4.11 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.00–3.87 (m, 12 H, 3 × OCH_2CH_3, 2 × 2-H, 3-H/4-H, OCH_3), 3.76 (m, 8 H, $CNOCH_3$, OCH_3, 2 × 3-H/4-H), 3.74–3.70 (m, 4 H, $CNOCH_3$, 3-H/4-H), 2.89 (dd, *J* = 13.5, 9.9 Hz, 2 H, 2 × 4a-H), 2.42 (td, *J* = 13.2, 3.6 Hz, 2 H, 2 × 10b-H), 2.17–2.14 (m, 2 H, 2 × 1-H_α), 1.71–1.68 (m, 2 H, 2 × 1-H_β), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.31–1.24 (m, 9 H, 3 × OCH_2CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.2 (2 × 6-C), 155.2 (7-C), 154.5 (7-C), 151.6 (9-C), 150.5 (9-C), 140.4 (2 × 10a-C), 139.7 (2 × 8-C), 112.3 (6a-C), 111.9 (6a-C), 104.3 (10-C), 103.4 (10-C), 71.8 (2 × 3-C), 71.2 (2 × 4-C), 69.4 (OCH_2CH_3), 68.5 (2 × 2-C), 68.3 (OCH_2CH_3), 68.2 (OCH_2CH_3), 63.9 (OCH_2CH_3), 61.1 (OCH_3), 58.8 (2 × 4a-C), 55.8 (OCH_3), 52.1 ($CNOCH_3$), 51.9 ($CNOCH_3$), 32.8 (2 × 10b-C), 28.9 (2 × 1-C), 15.5 (2 × OCH_2CH_3), 15.4 (OCH_2CH_3), 14.6 (OCH_2CH_3).

Anal. Calcd for $C_{19}H_{27}NO_7$: C, 59.83; H, 7.17; N, 3.67. Found: C, 59.82; H, 7.19; N, 3.66.

(–)-7,8,9-Triethoxy-6-methoxy-1,2,3,4,4a,10b-hexahydrophenanthridine-2,3,4-triol [(–)-27c]

Isolated by column chromatography (EtOAc–MeOH, 40:1) to give a white solid.

Yield: 0.22 g (85%); mp 111–113 °C; $[\alpha]_D^{22}$ –52.4 (*c* 1, THF); R_f = 0.37 (EtOAc–MeOH, 10:1).

IR (KBr): 3421, 2978, 2928, 1625, 1593, 1560, 1491, 1456, 1385, 1242, 1210, 1120, 714 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.66 (s, 1 H, 10-H), 4.86 (d, *J* = 3.6 Hz, 1 H, OH), 4.55 (d, *J* = 3.6 Hz, 1 H, OH), 4.19 (d, *J* = 4.8 Hz, 1 H, OH), 4.11 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.03–3.82 (m, 5 H, 2 × OCH_2CH_3, 2-H), 3.78–3.68 (m, 5 H, $CNOCH_3$, 3-H, 4-H), 2.88 (dd, *J* = 13.5, 9.9 Hz, 1 H, 4a-H), 2.44 (td, *J* = 13.2, 3.6 Hz, 1 H, 10b-H), 2.14 (dt, *J* = 13.2, 3.0 Hz, 1 H, 1-H_α), 1.68 (ddd, *J* = 14.7, 11.1, 1.5 Hz, 1 H, 1-H_β), 1.34 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 1.28 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.26 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.3 (6-C), 154.4 (7-C), 150.6 (9-C), 140.3 (10a-C), 139.9 (8-C), 112.3 (6a-C), 104.2 (10-C), 71.8 (3-C), 71.2 (4-C), 69.4 (OCH_2CH_3), 68.6 (2-C), 68.3 (OCH_2CH_3), 63.9 (OCH_2CH_3), 58.8 (4a-C), 51.9 ($CNOCH_3$), 32.8 (10b-C), 28.9 (1-C), 15.5 (2 × OCH_2CH_3), 14.6 (OCH_2CH_3).

Anal. Calcd for $C_{20}H_{29}NO_7$: C, 60.74; H, 7.39; N, 3.54. Found: C, 60.73; H, 7.40; N, 3.53.

(Trialkyloxyphenyl)lactams (–)-28a, (–)-28b/d and (–)-28c; General Procedure

To a solution of compound (–)-**27a**, (–)-**27b**/**d** or (–)-**27c** (0.29 mmol) in THF (14 mL) was added a 2 M aqueous HCl solution (0.7 mL) and the reaction mixture was stirred at r.t. for 24 h. Then, it was concentrated in vacuo. The crude product was purified as specified.

(–)-2,3,4-Trihydroxy-7,8,9-trimethoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-28a]

Purified by preparative TLC (EtOAc–MeOH, 4:1) to give a white solid.

Yield: 0.03 g (26%); mp 128–131 °C; $[\alpha]_D^{22}$ –70.6 (*c* 0.35, EtOH); R_f = 0.40 (EtOAc–MeOH, 4:1).

IR (KBr): 3435, 3374, 2940, 1647, 1595, 1488, 1458, 1372, 1250, 1122, 1041, 668 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.93 (s, 1 H, NH), 6.68 (s, 1 H, 10-H), 5.02–4.99 (m, 2 H, 2 × OH), 4.82–4.79 (m, 1 H, OH), 3.90–3.87 (m, 1 H, 2-H), 3.86 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 3.72–3.70 (m, 5 H, OCH_3, 3-H, 4-H), 3.21 (dd, *J* = 11.4, 10.5 Hz, 1 H, 4a-H), 2.81 (td, *J* = 12.0, 3.3 Hz, 1 H, 10b-H), 2.17 (dt, *J* = 13.2, 3.0 Hz, 1 H, 1-H_α), 1.66 (ddd, *J* = 14.4, 11.7, 2.1 Hz, 1 H, 1-H_β).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.6 (6-C), 155.3 (9-C), 154.1 (7-C), 140.9 (10a-C), 139.8 (8-C), 116.1 (6a-C), 103.3 (10-C), 71.6 (3-C), 69.5 (4-C), 68.6 (2-C), 61.4 (OCH_3), 60.4 (OCH_3), 55.8 (OCH_3), 54.4 (4a-C), 35.4 (10b-C), 28.3 (1-C).

Anal. Calcd for $C_{16}H_{21}NO_7$: C, 56.63; H, 6.24; N, 4.13. Found: C, 56.63; H, 6.25; N, 4.12.

(–)-8,9-Diethoxy-2,3,4-trihydroxy-7-methoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one/(–)-7,8-Diethoxy-2,3,4-trihydroxy-9-methoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-28b/d]

The mixture of these regioisomers (1:1) proved to be inseparable in this step. Their isolation was achieved after triacetylation, as described below.

(–)-7,8,9-Triethoxy-2,3,4-trihydroxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-28c]

Purified by preparative TLC (EtOAc–MeOH, 8:1) to afford a white solid.

Yield: 0.08 g (76%); mp 201–205 °C; $[\alpha]_D^{22}$ –34.7 (*c* 0.5, THF); R_f = 0.64 (EtOAc–MeOH, 4:1).

IR (KBr): 3481, 3432, 2927, 2857, 1667, 1595, 1459, 1378, 1239, 1127, 1040, 802 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.84 (s, 1 H, NH), 6.64 (s, 1 H, 10-H), 4.98–4.94 (m, 2 H, 2 × OH), 4.82–4.79 (m, 1 H, OH), 4.12 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 4.02–3.90 (m, 4 H, 2 × O*CH*$_2$CH$_3$), 3.90–3.87 (m, 1 H, 2-H), 3.73–3.68 (m, 2 H, 3-H, 4-H), 3.20 (dd, *J* = 12.6, 10.2 Hz, 1 H, 4a-H), 2.80 (td, *J* = 12.3, 3.3 Hz, 1 H, 10b-H), 2.14 (dt, *J* = 13.5, 3.3 Hz, 1 H, 1-H$_\alpha$), 1.65 (ddd, *J* = 14.1, 11.7, 2.4 Hz, 1 H, 1-H$_\beta$), 1.34 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.28 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.27 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.7 (6-C), 154.9 (9-C), 153.3 (7-C), 140.3 (10a-C), 139.4 (8-C), 116.4 (6a-C), 103.9 (10-C), 71.6 (3-C), 69.5 (4-C), 69.3 (O*CH*$_2$CH$_3$), 68.5 (2-C), 68.2 (O*CH*$_2$CH$_3$), 63.8 (O*CH*$_2$CH$_3$), 54.4 (4a-C), 35.3 (10b-C), 28.3 (1-C), 15.6 (OCH$_2$*CH*$_3$), 15.5 (OCH$_2$*CH*$_3$), 14.6 (OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{19}H_{27}NO_7$: C, 59.83; H, 7.14; N, 3.67. Found: C, 56.82; H, 7.15; N, 3.66.

Trialkyloxyphenanthridinetriyl Triacetates (–)-29a, (–)-29b and (–)-29d; General Procedure

Compound (–)-**28a** or (–)-**28b/d** (0.28 mmol) was dissolved in acetyl chloride (1.06 mL, 1.17 g, 14.90 mmol) and the solution was stirred at r.t. for 20–24 h. Then, it was poured into a saturated $NaHCO_3$ solution (135 mL) at 0 °C and extracted with EtOAc (4 × 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified as specified.

(–)-7,8,9-Trimethoxy-6-oxo-1,2,3,4,4a,5,6,10b-octahydrophenanthridine-2,3,4-triyl Triacetate [(–)-29a]

Purified by preparative TLC (hexane–EtOAc, 1:2) to give a white solid.

Yield: 0.05 g (42%); mp 124–130 °C; $[\alpha]_D^{22}$ –102.4 (*c* 1, THF); R_f = 0.05 (hexane–EtOAc, 1:1).

IR (KBr): 3196, 2933, 1748, 1673, 1592, 1473, 1457, 1375, 1253, 1227, 1121, 1020, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.52 (s, 1 H, 10-H), 6.00 (s, 1 H, NH), 5.44–5.40 (m, 1 H, 2-H/3-H/4-H), 5.21–5.16 (m, 2 H, 2-H/3-H/4-H, 2-H/3-H/4-H), 3.94 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.72–3.69 (m, 1 H, 4a-H), 3.12 (td, *J* = 12.3, 3.3 Hz, 1 H, 10b-H), 2.50 (dt, *J* = 14.1, 3.0 Hz, 1 H, 1-H$_\alpha$), 2.15 (s, 3 H, CH_3CO), 2.08 (s, 6 H, 2 × CH_3CO), 1.94–1.91 (m, 1 H, 1-H$_\beta$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (CH_3*CO*), 169.5 (CH_3*CO*), 169.1 (CH_3*CO*), 163.6 (6-C), 156.4 (9-C), 155.7 (7-C), 142.3 (10a-C), 137.4 (8-C), 115.7 (6a-C), 102.9 (10-C), 71.6 (4-C), 68.6 (2-C), 67.4 (3-C), 61.9 (OCH_3), 61.1 (OCH_3), 56.1 (OCH_3), 52.1 (4a-C), 35.7 (10b-C), 26.8 (1-C), 21.0 (*CH*$_3$CO), 20.8 (*CH*$_3$CO), 20.7 (*CH*$_3$CO).

Anal. Calcd for $C_{22}H_{27}NO_{10}$: C, 56.77; H, 5.85; N, 3.01. Found: C, 56.78; H, 5.87; N, 3.00.

(–)-8,9-Diethoxy-7-methoxy-6-oxo-1,2,3,4,4a,5,6,10b-octahydrophenanthridine-2,3,4-triyl Triacetate [(–)-29b]

Purified and separated from the regioisomer (–)-**29d** by preparative TLC (hexane–EtOAc, 1:1) to give a white solid (fluffy).

Yield: 0.03 g (20%); mp 100–106 °C; $[\alpha]_D^{22}$ –99.3 (*c* 1.2, $CHCl_3$); R_f = 0.17 (hexane–EtOAc, 1:1).

IR (KBr): 3196, 2933, 1748, 1673, 1592, 1473, 1457, 1375, 1253, 1227, 1121, 1020, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.49 (s, 1 H, 10-H), 6.14 (s, 1 H, NH), 5.44–5.41 (m, 1 H, 2-H/3-H/4-H), 5.20–5.15 (m, 2 H, 2-H/3-H/4-H, 2-H/3-H/4-H), 4.11 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 4.06 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 3.93 (s, 3 H, OCH_3), 3.72–3.69 (m, 1 H, 4a-H), 3.11 (td, *J* = 12.3, 3.6 Hz, 1 H, 10b-H), 2.46 (dt, *J* = 14.4, 2.7 Hz, 1 H, 1-H$_\alpha$), 2.14 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 1.91 (ddd, *J* = 14.1, 12.9, 3.0 Hz, 1 H, 1-H$_\beta$), 1.47 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.37 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (CH_3*CO*), 169.5 (CH_3*CO*), 169.1 (CH_3*CO*), 163.8 (6-C), 156.2 (9-C), 156.0 (7-C), 141.4 (10a-C), 137.1 (8-C), 115.4 (6a-C), 103.5 (10-C), 71.6 (4-C), 69.4 (O*CH*$_2$CH$_3$), 68.6 (2-C), 67.4 (3-C), 64.5 (O*CH*$_2$CH$_3$), 61.8 (OCH_3), 52.1 (4a-C), 35.6 (10b-C), 26.8 (1-C), 21.0 (*CH*$_3$CO), 20.8 (*CH*$_3$CO), 20.7 (*CH*$_3$CO), 15.6 (OCH$_2$*CH*$_3$), 14.6 (OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{24}H_{31}NO_{10}$: C, 58.41; H, 6.33; N, 2.84. Found: C, 58.41; H, 6.32; N, 2.83.

(–)-7,8-Diethoxy-9-methoxy-6-oxo-1,2,3,4,4a,5,6,10b-octahydrophenanthridine-2,3,4-triyl Triacetate [(–)-29d]

Purified and separated from the regioisomer (–)-**29b** by preparative TLC (hexane–EtOAc, 1:1) to give a white solid (fluffy).

Yield: 0.05 g (38%); mp 100–106 °C; $[\alpha]_D^{22}$ –95.0 (*c* 0.5, $CHCl_3$); R_f = 0.22 (hexane–EtOAc, 1:1).

IR (KBr): 3190, 3083, 2979, 2938, 1754, 1667, 1592, 1448, 1370, 1238, 1121, 1094, 1040, 789 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.51 (s, 1 H, 10-H), 5.90 (s, 1 H, NH), 5.44–5.41 (m, 1 H, 2-H/3-H/4-H), 5.22–5.17 (m, 2 H, 2-H/3-H/4-H, 2-H/3-H/4-H), 4.13 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 4.07 (q, *J* = 6.9 Hz, 2 H, O*CH*$_2$CH$_3$), 3.90 (s, 3 H, OCH_3), 3.70 (dd, *J* = 12.3, 10.5 Hz, 1 H, 4a-H), 3.13 (td, *J* = 12.6, 3.6 Hz, 1 H, 10b-H), 2.49 (dt, *J* = 14.4, 3.0 Hz, 1 H, 1-H$_\alpha$), 2.15 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 1.93 (ddd, *J* = 14.4, 12.9, 2.7 Hz, 1 H, 1-H$_\beta$), 1.42 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$), 1.37 (t, *J* = 6.9 Hz, 3 H, OCH$_2$*CH*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (CH_3*CO*), 169.5 (CH_3*CO*), 169.2 (CH_3*CO*), 163.7 (6-C), 156.9 (9-C), 156.7 (7-C), 141.6 (10a-C), 137.2 (8-C), 116.0 (6a-C), 102.5 (10-C), 71.7 (4-C), 70.5 (O*CH*$_2$CH$_3$), 69.4 (O*CH*$_2$CH$_3$), 68.7 (2-C), 67.5 (3-C), 56.0 (OCH_3), 52.1 (4a-C), 35.7 (10b-C), 26.7 (1-C), 21.1 (*CH*$_3$CO), 20.7 (2 × *CH*$_3$CO), 15.7 (2 × OCH$_2$*CH*$_3$).

Anal. Calcd for $C_{24}H_{31}NO_{10}$: C, 58.41; H, 6.33; N, 2.84. Found: C, 58.40; H, 6.34; N, 2.83.

Dialkyloxyphenanthridinetriyl Triacetates (–)-30a, (–)-30b and (–)-30d; General Procedure

To a solution of compound (–)-**29a**, (–)-**29b** or (–)-**29d** (0.12 mmol) and KI (20.30 mg, 0.12 mmol) in anhydrous MeCN (5.5 mL) was added a solution of TMSCl (17.30 mg, 0.16 mmol) in anhydrous MeCN (2.6 mL). The reaction mixture was heated to 50–60 °C and stirred for

3–5 h. Then, it was cooled to 0 °C and H_2O (7 mL) was added dropwise to quench the reaction. After extraction with EtOAc (4 × 10 mL), the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified as specified.

(–)-7-Hydroxy-8,9-dimethoxy-6-oxo-1,2,3,4,4a,5,6,10b-octahydrophenanthridine-2,3,4-triyl Triacetate[(–)-30a]

Purified by preparative TLC (hexane–EtOAc, 1:1) to afford a white solid.

Yield: 0.04 g (76%); mp 207–209 °C; $[\alpha]_D^{22}$ –49.2 (*c* 0.65, $CHCl_3$); R_f = 0.32 (hexane–EtOAc, 1:1).

IR (KBr): 3357, 2937, 1762, 1646, 1507, 1457, 1370, 1248, 1221, 1120, 1051, 652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 12.36 (s, 1 H, OH), 6.28 (s, 1 H, 10-H), 6.17 (br s, 1 H, NH), 5.46–5.43 (m, 1 H, 2-H), 5.23–5.18 (m, 2 H, 3-H, 4-H), 3.91 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.79 (dd, *J* = 12.6, 11.1 Hz, 1 H, 4a-H), 3.14 (td, *J* = 12.3, 3.3 Hz, 1 H, 10b-H), 2.51 (dt, *J* = 13.8, 3.0 Hz, 1 H, 1-H_α), 2.14 (s, 3 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 1.95 (ddd, *J* = 14.1, 12.9, 2.7 Hz, 1 H, 1-H_β).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2 (CH_3CO), 170.1 (CH_3CO), 169.4 (CH_3CO), 169.1 (6-C), 157.3 (9-C), 156.3 (7-C), 135.9 (10a-C), 135.7 (8-C), 105.5 (6a-C), 98.6 (10-C), 71.6 (4-C), 68.5 (2-C), 67.3 (3-C), 60.7 (OCH_3), 56.1 (OCH_3), 52.7 (4a-C), 34.5 (10b-C), 26.5 (1-C), 21.0 (CH_3CO), 20.8 (CH_3CO), 20.7 (CH_3CO).

Anal. Calcd for $C_{21}H_{25}NO_{10}$: C, 55.87; H, 5.58; N, 3.10. Found: C, 55.86; H, 5.59; N, 3.09.

(–)-8,9-Diethoxy-7-hydroxy-6-oxo-1,2,3,4,4a,5,6,10b-octahydrophenanthridine-2,3,4-triyl Triacetate [(–)-30b]

Purified by preparative TLC (hexane–EtOAc, 3:2) to give a white solid.

Yield: 0.04 g (77%); mp 166–168 °C; $[\alpha]_D^{22}$ –33.3 (*c* 0.58, $CHCl_3$); R_f = 0.43 (hexane–EtOAc, 1:1).

IR (KBr): 3367, 2983, 2933, 2888, 1752, 1651, 1574, 1501, 1449, 1373, 1247, 1222, 1123, 1045, 826, 662 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 12.33 (s, 1 H, OH), 6.26 (s, 1 H, 10-H), 6.05 (br s, 1 H, NH), 5.45–5.42 (m, 1 H, 2-H), 5.22–5.17 (m, 2 H, 3-H, 4-H), 4.12 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 4.08 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 3.79 (dd, *J* = 12.6, 11.1 Hz, 1 H, 4a-H), 3.13 (td, *J* = 12.9, 3.6 Hz, 1 H, 10b-H), 2.48 (dt, *J* = 14.4, 3.0 Hz, 1 H, 1-H_α), 2.14 (s, 3 H, CH_3CO), 2.08 (s, 6 H, 2 × CH_3CO), 1.93 (ddd, *J* = 14.1, 13.2, 2.7 Hz, 1 H, 1-H_β), 1.46 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.36 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (CH_3CO), 170.2 (CH_3CO), 169.4 (CH_3CO), 169.2 (6-C), 157.0 (9-C), 156.8 (7-C), 135.6 (10a-C), 134.8 (8-C), 105.3 (6a-C), 99.7 (10-C), 71.7 (4-C), 68.7 (OCH_2CH_3), 68.6 (2-C), 67.3 (3-C), 64.6 (OCH_2CH_3), 52.6 (4a-C), 34.4 (10b-C), 26.5 (1-C), 21.0 (CH_3CO), 20.8 (CH_3CO), 20.7 (CH_3CO), 15.5 (OCH_2CH_3), 14.8 (OCH_2CH_3).

Anal. Calcd for $C_{23}H_{29}NO_{10}$: C, 57.61; H, 6.10; N, 2.92. Found: C, 57.62; H, 6.09; N, 2.91.

(–)-8-Ethoxy-7-hydroxy-9-methoxy-6-oxo-1,2,3,4,4a,5,6,10b-octahydrophenanthridine-2,3,4-triyl Triacetate [(–)-30d]

Purified by preparative TLC (hexane–EtOAc, 3:2) to give a white solid.

Yield: 0.03 g (58%); mp 209–210 °C; $[\alpha]_D^{22}$ –52.2 (*c* 0.64, $CHCl_3$); R_f = 0.36 (hexane–EtOAc, 1:1).

IR (KBr): 3231, 2977, 1749, 1653, 1572, 1451, 1371, 1241, 1220, 1037, 809 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 12.35 (s, 1 H, OH), 6.28 (s, 1 H, 10-H), 6.13 (br s, 1 H, NH), 5.46–5.43 (m, 1 H, 2-H), 5.22–5.18 (m, 2 H, 3-H, 4-H), 4.09 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3), 3.90 (s, 3 H, OCH_3), 3.80 (dd, *J* = 12.6, 11.1 Hz, 1 H, 4a-H), 3.14 (td, *J* = 12.9, 3.6 Hz, 1 H, 10b-H), 2.51 (dt, *J* = 14.4, 3.0 Hz, 1 H, 1-H_α), 2.14 (s, 3 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 1.95 (ddd, *J* = 14.4, 12.6, 2.7 Hz, 1 H, 1-H_β), 1.37 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (CH_3CO), 170.2 (CH_3CO), 169.4 (CH_3CO), 169.1 (6-C), 157.6 (9-C), 156.6 (7-C), 135.8 (10a-C), 134.6 (8-C), 105.4 (6a-C), 98.6 (10-C), 71.7 (4-C), 68.7 (OCH_2CH_3), 68.6 (2-C), 67.4 (3-C), 56.1 (OCH_3), 52.7 (4a-C), 34.5 (10b-C), 26.5 (1-C), 21.0 (CH_3CO), 20.8 (CH_3CO), 20.7 (CH_3CO), 15.5 (OCH_2CH_3).

Anal. Calcd for $C_{22}H_{27}NO_{10}$: C, 56.77; H, 5.85; N, 3.01. Found: C, 56.76; H, 5.86; N, 3.00.

Dialkyloxyphenanthridones (–)-31a, (–)-31b and (–)-31d, as well as Trialkyloxyphenanthridones (–)-28b and (–)-28d, by Zemplén Deacetylation; General Procedure

To a solution of compound (–)-**30a**, (–)-**30b**, (–)-**30d**, (–)-**29b** or (–)-**29d** (0.07 mmol) in anhydrous THF (5.2 mL) was added dropwise a 0.5 M methanolic solution of NaOMe (2.9 mL) at r.t. and the mixture was stirred for 2 h. Amberlite IR-120 (strongly acidic resin) was added until the pH became 7. The solid resin was collected by filtration and washed with THF (5 mL), and the filtrate was concentrated in vacuo. The residue was purified as specified.

(–)-2,3,4,7-Tetrahydroxy-8,9-dimethoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-31a]

Purified by preparative TLC (EtOAc–MeOH, 6:1) to afford a white solid.

Yield: 0.02 g (79%); mp 108–111 °C; $[\alpha]_D^{22}$ –8.1 (*c* 0.37, EtOH); R_f = 0.62 (EtOAc–MeOH, 4:1).

IR (KBr): 3381, 2927, 1633, 1610, 1572, 1508, 1457, 1395, 1249, 1127, 1062, 1032, 799 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 12.98 (s, 1 H, OH), 7.49 (s, 1 H, NH), 6.44 (s, 1 H, 10-H), 5.03–4.89 (m, 2 H, 2 × OH), 4.88–4.85 (m, 1 H, OH), 3.90–3.87 (m, 1 H, 2-H), 3.85 (s, 3 H, OCH_3), 3.74–3.70 (m, 2 H, 3-H, 4-H), 3.67 (s, 3 H, OCH_3), 3.34 (m, 1 H, 4a-H), 2.88 (td, *J* = 12.3, 3.6 Hz, 1 H, 10b-H), 2.19 (dt, *J* = 12.9, 3.0 Hz, 1 H, 1-H_α), 1.70–1.67 (m, 1 H, 1-H_β).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.6 (6-C), 156.5 (9-C), 155.1 (7-C), 138.5 (10a-C), 134.1 (8-C), 105.2 (6a-C), 98.8 (10-C), 71.5 (3-C), 69.5 (4-C), 68.4 (2-C), 59.7 (OCH_3), 55.8 (OCH_3), 55.0 (4a-C), 33.7 (10b-C), 27.8 (1-C).

Anal. Calcd for $C_{15}H_{19}NO_7$: C, 55.38; H, 5.89; N, 4.31. Found: C, 55.39; H, 5.90; N, 4.30.

(–)-8,9-Diethoxy-2,3,4,7-tetrahydroxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-31b]

Purified by preparative TLC (EtOAc–MeOH, 8:1) to afford a white solid.

Yield: 0.02 g (80%); mp 241–243 °C; $[\alpha]_D^{22}$ –8.8 (*c* 0.45, EtOH); R_f = 0.71 (EtOAc–MeOH, 4:1).

IR (KBr): 3382, 2980, 2933, 2887, 1646, 1611, 1573, 1507, 1444, 1377, 1245, 1125, 1067, 1040, 816 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 12.92 (s, 1 H, OH), 7.42 (s, 1 H, NH), 6.39 (s, 1 H, 10-H), 4.99 (d, *J* = 3.6 Hz, 1 H, OH), 4.94 (d, *J* = 6.0 Hz, 1 H, OH), 4.84 (d, *J* = 3.3 Hz, 1 H, OH), 4.12 (q, *J* = 6.9 Hz, 2 H, OCH_2CH_3),

3.92 (q, J = 6.9 Hz, 2 H, OCH_2CH$_3$), 3.90–3.87 (m, 1 H, 2-H), 3.73–3.68 (m, 2 H, 3-H, 4-H), 3.35–3.32 (m, 1 H, 4a-H), 2.86 (td, J = 12.6, 3.6 Hz, 1 H, 10b-H), 2.15 (dt, J = 13.2, 3.3 Hz, 1 H, 1-H$_\alpha$), 1.69–1.66 (m, 1 H, 1-H$_\beta$), 1.33 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$), 1.23 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.7 (6-C), 156.1 (9-C), 155.5 (7-C), 138.2 (10a-C), 133.2 (8-C), 105.1 (6a-C), 99.6 (10-C), 71.6 (3-C), 69.5 (4-C), 68.4 (2-C), 67.5 (OCH_2CH$_3$), 63.9 (OCH_2CH$_3$), 55.0 (4a-C), 33.6 (10b-C), 27.8 (1-C), 15.4 (OCH$_2$$CH_3$), 14.6 (OCH$_2$$CH_3$).

Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.77; H, 6.55; N, 3.97.

(–)-8-Ethoxy-2,3,4,7-tetrahydroxy-9-methoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-31d]

Purified by preparative TLC (EtOAc–MeOH, 8:1) to afford a white solid.

Yield: 0.02 g (78%); mp 240–242 °C; $[\alpha]_D^{22}$ –4.7 (*c* 0.42, EtOH); R_f = 0.67 (EtOAc–MeOH, 4:1).

IR (KBr): 3382, 2980, 2933, 2887, 1646, 1611, 1573, 1507, 1444, 1377, 1245, 1125, 1067, 1040, 816 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.94 (s, 1 H, OH), 7.45 (s, 1 H, NH), 6.43 (s, 1 H, 10-H), 5.00 (d, J = 3.3 Hz, 1 H, OH), 4.95 (d, J = 6.0 Hz, 1 H, OH), 4.85 (d, J = 3.6 Hz, 1 H, OH), 3.91 (q, J = 6.9 Hz, 2 H, OCH_2CH$_3$), 3.91–3.88 (m, 1 H, 2-H), 3.84 (s, 3 H, OCH$_3$), 3.75–3.71 (m, 2 H, 3-H, 4-H), 3.35–3.32 (m, 1 H, 4a-H), 2.88 (td, J = 12.3, 3.3 Hz, 1 H, 10b-H), 2.19 (dt, J = 13.5, 3.0 Hz, 1 H, 1-H$_\alpha$), 1.71–1.68 (m, 1 H, 1-H$_\beta$), 1.23 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.7 (6-C), 156.8 (9-C), 155.3 (7-C), 138.3 (10a-C), 133.0 (8-C), 105.2 (6a-C), 98.8 (10-C), 71.6 (3-C), 69.5 (4-C), 68.4 (2-C), 67.5 (OCH_2CH$_3$), 55.8 (OCH$_3$), 55.0 (4a-C), 33.7 (10b-C), 27.8 (1-C), 15.4 (OCH$_2$$CH_3$).

Anal. Calcd for $C_{16}H_{21}NO_7$: C, 56.63; H, 6.24; N, 4.13. Found: C, 56.64; H, 6.23; N, 4.12.

(–)-8,9-Diethoxy-2,3,4-trihydroxy-7-methoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-28b]

Purified by preparative TLC (EtOAc–MeOH, 8:1) to afford a white solid.

Yield: 0.02 g (73%); mp 191–194 °C; $[\alpha]_D^{22}$ –40.9 (*c* 0.22, EtOH); R_f = 0.61 (EtOAc–MeOH, 4:1).

IR (KBr): 3438, 3369, 2978, 2924, 1650, 1595, 1457, 1370, 1247, 1223, 1122, 1049, 802 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.89 (s, 1 H, NH), 6.65 (s, 1 H, 10-H), 4.99–4.96 (m, 1 H, OH), 4.93–4.90 (m, 1 H, OH), 4.80–4.77 (m, 1 H, OH), 4.12 (q, J = 6.9 Hz, 2 H, OCH_2CH$_3$), 3.94 (q, J = 6.9 Hz, 2 H, OCH_2CH$_3$), 3.90–3.87 (m, 1 H, 2-H), 3.76 (s, 3 H, OCH$_3$), 3.73–3.69 (m, 2 H, 3-H, 4-H), 3.21 (dd, J = 12.9, 9.9 Hz, 1 H, 4a-H), 2.80 (td, J = 12.0, 3.3 Hz, 1 H, 10b-H), 2.14 (dt, J = 13.2, 3.3 Hz, 1 H, 1-H$_\alpha$), 1.65 (ddd, J = 14.1, 11.7, 2.4 Hz, 1 H, 1-H$_\beta$), 1.34 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$), 1.27 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.7 (6-C), 154.8 (9-C), 154.3 (7-C), 140.0 (10a-C), 139.6 (8-C), 116.0 (6a-C), 104.0 (10-C), 71.6 (3-C), 69.4 (4-C), 68.5 (2-C), 68.3 (OCH_2CH$_3$), 63.9 (OCH_2CH$_3$), 61.3 (OCH$_3$), 54.5 (4a-C), 35.3 (10b-C), 28.3 (1-C), 15.5 (OCH$_2$$CH_3$), 14.6 (OCH$_2$$CH_3$).

Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 6.86; N, 3.81. Found: C, 58.83; H, 6.87; N, 3.80.

(–)-7,8-Diethoxy-2,3,4-trihydroxy-9-methoxy-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2*H*)-one [(–)-28d]

Purified by preparative TLC (EtOAc–MeOH, 8:1) to afford a white solid.

Yield: 0.01 g (49%); mp 171–174 °C; $[\alpha]_D^{22}$ –52.5 (*c* 0.32, EtOH); R_f = 0.57 (EtOAc–MeOH, 4:1).

IR (KBr): 3393, 2975, 1653, 1593, 1559, 1508, 1456, 1386, 1240, 1121, 1038, 804 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.85 (s, 1 H, NH), 6.66 (s, 1 H, 10-H), 5.00 (d, J = 3.0 Hz, 1 H, OH), 4.93 (d, J = 5.7 Hz, 1 H, OH), 4.80 (d, J = 3.3 Hz, 1 H, OH), 3.98 (q, J = 7.2 Hz, 2 H, OCH_2CH$_3$), 3.92 (q, J = 7.2 Hz, 2 H, OCH_2CH$_3$), 3.90–3.87 (m, 1 H, 2-H), 3.84 (s, 3 H, OCH$_3$), 3.73–3.69 (m, 2 H, 3-H, 4-H), 3.21 (dd, J = 12.6, 10.2 Hz, 1 H, 4a-H), 2.81 (td, J = 12.0, 3.3 Hz, 1 H, 10b-H), 2.16 (dt, J = 12.3, 3.9 Hz, 1 H, 1-H$_\alpha$), 1.67 (ddd, J = 14.4, 11.7, 2.4 Hz, 1 H, 1-H$_\beta$), 1.28 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$), 1.26 (t, J = 6.9 Hz, 3 H, OCH$_2$$CH_3$).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 166.8 (6-C), 158.3 (9-C), 155.5 (7-C), 142.1 (10a-C), 141.4 (8-C), 116.9 (6a-C), 104.4 (10-C), 73.4 (3-C), 71.5 (4-C and OCH_2CH$_3$), 70.7 (2-C), 70.3 (OCH_2CH$_3$), 56.6 (OCH$_3$), 55.7 (4a-C), 36.5 (10b-C), 29.7 (1-C), 16.0 (2 × OCH$_2$$CH_3$).

Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 6.86; N, 3.81. Found: C, 58.84; H, 6.85; N, 3.82.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591514.

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