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Graphical Abstract

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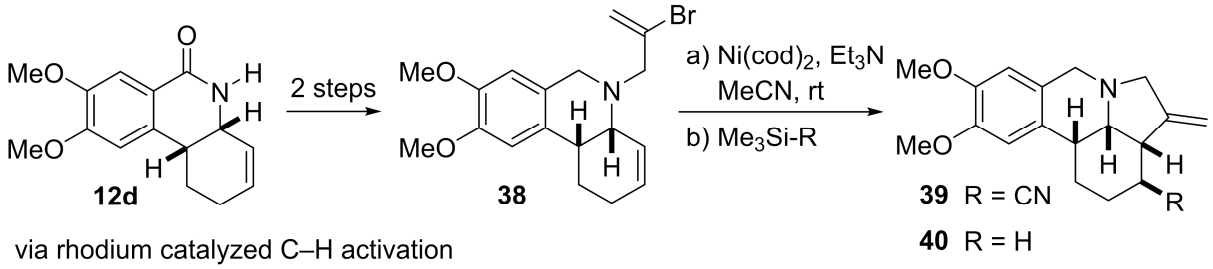

via rhodium catalyzed C–H activation

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ABSTRACT

With a view towards the synthesis of lycorane-like structures several *N*-(pivaloyloxy)-benzamides were reacted with cyclohexa-1,3-diene in presence of a rhodium(III) catalyst which resulted via C–H activation in the corresponding tetrahydrophenanthridinones **12a-d** and **19**. Subsequently, various strategies were explored to convert these tricyclic phenanthridinones to the tetracyclic core structure of the lycoranes. While radical based approaches were not successful, we were able to form ring D (pyrrolidine ring) by a nickel catalyzed reaction, resulting in alkaloid derivatives **39** and **40**.

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1. Introduction

Among alkaloids derived from phenylalanine and tyrosine, amaryllidaceae alkaloids, hold a prominent place among natural products. They comprise eight different ring systems, with lycorine (**1**) representing one of them (Figure 1).[1] Alkaloids related to lycorine feature a tetracyclic pyrrolo[d,e]phenanthridine core structure (galanthan ring system). Some of these alkaloids seem to have interesting biological activity. Thus, lycorine (**1**), displays plant growth inhibiting properties. Another structurally related alkaloid is (+)-fortucine (**2**) which features a *cis*-B/C-ring junction. Its correct absolute configuration could recently be determined by total synthesis.[2] During degradation studies on lycorine the deoxygenated derivative called α-lycorane (**3**) was obtained.[3] Besides the *trans-cis*- (α) and the *trans-trans*- (β), the *cis-cis*-isomer [γ-lycorane (**5**)] has also been prepared.[4] While not biologically active, the lycoranes are timeless synthetic targets for demonstrating potential new strategies towards such polycyclic alkaloids.

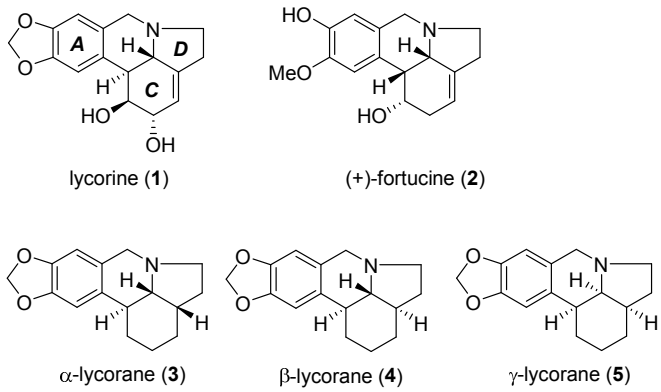
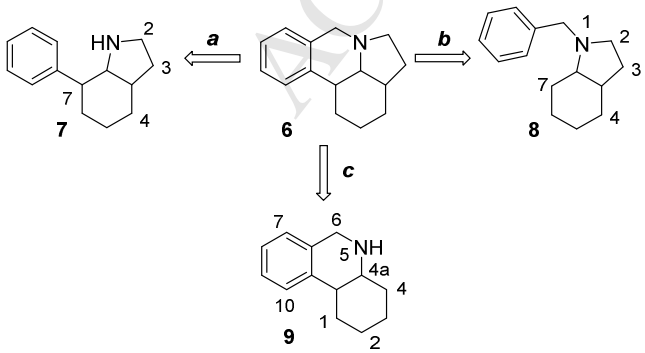


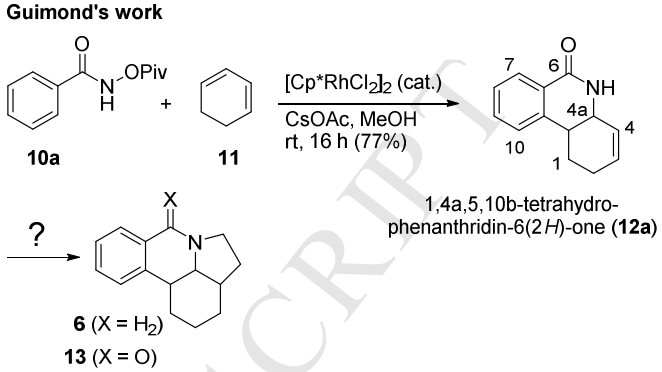
Figure 1. Structures of alkaloids with galanthan ring system.

The main strategies towards lycoranes **6** can be grouped according to formation of the final ring (Scheme 1). Thus, major approaches path through 7-phenyl-octahydro-1*H*-indole derivatives **7** (route ***a***) and close ring B, for example by Pictet-Spengler cyclization.[5] Alternatively, 1-benzyloctahydro-1*H*-indole derivatives **8** have served as advanced intermediates prior to formation of the B-ring (route ***b***).[6] These major strategies then distinguish themselves in the synthetic strategies towards the key octahydroindole derivatives. A quite unique synthesis of lycorine (**1**) features an intramolecular Diels-Alder reaction to simultaneously create the B and C rings.[7] There are two syntheses of lycoranes where the pyrrolidine ring D is formed in the final step by reductive amination and ketone alkylation, respectively, from derivatives of **9** (route ***c***).[8,9,10]



Scheme 1. Major strategies for formation of the last ring of the galanthan ring system.

With the advent of Rh(III)-catalyzed synthesis of fused heterocycles from *N*-hydroxybenzamide derivatives and alkenes, a new approach to lycorane analogs based on route ***c*** seemed possible (Scheme 2). Thus, extending on the example reported by Guimond et al.[11,12,13] who described the annulation of *N*-(pivaloxyloxy)benzamide **10a** with cyclohexa-1,3-diene to tetrahydrophenanthridinone **12a**, the synthesis of lycorane-like structures seemed possible by annexing the D-ring to a properly substituted tetrahydrophenanthridinone.

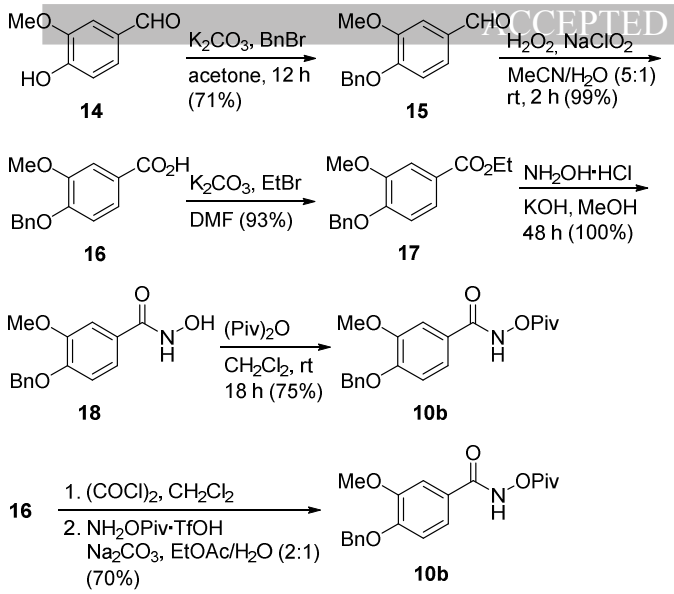


Scheme 2. Possible route to lycorane derivatives via Rh(III)-catalyzed C–H-activation on benzamide derivatives with annulation of cyclohexadienes followed by formation of ring D.

However, this would require to study the effect of substituted benzamide derivatives on this rhodium(III)-catalyzed phenanthridinone synthesis. In this paper we describe our results of this study and investigations toward D-ring formation.

2. Results and discussion

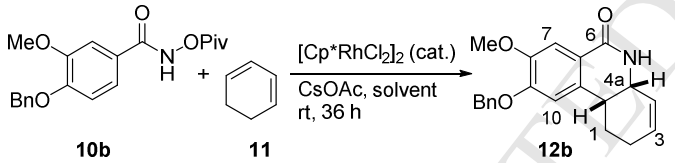
With a view towards the synthesis of lycorane using this strategy, 3,4-dialkoxy-substituted *N*-(pivaloyloxy)-benzamide **10b** was prepared as a model compound. The synthesis of this amide from vanillin is summarized in Scheme 3. Thus, benzylation of 4-hydroxy-3-methoxy-benzaldehyde (vanillin, **14**) to benzyl ether[14] **15** was followed by oxidation[15] of the aldehyde function to benzoic acid[16] **16**. For the conversion of benzoic acid **16** to *N*-pivaloyloxy)amide **10b** two variants were explored. In the first one, acid **16** was converted to ethyl benzoate[17] **17** under alkylating conditions. Subsequent reaction of **17** with hydroxylamine led to hydroxamic acid **18**.[18] A final reaction with pivalic anhydride provided benzamide derivative **10b**. The second variant utilizes the acid chloride, derived from **16**. Its reaction with, *O*-pivaloylhydroxylamine,[19] generated from its triflate salt with Na_2CO_3 gave amide **10b** as well.



Scheme 3. Synthesis of benzamide derivative **10b** from vanillin (**14**).

With amide **10b** a brief survey of reaction conditions (amount of catalyst $[Cp^*RhCl_2]_2$,[20] solvent) was carried out (Table 1). In methanol the reaction led to successful C–H activation, cross-coupling and cyclization. However, despite relatively high catalyst loadings (up to 5 mol%) the yield of tricyclic amide **12b** did not exceed 20%. Acetonitrile as solvent was even worse with a 10% yield of **12b** in presence of 5 mol% catalyst. Much better results were obtained in ethanol as solvent. Here up to 55% of **12b** (2.5 mol% of catalyst) could be obtained.

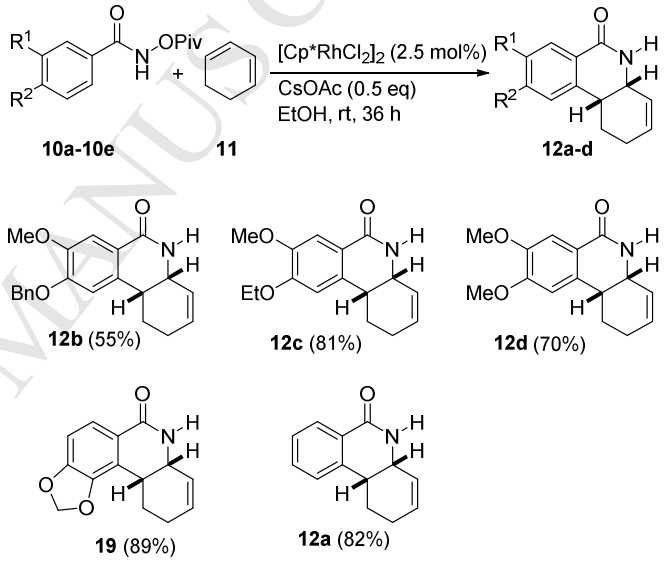
Table 1. Screening of conditions for the rhodium(III)-catalyzed synthesis of phenanthridinone **12b**.



entry	mol% of catalyst	solvent	yield of **12b** (%)
1	5	MeOH	20
2	2.5	MeOH	20
3	1	MeOH	10
4	5	MeCN	10
5	2.5	MeCN	5
6	1	MeCN	0
7	5	EtOH	50
8	2.5	EtOH	55
9	1	EtOH	40

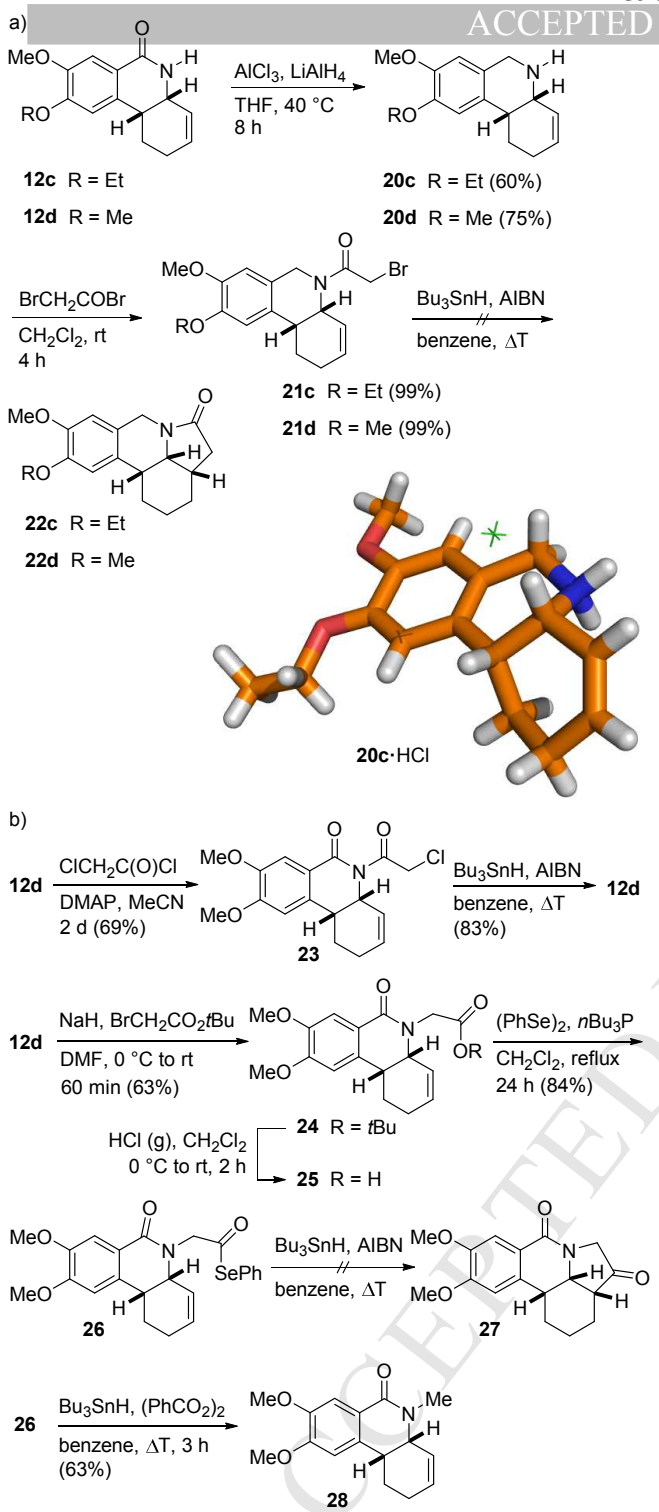
In a larger scale reaction besides the *cis*-product **12b** a small amount of the corresponding *trans*-fused compound could be isolated (*cis*/*trans* = 98:02). As can be seen, the C–H activation is regioselective with the insertion taking place only at 6-H.

With a view towards delineating the scope of this reaction, various 3,4-dialkoxy-substituted *N*-(pivaloyloxy)benzamides **10c**-**10e** were prepared (Scheme 4) and then reacted with cyclohexadiene (**11**). These other *N*-(pivaloyloxy)benzamides were prepared analogously to **10b** as described in the Supporting Information. The optimized conditions (2.5 mol% of catalyst, 0.5 equiv of (CsOAc, EtOH 0 °C to rt, 36 h) were then applied to benzamides **10a**–**10e**. The results are summarized in Scheme 4. With the exception of **12b**, all annulations proceeded in quite good yields. In all cases essentially only the *cis*-fused products were obtained (dr > 98:02). A surprising result was obtained with the amide **10e** derived from 3,4-(methylendioxy)benzoic acid. In this case only the isomer resulting from activation of 2-H was observed. This was clearly evident from observation of two doublets for the aromatic protons. As is known, the electron-donating effect of the methylenedioxy function is significantly reduced due to conformational reasons, since the free election pairs of the oxygen atoms cannot be in line with the π-system. Moreover, the steric demand of the methylenedioxy group might be less. Similar regioselectivtiy has been observed for other Rh(III)-catalyzed reactions of **10e**.[21] Therefore, access to the lycorane skeleton would not be possible from **10e** via this strategy. Thus, it seems that electronic factors govern the regiochemistry in the C–H activation step.



Scheme 4. Rhodium(III)-catalyzed synthesis of phenanthridinones **12a–12d** and **19** using the optimized conditions from Table 1.

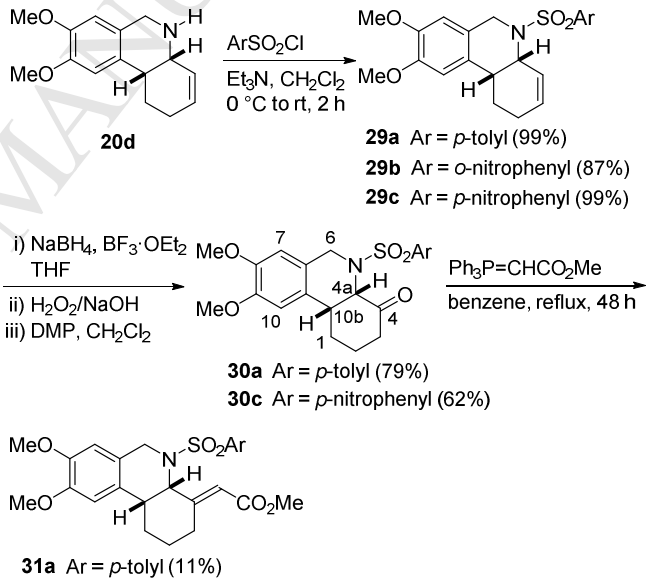
Accordingly, studies towards formation of ring D were carried out with tetrahydrophenanthridinones **12c** and **12d**. However, this turned out to be rather difficult. Some of these experiments with **12c** and **12d** are summarized in Scheme 5. Thus, reduction of the amide function of **12** with the reagent combination $LiAlH_4/AlCl_3$ led to secondary amines **20**.[22] The structure of **20c**·HCl was secured by X-ray analysis, which proved the B/C-*cis*-function (Scheme 5). Amines **20c** and **20d** could be acylated with bromoacetyl bromide to the corresponding amides **21**. However, neither radical conditions[23] nor reaction in presence of $Pd(OAc)_2$ (30 mol%), tBu$_3$P (40 mol%), Et_3N (2 equiv), toluene, 110 °C, 12 h, led to the desired tetracycles **22c** or **22d**. Rather decomposition of these bromoacetamides with the formation of a complex mixture was observed.



Scheme 5. a) Reduction of amides **12c,d** to amines **20c,d** and attempts to form lactams **22c,d** by radical cyclization. X-ray structure of amine **20c** (as hydrochloride) showing the *cis*-fusion. b) Attempts to cyclize amide derivatives **23** and **26** to the corresponding galanthan ring systems.

Diacylamine **23**, obtained from amide **12d**, underwent cleavage of the acylic amide bond upon reaction with Bu_3SnH given back the starting amide. (Scheme 5). As it is known that phenyl selenoesters can serve as precursors for acyl radicals, selenoester **26** was prepared from amide **12d** in three steps. However, reaction of **26** with Bu_3SnH in presence of AIBN did not lead to the desired tetracyclic compound. Here only starting material (16 mg of 25 mg) was recovered. Using benzoylperoxide as radical initiator led to formation of the intermediate acyl radical followed by decarbonylation and formation of *N*-methylamide **28**.

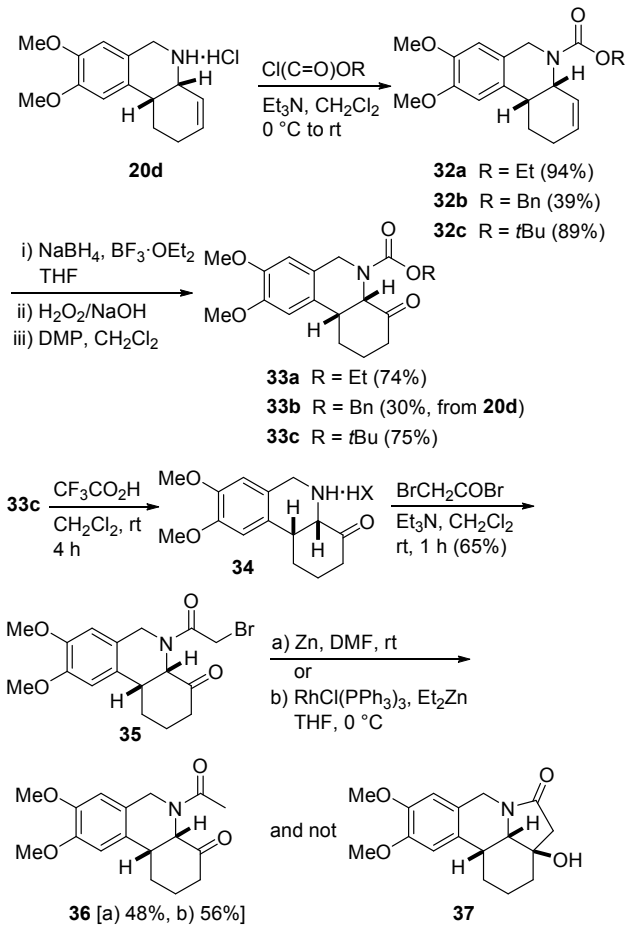
Our next plans focused on derivatization reactions of the double bond of ring C. This might open additional options for creation of ring D. Initially, amine **20d** was converted to sulfonamides **29a**–**29c** (Scheme 6). As it turned out, hydroboration[24] of the double bond was highly selective, with the borane attacking the double bond at the more hindered position. The alcohol derivatives were not further purified but rather oxidized to the α-aminoketone derivatives **30a**–**30c** using the Dess-Martin periodinane reagent. The regiochemistry of the hydroboration was inferred from the ^{1}H NMR spectra. Indicative of the regiochemistry was the signal for 4a-H in alcohol **30a-OH** which appeared as a doublet of doublet (δ = 3.90, *J* = 8.0, 4.0 Hz). The hydroboration was also diastereoselective. While this was not further investigated, we assume attack of the borane from the *exo* face, *syn* to 4a-H and 10b-H. For the other regioisomer a multiplet would be expected instead. In order to attach ring D, extension of the ketone by a suitable C2-building block is required. Reaction of the two ketones **30a** and **30c** with methyl 2-(triphenylphosphoranylidine) acetate gave the desired enoates **31a** and **31c**, respectively. However, the yields were too low to be of practical value.



Scheme 6. Conversion of tricyclic amine **20d** to sulfonamides **29a**–**29c** and the regioselective hydroboration of the ring C double bond.

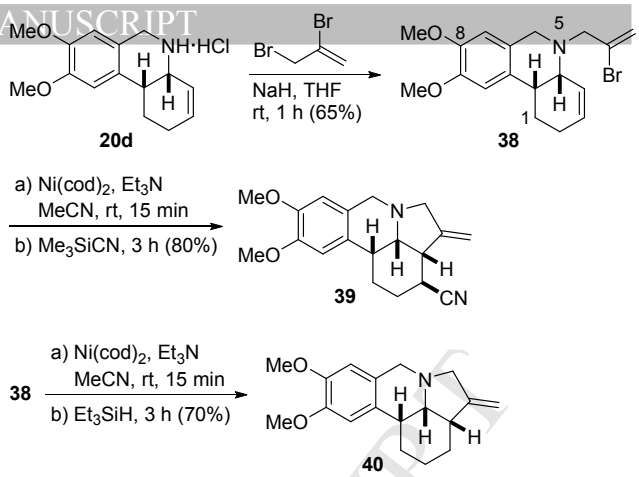
In order to check whether the protecting group on the nitrogen influences the regiochemistry of the hydroboration reaction, amine **20d** was converted to the carbamates **32a**–**32c** (Scheme 7). Subjecting these carbamates to the hydroboration/oxidation sequence led to the α-aminoketone derivatives **33a**–**33c**, respectively. Carbamate **33c** was deprotected under acid conditions giving amine salt **34**. After its acylation with 2-bromoacetyl bromide the obtained 2-bromoacetamide **35** was subjected to conditions for a Reformatsky reaction. However instead of the desired intramolecular aldol reaction, only reductive dehalogenation to acetamide **36** could be observed. The reasons for the failure of the above-mentioned cyclizations are unclear, as visual inspection of amine **20c** indicates that cyclization of an amide derivative via attack at the double bond should be possible. Most likely, the tricyclic ring system already

suffers from some strain so the additional ring D would increase the ring strain even more.



Scheme 7. Conversion of tricyclic amine **20d** to carbamates **32a**–**32c**, their regioselective hydroboration of the ring C double bond followed by oxidation to ketones **33a**–**33c**, and attempts on intramolecular Reformatsky reaction of keto amide **35**.

Eventually we turned to transition metal catalyzed cyclization where the cyclization would be initiated from a vinylmetal species. Accordingly, amine **20d** was alkylated with 2-bromoallyl bromide to yield allylamine **38** (Scheme 8). With this substrate successful cyclization was observed in presence of $Ni(cod)_2$, Et_3N and a suitable nucleophile, like trimethylsilyl cyanide or triethylsilane.[25] This way the two tetracyclic compounds **39** and **40** were obtained. Both feature the *cis*/*cis*-ring fusion of the γ-lycorane ring system. Brief attempts at epoxidation or oxidative cleavage (O_3) were unsuccessful.



Scheme 8. Conversion of amine **20d** to 5-(2-bromoallyl)-hexahydrophenanthridine derivative **38** and its nickel-mediated cyclization to 4-methylene-octahydro-1*H*-pyrrolo[3,2,1-de]phenanthridines **39** and **40**.

3. Conclusion

In this paper we present a new approach to lycorane-like structures that relies on the fusion of substituted benzamide derivatives with cyclohexadiene by C–H-activation. After reduction of the tricyclic secondary amine, N-allylation with 2-bromoallyl bromide and Ni-induced cyclization led to the tetracyclic γ-lycorane analogs **39** and **40**. In the course of this study we discovered a strong influence of the type of the 3,4-dialkoxy substituents on the regiochemistry of the C–H-activation. While for the non-constrained *N*-(pivaloyloxy) benzamides activation of 6-H takes place, with 3,4-methylendioxyamide **10e** insertion occurs selectively at 2-H. Furthermore *N*-protected phenanthridine derivatives **29** and **32** underwent a regioselective hydroboration/oxidation to the corresponding α-aminoketone compounds.

4. Experimental section

4.1. Preparation of catalyst $[Cp^*RhCl_2]_2$

To a stirred solution of $RhCl_3$ (0.5 g, 1.95 mmol) in MeOH (12 mL) was added excess pentamethylcyclopentadiene (0.5 mL). The mixture was reflux for 21 h, cooled to room temperature, filtered through sintered funnel, washed with diethylether (2 × 5 mL), dried under vacuum to give the rhodium catalyst (1.02 g, 85%) as dark brown powder.[20]

4.2. Preparation of O-pivaloyl hydroxamic acids

4.2.1. (Procedure 1, via hydroxamic acid)

(a) To a stirred solution of ethyl benzoate (1.0 equiv) and hydroxylamine hydrochloride (4.0 equiv) in MeOH (2 mL per mmol of benzoate) was added KOH solution (1M in methanol, 5.0 equiv) in a dropwise fashion. The resulting solution was stirred 48 h at room temperature. Thereafter most of the MeOH was distilled out in vacuo and the solid residue was dissolved in a mixture of acetic acid/water (1/1, 4 mL per mmol of benzoate). The mixture was extracted with EtOAc (3 × 5 mL (per mmol of benzoate)). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to provide the crude hydroxamic acid which was washed with diethyl ether (5 mL per mmol of benzoate) to afford the pure hydroxamic acid as transparent solid.

(b) To the suspension of hydroxamic acid (1.0 equiv) in CH_2Cl_2 (5 mL per mmol of acid) was added pivalic anhydride

(0.8 equiv). The resulting mixture was stirred for 16 h at room temperature. The reaction mixture was diluted with saturated $NaHCO_3$ (4 mL per mmol of acid) and extracted with EtOAc (2 × 5 mL (per mmol of acid)). The combined organic layers were washed with saturated $NaHCO_3$ solution (4 mL per mmol of acid), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford the pure *O*-pivaloyl hydroxamic acid.

4.2.2. Procedure 2 (reaction of acid chloride with O-pivaloylhydroxylamine)

To a solution of benzoic acid (1.0 equiv) in dry CH_2Cl_2 (3 mL per mmol of acid) was added $SOCl_2$ (5.0 equiv) at room temperature followed by the addition of a catalytic amount of DMF (4 drops per 10 mmol of acid). The mixture was refluxed for 8 h. After cooling, solvent and excess reagent were removed in vacuo to afford the crude acid chloride, which was used in the next step without further purification.

O-Pivaloylhydroxylamine triflate[19] (1.2 equiv) was added to a biphasic mixture of Na_2CO_3 (2.0 equiv) in EtOAc/H_2O (9 mL per mmol of acid chloride, 2:1). To the cooled mixture containing the pivaloylhydroxylamine at 0 °C was added crude acid chloride (1.0 equiv) in EtOAc (1 mL per mmol of acid chloride) dropwise. The reaction mixture was allowed to reach room temperature within 5 h. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 10 mL (per mmol of acid chloride)). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo to provide. The crude product was purified by flash chromatography to afford pure *O*-pivaloyl hydroxamic acid.

*4.2.3. 4-(Benzyloxy)-N-hydroxy-3-methoxybenzamide (**18**)*

Prepared from benzoic acid **16** (300 mg, 1.05 mmol) according to procedure 1 (a). The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:2) to give hydroxamic acid **18** (280 mg, 95%) as colorless solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.78 (s, 3H, OMe), 5.11 (s, 2H, CH_2Ph), 7.1 (d, *J* = 8.3 Hz, 1H, Ar), 7.28-7.47 (m, 7H, Ar); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 55.8 (OMe), 70.0 (CH_2Ph), 110.6 (C-5), 112.8 (C-2), 120.1 (C-6), 125.4 (Ar), 128.14 (Ar), 128.3 (Ar), 128.7 (Ar), 136.9 (Ar), 148.8 (Ar), 150.3 (Ar), 164.2 (CONHOH); HRMS (ESI): calcd for $C_{15}H_{15}NO_4$ $[M+Na]^+$ 296.08933, found 296.08989.

*4.2.4. N-(Pivaloyloxy)benzamide[11] (**10a**)*

Prepared from the corresponding *N*-hydroxybenzamide (850 mg, 6.20 mmol) according to procedure 1 (b). The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:10) to give pure *N*-(pivaloyloxy)benzamide **10a** (1.260 g, 92%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 9H, OPiv), 7.39-7.46 (m, 2H, Ar), 7.50-7.57 (m, 1H, Ar), 7.76-7.82 (m, 2H, Ar), 9.48 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.0 (OPiv), 38.4 (*t*Bu), 127.4 (Ar), 128.8 (Ar), 130.8 (Ar), 132.6 (Ar), 166.7 (CONH), 177.0 (*t*Bu*C*O_2).

*4.2.5. 4-(Benzyloxy)-3-methoxy-N-(pivaloyloxy)benzamide (**10b**)*

Prepared from *N*-hydroxybenzamide **18** (250 mg, 0.91 mmol) according to procedure 1 (b). The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:5) to give pure *N*-(pivaloyloxy)benzamide **10b** (240 mg, 75%) as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9H, OPiv), 3.91 (s, 3H, OMe), 5.21 (s, 2H, CH_2Ph), 6.87 (d, *J* = 8.6 Hz, 1H, 5-H), 7.28-7.47 (m, 7H, Ar), 9.24 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.0 (OPiv), 38.4 (*t*Bu), 56.1 (OMe), 70.84 (CH_2Ph), 111.0 (C-5), 112.7 (C-2), 120.3 (C-6), 123.5 (Ar), 127.2 (Ar), 128.1 (Ar), 128.7 (Ar), 136.2 (Ar), 149.7 (Ar), 151.9 (Ar), 177.3 (CONH), 177.7 (*t*Bu*C*O_2); HRMS (ESI): calcd for $C_{20}H_{23}NO_5$ $[M+Na]^+$ 380.14684, found 380.14715.

*4.2.6. 4-Ethoxy-3-methoxy-N-(pivaloyloxy)benzamide (**10c**)*

Prepared from the corresponding benzoic acid (1.00 g, 5.09 mmol) according to procedure 2. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:5) to give pure *N*-(pivaloyloxy)benzamide **10c** (1.5 g, 98%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (s, 9H, OPiv), 1.41 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 3.79 (s, 3H, OMe), 4.05 (q, *J* = 7.1 Hz, OCH_2CH_3), 6.71-6.77 (m, 1H, Ar), 7.29-7.35 (m, 2H, Ar), 9.79 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4 (OCH_2CH_3), 26.9 (OPiv), 38.3 (*t*Bu), 55.7 (OMe), 64.2 (OCH_2CH_3), 110.5 (Ar), 111.17 (Ar), 120.5 (Ar), 122.7 (Ar), 148.9 (Ar), 151.8 (Ar), 166.5 (CONH), 177.0 (*t*Bu*C*O_2); HRMS (ESI): calcd for $C_{15}H_{21}NO_5$ $[M+Na]^+$ 318.13119, found 318.13121.

*4.2.7. 3,4-(Dimethoxy)-N-(pivaloyloxy)benzamide (**10d**)*

Prepared either from the corresponding *N*-hydroxybenzamide (3.00 g, 15.2 mmol, procedure 1) or the benzoic acid (3.0 g, 14.48 mmol, procedure 2). The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:3) to give pure *N*-(pivaloyloxy)benzamide[26] **10d** (3.70 g, 86%, procedure 1; 3.70 g, 80%, procedure 2) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 9H, OPiv), 3.75 (s, 3H, OMe), 3.78 (s, 3H, OMe), 6.65-6.73 (m, 1H, 5-H), 7.26-7.36 (m, 2H, 2-H, 3-H), 9.65 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.8 (OPiv), 38.2 (*t*Bu), 55.6 (OMe), 55.7 (OMe), 110.1 (Ar), 110.2 (Ar), 120.5 (Ar), 122.9 (Ar), 148.6 (Ar), 152.2 (Ar), 166.3 (CONH), 176.9 (*t*Bu*C*O_2); HRMS (ESI): calcd for $C_{14}H_{19}NO_5$ $[M+Na]^+$ 304.11554, found 304.11566.

*4.2.8. N-(pivaloyloxy) benzo[d][1,3]dioxole-5-carboxamide (**10e**)*

Prepared from the corresponding benzoyl chloride (500 mg, 2.71 mmol) according to procedure 2. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:3) to give pure *N*-(pivaloyloxy)benzamide[21] **10e** (650 mg, 90%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 9H, OPiv), 5.99 (s, 2H, OCH_2O), 6.76 (d, *J* = 8.3 Hz, 5-H), 7.21 (d, *J* = 2.0 Hz, 2-H), 7.22 (dd, *J* = 8.3, 2.0 Hz, 1H, 6-H), 9.58 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.9 (OPiv), 38.5 (*t*Bu), 101.8 (OCH_2O), 107.8 (C-5), 108.1 (C-2), 122.6 (C-6), 124.6 (Ar), 147.9 (Ar), 151.2 (Ar), 166.2 (CONH), 177.1 (*t*Bu*C*O_2); HRMS (ESI): calcd for $C_{13}H_{15}NO_5$ $[M+Na]^+$ 288.08424, found 288.08450.

4.3. Rhodium catalyzed annulation (Procedure 3)

An oven dried, cooled Schlenk tube under N_2, was charged with *N*-(pivaloyloxy)benzamide (1.0 equiv), $[Cp^*RhCl_2]_2$ (2.5 mol%), CsOAc (50 mol%) and dry EtOH (1 mL per mmol of amide). The mixture was cooled to 0 °C, whereupon 1,3-cyclohexadiene (1.3 equiv) was added in one shot. The screw cap was closed tightly under positive pressure of N_2 followed by stirring of the reaction mixture at room temperature for 35 h (TLC control). The mixture was concentrated in vacuo and the residue purified by flash chromatography to afford the pure annulation product.

*4.3.1. 1,4a,5,10b-Tetrahydrophenanthridin-6(2H)-one (**12a**)*

Prepared from *N*-(pivaloyloxy)benzamide **10a** (100 mg, 0.45 mmol) according to procedure 3. TLC showed consumption of

starting material after 19 h. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:1) to give pure phenanthridinone[11] **12a** (74 mg, 82%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62-1.73 (m, 1H, 1-H), 1.88-2.05 (m, 1H, 2-H), 2.10-2.28 (m, 2H, 1-H, 2-H), 2.92 (td, *J* = 3.8, 12.2 Hz, 1H, 10b-H), 4.22-4.30 (m, 1H, 4a-H), 5.79 (ddt, *J* = 2.1, 4.5, 9.3 Hz, 1H, 4-H), 5.94-6.06 (m, 1H, 3-H), 6.26 (s, br, 1H, NH), 6.23 (d, *J* = 7.5 Hz, 1H, Ar), 7.33 (td, *J* = 1.1, 7.6 Hz, 1H, Ar), 7.46 (td, *J* = 1.3, 7.5 Hz, 1H, Ar), 8.06 (dd, *J* = 1.2, 7.8 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0 (C-2), 25.1 (C-1), 37.7 (C-10b), 47.9 (C-4a), 124.4 (Ar), 127.0 (Ar), 127.2 (Ar), 127.5 (Ar), 127.9 (Ar) 132.2 (C-4), 132.5 (C-3), 142.7 (Ar), 165.4 (CONH); HRMS (ESI): calcd for $C_{13}H_{13}NO$ $[M+Na]^+$ 222.08893, found 222.08894.

*4.3.2. 9-(Benzyloxy)-8-methoxy-1,4a,5,10b-tetrahydrophenanthridin-6(2H)-one (**12b**)*

Prepared from *N*-(pivaloyloxy)benzamide **10b** (50 mg, 0.14 mmol) according to procedure 3. TLC showed consumption of starting material after 39 h. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 1:1) to give pure phenanthridinone **12b** (26 mg, 55%) as slightly yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54-1.65 (m, 1H, 1-H), 1.82-1.97 (m, 1H, 1-H), 2.06-2.26 (m, 2H, 1-H), 2.78 (td, *J* = 3.3, 12.1 Hz, 1H, 10a-H), 3.92 (s, 3H, OMe), 4.21 (m, 1H, 4a-H), 5.20 (OCH_2Ph), 5.57 (s, br, NH), 5.68-5.78 (m, 1H, 4-H), 5.94-6.05 (m, 1H, 3-H), 6.70 (s, 1H, 10-H), 7.28-7.34 (m, 1H, Ar), 7.34-7.41 (m, 2H, Ar), 7.41-7.48 (m, 2H, Ar), 7.58 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9 (C-2), 25.0 (C-1), 37.4 (C-10b), 48.2 (C-4a), 56.1 (OMe), 70.9 (OCH_2Ph), 110.4 (C-7), 111.6 (C-10), 120.4 (Ar), 124.4, 127.2, 128.0, 128.6, 132.2, 136.2, 136.4, 148.6 (Ar), 151.6 (Ar), 164.9 (CONH); HRMS (ESI): calcd for $C_{21}H_{21}O_3$ $[M+H]^+$ 336.159420, found 336.159327.

*4.3.3. 9-Ethoxy-8-methoxy-1,4a,5,10b-tetrahydrophenanthridin-6(2H)-one (**12c**)*

Prepared from *N*-(pivaloyloxy)benzamide **10c** (100 mg, 0.34 mmol) according to procedure 3. TLC showed consumption of starting material after 20 h. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 2:1) to give pure phenanthridinone **12c** (75 mg, 81%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (t, *J* = 6.8 Hz, 3H, OCH_2CH_3), 1.58-1.68 (m, 1H, 1-H), 1.82-1.95 (m, 1H, 1-H), 2.11-2.21 (m, 2H, 2-H), 2.78 (td, *J* = 3.3, 12.4 Hz, 1H, 10a-H), 3.87 (s, 3H, OMe), 4.11 (q, *J* = 6.8 Hz, 2H, OCH_2CH_3), 4.18-4.23 (m, 1H, 4a-H), 5.72-5.80 (m, 1H, 4-H), 5.93-6.01 (m, 1H, 3-H), 6.40 (s, 1H, NH), 6.65 (s, 1H, 10-H), 7.51 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): d = 14.6 (OCH_2CH_3), 24.9 (C-2), 25.1 (C-1), 37.4 (C-10b), 48.1 (C-4a), 56.0 (OMe), 64.3 (OCH_2CH_3), 110.0 (C-7), 110.2 (C-10), 119.6 (Ar), 124.3 (C-4), 132.0 (Ar), 136.5 (C-3), 148.1 (Ar), 151.9 (Ar), 165.4 (CONH).

*4.3.4. 8,9-Dimethoxy-1,4a,5,10b-tetrahydrophenanthridin-6(2H)-one (**12d**)*

Prepared from *N*-(pivaloyloxy)benzamide **10d** (500 mg, 1.78 mmol) according to procedure 3. TLC showed consumption of starting material after 55 h. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 4:1) to give pure phenanthridinone **12d** (325 mg, 70%) as slightly brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.61-1.71 (m, 1H, 1-H), 1.84-1.99 (m, 1H, 1-H), 2.15-2.24 (m, 2H, 2-H), 2.82 (td, *J* = 4.0, 12.4 Hz, 1H, 10b-H), 3.91 (s, 3H, OMe), 3.91 (s, 3H, OMe), 4.23 (t, *J* = 4.0 Hz, 1H, 4a-H), 5.72-5.84 (m, 2H, 4-H, NH), 5.97-6.05 (m, 1H, 3-H), 6.67 (s, 1H, 10-H), 7.51 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.9 (C-2), 25.2 (C-1), 37.7 (C-10b), 48.2 (C-4a), 56.0 (OMe), 56.1 (OMe), 109.3 (C-7), 109.9 (C-10), 120.0 (Ar), 124.4 (C-4), 132.2 (Ar), 136.6 (C-3), 148.0 (Ar), 152.5 (Ar), 164.9 (CONH); HRMS (ESI): calcd for $C_{15}H_{17}NO_3$ $[M+Na]^+$ 282.11006, found 282.11030.

*4.3.5. 7a,8,9,11a-Tetrahydro-[1,3]dioxolo[4,5-k]phenanthridin-6(7H)-one (**19**)*

Prepared from *N*-(pivaloyloxy)benzamide **10e** (500 mg, 2.00 mmol) according to procedure 3. TLC showed consumption of starting material after 35 h. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether, 4:1) to give pure phenanthridinone **19** (435 mg, 89%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69-1.78 (m, 1H, 11-H), 1.80-1.97 (m, 1H, 11-H), 2.14-2.26 (m, 2H, 10-H_2), 2.98-3.12 (m, 1H, 11a-H), 4.14-4.26 (m, 1H, 7a-H), 5.68-5.85 (m, 2H, 8-H, NH), 6.00-6.11 (m, 1H, 9-H), 6.02 (d, *J* = 1.3 Hz, 2-H), 6.79 (d, *J* = 1.3 Hz, 2-H), 6.79 (d, *J* = 8.2 Hz, 1H, 4-H), 7.68 (d, *J* = 8.3 Hz, 1H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6 (C-10), 25.2 (C-11), 32.4 (C-11a), 47.6 (C-7a), 101.9 (C-2), 107.1 (C-4), 121.7 (Ar), 123.4 (C-5), 123.9 (Ar), 124.0 (C-8), 132.6 (C-9), 143.9 (Ar), 150.6 (Ar), 164.6 (CONH); HRMS (ESI): calcd for $C_{14}H_{13}NO_3$ $[M+Na]^+$ 266.07876, found 266.07918.

4.4. Reduction of the tetrahydrophenanthridinones to hexahydrophenanthridines (Procedure 4)

To a cooled (0 °C) solution of $AlCl_3$ (1 equiv) in THF (10 mL per mmol $AlCl_3$) under N_2 was added $LiAlH_4$ (3 equiv). The mixture was allowed to stir at room temperature for 1 h, before it was added dropwise via cannula to a separately stirred solution of the amide (1 equiv) in THF (20 mL per mmol of amide). The reaction mixture was allowed to reach room temperature within 1 h. Then the flask was moved to a preheated oil bath (40 °C) and the mixture stirred for 8 h. Thereafter, the reaction mixture was cooled to 0 °C and quenched with saturated NH_4Cl solution (10 mL per mmol of $AlCl_3$). The organic layer was separated and the aqueous semisolid washed with diethyl ether (10 mL per mmol of amide). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude material was dissolved in diethyl ether (10 mL per mmol of amide) and cooled to 0 °C, then ethereal HCl (3M, 0.5 mL per mmol of amide) was added dropwise. The white solid amine salt which precipitated, was collected by filtration through a G4 frit. It was found to be of sufficient purity.

*4.4.1. 9-Ethoxy-8-methoxy-1,2,4a,5,6,10b-hexahydrophenanthridin-5-iumchloride (**20c**)*

Prepared from tetrahydrophenanthridinone **12c** (127 mg, 0.46 mmol) according to procedure 4 to give pure hydrochloride **20c** (115 mg, 80%) as colorless solid. ^{1}H NMR (400 MHz, CD_3OD): δ = 1.40 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.79-1.91 (m, 1H, 1-H), 2.04-2.12 (m, 1H, 1-H), 2.16-2.35 (m, 2H, 2-H), 3.16 (dt, *J* = 4.3, 12.1 Hz, 1H, 10b-H), 3.82 (s, 3H, OMe), 4.06 (q, *J* = 7.1 Hz, 3H, OCH_2CH_3, 4a-H), 4.28 (dd, *J* = 11.4, 15.4 Hz, 2H, 6-H), 5.86-5.93 (m, 1H, 4-H), 6.28-6.34 (m, 1H, 3-H), 6.79 (s, 1H, 10-H), 6.93 (s, 1H, 7-H); ^{13}C NMR (100 MHz, CD_3OD): δ = 15.2 (OCH_2CH_3), 25.8 (C-2), 27.8 (C-1), 35.5 (C-10b), 45.2 (C-6), 52.2 (C-4a), 56.7 (OMe), 65.8 (OCH_2CH_3), 110.7 (C-7), 114.2 (C-10), 120.5 (Ar), 122.0 (C-4), 129.2 (Ar), 138.2 (C-3), 150.2 (Ar), 150.3 (Ar); HRMS (ESI): calcd for $C_{16}H_{22}ClNO_2$ $[M]^+$ 260.164505, found 260.164354.

*4.4.2. 8,9-Dimethoxy-1,2,4a,5,6,10b-hexahydrophenanthridin-5-iumchloride (**20d**)*

Prepared from tetrahydrophenanthridinone **12d** (500 mg, 1.90 mmol) according to procedure 4 to give pure hydrochloride **20d** (425 mg, 75%) as colorless solid. ^{1}H NMR (400 MHz, CD_3OD): δ = 1.77-1.93 (m, 1H, 1-H), 2.04-2.17 (m, 1H, 1-H), 2.18-2.37 (m, 2H, 2-H), 3.18 (dt, *J* = 4.0, 12.0 Hz, 1H, 10b-H), 3.82 (s, 3H,

OMe), 3.84 (s, 3H, OMe), 4.02-4.10 (m, 1H, 4a-H), 4.29 (dd, *J* = 14.4, 15.7 Hz, 2H, 6-H), 5.84-5.91 (m, 1H, 4-H), 6.28-6.37 (m, 1H, 3-H), 6.78 (s, 1H, 10-H), 6.95 (s, 1H, 7-H); ^{13}C NMR (100 MHz, CD_3OD): δ = 25.8 (C-2), 27.8 (C-1), 35.6 (C-10b), 45.2 (C-6), 52.3 (C-4a), 56.6 (OMe), 56.7 (OMe), 110.5 (C-7), 112.9 (C-10), 120.5 (Ar), 121.9 (C-4), 129.3 (Ar), 138.3 (C-3), 150.2 (Ar), 151.0 (Ar); HRMS (ESI): calcd for $C_{15}H_{20}ClNO_2$ $[M+Na]^+$ 246.14886, found 246.14873.

4.5. Preparation of α-haloamides from amine hydrochlorides (Procedure 5)

To a stirred solution of the amine·HCl (1 equiv) and trimethylamine (2 equiv) in THF (3 mL per mmol of salt) at 0 °C was added 2-bromoacetyl bromide (2 equiv). The stirred reaction mixture was allowed to reach room temperature within 1 h. For work-up the mixture was diluted with saturated $NaHCO_3$ solution (20 mL per mmol of salt) and extracted with Et_2O (3 × 15 mL (per mmol of salt). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude amide was purified by flash chromatography (petroleum ether/ethyl acetate, 3:1) to provide pure product.

*4.5.1. 2-Bromo-1-(9-ethoxy-8-methoxy-2,4a,6,10b-tetrahydrophenanthridin-5(1H)-yl)ethan-1-one (**21c**)*

Prepared from amine hydrochloride **20c** (50 mg, 0.16 mmol) according to procedure 5 to give pure bromoacetylamide **21c** (67 mg, 99%) as brown solid. R_f = 0.5 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers): δ = 1.43 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.68-1.93 (m, 2H, 1-H, 2-H), 1.93-2.09 (m, 1H, 1-H), 2.21-2.43 (m, 1H, 2-H), 3.16-3.43 (m, 1H, 10b-H), 3.81 (s, 3H, OMe), 4.00-4.23 (m, 5H, OCH_2CH_3, CH_2Br, 4a-H), 4.40-4.64 (m, 1H, 6-H), 5.12-5.46 (m, 1H, 6-H), 5.46-5.58 (m, 1H, 4-H), 5.70-5.85 (m, 1H, 3-H), 6.54 (s, 1H, 7-H), 6.80 (s, 1H, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 20.1, 25.3, 33.1, 34.4, 40.7, 41.1, 41.5, 44.6, 48.6, 53.4, 55.8, 64.5, 64.6, 108.5, 108.9, 111.0, 111.2, 124.4, 125.2, 125.6, 126.0, 132.1, 132.6, 147.3, 147.7, 147.8, 148.0, 165.3 (CO); HRMS (ESI): calcd for $C_{18}H_{22}BrNO_3$ $[M]^+$ 402.067527, found 402.067526.

*4.5.2. 2-Bromo-1-(8,9-dimethoxy-2,4a,6,10b-tetrahydrophenanthridin-5(1H)-yl)ethan-1-one (**21d**)*

Prepared from amine hydrochloride **20d** (200 mg, 0.71 mmol) according to procedure 5 to give pure bromoacetylamide **21d** (145 mg, 56%) as brown solid. R_f = 0.2 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers): δ = 1.66-1.92 (m, 2H, 1-H, 2-H), 1.93-2.11 (m, 1H, 1-H), 2.22-2.48 (m, 1H, 2-H), 3.13-3.48 (m, 1H, 10b-H), 3.81 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.97-4.24 (m, 1H, 4a-H), 4.15 (s, 2H, CH_2Br), 4.43-4.83 (m, 1H, 6-H), 5.12-5.45 (m, 1H, 6-H), 5.46-5.60 (m, 1H, 4-H), 5.71-5.88 (m, 1H, 3-H), 6.53 (s, 1H, 7-H), 6.78 (s, 1H, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1, 25.3, 33.2, 34.4, 40.7, 41.1, 41.4, 44.6, 48.6, 53.4, 55.7, 56.0, 108.2, 108.7, 109.2, 109.5, 124.4, 125.1, 125.6, 125.9, 132.1, 132.6, 148.1, 148.5, 165.4 (CO); HRMS (ESI): calcd for $C_{17}H_{20}BrNO_3$ $[M+Na]^+$ 388.05188, found 388.05197.

*4.5.3. tert-Butyl 2-(8,9-dimethoxy-6-oxo-2,4a,6,10b-tetrahydrophenanthridin-5(1H)-yl)acetate (**24**)*

Sodium hydride (20 mg, 0.50 mmol, 1.3 equiv, 60% dispersion in mineral oil) was added to a stirred, cold (0 °C) solution of amide **12d** (100 mg, 0.38 mmol) in dry DMF (2 mL). The solution was allowed to warm to room temperature for 20 min and then cooled to 0 °C, before *tert*-butyl bromoacetate (86 µL, 0.57 mmol, 1.5 equiv) was added. Then the reaction mixture was warmed to room temperature within 45 min. The reaction mixture was diluted with water (30 mL) and the aqueous phase was basified (10% NaOH, 5 mL) and extracted with ether (5 × 10 mL). The combined ether extracts were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate, 3:1) to provide pure *N*-alkyation product **24** (90 mg, 63%) as an amorphous solid. R_f = 0.6 (petroleum ether/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): d = 1.45 (s, 9H, *t*Bu), 1.70-1.80(m, 1H, 1-H), 2.03-2.20 (m, 3H, 1-H, 2-H), 2.99-3.09 (m, 1H, 10b-H), 3.86 (d, *J* = 17.2 Hz, 1H, NCH_2CO), 3.89 (s, 3H, OMe), 3.91 (s, 3H, OMe), 4.33 (m, 1H, 4a-H), 4.70 (d, *J* = 17.2 Hz, 1H, NCH_2CO), 5.66-5.72 (m, 1H, 4-H), 5.91-5.99 (m, 1H, 3-H), 6.67 (s, 1H, 10-H), 7.58 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3 (C-2), 24.4 (C-1), 28.0 (*t*Bu), 36.7 (C-10b), 46.0 (NCH_2CO), 53.5 (C-4a), 56.0 (OMe), 81.6 (C-$(CH_3)_3$), 108.5 (C-7), 110.7 (C-10), 120.6 (Ar), 123.8 (C-4), 132.6 (C-3), 135.2 (Ar), 147.8 (Ar), 152.2 (Ar), 164.3 (CON), 169.0 (CO_2tBu); HRMS (ESI): calcd for $C_{21}H_{27}NO_5$ $[M+Na]^+$ 396.17814, found 396.17849.

*4.5.4. 2-(8,9-Dimethoxy-6-oxo-2,4a,6,10b-tetrahydrophenanthridin-5(1H)-yl)acetic acid (**25**)*

Through a solution of ester **24** (67 mg, 0.18 mmol) in CH_2Cl_2 (5 mL) was bubbled HCl gas at 0 °C for 5 h. The solution was stirred for additional 1.5 h at 0 °C, warmed to room temperature over 30 min, and evaporated to dryness. This way acid **25** was obtained as a white solid in pure form. ^{1}H NMR (400 MHz, CD_3OD): δ = 1.73-1.92 (m, 1H, 1-H), 2.08-2.30 (m, 3H, 1-H, 2-H), 3.06-3.22 (m, 1H, 10b-H), 3.84 (s, 3H, OMe), 3.89 (s, 3H, OMe), 4.07 (d, *J* = 17.4 Hz, 1H, NCH_2CO), 4.35-4.42 (m, 1H, 4a-H), 4.62 (d, *J* = 17.4 Hz, 1H, NCH_2CO), 5.74-5.81 (m, 1H, 4-H), 5.94-6.01 (m, 1H, 3-H), 6.91 (s, 1H, 10-H), 7.41 (s, 1H, 7-H); ^{13}C NMR (100 MHz, CD_3OD): δ = 25.3 (C-2), 25.3 (C-1), 37.7 (C-10b), 46.0 (NCH_2CO), 55.8 (C-4a), 56.6 (OMe), 56.7 (OMe), 110.5 (C-7), 111.8 (C-10), 121.4 (Ar), 124.9 (C-4), 133.9 (C-3), 137.6 (Ar), 149.5 (Ar), 154.5 (Ar), 166.3 (CON), 173.1 (CO_2H).

*4.5.5. Se-phenyl 2-(8,9-dimethoxy-6-oxo-2,4a,6,10b-tetrahydrophenanthridine-5(1H)-yl)ethaneselenoate (**26**)*

$(PhSe)_2$ (60 mg, 0.20 mmol, 1.5 equiv) was added to a solution of acid **25** in CH_2Cl_2 (10 mL). The solution was cooled to 0 °C before *n*-Bu_3P (66 µL, 0.26 mmol, 2.0 equiv) was added. The reaction mixture was refluxed for 24 h, poured into water (20 mL) and then the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate, 3:1) to provide pure selenoester **26** (50 mg, 84%), as an amorphous solid. R_f = 0.5 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.75-1.94 (m, 1H, 1-H), 2.06-2.28 (m, 3H, 1-H, 2-H), 3.18-3.37 (m, 1H, 10b-H), 3.91 (s, 3H, OMe), 3.93 (s, 3H, OMe), 4.11 (d, *J* = 16.9 Hz, 1H, NCH_2CO), 4.37-4.44 (m, 1H, 4a-H), 5.05 (d, *J* = 16.9 Hz, 1H, NCH_2CO), 5.64-5.73 (m, 1H, 4-H), 5.92-6.01 (m, 1H, 3-H), 6.72 (s, 1H, 10-H), 7.32-7.40 (m, 3H, Ar), 7.46-7.53 (m, 2H, Ar), 7.62 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.8 (C-2), 24.3 (C-1), 36.2 (C-10b), 54.7 (NCH_2CO), 56.0 (OMe), 56.05 (OMe), 56.5 (C-4a), 108.3 (C-7), 110.8 (C-10), 120.1 (Ar), 123.4 (C-4), 125.4 (Ar), 128.9 (C-3), 129.1 (Ar),129 (Ar), 131.4 (Ar), 132.8 (Ar), 135.0 (Ar), 136.0 (Ar), 148.0 (Ar), 152.6 (Ar), 164.8 (CON), 199.0 (COSePh); HRMS (ESI): calcd for $C_{23}H_{23}NO_4Se$ $[M+Na]^+$ 480.06845, found 480.06836.

*4.5.6. 8,9-Dimethoxy-5-methyl-1,4a,5,10b-tetrahydrophenanthridin-6(2H)-one (**28**)*

To a boiling solution of compound selenoester **26** (16 mg, 0.035 mmol) in benzene (2 mL) was added dropwise a solution of Bu_3SnH (14 µL, 0.052 mmol, 1.5 equiv), and benzoyl peroxide (2 mg, 0.008 mmol, 23 mol%) in benzene (1 mL) over 1 h by employing a syringe pump. After complete addition, the reaction mixture was further refluxed for 2 h. The solvent was evaporated in vacuo, and the residue diluted with Et_2O (3 mL). This solution was washed with 10% aqueous solution of KF (2 × 5 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate, 1:2) to provide *N*-methylamide **28** (6 mg, 63%), as a colorless solid. R_f = 0.1 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.79-1.92(m, 1H, 1-H), 2.02-2.15 (m, 2H, 1-H, 2-H), 2.16-2.27 (m, 1H, 2-H), 3.14 (s, 3H, NCH_3), 3.17-3.28 (m, 1H, 10b-H), 3.91 (s, 3H, OMe), 3.92 (s, 3H, OMe), 4.08-4.20 (m, 1H, 4a-H), 5.64-5.75 (m, 1H, 4-H), 5.78-5.90 (m, 1H, 3-H), 6.71 (s, 1H, 10-H), 7.60 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9 (C-2), 24.0 (C-1), 32.2 (NCH_3), 35.3 (C-10b), 56.0 (OMe), 56.2 (C-4a), 107.9 (C-7), 110.7 (C-10), 121.5 (Ar), 124.5 (C-4), 130.6 (C-3), 133.4 (Ar), 147.8 (Ar), 151.9 (Ar), 164.1 (CON); HRMS (ESI): calcd for $C_{16}H_{19}NO_2$ $[M+Na]^+$ 296.12571, found 296.12582.

4.6. Preparation of sulfonamides from amine hydrochlorides (Procedure 6)

To a cooled (0 °C) suspension of amine·HCl (1.0 equiv) in CH_2Cl_2 (9 mL per mmol of hydrochloride) were added Et_3N (2.0 equiv) and arylsulfonyl chloride (1.5 equiv). The stirred reaction mixture was allowed reach room temperature within 2 h. Thereafter, saturated $NaHCO_3$ solution (9 mL per mmol of hydrochloride) was added. After separation of the layers the aqueous layer was extracted with CH_2Cl_2 (2 × 9 mL per mmol of hydrochloride). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography to afford the pure sulfonamides.

*4.6.1. 8,9-Dimethoxy-5-tosyl-1,2,4a,5,6,10b-hexahydrophenanthridine (**29a**)*

Prepared from amine hydrochloride **20d** (305 mg, 1.03 mmol) according to procedure 6 to give pure sulfonamide **29a** (435 mg, 99%) as colorless solid. R_f = 0.3 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55-1.83 (m, 2H, 1-H, 2-H), 1.85-1.98 (m, 1H, 1-H), 2.18-2.31 (m, 1H, 2-H), 2.38 (s, 3H, SO_2CH_2Ph), 3.07-3.21 (m, 1H, 10b-H), 3.81 (s, 6H, 2 OMe), 4.13 (d, *J* = 15.6 Hz, 1H, 6-H), 4.59 (d, *J* = 15.6 Hz, 1H, 6-H), 4.76-4.88 (m, 1H, 4a-H), 5.10-5.20 (m, 1H, 4-H), 5.56-5.73 (m, 1H, 3-H), 6.48 (s, 1H, 7-H), 6.69 (s, 1H, 10-H), 7.22 (d, *J* = 8.0 Hz, 2H, Ar), 7.69 (d, *J* = 8.0 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2 (C-2), 21.4 (Me), 25.5 (C-1), 34.0 (C-10b), 43.2 (C-6), 52.4 (C-4a), 55.7 (OMe), 56.0 (OMe), 108.4 (C-8), 109.4 (C-10), 124.7 (Ar), 125.2 (C-4), 126.5 (Ar), 127.1 (Ar), 129.6 (Ar), 132.6 (C-3), 137.4 (Ar), 143.2 (Ar), 147.3 (Ar), 148.2 (Ar); HRMS (ESI): calcd for $C_{22}H_{25}NO_4S$ $[M+Na]^+$ 422.13965, found 422.13960.

*4.6.2. 8,9-Dimethoxy-5-((2-nitrophenyl)sulfonyl)-1,2,4a,5,6,10b-hexahydrophenanthridine (**29b**)*

Prepared from amine hydrochloride **20d** (350 mg, 1.01 mmol) according to procedure 6 to give pure sulfonamide **29b** (377 mg, 87%) as yellow amorphous solid. R_f = 0.2 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63-1.87 (m, 2H, 1-H, 2-H), 1.93-2.03 (m, 1H, 1-H), 2.25-2.37 (m, 1H, 2-H), 3.26-3.36 (m, 1H, 10b-H), 3.82 (s, 3H, OMe), 3.83 (s, 3H, OMe), 4.39 (d, *J* = 16.2 Hz, 1H, 6-H), 4.56 (d, *J* = 16.2 Hz, 1H, 6-H), 4.81-4.89 (m, 1H, 4a-H), 5.34-5.43 (m, 1H, 4-H), 5.68-5.79 (m, 1H, 3-H), 6.52 (s, 1H, 7-H), 6.76 (s, 1H, 10-H), 7.58-7.70 (m, 3H, Ar), 8.01-8.08 (m, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1 (C-2), 25.5 (C-1), 33.9 (C-10b), 43.5 (C-6), 52.9 (C-4a), 55.8 (OMe), 56.0 (OMe), 108.4 (C-7), 109.4 (C-10), 124.7 (Ar), 124.2 (Ar), 124.7 (Ar), 126.2 (Ar), 130.7 (C-4), 131.7 (C-3), 133.1 (Ar), 133.3 (Ar), 133.7 (Ar), 147.4 (Ar), 147.9 (Ar), 148.3 (Ar); HRMS (ESI): calcd for $C_{21}H_{22}N_2O_6S$ $[M+Na]^+$ 453.10908, found 453.10940.

*4.6.3. 8,9-Dimethoxy-5-((4-nitrophenyl)sulfonyl)-1,2,4a,5,6,10b-hexahydrophenanthridine (**29c**)*

Prepared from amine hydrochloride **20d** (100 mg, 0.35 mmol) according to procedure 6 to give pure sulfonamide **29c** (140 mg, 99%) as yellow amorphous solid. R_f = 0.2 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62-1.73 (m, 1H, 1-H), 1.74-1.85 (m, 1H, 2-H), 1.85-1.98 (m, 1H, 1-H), 2.18-2.31 (m, 1H, 2-H), 2.99-3.13 (m, 1H, 10b-H), 3.80 (s, 3H, OMe), 3.82 (s, 3H, OMe), 4.23 (d, *J* = 15.9 Hz, 1H, 6-H), 4.64 (d, *J* = 15.9 Hz, 1H, 6-H), 4.81-4.89 (m, 1H, 4a-H), 5.14-5.21 (m, 1H, 4-H), 5.67-5.75 (m, 1H, 3-H), 6.49 (s, 1H, 7-H), 6.66 (s, 1H, 10-H), 7.97 (d, *J* = 8.8 Hz, 2H, Ar), 8.26 (d, *J* = 8.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1 (C-2), 25.5 (C-1), 33.8 (C-10b), 43.4 (C-6), 52.8 (C-4a), 55.8 (OMe), 56.0 (OMe), 108.4 (C-7), 109.4 (C-10), 124.7 (Ar), 124.2 (Ar), 124.7 (C-4), 126.5 (Ar), 128.2 (Ar), 133.5 (C-3), 146.4 (Ar), 147.6 (Ar), 148.5 (Ar), 149.8 (Ar); HRMS (ESI): calcd for $C_{21}H_{22}N_2O_6S$ $[M+Na]^+$ 453.10908, found 453.10940.

4.7. Preparation of carbamates from amine hydrochlorides (Procedure 7)

To a cooled (0 °C) suspension of amine·HCl (1.0 equiv) in CH_2Cl_2 (9 mL per mmol of hydrochloride) were added Et_3N (2.0 equiv) and the corresponding chloroformate (2.0 equiv) or Boc_2O (2.5 equiv). The stirred reaction mixture was allowed reach room temperature within 1 h (in case chloroformate) or 2 h (in case of Boc_2O), respectively. Thereafter, saturated $NaHCO_3$ solution (9 mL per mmol of hydrochloride) was added. After separation of the layers the aqueous layer was extracted with CH_2Cl_2 (2 × 9 mL per mmol of hydrochloride). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash chromatography to afford the pure carbamates.

*4.7.1. Ethyl 8,9-dimethoxy-2,4a,6,10b-tetrahydrophenanthridine-5(1H)-carboxylate (**32a**)*

Prepared from amine hydrochloride **20d** (10 mg, 0.03 mmol) according to procedure 7 to give pure carbamate **32a** (9 mg, 94%) as colorless amorphous solid. R_f = 0.5 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.71-1.91 (m, 2H, 1H, 2-H), 1.94-2.08 (m, 1H, 1-H), 2.28-2.38 (m, 1H, 2-H), 3.19-3.29 (m, 1H, 10b-H), 3.83 (s, 3H, OMe), 3.85 (s, 3H, OMe), 4.18 (q, *J* = 7.1 Hz, 3H, OCH_2, 6-H) 4.81 (d, *J* = 15.7 Hz, 1H, 6-H), 4.96-5.28 (m, 1H, 4a-H), 5.44-5.55 (m, 1H, 4-H), 5.65-5.78 (m, 1H, 3-H), 6.52 (s, 1H, 7-H), 6.81 (s, 1H, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7 (OCH_2CH_3), 20.3 (C-2), 25.3 (C-1), 33.5 (C-10b), 42.2 (C-6), 50.3 (C-4a), 55.8 (OMe), 56.1 (OMe), 61.5 (OCH_2), 108.5 (C-7), 109.5 (C-10), 127.3 (C-4), 131.2 (C-3), 147.4 (Ar), 148.0 (Ar), 155.4 (CO).

*4.7.2. Benzyl 8,9-Dimethoxy-2,4a,6,10b-tetrahydrophenanthridine-5(1H)-carboxylate (**32b**)*

Prepared from amine hydrochloride **20d** (100 mg, 0.34 mmol) according to procedure 7 to give pure carbamate **32b** (50 mg, 39%) as colorless amorphous solid. R_f = 0.2 (petroleum

ether/ethyl acetate, 2:1); 1H NMR (400 MHz, $CDCl_3$): δ = 1.69-1.90 (m, 2H, 1-H, 2-H), 1.91-2.09 (m, 1H, 1-H), 2.26-2.41 (m, 2H, 2-H), 3.18-3.35 (m, 1H, 10b-H), 3.82 (s, 3H, OMe), 3.85 (s, 3H, OMe), 4.21 (d, *J* = 16.0 Hz, 1H, 6-H), 4.84 (d, *J* = 16.0 Hz, 1H, 6-H), 5.02-5.26 (m, 1H, 4a-H), 5.17 (s, 2H, OCH_2Ph), 5.46-5.55 (m, 1H, 4-H), 5.67-5.77 (m, 1H, 3-H), 6.52 (s, 1H, 7-H), 6.81 (s, 1H, 10-H), 7.28-7.34 (m, 1H, Ar), 7.35-7.44 (m, 4H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2 (C-2), 25.2 (C-1), 33.4 (C-10b), 42.3 (C-6), 50.4 (C-4a), 55.7 (OMe), 56.0 (OMe), 67.2 (OCH_2Ph), 108.5 (C-7), 109.4 (C-10), 127.6 (C-4), 128.4 (Ar), 128.9 (Ar), 131.8 (C-3), 136.6 (Ar), 147.3 (Ar), 148.0 (Ar), 155.4 (CO); HRMS (ESI): calcd for $C_{23}H_{25}NO_4$ $[M+Na]^+$ 402.16758, found 402.16774.

*4.7.3. Ethyl 8,9-Dimethoxy-2,4a,6,10b-tetrahydrophenanthridine-5(1H)-carboxylate (**32c**)*

Prepared from amine hydrochloride **20d** (173 mg, 0.68 mmol) according to procedure 7 to give pure carbamate **32c** (210 mg, 89%) as colorless amorphous solid. R_f = 0.3 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 9H, O*t*Bu), 1.69-1.89 (m, 2H, 1-H, 2-H), 1.91-2.06 (m, 1H, 1-H), 2.26-2.38 (m, 1H, 2-H), 3.16-3.26 (m, 1H, 10b-H), 3.83 (s, 3H, OMe), 3.84 (s, 3H, OMe), 4.12 (d, *J* = 16.7 Hz, 6-H), 4.75 (d, *J* = 16.7 Hz, 1H, 6-H), 4.87-5.20 (m, 1H, 4a-H), 5.41-5.53 (m, 1H, 4-H), 5.63-5.76 (m, 1H, 3-H), 6.52 (s, 1H, 7-H), 6.81 (s, 1H, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3 (C-2), 25.4 (C-1), 28.4 (O*t*Bu), 33.6 (C-10b), 42.2 (C-6), 55.7 (OMe), 56.0 (C-4a), 56.1 (OMe), 79.8 (O^{t}Bu), 108.6 (C-7), 109.5 (C-10), 127.6 (C-4), 130.8 (C-3), 147.3 (Ar), 147.9 (Ar), 154.8 (CO). HRMS (ESI): calcd for $C_{20}H_{27}NO_4$ $[M+Na]^+$ 368.18323, found 368.18325.

*4.8. Directed hydroboration of arylsulfonyl)-hexahydrophenanthridines **29** and carbamates **32** (Procedure 8)*

To a magnetically stirred suspension of $NaBH_4$ (6.0 equiv) in dry THF (3 mL per mmol of $NaBH_4$) was added neat $BF_3{\cdot}OEt_2$ (5.5 equiv) at 0 °C. The reaction mixture was allowed to stir at room temperature for 30 min before the alkene **29** or **32** (1.0 equiv) respectively, in dry THF (30 mL per mmol of alkene) was added dropwise to the mixture at 0 °C. Thereafter, the mixture was allowed to reach room temperature within 1.5 h. For work-up 3N aqueous NaOH (30 mL per mmol of alkene) and 30% H_2O_2 (30 mL per mmol of alkene) were added sequentially to the reaction mixture at 0 °C. The mixture was stirred at room temperature for 5 h, before it was extracted with Et_2O (3 × 50 mL per mmol of alkene). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography gave the pure secondary alcohol.

*4.8.1. 8,9-Dimethoxy-5-tosyl-1,2,3,4,4a,5,6,10b-octahydrophenanthridin-4-ol (**30a-OH**)*

Prepared from alkene **29a** (220 mg, 0.55 mmol) according to procedure 8 to give alcohol **30a-OH** (206 mg, 90%) as colorless solid. R_f = 0.4 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11-1.26 (m, 1H, 2-H), 1.29-1.43 (m, 1H, 2-H), 1.48-1.68 (m, 2H, 1-H), 1.94-2.05 (m, 1H, 3-H), 2.23-2.33 (m, 1H, 3-H), 2.36 (s, 3H, CH_3), 2.87-2.98 (m, 1H, 10b-H), 3.44 (td, *J* = 10.6, 4.8 Hz, 1H, 4-H), 3.80 (s, 3H, OMe), 3.81 (s, 3H, OMe), 3.90 (dd, *J* = 8.0, 4.0 Hz, 1H, 4a-H), 4.41 (d, *J* = 16.0 Hz, 1H, 6-H), 4.64 (d, *J* = 16.0 Hz, 1H, 6-H), 6.53 (s, 1H, 7-H), 6.64 (s, 1H, 10-H), 7.23 (d, *J* = 8.1 Hz, 2H, Ar), 7.71 (d, *J* = 8.1 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2 (C-2), 21.5 (CH_3), 27.6 (C-1), 33.9 (C-3), 36.0 (C-10b), 43.5 (C-6), 55.8 (OMe), 56.0 (OMe), 60.6 (C-4), 66.3 (C-4a), 108.6 (C-7), 108.9 (C-10), 123.8 (Ar), 126.4 (Ar), 127.1 (Ar), 129.7 (Ar), 137.0 (Ar), 143.5 (Ar), 147.6 (Ar), 148.2 (Ar).

*4.8.2. 8,9-Dimethoxy-5-((4-nitrophenyl)sulfonyl)-1,2,3,4,4a,5,6,10b-octahydrophenanthridin-4-ol (**30c-OH**)*

Prepared from alkene **29c** (120 mg, 0.29 mmol) according to procedure 8 to give alcohol **30c-OH** (80 mg, 63%) as yellow solid. R_f = 0.4 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15-1.30 (m, 1H), 1.34-1.48 (m, 1H), 1.54-1.75 (m, 3H), 1.97-2.08 (m, 1H), 2.31-2.43 (m, 1H), 3.01-3.10 (m, 1H, 4a-H), 3.5 (td, *J* = 10.4, 4.5 Hz, 1H, 4-H), 3.81 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.90 (dd, *J* = 10.1, 5.0 Hz, 1H, 4a-H), 4.40 (d, *J* = 16.4 Hz, 1H, 6-H), 4.72 (d, *J* = 16.4 Hz, 1H, 6-H), 6.53 (s, 1H, 7-H), 6.67 (s, 1H, 10-H), 8.04 (d, *J* = 8.8 Hz, 2H, Ar), 8.28 (d, *J* = 8.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3 (C-2), 27.7 (C-1), 34.5 (C-3), 36.8 (C-10b), 43.5 (C-6), 55.9 (OMe), 56.0 (OMe), 60.9 (C-4), 66.2 (C-4a), 108.6 (C-7), 108.7 (C-10), 123.2 (Ar), 124.2 (Ar), 126.1 (Ar), 128.3 (Ar), 146.2 (Ar), 147.8 (Ar), 148.5 (Ar).

4.9. Oxidation of the secondary alcohols to the corresponding ketones using Dess-Martin periodinane (Procedure 9)

To a stirred solution of alcohol (1 equiv) in CH_2Cl_2 (50 mL per mmol of alcohol) was added DMP (1.5 equiv) and the mixture was allowed to stir at room temperature for 1.5 h. Then it was diluted with saturated $NaHCO_3$ solution (30 mL per mmol of alcohol) and concentrated sodium thiosulfate solution (30 mL per mmol of alcohol). This mixture was stirred until both the organic and aqueous layers appeared clear. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL per mmol of alcohol). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Purification of the residue by flash chromatography afforded the pure ketone.

*4.9.1. 8,9-Dimethoxy-5-tosyl-2,3,4,4a,5,6,10b-hexahydrophenanthridin-4-(1H)-one (**30a**)*

Prepared from alcohol **30a-OH** (120 mg, 0.30 mmol) according to procedure 9 to give ketone **30a** (98 mg, 79%) as colorless solid. R_f = 0.5 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45-1.96 (m, 2H, 2-H), 2.07-2.24 (m, 1H, 1-H), 2.25-2.36 (m, 2H, 1-H, 3-H), 2.42 (s, 3H, CH_3), 2.52-2.66 (m, 1H, 3-H), 3.59-3.72 (m, 1H, 10b-H), 3.81 (s, 3H, OMe), 3.84 (s, 3H, OMe), 4.47 (d, *J* = 15.2 Hz, 1H, 6-H), 4.58 (d, *J* = 15.2 Hz, 1H, 6-H), 4.79 (d, *J* = 5.6 Hz, 1H, 4a-H), 6.49 (s, 1H, 7-H), 6.70 (s, 1H, 10-H), 7.29 (d, *J* = 8.1 Hz, 2H, Ar), 7.73 (d, *J* = 8.1 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (C-1), 21.5 (CH_3), 27.6 (C-2), 41.0 (C-3), 41.1 (C-10b), 44.2 (C-6), 55.7 (OMe), 56.0 (OMe), 62.5 (C-4a), 108.1 (C-7), 108.8 (C-10), 124.5 (Ar), 125.0 (Ar), 127.4 (Ar), 129.4 (Ar), 136.2 (Ar), 143.3 (Ar), 148.0 (Ar), 148.1 (Ar), 205.1 (CO); HRMS (ESI): calcd for $C_{22}H_{25}NO_5S$ $[M+Na]^+$ 438.13456, found 438.13454.

*4.9.2. 8,9-Dimethoxy-5-((4-nitrophenyl)sulfonyl)-2,3,4,4a,5,6,10b-hexahydrophenanthridin-4-(1H)-one (**30c**)*

Prepared from alcohol **30c-OH** (50 mg, 0.10 mmol) according to procedure 9 to give ketone **30c** (47 mg, 99%) as yellow amorphous solid, R_f = 0.5 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54-1.61 (m, 1H, 2-H), 1.82-1.92 (m, 1H, 2-H), 2.12-2.34 (m, 3H, 1-H, 3-H), 2.56-2.67 (m, 1H, 3-H), 3.70-3.77 (m, 1H, 10b-H), 3.80 (s, 3H, OMe), 3.83 (s, 3H, OMe), 4.39 (d, *J* = 14.6 Hz, 1H, 6-H), 4.68 (d, *J* = 14.6 Hz, 1H, 6-H), 4.85 (d, *J* = 6.1 Hz, 1H, 4a-H), 6.48 (s, 1H, 7-H), 6.70 (s, 1H, 10-H), 8.00 (d, *J* = 8.8 Hz, 2H, Ar), 8.34 (d, *J* = 8.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (C-1), 27.6 (C-2), 40.9 (C-10b), 41.0 (C-3), 44.3 (C-6), 55.8 (OMe), 56.1 (OMe), 62.8 (C-4a), 108.1 (C-7), 108.8 (C-10), 124.1 (Ar), 124.3 (Ar),

128.6 (Ar), 144.9 (Ar), 148.4 (Ar), 150.0 (Ar), 204.9 (CO). HRMS (ESI): calcd for $C_{21}H_{22}N_2O_7S$ $[M+Na]^+$ 469.10399, found 469.10415.

*4.9.3. 5-(2-Bromoacetyl)-8,9-dimethoxy-2,3,4a,5,6,10b-hexahydrophe-nanthridin-4(1H)-one (**35**)*

To a cooled (0 °C) stirred solution of carbamate **33c** (30 mg, 0.08 mmol) in CH_2Cl_2 (1 mL) was added TFA (0.5 mL). The reaction mixture was allowed to stir at room temperature for 4 h. Excess solvent and TFA were removed on a rotavapor in vacuo and the residual TFA was removed by adding several times CH_2Cl_2 and concentration of the solution in vacuo to give the solid amine salt, which was directly used in next step without further purification.

To a cooled (0 °C) solution of salt and Et_3N (36 µL, 0.25 mmol, 3 equiv) in CH_2Cl_2 (1 mL) was added bromoacetyl bromide (8 µL, 0.10 mmol, 1.2 equiv) dropwise. The stirred reaction mixture was allowed to reach room temperature within 1 h. For work-up, the mixture was treated with saturated $NaHCO_3$ (2 mL), and this mixture was extracted with Et_2O (3 × 2mL). The combined organic layers was dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude amide was purified by flash chromatography (petroleum ether/ethyl acetate, 2:1) to provide pure amide **35** (20 mg, 65% over two steps) as yellow solid. R_f = 0.3 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers): δ = 1.53-1.81 (m, 2H, 2-H), 1.82-2.01 (m, 1H, 2-H), 2.13-2.27 (m, 2H, 1-H), 2.28-2.46 (m, 2H, 1-H, 3-H), 2.54-2.75 (m, 1H, 3-H), 3.52-3.67 (m, 1H, 10b-H), 3.78-3.86 (6H, 2 OMe), 3.90-4.08 (s, 1H, $COCH_2Br$), 4.14-4.31 (m, 1H, $COCH_2Br$), 4.59-4.73 (m, 1H, 6-H), 4.76-4.92 (m, 1H, 6-H), 5.44 (d, *J* = 6.1 Hz, 1H, 4a-H), 6.52-6.59 (1H, 7-H), 6.68-6.75 (1H, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 21.1, 25.9, 26.1, 27.0, 27.2, 38.9, 40.8, 41.2, 45.4, 45.8, 55.8, 55.8, 56.0, 56.1, 59.6, 59.64, 107.8, 107.9, 108.8, 109.2, 123.5, 124.4, 124.5, 124.7, 124.7, 148.3, 148.4, 166.5, 166.8, 205.1, 205.2; HRMS (ESI): calcd for $C_{17}H_{20}BrNO_4$ $[M+Na]^+$ 404.04679, found 404.04670.

*4.9.4. 5-(2'-Bromoallyl)-8,9-dimethoxy-1,2,4a,5,6,10b-hexahydro phenanthridine (**38**)*

To a stirred solution of amine·HCl **20d** (110 mg, 0.34 mmol) in DMF (1 mL) was added NaH (60% dispersion in oil, 35 mg, 0.85 mmol, 2.5 equiv) and bromoallyl bromide (51 µL, 0.51 mmol, 1.5 equiv). The reaction mixture was allowed to stir at room temperature for 1 h, before it was cooled to 0 °C and quenched with H_2O (2 mL). The mixture was extracted with EtOAc (3 × 3mL). The combined organic layers were was washed with H_2O (3 × 3 mL) and saturated NaCl solution (3 mL), drieed with anhydrous Na_2SO, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/ethyl acetate, 3:1) provided pure allylamine **38** (80 mg, 65%) as yellow oil. R_f = 0.6 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.80-1.89 (m, 1H, 1-H), 1.92-2.03 (m, 2H, 2-H), 2.11-2.24 (m, 1H, 1-H), 2.92-3.01 (m, 1H, 10b-H), 3.40 (d, *J* = 16.0 Hz, 1H, 1'-H), 3.46-3.50 (m, 1H, 4a-H), 3.53 (d, *J* = 16.0 Hz, 1H, 1'-H), 3.58 (d, *J* = 15.2 Hz, 1H, 6-H), 3.81 (s, 3H, OMe), 3.84 (d, *J* = 15.2 Hz, 6-H), 3.85 (s, 3H, OMe), 5.57 (s, 1H, 3'-H), 5.71-5.79 (m, 1H, 4-H), 5.82-5.89 (m, 1H, 3-H), 5.91 (s, 1H, 3'-H), 6.48 (s, 1H, 10-H), 6.74 (s, 1H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = C-2), 26.6 (C-1), 35.2 (C-10b), 51.3 (C-6), 55.7 (OMe), 55.9 (C-1'), 56.0 (OMe), 60.9 (C-4a), 109.0 (C-7), 110.2 (C-10), 117.8 (C-2'), 126.0 (C-3'), 126.6 (Ar), 129.1 (Ar), 131.7 (C-4), 132.1 (C-3), 147.1 (Ar), 147.8 (Ar).

*4.9.5. 9,10-Dimethoxy-4-methylene-2,3,3a,3a,1,4,5,7,11b-octahydro-1H-pyrrolo[3,2,1-de]phenanthridine-3-carbonitrile (**39**)*

To a solution of $Ni(COD)_2$ (149 mg, 0.54 mmol, 2.0 equiv) in dry acetonitrile (1 mL), at room temperature and under nitrogen atmosphere, was added a solution of vinyl bromide **38** (100 mg, 0.27 mmol) and Et_3N (117 µL, 0.81 mmol, 3.0 equiv) in dry acetonitrile (1 mL). The reaction mixture was stirred at room temperature for about 15 min, resulting in a color change from yellow to black. When all starting material had been consumed (checked by TLC), the quencher TMSCN (100 µL, 0.66 mmol, 2.5 equiv) was added and the mixture stirred for additional 3 h. It was filtered through Celite and the filter cake washed several times with CH_2Cl_2. The filtrate was washed with saturated Na_2CO_3 solution. The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH, 9/1) afforded the cyclization product **39** (67 mg, 80%) as yellow solid. R_f = 0.6 (CH_2Cl_2/MeOH, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68 (tt, *J* = 3.3, 13.6 Hz, 1H, 1-H), 1.75-2.87 (m, 1H, 2-H), 1.91-2.02 (m, 1H, 1-H), 2.02-2.13 (m, 1H, 2-H), 2.68 (t, *J* = 4.8 Hz, 1H, 3a-H), 2.72-2.82 (m, 2H, 3-H, 11b-H), 2.94 (d, *J* = 14.1 Hz, 1H, 5-H), 3.00-3.07 (m, 1H, 3b-H), 3.28 (d, *J* = 14.1 Hz, 1H, 5-H), 3.82 (s, 3H, OMe), 3.84 (s, 3H, OMe), 4.09 (d, *J* = 14.4 Hz, 1H, 7-H), 4.11 (d, *J* = 14.4 Hz, 1H, 7-H), 5.08 (s, 1H, 4-CH_2), 5.13 (s, 1H, 4-CH_2), 6.52 (s, 1H, 11-H), 6.62 (s, 1H, 8-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.6 (C-3), 27.3 (C-2), 31.1 (C-1), 38.1 (C-11b), 44.8 (C-3a), 55.7 (C-7), 55.89 (OMe), 55.92 (OMe), 59.5 (C-5), 61.1 (C-3b), 107.6 (4-CH_2), 109.2 (C-8), 111.2 (C-11), 121.6 (CN), 126.0 (Ar), 129.9 (Ar), 147.5 (Ar), 147.6 (Ar), 148.4 (C-4); HRMS (ESI): calcd for $C_{19}H_{22}N_2O_2$ $[M+H]^+$ 311.17540, found 311.17548.

*4.9.6. 9,10-Dimethoxy-4-methylene-2,3,3a,3a,1,4,5,7,11b-octahydro-1H-pyrrolo[3,2,1-de]phenanthridine (**40**)*

To a solution of $Ni(COD)_2$ (149 mg, 0.54 mmol, 2.0 equiv) in dry acetonitrile (1 mL), at room temperature and under nitrogen atmosphere, was added a solution of vinyl bromide **38** (100 mg, 0.27 mmol) and Et_3N (117 µL, 0.81 mmol, 3.0 equiv) in dry acetonitrile (1 mL). The reaction mixture was stirred at room temperature for about 15 min, resulting in a color change from yellow to black. When all starting material had been consumed (checked by TLC), the quencher Et_3SiH (137 µL, 0.85 mmol, 3.2 equiv) was added and the mixture stirred for additional 3 h. It was filtered through Celite and the filter cake washed several times with CH_2Cl_2. The filtrate was washed with saturated Na_2CO_3 solution. The organic laywer was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH, 9/1) afforded the cyclization product **40** (54 mg, 70%) as yellow solid. R_f = 0.5 (CH_2Cl_2/MeOH, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23-1.48 (m, 3H, 3-H, 2-H), 1.55-1.80 (m, 3H, 2-H, 1-H), 2.48-2.59 (m, 2H, 3a-H, 11b-H), 2.64-2.75 (m, 1H, 3b-H), 2.83 (d, *J* = 14.0 Hz, 1H, 5-H), 3.20 (d, *J* = 14.0 Hz, 1H, 5-H), 3.75 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.88 (d, *J* = 14.0 Hz, 1H, 7-H), 3.97 (d, *J* = 14.0 Hz, 1H, 7-H), 4.81 (s, 1H, 4-H), 4.82 (s, 1H, 4-H), 6.45 (s, 1H, 11-H), 6.57 (s, 1H, 8-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.8 (C-2), 29.8 (C-3), 31.4 (C-1), 38.5 (C-11b), 43.5 (C-3a), 55.8 (OMe), 56.4 (C-7), 59.9 (C-5), 62.9 (C-3b), 103.9 (4-*C*H_2), 109.2 (C-8), 111.3 (C-11), 125.7 (Ar), 131.5 (Ar), 147.2 (Ar), 147.6 (Ar), 152.2 (C-4); HRMS (ESI): calcd for $C_{18}H_{23}NO_2$ $[M+H]^+$ 286.18016 found 286.18043.

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Supplementary data

General information, some procedures not included in the main part and copies of NMR spectra. Supplementary data associated with this article can be found in the online version, at doi:

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