In-depth examination of the pterolactams behaviour in Lewis/Brönsted acid catalysis environment: Total isolation of the reaction products

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Dedicated to our colleague and friend, Professor Benoît Rigo, on the occasion of his retirement.

Abstract

To gain some insights on the amidoalkylation process, we were interested in studying the product distribution when pterolactam was exposed to acids. The reactivity of pterolactam and its *N*-aryl derivatives towards TMSOTf or TfOH has been carefully examined in presence and absence of TMS-protected anilines. Under these conditions, the *N*-acyliminium precursors showed high reactivity at both α- and β-positions of the nitrogen atom. In this context, these salts can induce cascade processes including Povarov type reaction among other transformations. In that way, novel quinolines and tetrahydro-quinolines, among other compounds, were isolated for the first time.
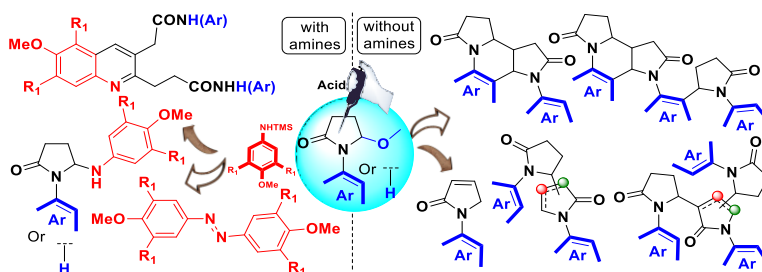
Introduction

Coupling reactions between nucleophiles and linear *N*-acyliminium ions (NAI) usually result in low to medium regio- and stereoselectivity, generally due to the high degrees of freedom of cationic precursor species. The use of cyclic NAI, having lower degrees of freedom, allows better control of the regio- and diastereoselectivity of the amido-alkylation process, which allowed the synthesis of natural and unnatural aza-heterocyclic complex molecules.[1-6] While the C–heteroatom bond formation proved to be scarce,[7] the C–C bond forming reactions, have extensively investigated, and are still of interest.

Of particular interest, the cyclic NAI are characterised by great structural variability, and among them two major families can be distinguished: the more stable aromatic ions of type (**I**) and the more reactive cyclic ions of type (**II**), which may themselves be endocyclic[8] or exocyclic[9,10] (Scheme 1). In the latter case, the acyl C=O group is attached to the *N* atom instead of the R group, however, these exocyclic NAI are not shown in Scheme 1 to simplify the Scheme.
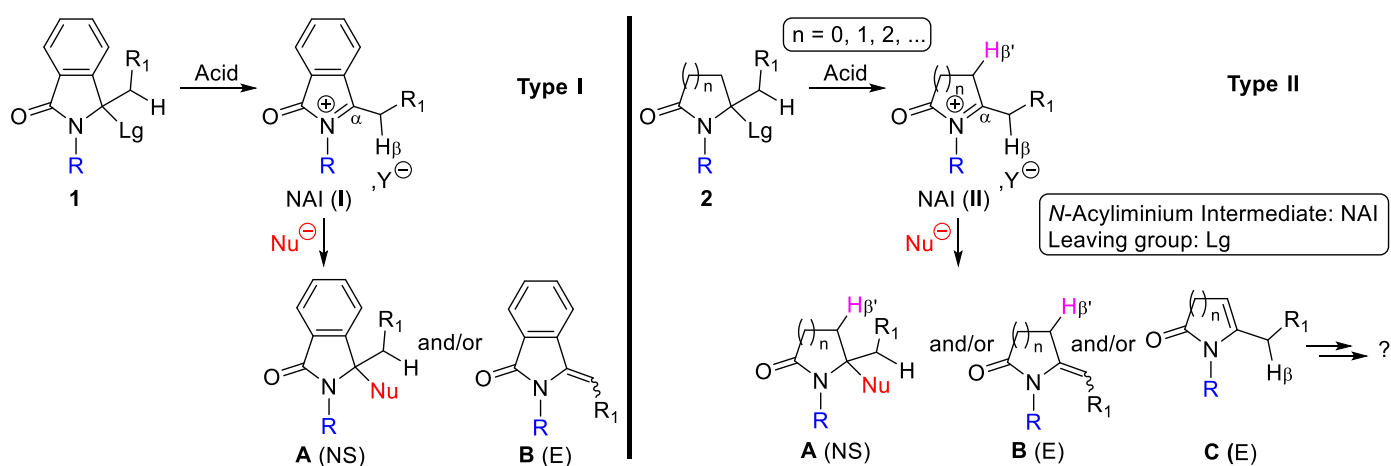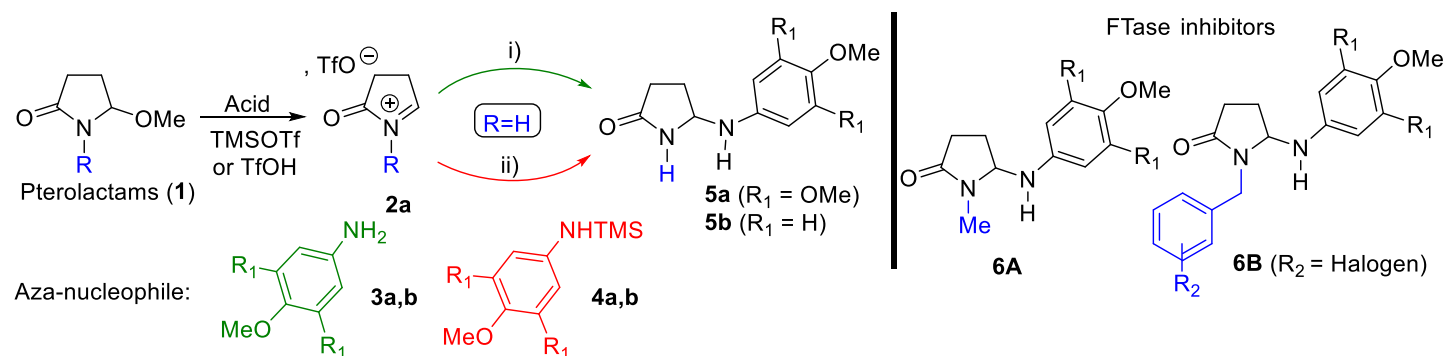

Scheme 1. Different reactivity modes of cyclic NAI generated form lactams **1** and **2** according to nucleophilic substitution (NS) *vs.* elimination (E).

In that context and according to Scheme 1, in addition to the classical nucleophilic substitution (NS) reaction products **A**, other products (**B**) can be obtained by H_β elimination (E). In the case of NAI of type (**II**), $H_{\beta'}$ elimination can occur giving endocyclic enamidones **C**[11] able to react further in the reaction medium forming complexes molecules. In order to deepen this question, our aim beyond the importance of the products that will be obtained, is to study the overall behavior of NAI (**II**) generated in an acid environment in the absence or presence of an external nucleophile. Due to the poor literature data on this area, the isolation of all the reaction products will be systematically undertaken.

Results and Discussion

During our previous studies on pterolactams[12-14] we have already explored the reactivity of pterolactam derivatives of type **1** (R = H, Me, CH$_2$Ar) with anilines **3** or *N*-trimethylsilylanilines **4** by using triflic acid (TfOH) or trimethylsilyl triflate (TMSOTf) as a catalyst (Scheme 2). The results showed that α-aminoalkylation reaction is clean and the use of TMS-protected amines **4** gives higher yields (55% instead of 40-50% with anilines **3**)

under shorter reaction time (Scheme 2).[15] In addition, *via* this reaction, compounds **5a,b**, and the potential farnesyltransferase (FTase) inhibitors **6A,B** could be synthesized (Scheme 2).[16-18] Of interest, attempts to generalize this amination method showed that the process is very sensitive to the acidity of the reaction medium and that addition, changing the concentrations and/or the nature of the acid used as catalyst completely modifies the reaction profile.

Reaction conditions: i) TfOH (10-15 mol%), **3**, CH$_2$Cl$_2$, 50 °C, 24-48 h (40-50%); ii) TMSOTf (5 mol%), **4**, CH$_2$Cl$_2$, 50 °C, 8 h (55%).

Scheme 2. α-Aminoalkylation of cyclic NAI **2a** into *N,N*-aminals **5-6** from pterolactams **1** under acid catalysis.

We began the study by re-examining the reaction of pterolactam **1a** with *N*-trimethylsilylamine **4a** under different acidic conditions by using a double amount of TMSOTf catalyst (10 mol%) that we have used in an earlier report in 5 mol%.[15] Thus after heating for 14 h at 50 °C, the *N,N*-aminal product **5a**[15] was isolated in only 10% yield after chromatography separation. The latter compound was accompanied by many new compounds identified as the quinolines **7a**, **8a** and **9a** in 0.15% to 2% yields, in addition to the amine **10a** (trance) and the azo-derivative **11a** in 1% yield (Scheme 3).
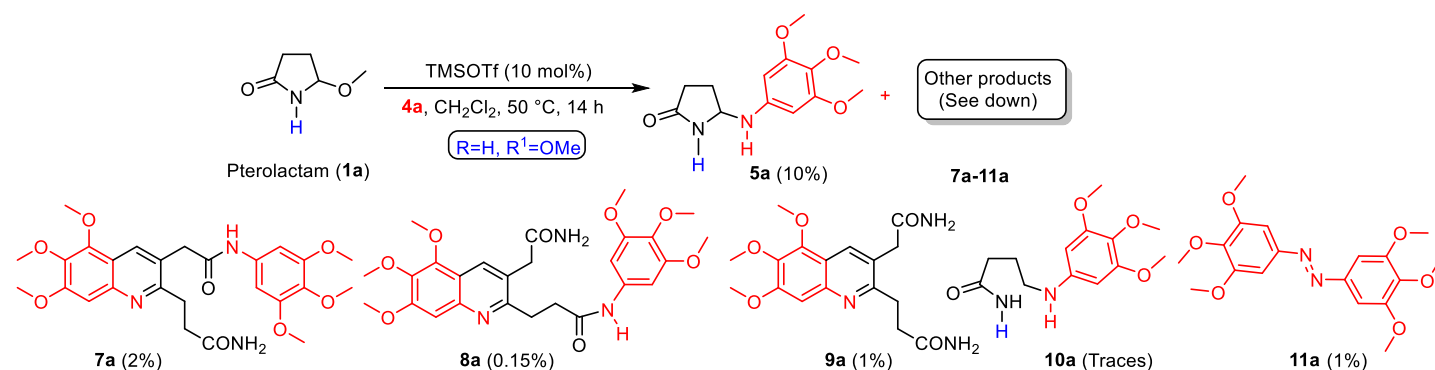
Scheme 3. α-Aminoalkylation of **1a** under TMSOTf catalysis.

Considering the literature on slightly related transformations, the formation of compounds **5a** and **7a-11a** can be explained as described in Scheme 4. Thus, pterolactam **1a** under acidic conditions can provide the NAI **2a** which gave the enamide **12a** by functional equilibration,[19-23] and also *N,N*-aminal derivative **5a** by α-aminoalkylation[15] when reacted with TMS aniline **4a**. All the three compounds **2a**, **5a**, and **12a** are in equilibrium in the acid medium. Ring opening of *N,N*-aminal derivative **5a** furnished aromatic imine **L**, which under acid catalyzed Povarov type reaction (aza-Diels-Alder reaction)[24-30] with enamide **12a** provided tetrahydroquinoline intermediate **M**. The latter after lactam ring cleavage[31-34] furnished dihydroquinoline **N**

whose air oxidation provided the isolated quinoline product **9a** (1%). Interestingly, no lactam cleavage was reported in related piperidinoquinolones.[24] Then the *trans*-amidification at the primary amides' sites of quinoline **9a** by TMS-protected amine **4a**, ultimately yielded dissymmetrical quinoline diamides **7a** (2%) and **8a** (0.15%). As for azo-benzene **11a**, it was formed by a standard oxidative dimerization of the starting aniline obtained by TMS-amine deprotection under acidic conditions.[31,34] Finally, the formation of **10a**, detected in the reaction medium only in trace amounts, could be due to the *in-situ* imine reduction of **L** by proton transfer from the fused tetrahydroquinoline **M** and/or dihydroquinoline **N** intermediates.[24-30]
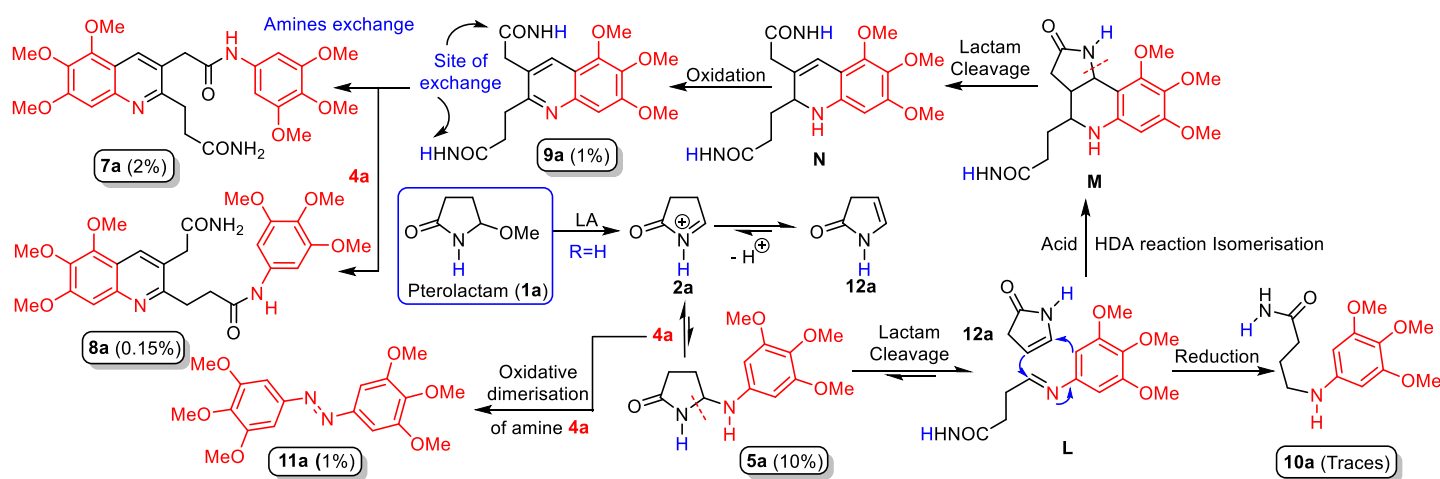

Scheme 4. Postulated mechanism for α-aminoalkylation of **1a** (R = H) leading to compounds **5a**, **7a-11a**.

Quinoline scaffold is present in many biologically important natural and unnatural compounds,[37-42] and the formation of these systems with substituents at privileged positions could lead to new compounds with important biological properties. Interestingly, many approaches on the synthesis of quinolines and their application domains were described in numerous reviews,[43,44] and to the best of our knowledge, neither pterolactam **1a** nor its *N*-aryl derivatives were used in these approaches to date. Thus, the control of this new synthesis in exploitable manner, in terms of yields and limitation of by-products, could render this methodology very attractive.

In order to collect additional information on the scope of this new quinoline synthesis, two *N*-aryl lactams, **1b** (R_2 = Ph) and **1c** (R_2 = 1,3-Cl$_2$Ph) were chosen. These substrates **1b,c** obtained by *N*-arylation of pterolactam (**1a**) under Buchwald type coupling reaction,[35] were submitted to reaction with TMS-protected anilines **4b** and **4a** (Scheme 2), respectively, under acidic conditions (Scheme 5).

As highlighted in Scheme 5, the reaction between *N*-phenylpterolactam (**1b,** R = Ph; R_2 = H) and TMS-aniline **4b**, was complete after heating for 96 h in the presence 20 mol% of TfOH, where only three products were isolated. The trisubstituted quinoline **9b** was obtained as a major compound in 30% yield, accompanied by amino-amide **10b** in 5% yield and the azo-derivative **11b** in only 1% yield. No *N*-phenyl *N,N*-aminal **5b**, or dissymmetrical quinoline amides analogs to **7a** and **8a** (Scheme 3) could be detected in the reaction mixture. However, the reaction between of *N*-(3,5-dichlorophenyl)-pterolactam (**1c**) and TMS-aniline **4a** in the presence of TfOH required the use AcOH as a solvent, because of the high melting point of the reaction mixture The reaction showed the same profile as for **1b** (Scheme 5) where the trisubstituted quinoline **9c** was isolated in good yield (53%), accompanied with only insignificant amounts of amino-amide **8c** (traces) and 18% of the azo-compound **11c**. Also, no compounds such as **5c**, **7c** and **8c** were isolated from the reaction mixture. From these results, it seems that *N*-aryl-*N,N*-aminal moiety such as in **5b** or **5c** is unstable in acid medium. This is

beneficial and favors the reaction profile to give quinolines. The quinolines **9** (**9c**>>**9b**>>**9a**) and azo-compounds **11** (**11c**>>**11b**≈**11a**) was obtained instead of the formation of amino-amides **10** which becomes totally marginal. Finally, the *N*-aryl amides **9b,c** were not subjected to the *trans*-amidification observed in case of reagent **1a**.
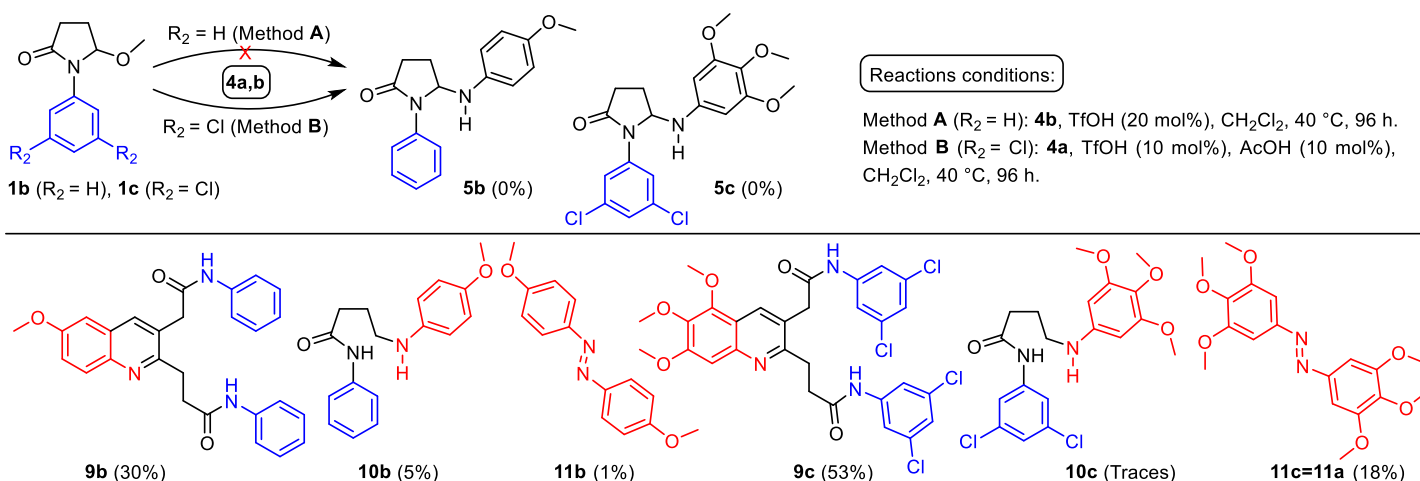

Scheme 5. Influence of *N*-aryl substituent on reaction of **1b,c** with amines **4a,b** under acid catalysis.

Furthermore, in the hope of obtaining *N*-aryl-*N,N*-aminal products, parallel investigations were done on the Buchwald reaction between *N,N*-hemi-aminal **5a** and 1,3-dichloro-5-iodobenzene (**13a**). As illustrated in Scheme 6, the reaction realized under the conditions published earlier,[35] provides regiochemically the expected product **5c** in 72% yield. This is in accordance with our report[35] and demonstrates in the same time that *N,N*-aminal functionality is stable in alkaline media compared with acidic one.[45,46]
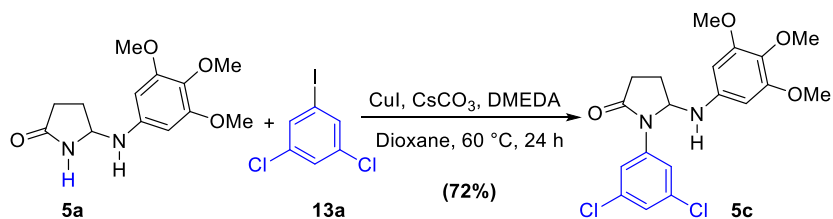
Scheme 6. Synthesis of *N,N*-aminal **5c** under coupling *N*-arylation conditions.

In all α-aminoalkylation reactions of *N*-aryl pterolactams **1** with TMS-protected anilines described above, very few amounts of unknown by-products were also observed by ^{1}H-NMR studies. They do not present elements of the used aniline as copartner. In an attempt to identify these compounds, obtain them in measurable amounts, and understand the possible mechanism allowing their formation, the reaction was realized without TMS-anilines. Also, to determine the influence of acid amount on the reaction profile, the NAI precursors *N*-aryl pterolactams **1** were stirred in CH_2Cl_2 under different conditions of temperature and amount of TMSOTf (see Scheme 8 and Table 1).
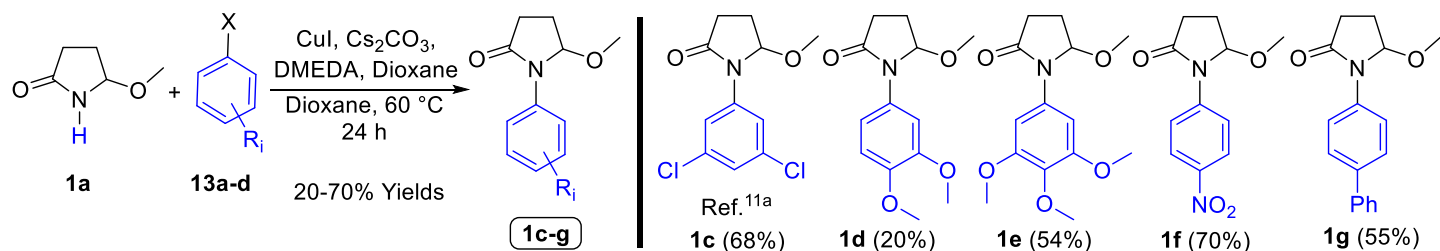
Scheme 7. Production of *N*-arylpterolactams **1c-g** necessary for next investigations by *N*-arylation coupling.

In that line, selected *N*-aryl pterolactams **1c-g** with different substituents on the phenyl group necessary for our next investigations in acid medium, were firstly prepared in good yields from pterolactam **1a** (R = H) as highlighted in Scheme 7.
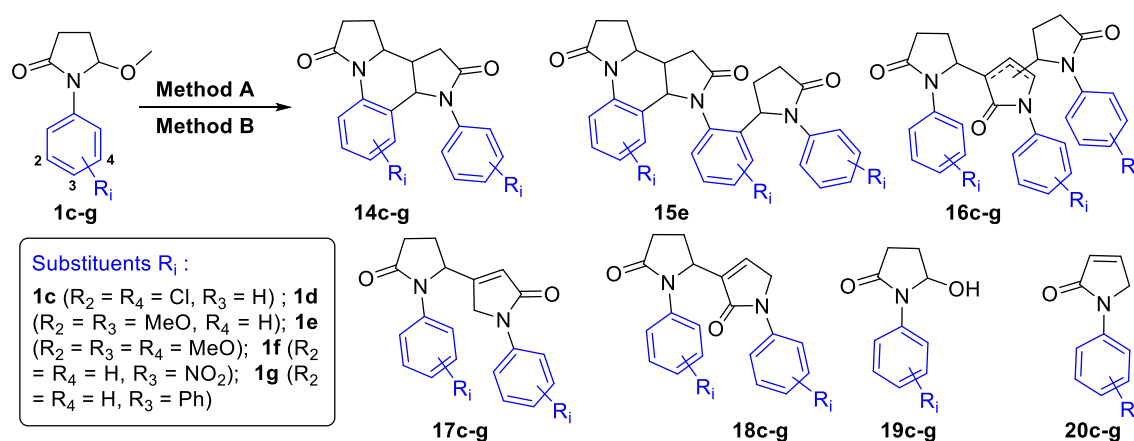
Scheme 8. Transformation of pterolactams **1c-g** without amines under acid catalysis. *Reactions conditions*: Method A: TMSOTf (5 mol%), CH_2Cl_2, 20-50 °C, 2-4 days. Method B: TMSOTf (50 mol%), CH_2Cl_2, rt., 1-2 h.

Table 1. Casting (%) of formed products stemming from the evolution of **1c-g** in acid medium as in Scheme 8.

| Product[a]	14	15	16 (16')	17	18	19	20
SM: **1c**[b]	30%[c]	-	-	-	-	-	-
	5%[d]	-	**90%**	-	-	-	-
SM: **1d**	42%	-	-	-	-	40%	-
	52% (7%)[e]	-	-	-	-	Traces	-
SM: **1e**	35%	Traces	-	-	-	40%	-
	60%	**24%**	-	-	-	5%	-
SM: **1f**	-	-	-	-	-	-	-
	-	-	-	**25%**	**5%**	-	-
SM: **1g**	-	-	-	-	-	-	-
	50%[f]	-	**10% (8%)**[e]	-	**7%**	**2%**	**2%**

[a] Yields of isolated products. [b] SM: Starting material: pterolactams **1c-g**. [c] Yields obtained from **Method A**. [d] Yields (in bold) obtained from **Method B**. [e] Other stereoisomer. [f] Mixture containing two stereoisomers.

The Cu(I)-catalyzed Csp^2-N coupling process conditions used in Scheme 7 are same as for products **1b** and **5c** (Scheme 6).[35] The low yield isolated in the case of product **1d** reflects mainly the purification difficulties encountered during the reaction work up.

From the results reported in Table 1, it appears that the use of 5 mol% of TMSOTf in CH_2Cl_2 at 20-50 °C for 2-4 days (**Method A**), or reactions in CH_2Cl_2 at room temperature, with 50 mol% of TMSOTf for 1-2 hours (**Method B**), lead to different reaction profiles (Scheme 8). In the case of **Method A**, with low amount of catalyst, the reaction with **1c-e** gave a mixture of *N*-aryl polyhydropyrroloquinolines (**14c-e**) in 30-42% yield and 5-hydroxy-1-arylpyrrolidin-2-ones (**19c-e**) in 40% yields, except for pterolactam derivative **1c**. The formation of tricyclic systems **14c-e** can be explained by the already reported dimerization process for related compounds *via* an interesting intermolecular π-cationic cyclisation.[24,47-50] As for hydroxyl lactams **19c-g**, they were generated by hydrolysis of the unreacted NAI intermediates during the reaction work up. Only traces of compounds **15e** were detected, and no reaction in cases of methoxy lactams **1f,g** was observed when using **Method A**.

On the other hand, as outlined in Table 1, treatment of pterolactams **1c-e** using 50 mol% of TMSOTf according to the **Method B,** provides mainly cyclized dimers **14** and also trimers **15** formed from reaction of **14** with aryl pterolactam **1**, with very low amounts of hydroxyl lactams **19**. Interestingly, starting from reactants **1c** and **1g** also uncyclized trimers **16** formed from the reaction of **17** and **18** were isolated in 90% and cumulated 18%, respectively (Scheme 8, Table 1). The reactions proceeded with high yields which are globally inverted from **1c** to **1e**. In addition, the short reaction time (1-2 h for completion determined by TLC) and the room temperature needed under these conditions, outline the importance of the acid concentration for the kinetic, the selectivity and the yields of these reactions.

In particular with *N*-(*p*-nitrophenyl)pterolactam **1f**, the reaction leads to only uncyclized dimers **17f** (25%) and **18f** (5%), whereas starting from *N*-(*p*-diphenyl)pterolactam **1g**, a plethora of compounds including monomers **19f** (2%) and **20f** (2%), dimer **18f** (7%) and cyclized dimer **14g** (50%) were obtained. In addition, the latter compounds were accompanied with uncyclized trimer **16g** (10%) and its regioisomer **16'g** (8%) with **14g** obtained as mixture of two isomers (see Table 1). Thus, it appears that the strong electro-withdrawing effect of the nitro group on NAI precursor **1f** aborted the π-cationic cyclization whatever the dimer resulting from the α-amidoalkylation. This result is contradictory to that of the bis-phenyl group which exerts non-selectivity on the reaction profile.
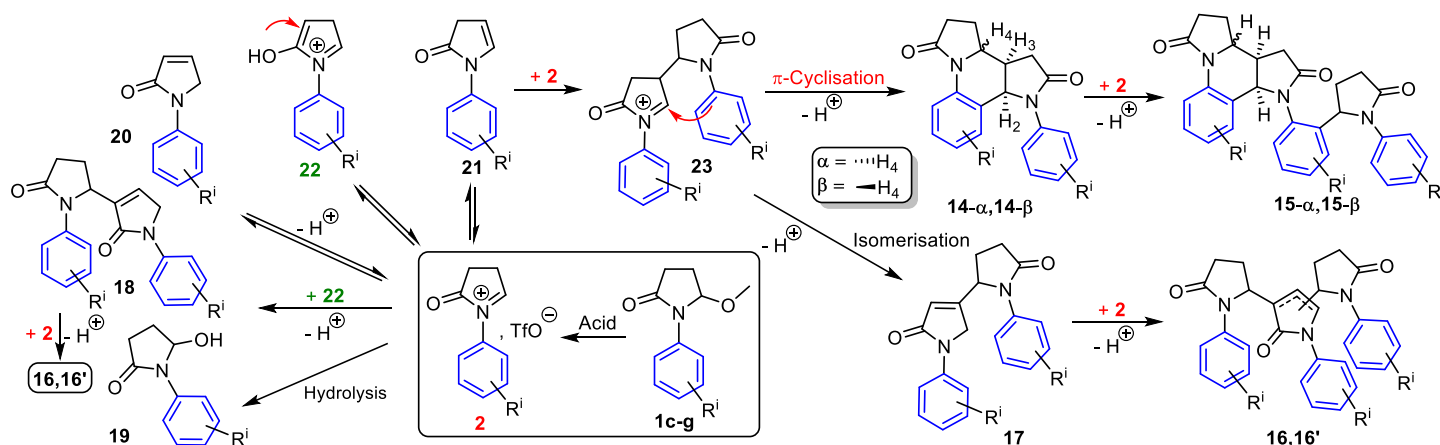
Scheme 9. Plausible mechanism for the formation of **14-20** from pterolactams **1c-g** (R[i] are substituents).

The pioneer work of Speckamp's group in the chemistry of NAI has demonstrated that ω-alkoxy lactams treated with an acid decomposed into several kinds of compounds. Some of them are mentioned in the general mechanism we proposed for the production of derivatives **14-19** (Scheme 9).[22,23,32,33,51-53] Structurally speaking, identification of the obtained products and their stereochemistry in particular of the cyclic dimers **14** and the trimers **15** and **16** were determined by MS, NMM NOESY experiments, and crystallographic analysis, in addition to traditional physico-chemical methodologies.

On the basis of the contributions of Speckamp's group and others in this area,[22,23,32,33,51-53] we identified easily some derivatives such as ω-carbinol lactams **19** and enamides **20**. They, respectively, were formed by a facile hydrolysis or isomerization of the NAI of type **2** in the acid medium. The formation of dimers **17** can be explained by steps-sequence involving the formation of enamides **21** (never isolated in our case), their reaction with NAI **2** followed by deprotonation of intermediate salt **23**, and their spontaneous isomerization. For dimers **18**, the same sequence can be considered, being preceded by the isomerization of the cation **2** into **22** which now acted as carba-nucleophile. Some of these uncyclized dimers scaffolds are described to be unstable depending on the acid used as catalyst.[32,33,51,53]

In another way, the NAI intermediates **23** provided, *via* π-cationic cyclization, the cyclic dimers **14** as two stereoisomers **14**-α and **14**-β. In certain cases, these products were separated by chromatography on silica gel column. Finally, the cyclized trimers **15**-α and **15**-β, for which no-equivalent structure was published yet in the literature, were obtained by regioselective α-amidoalkylation reaction of **14**-α and **14**-β with NAI **2** as nucleophilic and electrophilic partners, respectively.

Part I (Stick drawing **of 14e**-α)   Part II (Stick drawing **of 14e**-β)
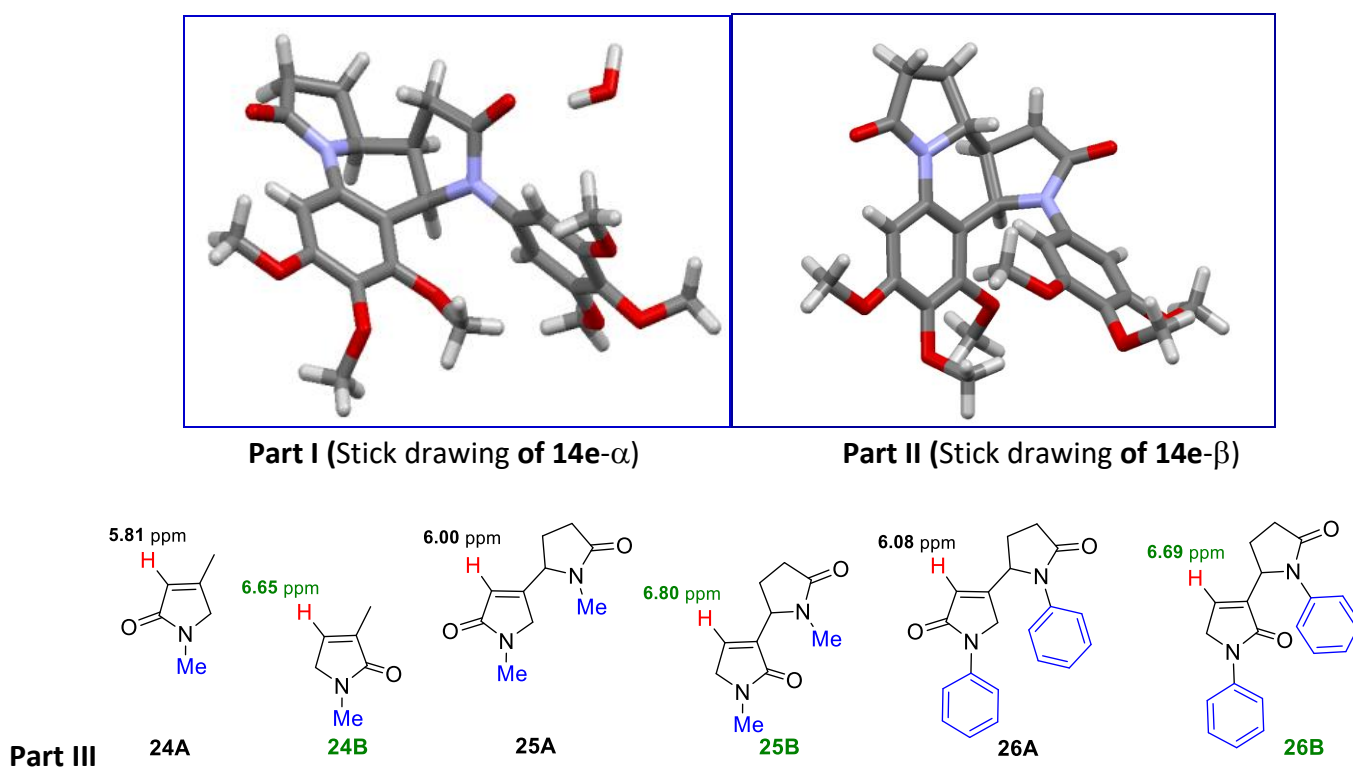
Figure 2. X-ray structure of **14e**-α (**Part I**) and **14e**-β (**Part II**) crystallized, respectively, with one molecule of water or alone. Chemical shifts of the ethylenic proton for **24-26(A,B)** extracted from the literature (**Part III**).

Thanks to the careful NMR interpretation, and especially the chemical shifts of the ethylenic proton extracted from the literature for compounds **24-26(A,B)** (Figure 2),[22,23,48,52] associated with ²D NMR, have

constituted important backgrounds for the identification of a big part of products **14-20** (Schemes 8, 9). On the other side, the X-ray crystal structure of the representative cyclized major isomer **14e**-α and minor isomer **14e**-β was realized;[54] the three contiguous angular protons H_2, H_3 and H_4 (as outlined in Scheme 9) are in the same side for the isomer **14e**-α while H_4 in the opposite side to H_2, H_3 for the isomer **14e**-β (Figure 2). This stereochemistry relationship between the three angular protons is transferred to the high-ranking compounds, the trimers **15**-α and **15**-β, and that was confirmed by the rather simple ^{1}H NMR of trimer **15e**-α for example. Finally, the relative configuration of the contiguous three tertiary stereocenters are found in the structure of natural Incargranine-B (H_{2-4} and H_{3-4} all *cis*)[55] and aglycon of Incargranine-B (H_{2-3} *cis* and H_{3-4} *trans*) whose syntheses were described very recently from an efficient Cu(OTf)$_2$-catalyzed cascade cyclization reaction of simple homopropargylic amines.[56] Noteworthy, taking into account that crystals of trimers **16c** and **16g/16'g** suitable for an X-ray structure confirmation cannot be obtained, and these compounds degrade rapidly in the NMR solvents tried. Their structure was however deduced from their ^{1}D NMR which highlights no similarity with the cyclized trimer **15e**.

Conclusions

Beyond the utility of the amidoalkylation reaction of NAI for the preparation of *N,N*-aminals which can possess desirable FTase activities,[15] we were interested in this contribution to isolate all the products stemming from this reaction conducted with pterolactms under acidic conditions. Surprisingly, in addition to conventional products, we showed that this reaction gives rise to several transformations, sometimes complex, in which the products obtained in small quantities were often ignored in the literature.

    Concisely, the reactivity of pterolactam and its corresponding *N*-aryl derivatives towards TMSOTf and TfOH has been investigated in presence and absence of TMS-protected anilines as aza-nucleophiles. The first set of amines lead to original functionalized quinolines by cascade reactions. The latter include the formation of enamides and *N,N*-aminals *via* NAI, ring opening of *N,N*-aminals into aldimines which are reduced by proton transfer or embarked in an interesting Povarov type reaction (aza-Diels-Alder). The quinolines were finally reached by lactam cleavage, oxidation followed by a trans-amidification.

    On the contrary, without amines, the starting pterolactams under similar acidic conditions generate the classical NAI. The latter NAI unstable undergo hydrolysis in certain cases, or deprotonation into corresponding enamides. These species by α-amidoalkylation furnish cyclized or uncyclized dimers *via* another intermolecular or intramolecular π-cationic cyclisation. These reactions generate the creation of three angular tertiary stereocenters present in different complex alkaloids, whose stereochemical integrity rests intact in trimers obtained ultimately by another α-amidoalkylation with the initially cation. Finally, the relative stereochemistry of the stereocenters being formed was confirmed by X-ray analysis.

Experimental Section

General. Starting materials are commercially available and were used without further purification (suppliers: Carlo Erba Reagents S.A.S., Thermo Fisher Scientific Inc., and Sigma-Aldrich Co.). Melting points were measured on a MPA 100 OptiMelt® apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were acquired at 400 MHz for ^{1}H NMR and at 100 MHz for ^{13}C NMR on a Varian 400-MR spectrometer with tetramethylsilane (TMS) as internal standard, at room temperature (rt). Chemical shifts (δ) are expressed

in ppm relative to TMS. Splitting patterns are designed: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; m, multiplet; sym m, symmetric multiplet; br s, broaden singlet; br t, broaden triplet. Coupling constants (J) are reported in Hertz (Hz). Thin layer chromatography (TLC) was realized on Macherey Nagel silica gel plates with fluorescent indicator and were visualized under a UV-lamp at 254 nm and 365 nm. Column chromatography was performed with a CombiFlash R$_f$ Companion (Teledyne-Isco System) using RediSep packed columns. IR spectra were recorded on a Varian 640-IR FT-IR Spectrometer. Elemental analyses (C, H, N) of new compounds were determined on a Thermo Electron apparatus by 'Pôle Chimie Moléculaire-Welience', Faculté de Sciences Mirande, Université de Bourgogne, Dijon, France. LC-MS was accomplished using an HPLC combined with a Surveyor MSQ (Thermo Electron) equipped with APCI source.

General procedure for the *N*-Csp^2 bond formation (copper-catalyzed coupling). To a suspension of pyrrolidin-2-one (**5a**) or pterolactam (**1a**) (1 equiv.), copper(I) iodide (0.5 equiv.), cesium carbonate (2 equiv.) and the appropriate aryl halide (iodide or bromide) (1.0 equiv.) in anhydrous 1,4-dioxane under inert atmosphere, was added dropwise the coupling ligand, *N,N'*-dimethylethylene diamine (DMEDA, 1-1.2 equiv.) *via* a syringe. The mixture was then stirred at 60 °C for 24 hours, turning blue very quickly. After cooling to rt, the mixture was filtered to remove insoluble salts and the filter cake was washed with dichloromethane. The filtrate was concentrated *in vacuo* and the residue was partitioned between distilled water and dichloromethane. The organic layer was dried over MgSO$_4$ and evaporated to dryness. The crude product was purified by flash chromatography on prepacked SiOH columns (40-63 μm) (eluent EtOAc/*n*-heptane, gradient 0/100 to 100/0) to afford pure N-arylated compounds **5c** or **1c-g**.

5-(3,4,5-Trimethoxyphenylamino)-1-(3,5-dichlorophenyl)-pyrrolidin-2-one (5c). The general copper coupling procedure was followed using 5-(3,4,5-trimethoxyphenylamino)pyrrolidin-2-one (**5a**, 1.00 g, 3.7 mmol, 1,3-dichloro-5-iodobenzene (1.02 g, 3.7 mmol), cesium carbonate (2.44 g, 7.5 mmol), copper(I) iodide (0.36 g, 1.9 mmol), dioxane (30 mL) and DMEDA (0.38 g, 0.47 mL, 4.3 mmol). The crude product was purified by flash chromatography to afford amine **5c** as a white solid in 72% yield (1.1 g); mp (EtOAc/*n*-heptane) 181-182 °C; IR (KBr): v 3329, 3068, 2956, 2886, 1691, 1610, 1545, 1498, 1435, 1389, 1255, 1201, 1128, 1075, 1010, 985, 839, 758 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.08-2.20 (m, 1H, C*H*$_2$CH$_2$CH), 2.47-2.65 (m, 2H, CH$_2$C*H*$_2$CH), 2.69-2.81 (m, 1H, C*H*$_2$CH$_2$CH), 3.76 (s, 3H, OC*H*$_3$), 3.79 (s, 6H, 2OC*H*$_3$), 3.86 (d, *J* 9.4 Hz, 1H, N*H*), 5.53-5.62 (m, 1H, CH$_2$CH$_2$C*H*), 5.82 (s, 2H, Ar*H*), 7.17 (t, *J* 1.9 Hz, 1H, Ar*H*), 7.46 (d, *J* 1.9 Hz, 2H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 26.7 (CH$_2$), 30.2 (CH$_2$), 56.1 (2CH$_3$), 61.0 (CH$_3$), 72.1 (CH), 92.8 (2CH), 121.8 (2CH), 126.0 (CH), 131.8 (C), 135.2 (2C), 139.4 (C), 141.1 (C), 154.2 (2C), 173.6 (C) ppm; LC/MS (APCI$^+$) *m/z* 412.06 (MH$^+$) (calcd for C$_{19}$H$_{20}$Cl$_2$N$_2$O$_4$: 411.29 g/mol).

5-Methoxy-1-(3,4-dimethoxyphenyl)pyrrolidin-2-one (1d). The general copper coupling procedure was followed using pterolactam (**1a**, 5.00 g, 43.5 mmol), 4-bromoveratrole (9.43 g, 43.5 mmol), cesium carbonate (30.68 g, 94.2 mmol), copper(I) iodide (4.10 g, 21.7 mmol), dioxane (100 mL) and DMEDA (3.83 g, 5.50 mL, 43.47 mmol). The crude product was purified by flash chromatography to provide 5-methoxy-1-(3,4-dimethoxyphenyl)-pyrrolidin-2-one (**1d**) as a yellow oil in 20% yield (2.18 g); IR (KBr): v 1696, 1593, 1513, 1452, 1172, 1117 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.99 (bdd, *J* 9.5, 9.2 Hz, 1H, C*H*$_2$CH$_2$CH), 2.09-2.21 (m, 1H, CH$_2$C*H*$_2$CH), 2.33 (ddd, *J* 17.6, 9.7, 2.2 Hz, 1H, C*H*$_2$CH$_2$CH), 2.59 (dt, *J* 17.4, 9.3 Hz, 1H, CH$_2$C*H*$_2$CH), 3.15 (s, 3H, C*H*$_3$), 3.73 (s, 3H, OC*H*$_3$), 3.74 (s, 3H, 2OC*H*$_3$), 5.13 (dd, *J* 6.1 Hz, 1H, CH$_2$CH$_2$C*H*), 6.74 (d, *J* 6.7 Hz, 2H, Ar*H*), 6.84 (dd, *J* 6.1, 2.1 Hz, 1H, Ar*H*), 7.02 (d, *J* 2.1 Hz, 1H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 24.4 (CH$_2$), 29.6 (CH$_2$), 53.8 (CH$_3$), 55.8 (CH$_3$), 55.9 (CH$_3$), 92.4 (CH), 108.1 (CH), 111.2 (C), 115.9 (C), 131.0 (C), 147.3 (C), 148.9 (C), 174.4 (C) ppm; Anal. Calcd for C$_{13}$H$_{17}$NO$_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.32; H, 6.91; N, 5.83%.

5-Methoxy-1-(3,4,5-trimethoxyphenyl)pyrrolidin-2-one (1e). The general copper coupling procedure was followed using pterolactam (**1a**, 2.33 g, 20.2 mmol), 5-bromo-1,2,3-trimethoxy-benzene (5.00 g, 20.2 mmol), cesium carbonate (13.19 g, 40.5 mmol), copper(I) iodide (1.93 g, 10.1 mmol), dioxane (25 mL) and DMEDA (1.78 g, 2.56 mL, 20.2 mmol). The crude product was purified by flash chromatography (EtOAc/*n*-heptane gradient 0/100 to 100/0) to provide 5-methoxy-1-(3,4,5-trimethoxy-phenyl)pyrrolidin-2-one (**1e**) as a white solid in 54% yield (3.06 g); mp (EtOAc/*n*-heptane) 92-93 °C (decomposition); IR (KBr): v 1708, 1585, 1503, 1453, 1126, 1075 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.11-2.19 (dddd, *J* 13.7, 9.4, 2.3, 1.0 Hz, 1H, C*H*$_2$CH$_2$CH), 2.25-2.36 (m, 1H, CH$_2$C*H*$_2$CH), 2.51 (ddd, *J* 17.4, 9.8, 2.5 Hz, 1H, C*H*$_2$CH$_2$CH), 2.76 (dt, *J* 17.4, 9.4 Hz, 1H, CH$_2$C*H*$_2$CH), 3.32 (s, 3H, C*H*$_3$), 3.84 (s, 3H, OC*H*$_3$), 3.86 (s, 6H, 2OC*H*$_3$), 5.26 (dd, *J* 6.1, 1.2 Hz, 1H, CH$_2$CH$_2$C*H*), 6.76 (s, 2H, Ar*H*) *ppm;* ^{13}C NMR (CDCl$_3$, 100 MHz): δ 24.6 (CH$_2$), 29.8 (CH$_2$), 53.9 (CH$_3$), 56.2 (2CH$_3$), 60.9 (CH$_3$), 92.6 (CH), 101.6 (2CH), 133.7 (C), 136.4 (C), 153.3 (2C), 174.5 (C) ppm; LC/MS (APCI$^+$) *m/z* 282.11 (MH$^+$) (calcd for C$_{14}$H$_{19}$NO$_5$: 281.31 g/mol).

5-Methoxy-1-(4-nitrophenyl)pyrrolidin-2-one (1f). The general copper coupling procedure was followed using pterolactam (**1a**, 2.31 g, 20.1 mmol), 1-iodo-4-nitrobenzene (5.02 g, 20.1 mmol), cesium carbonate (13.06 g, 40.1 mmol), copper(I) iodide (1.91 g, 10.0 mmol), dioxane (50 mL) and DMEDA (1.77 g, 2.56 mL, 20.1 mmol). The crude product was purified by flash chromatography to provide 5-methoxy-1-(4-nitrophenyl)-pyrrolidin-2-one (**1f**) as a cream solid in 70% yield (3.3 g); mp (EtOAc/*n*-heptane) 85-86 °C; IR (KBr): v 1707, 1594, 1498, 1192, 1164, 1113 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.20-2.36 (m, 2H, C*H*$_2$CH$_2$CH), 2.56 (ddd, *J* 17.7, 9.2, 2.9 Hz, 1H, CH$_2$C*H*$_2$CH), 2.76 (dt, *J* 19.3, 9.6 Hz, 1H, CH$_2$C*H*$_2$CH), 3.37 (s, 3H, OC*H*$_3$), 5.42 (dd, *J* 5.6, 1.3 Hz, 1H, CHCH$_2$C*H*), 7.83 (d, *J* 9.6 Hz, 2H, Ar*H*), 8.20 (d, *J* 9.6 Hz, 2H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 23.5 (CH$_2$), 30.1 (CH$_2$), 53.0 (CH$_3$), 90.9 (CH), 120.9 (2CH), 124.4 (2CH), 143.3 (C), 144.0 (C), 174.5 (C). Anal. Calcd for C$_{11}$H$_{12}$N$_2$O$_4$: C, 55.93; H, 5.12; N, 11.86. Found: C, 56.27; H, 5.29; N, 12.09%.

1-(1,1'-Biphenyl-4-yl)-5-methoxypyrrolidin-2-one (1g). The general copper coupling procedure was followed using pterolactam (**1a**, 1.65 g, 14.3 mmol), 4-iodobiphenyl (4.00 g, 14.3 mmol), cesium carbonate (9.31 g, 28.6 mmol), copper(I) iodide (1.36 g, 7.1 mmol), dioxane (30 mL) and *N,N'*-dimethyl-ethylenediamine (1.92 mL, 14.34 mmol). The crude product was purified by flash chromatography to provide 5-methoxy-1-biphenyl-pyrrolidin-2-one (**1g**) a white solid in 55% yield (2.10 g); mp (EtOAc/*n*-heptane) 75-76 °C; IR (KBr): v 1709, 1609, 1520, 1485, 1456, 1192, 1166, 1129 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.13 (dddd, *J* 13.7, 9.3, 2.4, 1.1 Hz, 1H, C*H*$_2$CH$_2$CH), 2.20-2.30 (m, 1H, C*H*$_2$CH$_2$CH), 2.49 (m, *J* 17.3, 9.7, 2.4 Hz, 1H, CH$_2$C*H*$_2$CH), 2.76 (dt, *J* 17.4, 8.7 Hz, 1H, CH$_2$C*H*$_2$CH), 3.29 (s, 3H, OC*H*$_3$), 5.35 (dd, *J* 6.0, 1.2 Hz, 1H, CH$_2$CH$_2$C*H*), 7.34 (ddt, *J* 8.1, 6.7, 1.3 Hz, 1H, Ar*H*), 7.42 (bt, *J* 7.6 Hz, 2H, Ar*H*), 7.56 (bd, *J* 7.3 Hz, 2H, ArH), 7.60 (s, 4H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 24.3 (CH$_2$), 30.0 (CH$_2$), 53.5 (CH$_3$), 91.8 (CH), 123.2 (2CH), 127.0 (2CH), 127.3 (CH), 127.6 (2CH), 128.8 (2CH), 137.2 (C), 138.7 (C), 140.4 (C), 174.4 (C) ppm; Anal. Calcd for C$_{17}$H$_{17}$NO$_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.49; H, 6.66; N, 5.17%.

5-(3,4,5-Trimethoxyphenylamino)pyrrolidin-2-one (5a).[15] *N*-(Trimethylsilyl)-3,4,5-trimethoxyaniline (**4a**, 12.21 g, 47.8 mmol) was added to pterolactam (**1a**, 5.00 g, 43.4 mmol) in anhydrous dichloromethane (40 mL) and the solution was stirred under nitrogen atmosphere. TMSOTf (0.25 mL, 0.307 g, 1.4 mmol) (5% vol.) was added through a syringe, and the resulting brownish, homogeneous solution was heated at 50 °C for 8 h. After cooling to room temperature, water (100 mL) and dichloromethane (100 mL) were added, and the mixture was intensively shaken in an extraction funnel, upon which the organic phase lost its brown color and remained slightly beige. The organic phase was washed with water (3 x 100 mL) and dried (MgSO$_4$). The residue obtained upon evaporation was purified by flash chromatography (EtOAc/*n*-heptane gradient 0/100 to 100/0) to provide amine **5a** as a white solid in 55% yield (6.36 g); mp (EtOH) 181-182 °C. IR (KBr): v 3312, 1685, 1598, 1530, 1508, 1467, 1447, 1191, 1114 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.85-1.96 (m, 1H, C*H*$_2$CH$_2$CH),

2.30-2.51 (m, 2H, CH$_2$C*H*$_2$CH), 2.52-2.63 (m, 1H, C*H*$_2$CH$_2$CH), 3.77 (s, 3H, OC*H*$_3$), 3.82 (s, 6H, 2OC*H*$_3$), 3.99 (d, *J* 9.6 Hz, 1H, N*H*), 5.20-5.27 (m, 1H, CH$_2$CH$_2$C*H*), 5.90 (s, 2H, Ar*H*), 6.76 (s, 1H, N*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 28.9 (CH$_2$), 29.2 (CH$_2$), 56.0 (2CH$_3$), 61.1 (CH$_3$), 65.5 (CH), 92.0 (2CH), 131.5 (C), 142.1 (C), 154.2 (2C), 177.0 (C) ppm; LC/MS (APCI$^+$) *m/z* 267.16 (MH$^+$) (calcd for C$_{13}$H$_{18}$N$_2$O$_4$: 266.29 g/mol).

Reaction of pterolactam 1a with *N*-trimethylsilyl-3,4,5-trimethoxyaniline (4a). *N*-(Trimethylsilyl)-3,4,5-trimethoxyaniline (**4a**, 12.21 g, 47.8 mmol) was added under nitrogen to pterolactam (**1a**, 5.00 g, 43.4 mmol) in anhydrous dichloromethane (40 mL). Under stirring, TMSOTf (0.5 mL, 0.704 g, 2.8 mmol) (10% vol.) was added through a syringe, and the resulting brownish, homogeneous solution was heated at 50 °C for 14 h. After cooling to room temperature, water (100 mL) and dichloromethane (100 mL) were added, and the mixture was intensively shaken in an extraction funnel, upon which the organic phase lost its brown color and remained slightly beige. The organic phase was washed with water (3 x 100 mL) and dried (MgSO$_4$). The residue obtained upon evaporation was purified by flash chromatography (EtOAc/*n*-heptane gradient 0/100 to 100/0) to provide the following compounds.

5-(3,4,5-Trimethoxyphenylamino)pyrrolidin-2-one (5a).[15] This product was obtained in 10% yield (1.15 g) as white crystals having a mp and spectral pattern identical to those of **5a** obtained by the former above procedure.

3-(3-((3,4,5-Trimethoxyphenylcarbamoyl)-methyl)-5,6,7-trimethoxyquinol-in-2-yl)propanamide (7a). This product was obtained as white solid in 2% yield (0.2 g); mp (EtOAc/*n*-heptane) 201-203 °C; IR (KBr): ν 3374, 3259, 1662, 1601, 1538, 1509, 1486, 1450, 1126 cm^{-1}; ^{1}H NMR (DMSO-*d$_6$*, 400 MHz): δ 2.87 (t, *J* 7.4 Hz, 2H, C*H*$_2$), 3.19 (t, *J* 7.4 Hz, 2H, C*H*$_2$), 3.61 (s, 3H, OC*H*$_3$), 3.70 (s, 2H, C*H*$_2$), 3.72 (s, 6H, 2OC*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 3.91 (s, 3H, OC*H*$_3$), 3.97 (s, 3H, OC*H*$_3$), 7.02 (s, 2H, Ar*H*), 7.03 (bs, 1H, N*H*$_2$), 7.11 (s, 1H, Ar*H*), 7.66 (bs, 1H, N*H*$_2$), 8.10 (s, 1H, Ar*H*), 9.97 (bs, 1H, N*H*) ppm; ^{13}C NMR (DMSO-*d$_6$*, 100 MHz): δ 30.4 (CH$_2$), 34.7 (CH$_2$), 39.4 (CH$_2$), 56.1 (2CH$_3$), 56.3 (CH$_3$), 60.5 (CH$_3$), 61.3 (CH$_3$), 61.9 (CH$_3$), 97.1 (2CH), 103.9 (CH), 117.4 (C), 126.9 (C), 131.1 (CH), 133.5 (C), 136.1 (C), 140.3 (C), 144.1 (C), 146.7 (C), 153.1 (2C), 155.5 (C), 159.8 (C), 171.4 (C), 172.3 (C) ppm; LC/MS (APCI$^+$) *m/z* 514.23 (MH$^+$) (calcd for C$_{26}$H$_{31}$N$_3$O$_8$: 513.55 g/mol).

3-(3-(Carbamoylmethyl)-5,6,7-trimethoxy-quinolin-2-yl)-*N*-(3,4,5-tri-methoxyphenyl)propanamide (8a). This product was obtained as white solid; 0.15% yield (0.017 g); mp (EtOAc/*n*-heptane) 197-199 °C (decomposition); IR (KBr): ν 3405, 3257, 1664, 1602, 1537, 1510, 1452, 1131 cm^{-1}; ^{1}H NMR (DMSO-*d$_6$*, 400 MHz): δ 2.87 (t, *J* 7.5 Hz, 2H, C*H*$_2$), 3.18 (t, *J* 7.5 Hz, 2H, C*H*$_2$), 3.60 (s, 3H, OC*H*$_3$), 3.68 (s, 2H, C*H*$_2$), 3.72 (s, 6H, 2OC*H*$_3$), 3.84 (s, 3H, OC*H*$_3$), 3.90 (s, 3H, OC*H*$_3$), 3.97 (s, 3H, OC*H*$_3$), 7.02 (bs, 3H, 2Ar*H* + N*H*$_2$), 7.11 (s, 1H, Ar*H*), 7.59 (bs, 1H, N*H*$_2$), 8.09 (s, 1H, Ar*H*), 9.96 (bs, 1H, N*H*) ppm; ^{13}C NMR (DMSO-*d$_6$*, 100 MHz): δ 30.3 (CH$_2$), 34.7 (CH$_2$), 39.3 (CH$_2$), 56.1 (2CH$_3$), 56.2 (CH$_3$), 60.5 (CH$_3$), 61.3 (CH$_3$), 61.9 (CH$_3$), 97.1 (2CH), 103.9 (CH), 117.4 (C), 126.9 (CH), 131.0 (C), 131.8 (C), 136.1 (C), 140.3 (C), 144.1 (C), 146.7 (C), 153.1 (2C), 155.5 (C), 159.8 (C), 171.4 (C), 172.3 (C) ppm; LC/MS (APCI$^+$) *m/z* 514.23 (MH$^+$) (calcd for C$_{26}$H$_{31}$N$_3$O$_8$: 513.55 g/mol).

3-(3-(Carbamoylmethylene)-5,6,7-trimethoxyquinolin-2-yl)propanamide (9a). This product was obtained as white solid; 1% yield (0.076 g); mp (EtOAc/*n*-heptane) 197-199 °C; IR (KBr): ν 3414, 3328, 1661, 1616, 1571, 1484, 1092 cm^{-1}; ^{1}H NMR (DMSO-*d$_6$*, 400 MHz): δ 2.60 (t, *J* 7.8 Hz, 2H, C*H*$_2$), 3.07 (t, *J* 7.8 Hz, 2H, C*H*$_2$), 3.66 (s, 2H, C*H*$_2$), 3.85 (s, 3H, OC*H*$_3$), 3.94 (s, 3H, OC*H*$_3$), 3.97 (s, 3H, OC*H*$_3$), 6.75 (bs, 1H, N*H*$_2$), 7.00 (bs, 1H, N*H*$_2$), 7.13 (s, 1H, Ar*H*), 7.34 (bs, 1H, N*H*$_2$), 7.56 (bs, 1H, N*H*$_2$), 8.07 (s, 1H, Ar*H*) ppm; ^{13}C NMR (DMSO-*d$_6$*, 100 MHz): δ 30.6 (CH$_2$), 33.5 (CH$_2$), 39.3 (CH$_2$), 56.3 (CH$_3$), 61.3 (CH$_3$), 61.9 (CH$_3$), 104.0 (CH), 117.4 (C), 126.9 (C), 131.0 (CH), 140.2 (C), 144.2 (C), 146.6 (C), 155.5 (C), 160.2 (C), 172.4 (C), 174.5 (C) ppm; LC/MS (APCI$^+$) *m/z* 348.14 (MH$^+$) (calcd for C$_{17}$H$_{21}$N$_3$O$_5$: 347.37 g/mol).

4-(3,4,5-Trimethoxyphenylamino)butanamide (10a). This product was obtained in traces as slightly brown oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.93 (q, *J* 6.9 Hz 2H, C*H*$_2$), 2.33 (t, *J* 7.2 Hz, 2H, C*H*$_2$), 3.12 (t, *J* 6.39 Hz, 2H, C*H*$_2$),

3.74 (s, 3H, OCH_3), 3.80 (s, 6H, 2OCH_3), 5.85 (s, 2H, ArH), 6.07 (s, 1H, NH), 6.21 (s, 1H, NH) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 24.9 (CH$_2$), 33.0 (CH$_2$), 43.7 (CH$_2$), 55.9 (2CH$_3$), 61.0 (CH$_3$), 90.2 (2CH), 129.6 (C), 145.3 (C), 153.8 (2C), 175.7 (C).

Reaction of *N*-phenylpterolactam 1a with *N*-(trimethylsilyl)anisidine (4b). *N*-(Trimethylsilyl)anisidine (**4b**, 1.12 g, 5.7 mmol) was added under nitrogen to *N*-phenyl pterolactam (**1b**, 1.00 g, 5.2 mmol) in anhydrous dichloromethane (15 mL). Under stirring, triflic acid (0.20 mL, 0.339 g, 2.3 mmol) (20% vol.) was added through a syringe, and the resulting brownish, homogeneous solution was heated at 40 °C for 96 h. After cooling to room temperature, water (100 mL) and dichloromethane (100 mL) were added, and the mixture was intensively shaken in an extraction funnel, upon which the organic phase lost its brown color and remained slightly beige. The organic phase was washed with water (3 x 100 mL) and dried (MgSO$_4$). The residue obtained upon evaporation was purified by flash chromatography (EtOAc/*n*-heptane gradient 0/100 to 100/0) to provide the following compounds.

3-(3-((Phenylcarbamoyl)methyl)-6-methoxyquinolin-2-yl)-*N*-phenylpropanamide (9b). This product was obtained as white solid; 30% yield (0.345 g); mp (EtOAc/*n*-heptane) 202-204 °C; IR (KBr): ν 3299, 1656, 1599, 1533, 1493, 1235, 1029 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.94 (t, *J* 7.5 Hz, 2H, CH_2), 3.24 (t, *J* 7.5 Hz, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.98 (s, 2H, CH_2), 7.00 (t, *J* 7.4 Hz, 1H, ArH), 7.05 (t, *J* 7.4 Hz, 1H, ArH), 7.24-7.34 (m, 6H, ArH), 7.61 (t, *J* 8.8 Hz, 4H, ArH), 7.80 (d, *J* 8.8 Hz, 1H, ArH), 8.06 (s, 1H, ArH), 10.05 (s, 1H, NH), 10.31 (s, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 29.6 (CH$_2$), 34.0 (CH$_2$), 38.8 (CH$_2$), 55.4 (CH$_3$), 105.2 (CH), 118.9 (2CH), 119.2 (2CH), 121.1 (CH), 122.7 (CH), 123.2 (CH), 127.5 (CH), 128.5 (2CH), 128.6 (2CH), 129.4 (CH), 129.9 (C), 135.4 (CH), 139.0 (C), 139.4 (C), 141.9 (C), 156.8 (C), 157.3 (C), 168.5 (C), 171.0 (C) ppm; LC/MS (APCI$^+$) *m/z* 440.21 (MH$^+$) (calcd for C$_{27}$H$_{25}$N$_3$O$_3$: 439.52 g/mol).

4-(4-Methoxyphenylamino)-*N*-phenylbutanamide (10b). This product was obtained as brown solid; 5% yield (0.075 g); mp (EtOH) 88-89 °C; IR (KBr): ν 3335, 1650, 1597, 1512, 1441, 1233, 1030 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.95 (q, 2H, *J* 6.9 Hz, CH_2), 2.41 (t, *J* 7.2 Hz, 2H, CH_2), 3.09 (t, *J* 6.7 Hz, 2H, CH_2), 3.51-3.62 (m, 1H, NH), 3.71 (s, 3H, OCH_3), 6.54 (dt, *J* 8.9, 3.0 Hz, 2H, ArH), 6.75 (dt, *J* 8.9, 3.0 Hz, 2H, ArH), 7.06 (t, *J* 7.4 Hz, 1H, ArH), 7.26 (t, *J* 7.4 Hz, 2H, ArH), 7.46 (t, *J* 7.9 Hz, 2H, ArH), 7.92 (s, 1H, NH) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 25.2 (CH$_2$), 35.0 (CH$_2$), 44.3 (CH$_2$), 55.8 (CH$_3$), 114.2 (2CH), 114.9 (2CH), 120.0 (2CH), 124.2 (CH), 128.9 (2CH), 138.0 (C), 142.4 (2C), 152.1 (C), 171.3 (C) ppm; LC/MS (APCI$^+$) *m/z* 285.14 (MH$^+$) (calcd for C$_{17}$H$_{20}$N$_2$O$_2$: 284.36 g/mol).

1,2-Bis(4-Methoxyphenyl)diazene (11b). This product was obtained as yellow solid with the same physicochemical properties as described in the literature;[57] 1% yield (0.006 g); mp (EtOAc/*n*-heptane) 162-164 °C;[57] 155-159 °C); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 3.89 (s, 6H, 2OCH_3), 7.00 (d, *J* 8.9 Hz, 2H, ArH), 7.88 (d, *J* 8.9 Hz, 2H, ArH) ppm.

Reaction of *N*-3,5-dichlorophenylpterolactam 1c with *N*-trimethylsilyl-3,4,5-trimethoxyaniline (4a). *N*-Trimethylsilyl-3,4,5-trimethoxyaniline (**4a**, 1.08 g, 4.22 mmol) was added under nitrogen atmosphere to *N*-3,5-dichlorophenyl pterolactam (**1c**, 1.00 g, 3.84 mmol) in anhydrous dichloromethane (15 mL). Under stirring, triflic acid (0.10 mL, 0.17 g, 1.12 mmol) (10% vol.) and glacial acetic acid (0.10 mL) (10% vol.) were added through a syringe, and the resulting brownish, homogeneous solution was heated at 40 °C for 96 hours. After cooling of the reaction to room temperature, water (100 mL) and dichloromethane (100 mL) were added, and the mixture was intensively shaken in an extraction funnel, upon which the organic phase lost its brown color and remained slightly beige. The organic phase was washed with water (3 x 100 mL) and dried (MgSO$_4$). The residue obtained upon evaporation was purified by flash chromatography (EtOAc/*n*-heptane gradient 0/100 to 100/0) to provide the following compounds.

3-(3-((3,5-Dichlorophenylcarbamoyl)methyl)-5,6,7-trimethoxyquinolin-2-yl)-*N*-(3,5-dichlorophenyl)propan-amide (9c). This product was obtained as white solid in 53% yield (0.65 g); mp (EtOAc/*n*-heptane) 257-259 °C

(decomposition); IR (KBr): v 3292, 1680, 1583, 1520, 1443, 1099 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.92 (t, *J* 7.1 Hz, 2H, C*H$_2$*), 3.22 (t, *J* 7.1 Hz, 2H, C*H$_2$*), 3.85 (s, 3H, OC*H$_3$*), 3.91 (s, 3H, OC*H$_3$*), 3.98 (s, 3H, OC*H$_3$*), 4.01 (s, 2H, C*H$_2$*), 7.09 (s, 1H, Ar*H*), 7.22 (t, *J* 1.8 Hz, 1H, Ar*H*), 7.26 (t, *J* 1.8 Hz, 1H, Ar*H*), 7.66 (d, *J* 1.8 Hz, 2H, Ar*H*), 7.67 (d, *J* 1.8 Hz, 2H, Ar*H*) 8.17 (s, 1H, Ar*H*), 10.38 (s, 1H, N*H*), 10.62 (s, 1H, N*H*) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 30.0 (CH$_2$), 34.6 (CH$_2$), 40.4 (CH$_2$), 56.2 (CH$_3$), 61.3 (CH$_3$), 61.9 (CH$_3$), 103.8 (CH), 117.3 (C), 117.4 (2CH), 117.8 (2CH), 122.4 (CH), 123.0 (CH), 125.8 (C), 131.7 (CH), 134.5 (2C), 134.6 (2C), 140.4 (C), 141.8 (C), 142.2 (C), 144.2 (C), 146.7 (C), 155.7 (C), 159.5 (C), 170.1 (C), 172.4 (C) ppm; LC/MS (APCI$^+$) *m/z* 638.05 (MH$^+$) (calcd for C$_{29}$H$_{25}$Cl$_4$N$_3$O$_5$: 637.35 g/mol).

4-(3,4,5-Trimethoxyphenylamino)-*N*-(3,5-dichlorophenylbutanamide (10c). This product was obtained as brown oil in traces; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.97-2.06 (m, 2H, C*H$_2$*), 2.47 (t, *J* 7.0 Hz, 2H, C*H$_2$*), 3.17 (t, *J* 7.0 Hz, 2H, C*H$_2$*), 3.76 (s, 3H, OC*H$_3$*), 3.77 (s, 1H, N*H*), 3.79 (s, 6H, 2OC*H$_3$*), 5.84 (s, 2H, Ar*H*), 7.07 (t, *J* 2.0 Hz, 1H, Ar*H*), 7.45 (t, *J* 2.0 Hz, 2H, Ar*H*), 7.85 (s, 1H, N*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 24.9 (CH$_2$), 34.9 (CH$_2$), 43.7 (CH$_2$), 55.9 (2CH$_3$), 61.1 (CH$_3$), 90.5 (2CH), 117.9 (2CH), 124.0 (CH), 135.1 (2C), 139.8 (C), 143.0 (C), 145.4 (C), 154.0 (2C), 171.3 (C).

(*E*)-Bis(3,4,5-Trimethoxyphenyl)diazene (11c). This product was obtained as yellow-orange solid; 18% yield (0.138 g); mp (EtOAc/*n*-heptane) 208-209 °C;[58] 217-218 °C) with the same physicochemical characteristics as previously described in reference.[58]

General procedures of reaction of *N*-aryl pterolactam 1 with TMSOTf
Method A. TMSOTf (0.05 mL for 1 g of lactam, 5% vol.) was added through a syringe to a stirred solution of *N*-aryl pterolactam **1** in CH$_2$Cl$_2$ (5 mL) placed under nitrogen. The brownish homogeneous solution was stirred at 40 °C for 50-100 hours. After cooling to room temperature, water (25 mL) and dichloromethane (25 mL) were added, and the mixture was intensively shaken in an extraction funnel, upon which the organic phase lost its brown color and remained slightly beige. The organic phase was washed repeatedly with water (3 X 25 mL) and dried (MgSO$_4$). The residue obtained upon evaporation was purified by flash chromatography on prepacked SiOH column (40-63 µm) (eluent: EtOAc/*n*-heptane, gradient 0/100 to 100/0).
Method B. TMSOTf (0.5 mL for 1 g of lactam, 50% vol.) was added through a syringe to a stirred solution of *N*-aryl pterolactam **1** in CH$_2$Cl$_2$ (5 mL) placed under nitrogen. The brownish, homogeneous solution was stirred at rt for 1-2 h. Water (25 mL) and dichloromethane (25 mL) were added, and the mixture was intensively shaken in an extraction funnel, upon which the organic phase lost its brown color and remained slightly beige. The organic phase was washed repeatedly with water (3 x 25 mL) and dried (MgSO$_4$). The residue obtained upon evaporation was purified by flash chromatography on prepacked SiOH column (eluent: EtOAc/*n*-heptane, gradient 0/100 to 100/0).
Reaction of N-(3,5-dichlorophenyl) pterolactam 1c with TMSOTf. The following compounds were obtained using **Method A** and **Method B**.
Method A. *N*-(3,5-Dichlorophenyl)pterolactam (**1c**, 1.0 g, 3.85 mmol) and TMSOTf (0.05 mL, 0.04 g, 0.18 mmol) in CH$_2$Cl$_2$ were stirred at 40 °C for 72 h. **Method B.** *N*-(3,5-Dichlorophenyl)pterolactam (**1c**, 0.50 g, 1.92 mmol) and TMSOTf (0.25 mL, 0.204 g, 0.91 mmol) in 15 mL of CH$_2$Cl$_2$were stirred at rt for 1.5 h.
9,11-Dichloro-1-(3,5-dichlorophenyl)-3a,4,5,11*b*-tetrahydro-1*H*-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6(3*H*,3b*H*)-dione (14c). This product was obtained as white solid (**Method A.** 30% yield (0.263 g); **Method B.** 5% yield (0.022g)); mp (EtOAc/*n*-heptane) 197-200 °C; IR (KBr): v 1698, 1583, 1565, 1441, 1154, 1130 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.74 (quint, *J* 10.4 Hz, 1H, C*H$_2$*CH$_2$CH), 2.33 (d, *J* 16.5 Hz, 1H, C*H$_2$*CH$_2$CH), 2.53-2.58 (m, 2H, CH$_2$C*H$_2$*CH), 2.61-2.73 (m, 2H, C*H$_2$*CH$_2$CH), 3.02 (dd, *J* 16.5, 6.5 Hz, 1H, CH$_2$C*H$_2$*CH), 3.96-4.06 (sym m, *J* 6.7 Hz, 1H, C*H*), 5.36 (d, *J* 4.3 Hz, 1H, C*H*), 6.95 (d, *J* 2.1 Hz, 2H, Ar*H*), 7.22 (d, *J* 1.9 Hz, 1H, Ar*H*), 7.52 (t, *J*

1.9 Hz, 1H, Ar*H*), 8.92 (d, *J* 2.1 Hz, 1H, Ar*H*) ppm; ^{13}C NMR (DMSO-*d*$_6$, 100 MHz): δ 22.5 (CH$_2$), 31.5 (CH$_2$), 33.5 (CH$_2$), 36.0 (CH), 54.7 (CH), 57.6 (CH), 116.5 (2CH), 117.5 (CH), 122.7 (C), 126.9 (CH), 127.9 (2C), 133.1 (CH), 134.4 (C), 137.1 (C), 139.3 (C), 139.7 (C), 172.5 (C), 174.5 (C) ppm; Anal. Calcd for C$_{20}$H$_{14}$Cl$_4$N$_2$O$_2$: C, 52.66; H, 3.09; N, 6.14. Found: C, 52.98; H, 3.41; N, 5.88%.

5,5'-(1-(3,5-dichlorophenyl)-2-oxo-2,3-dihydro-1*H*-pyrrole-3,4-diyl)bis(1-(3,5-dichlorophenyl)pyrrolidin-2-one) (16c). Following the **Method B**, this product was obtained as white solid in 90% yield (0.395 g); mp (EtOH) 218-220 °C; IR (KBr): ν 1703, 1600, 1580, 1445, 1168, 1123 cm^{-1}; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz): δ 0.88-0.95 (m, 1H, C*H$_2$*CH$_2$CH), 1.46-1.58 (m, 1H, C*H$_2$*CH$_2$CH), 1.70-1.84 (m, 1H, CH$_2$C*H$_2$*CH), 1.88-2.06 (m, 2H, C*H$_2$*CH$_2$CH), 2.42-2.58 (m, 5H, C*H$_2$*CH$_2$C*H*), 2.60-2.71 (m, 1H, CH$_2$C*H$_2$*CH), 4.56-4.62 (m, 1H, C*H*), 5.08 (dd, *J* 3.6, 1.8 Hz, 1H, C*H*), 5.33 (d, *J* 8.0 Hz, 1H, C*H*), 7.33 (t, *J* 1.8 Hz, 1H, Ar*H*), 7.43 (t, *J* 1.8 Hz, 1H, Ar*H*), 7.45 (s, 1H, Ar*H*), 7.46 (d, *J* 1.8 Hz, 1H, Ar*H*), 7.56 (d, *J* 1.8 Hz, 1H, Ar*H*), 7.68 (d, *J* 1.8 Hz, 1H, Ar*H*) ppm; ^{13}C NMR (DMSO-*d*$_6$, 100 MHz): δ 16.7 (CH$_2$), 25.0 (CH$_2$), 30.2 (CH$_2$), 31.3 (2CH$_2$), 39.6 (CH), 54.9 (CH), 57.9 (CH), 61.5 (CH), 119.8 (CH), 119.9 (C), 121.4 (CH), 122.8 (2CH), 122.9 (C), 124.1 (CH), 125.3 (CH), 125.8 (CH), 134.6 (C), 134.8 (C), 135.0 (C), 138.9 (C), 139.8 (C), 140.2 (C), 140.9 (C), 141.1 (2C), 168.4 (C), 173.5 (C), 174.7 (C) ppm; Anal. Calcd for C$_{30}$H$_{21}$Cl$_6$N$_3$O$_3$: C, 52.66; H, 3.09; N, 6.14. Found: C, 52.78; H, 3.33; N, 6.37%.

Reaction of *N*-(3,4-dimethoxyphenyl)pterolactam 1d with TMSOTf. The following compounds were obtained following the use of **Method A** and **Method B**.

Method A: *N*-(3,5-Dimethoxyphenyl)pterolactam (**1d**, 0.7 g, 2.8 mmol) and TMSOTf (0.04 mL, 0.043 g, 0.19 mmol) in CH$_2$Cl$_2$ were stirred at 40 °C for 50 h. **Method B:** *N*-(3,5-Dimethoxyphenyl)pterolactam (**1d**, 0.7 g, 2.8 mmol) and TMSOTf (0.35 mL, 0.43 g, 1.9 mmol) in 15 mL of CH$_2$Cl$_2$ were stirred at rt for 1.5 h.

1-(3,4-Dimethoxyphenyl)-9,10-dimethoxy-3*a*,4,5,11*b*-tetrahydro-1*H*-dipyrrolo[1,2-*a*:3',2'-*c*]-quinoline-2,6(3*H*,3b*H*)-dione (14d-α,β). This product was obtained as white solid (**Method A:** 42% yield (0.256 g); **Method B:** 52% yield (0.318 g)); mp (EtOAc/*n*-heptane) 102-105 °C; IR (KBr): ν 1694, 1666, 1591, 1511, 1455, 1153, 1133 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.72-1.89 (m, 1H, C*H$_2$*CH$_2$CH), 2.46 (d, *J* 17.2 Hz, 1H, C*H$_2$*CH$_2$CH), 2.45-2.77 (m, 4H, C*H$_2$*CH$_2$C*H*), 2.98 (dd, *J* 17.2, 7.2 Hz, 1H, CH$_2$C*H$_2$*CH), 3.35 (s, 3H, OC*H$_3$*), 3.75 (s, 3H, OC*H$_3$*), 3.86 (s, 3H, OC*H$_3$*), 3.84-3.91 (m, 1H, C*H*), 3.90 (s, 3H, OC*H$_3$*), 4.88 (d, *J* 5.2 Hz, 1H, C*H*), 5.90 (s, 1H, Ar*H*), 6.46 (d, *J* 2.2 Hz, 1H, Ar*H*), 6.49 (dd, *J* 8.4, 2.2 Hz, 1H, Ar*H*), 6.83 (d, *J* 8.4 Hz, 1H, Ar*H*), 8.38 (s, 1H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 23.1 (CH$_2$), 31.6 (CH$_2$), 34.2 (CH$_2$), 38.3 (CH), 55.5 (CH$_3$), 55.9 (CH$_3$), 56.0 (CH, CH$_3$), 56.1 (CH$_3$), 60.6 (CH), 102.5 (CH), 111.4 (CH), 112.1 (CH), 112.9 (CH), 113.8 (CH), 121.6 (C), 129.4 (C), 130.4 (C), 144.2 (C), 149.0 (C), 149.2 (C), 149.6 (C), 173.0 (C), 173.4 (C) ppm; Anal. Calcd for C$_{24}$H$_{26}$N$_2$O$_6$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.86; H, 6.24; N, 6.70%.

1-(3,4-Dimethoxyphenyl)-5-hydroxypyrrolidin-2-one (19d). This product was obtained as yellow oil (**Method A:** 40% yield (0.264 g); **Method B:** T*races*); IR (KBr): ν 3347, 1668, 1594, 1512, 1452, 1199, 1168, 1109 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.90-1.97 (m, 1H, C*H$_2$*CH$_2$CH), 2.27-2.28 (m, 2H, CH$_2$C*H$_2$*CH), 2.59-2.69 (m, 1H, C*H$_2$*CH$_2$CH), 3.79 (s, 3H, OC*H$_3$*), 3.81 (s, 3H, OC*H$_3$*), 4.45 (d, *J* 7.1 Hz, 1H, O*H*), 5.45 (td, *J* 6.4, 2.0 Hz, 1H, CH$_2$CH$_2$C*H*), 6.78 (d, *J* 8.6 Hz, 1H, Ar*H*), 6.90 (dd, *J* 8.6, 2.4 Hz, 1H, Ar*H*), 7.04 (d, *J* 2.4 Hz, 1H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 28.1 (CH$_2$), 29.5 (CH$_2$), 55.9 (CH$_3$), 56.0 (CH$_3$), 85.6 (CH), 108.4 (CH), 111.2 (CH), 116.3 (CH), 130.3 (C), 147.4 (C), 149.0 (C), 174.7 (C) ppm; Anal. Calcd for C$_{12}$H$_{15}$NO$_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 61.01; H, 6.49; N, 6.22%.

Reaction of *N*-(3,4,5-trimethoxyphenyl)pterolactam 1e with TMSOTf. The following compounds were obtained using **Method A** and **Method B**.

Method A. *N*-(3,4,5-Trimethoxyphenyl)pterolactam (**1e**, 1.00 g, 3.55 mmol) and TMSOTf (0.05 mL, 0.061 g, 0.27 mmol) in CH$_2$Cl$_2$ were stirred at 40 °C for 100 h. **Method B.** *N*-(3,4,5-Trimethoxyphenyl)pterolactam (**1e**, 1.0 g, 3.55 mmol) and TMSOTf (0.5 mL, 0.61 g, 2.71 mmol) in 15 mL of CH$_2$Cl$_2$ were stirred at rt for 1.5 h.

9,10,11-trimethoxy-1-(3,4,5-trimethoxy-phenyl)-3a,4,5,11b-tetrahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6(3H,3bH)-dione (14e). This product was obtained as white solid (**Method A**: 35% yield (0.310 g); **Method B**: 60% yield (0.532 g)); mp (EtOAc/n-heptane) 225-227 °C; IR (KBr): ν 1687, 1591, 1492, 1454, 1132, 1114 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.69 (q, J 10.4 Hz, 1H, CH$_2$CH$_2$CH), 2.23 (d, J 16.4 Hz, 1H, CH$_2$CH$_2$CH), 2.35-2.46 (m, 3H, CH$_2$CH$_2$CH), 2.58-2.70 (m, 1H, CH$_2$CH$_2$CH), 2.92 (dd, J 16.4, 6.6 Hz, 1H, CH$_2$CH$_2$CH), 3.26 (s, 3H, OCH$_3$), 3.43 (s, 3H, OCH$_3$), 3.54 (s, 6H, 2OCH$_3$), 3.58 (s, 3H, OCH$_3$), 3.77 (s, 3H, OCH$_3$), 3.82-3.91 (m, 1H, CH), 5.11 (d, J 4.4 Hz, 1H, CH), 6.04 (s, 2H, ArH), 8.27 (s, 1H, ArH) ppm; ^{13}C NMR (DMSO-d_6, 400 MHz): δ 23.2 (CH$_2$), 32.2 (CH$_2$), 34.5 (CH$_2$), 37.4 (CH), 55.6 (2CH), 56.1 (2CH$_3$), 56.3 (CH$_3$), 59.8 (CH$_3$), 60.4 (CH$_3$), 60.5 (CH$_3$), 97.7 (CH), 106.7 (2CH), 108.0 (C), 133.6 (2C), 136.7 (C), 136.9 (C), 152.5 (C), 152.6 (2C), 154.1 (C), 172.6 (C), 174.3 (C) ppm; LC/MS (APCI^{+}) m/z 499.22 (MH^{+}) (calcd for C$_{26}$H$_{30}$N$_2$O$_8$: 498.54 g/mol).

9,10,11-Trimethoxy-1-{3,4,5-trimethoxy-2-[5-oxo-1-(3,4,5-trimethoxy-phenyl)pyrrolidin-2-yl]-phenyl}-3a,4,5,11b-tetrahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6(3H,3bH)-dione (15e). This product was obtained as white solid (**Method A.** Traces; **Method B.** 24% yield (0.213 g)); mp (EtOAc/n-heptane) 137-139 °C; IR (KBr): ν 3525, 3442, 1674, 1594, 1493, 1452, 1105 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.85-1.97 (m, 1H, CH$_2$CH$_2$CH), 2.25-2.40 (m, 2H, CH$_2$CH$_2$CH), 2.46-2.57 (m, 1H, CH$_2$CH$_2$CH), 2.58-2.74 (m, 6H, 3CH$_2$), 3.34 (s, 3H, OCH$_3$), 3.34-3.43 (m, 1H, CH), 3.56 (s, 3H, OCH$_3$), 3.75 (s, 6H, 2OCH$_3$), 3.80 (s, 6H, 2OCH$_3$), 3.83 (s, 6H, 2OCH$_3$), 3.87 (s, 3H, OCH$_3$), 4.01-4.08 (m, 1H, CH), 5.30 (t, J 7.9 Hz, 1H, CH), 5.49 (d, J 8.9 Hz, 1H, CH), 6.17 (s, 2H, ArH), 6.41 (s, 1H, ArH), 7.71 (s, 1H, ArH) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 20.2 (CH$_2$), 27.3 (CH$_2$), 30.6 (CH$_2$), 31.3 (CH$_2$), 31.6 (CH$_2$), 38.4 (CH), 55.9 (CH$_3$), 56.0 (CH$_3$), 56.1 (2CH$_3$), 57.7 (CH), 58.7 (CH), 59.8 (CH), 60.6 (CH$_3$), 60.7 (CH$_3$), 60.8 (2CH$_3$), 61.3 (CH$_3$), 98.7 (CH), 105.1 (2CH), 108.1 (CH), 111.6 (C), 124.9 (C), 130.8 (C), 133.6 (C), 133.9 (C), 137.2 (C), 137.6 (C), 142.2 (C), 151.5 (C), 152.3 (C), 153.2 (2C), 153.6 (C), 153.9 (C), 172.7 (C), 173.1 (C), 175.7 (C) ppm; LC/MS (APCI^{+}) m/z 748.33 (MH^{+}) (calcd for C$_{39}$H$_{45}$N$_3$O$_{12}$: 747.81 g/mol).

5-Hydroxy-1-(3,4,5-trimethoxyphenyl)pyrrolidin-2-one (19e). This product was obtained as yellow-brownish oil with **Method A** in 40% yield (0.380g). It was also obtained using **Method B** in only 5% yield (0.048 g); IR (KBr): ν 3344, 1671, 1591, 1504, 1451, 1121 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.99-2.09 (m, 1H, CH$_2$CH$_2$CH), 2.35-2.48 (m, 2H, CH$_2$CH$_2$CH), 2.68-2.78 (m, 1H, CH$_2$CH$_2$CH), 3.78 (s, 3H, OCH$_3$), 3.79 (s, 6H, 2OCH$_3$), 3.79 (bs, 1H, OH), 5.58 (dd, J 5.8, 1.6 Hz, 1H, CH$_2$CH$_2$CH), 6.66 (s, 2H, ArH) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 27.9 (CH$_2$), 29.7 (CH$_2$), 56.1 (2CH$_3$), 60.8 (CH$_3$), 85.5 (CH), 102.3 (2CH), 132.9 (C), 136.1 (C), 153.2 (2C), 174.6 (C) ppm; LC/MS (APCI^{+}) m/z 268.10 (MH^{+}) (calcd for C$_{13}$H$_{17}$NO$_5$: 267.28 g/mol).

Reaction of N-(4-nitrophenyl)pterolactam 1f with TMSOTf. The following compounds were obtained by using **Method B** N-(4-nitrophenyl)pterolactam (**1f**, 1.0 g, 4.23 mmol) and TMSOTf (0.5 mL, 0.61 g, 2.7 mmol) in 10 mL of CH$_2$Cl$_2$ were stirred at rt for 1.5 h.

1-(4-Nitrophenyl)-4-(1-(4-nitrophenyl)-5-oxopyrrolidin-2-yl)-1H-pyrrol-2(5H)-one (17f). This product was obtained as cream solid; 25% yield (0.43 g); mp (EtOAc/n-heptane) 149-151 °C; IR (KBr): ν 1711, 1593, 1498, 1156, 1112 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.15-2.26 (m, 1H, CH$_2$CH$_2$CH), 2.55-2.67 (m, 2H, CH$_2$CH$_2$CH), 2.72-2.85 (m, 1H, CH$_2$CH$_2$CH), 4.65 (dd, J 19.4, 1.6 Hz, 1H, CH$_2$), 4.90 (dd, J 19.4, 1.6 Hz, 1H, CH$_2$), 5.56 (dd, J 8.2, 3.1 Hz, 1H, CH), 6.02 (dt, J 1.6, 1.0 Hz, 1H, CH), 7.90 (dd, J 9.4, 2.4 Hz, 2H, ArH), 7.97 (dd, J 9.4, 2.4 Hz, 2H, ArH), 8.24 (dd, J 9.4, 2.4 Hz, 2H, ArH), 8.27 (dd, J 9.4, 2.4 Hz, 2H, ArH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 24.6 (CH$_2$), 31.2 (CH$_2$), 52.3 (CH), 57.9 (CH), 118.0 (2CH), 121.1 (2CH), 123.4 (CH), 125.0 (2CH), 125.4 (2CH), 142.6 (C), 143.4 (C), 144.3 (C), 145.2 (C), 160.9 (C), 170.0 (C), 175.1 (C) ppm; Anal. Calcd for C$_{20}$H$_{16}$N$_4$O$_6$: C, 58.82; H, 3.95; N, 13.72. Found: C, 59.24; H, 4.31; N, 14.01%.

1-(4-Nitrophenyl)-3-(1-(4-nitrophenyl)-5-oxopyrrolidin-2-yl)-1H-pyrol-2(5H)-one (18f). This product was obtained as cream solid; 5% yield (0.043 g); mp (EtOAc/n-heptane) 137-139 °C; IR (KBr): ν 1716, 1682, 1591, 1493, 1442, 1194, 1156, 1111, 1067 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.01-2.12 (m, 1H, CH$_2$CH$_2$CH), 2.53-

2.64 (m, 2H, CH$_2$CH$_2$C*H*), 2.69-2.84 (m, 1H, C*H*$_2$CH$_2$CH), 4.56 (dd, *J* 20.9, 1.2 Hz, 2H, C*H*$_2$), 5.44 (d, *J* 7.3 Hz, 1H, C*H*), 7.26 (dd, *J* 2.2, 1.2 Hz, 1H, C*H*), 7.89 (dd, *J* 9.5, 1.6 Hz, 2H, Ar*H*), 8.03 (dd, *J* 9.5, 1.6 Hz, 2H, Ar*H*), 8.23 (dd, *J* 9.4, 1.5 Hz, 2H, Ar*H*), 8.28 (dd, *J* 9.4, 1.5 Hz, 2H, Ar*H*) ppm; ^{13}C NMR (DMSO-*d$_6$*, 100 MHz) δ (ppm) 24.3 (CH$_2$), 31.3 (CH$_2$), 51.7 (CH), 55.9 (CH), 118.2 (2CH), 121.1 (2CH), 124.9 (2CH), 125.4 (2CH), 137.4 (CH), 141.4 (C), 142.9 (C), 143.3 (C), 144.5 (C), 145.1 (C), 169.1 (C), 175.4 (C) ppm; Anal. Calcd for C$_{20}$H$_{16}$N$_4$O$_6$: C, 58.82; H, 3.95; N, 13.72. Found: C, 59.07; H, 4.15; N, 13.99%.

Reaction of *N*-(biphenyl)pterolactam 1g with TMSOTf. The following compounds were obtained by us sing **Method B**: *N*-(Biphenyl)pterolactam (**1g**, 0.8 g, 2.99 mmol) and TMSOTf (0.4 mL, 0.49 g, 2.2 mmol) in 10 mL of CH$_2$Cl$_2$ were stirred at rt for 1.5 h. Trimers were not stable enough in deuterated solvents to conduct additional experiments to elucidate the exact stereochemical of the trimeric products.

5,5'-(1-([1,1'-Biphenyl]-4-yl)-2-oxo-2,3-dihydro-1*H*-pyrrole-3,4-diyl)bis(1-([1,1'-biphenyl]-4-yl)-pyrrolidin-2-one) (16g). This product was obtained as white solid; 10% yield (0.070 g); mp (EtOAc/*n*-heptane) 259-262 °C; IR (KBr): v 1697, 1606, 1521, 1487, 1156, 1081 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.91-1.05 (m, 1H, C*H*$_2$CH$_2$CH), 1.20-1.29 (m, 3H, C*H*$_2$CH$_2$CH), 1.63-1.68 (m, 1H, CH$_2$CH$_2$C*H*), 1.94-2.01 (m, 2H, C*H*$_2$CH$_2$CH), 2.63-2.74 (m, 3H, C*H*$_2$CH$_2$C*H*), 4.56-4.62 (m, 1H, C*H*), 4.97 (d, *J* 2.4 Hz, 1H, C*H*), 5.46-5.51 (m, 1H, C*H*), 6.70 (d, *J* 1.2 Hz, 1H, C*H*), 7.35-7.49 (m, 12H, Ar*H*), 7.59-7.62 (m, 6H, Ar*H*), 7.65-7.72 (m, 7H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 400 MHz): δ 16.4 (CH$_2$), 25.5 (CH$_2$), 29.8 (CH$_2$), 31.2 (CH$_2$), 55.4 (CH), 57.8 (CH), 61.2 (CH), 121.9 (2CH), 122.7 (2CH), 123.6 (2CH), 127.0 (6CH), 127.5 (CH), 127.7 (2CH), 128.0 (2CH), 128.2 (2CH), 128.3 (2CH), 128.9 (6CH), 134.8 (C), 135.6 (C), 136.2 (C), 136.9 (C), 138.6 (C), 139.2 (C), 139.5 (C), 140.0 (2C), 140.1 (C), 142.7 (C), 168.0 (C), 173.4 (C), 174.2 (C) ppm.

5,5'-(1-([1,1'-Biphenyl]-4-yl)-5-oxo-2,5-dihydro-1*H*-pyrrole-2,4-diyl)bis(1-([1,1'-biphenyl]-4-yl)pyrrolidin-2-one) (16'g). This product was obtained as white solid; 8% yield (0.056 g); mp (EtOAc/*n*-heptane) 175-178 °C; IR (KBr): v 1689, 1605, 1521, 1486, 1156, 1032 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.77-0.84 (m, 1H, C*H*$_2$CH$_2$CH), 1.61-1.67 (m, 1H, C*H*$_2$CH$_2$CH), 1.93-2.01 (m, 1H, CH$_2$CH$_2$C*H*), 2.18-2.23 (m, 3H, C*H*$_2$CH$_2$C*H*), 2.57-2.66 (m, 3H, C*H*$_2$CH$_2$C*H*), 2.90-3.01 (m, 1H, C*H*$_2$CH$_2$C*H*), 4.53-4.59 (m, 1H, C*H*), 4.93 (d, *J* 2.4 Hz, 1H, C*H*), 5.25-5.29 (m, 1H, C*H*), 6.86 (d, *J* 1.2 Hz, 1H, C*H*), 7.31-7.38 (m, 3H, Ar*H*), 7.41-7.48 (m, 9H, Ar*H*), 7.52-7.68 (m, 13H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 16.4 (CH$_2$), 23.5 (CH$_2$), 30.9 (CH$_2$), 31.6 (CH$_2$), 39.4 (CH$_2$), 40.6 (CH), 56.7 (CH), 57.7 (CH), 60.8 (CH), 123.4 (CH), 124.4 (2CH), 124.6 (CH), 126.9 (3CH), 127.0 (3CH), 127.1 (3CH), 127.3 (2CH), 127.7 (2CH), 127.8 (CH), 127.9 (CH), 129.4 (6CH), 135.9 (C), 136.6 (C), 137.4 (C), 137.5 (C), 137.9 (C), 138.0 (C), 139.7 (2C), 139.8 (2C), 139.9 (C), 140.5 (C), 140.8 (C), 167.8 (C), 173.6 (C), 174.6 (C) ppm.

1-(1,1'-Biphenyl-4-yl)-3-[1-(1,1'-biphenyl-4-yl)-5-oxo-pyrrolidin-2-yl]-1,5-dihydro-2*H*-pyrrol-2-one (18g). This product was obtained as white solid; 7% yield (0.049 g); mp (EtOAc/*n*-heptane) 257-260 °C; IR (KBr): v 1677, 1609, 1523, 1485, 1151, 1091 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.14-2.21 (sym m, 1H, C*H*$_2$CH$_2$CH), 2.59-2.72 (m, 2H, C*H*$_2$CH$_2$CH), 2.72-2.80 (m, 1H, CH$_2$CH$_2$C*H*), 4.37 (t, *J* 1.8 Hz, 2H, C*H*$_2$), 5.33 (bd, *J* 5.7 Hz, 1H, C*H*), 6.79 (dd, *J* 3.3, 1.8 Hz, 1H, C*H*), 7.30-7.37 (m, 2H, Ar*H*), 7.40-7.47 (m, 4H, Ar*H*), 7.54-7.67 (m, 10H, Ar*H*), 7.80 (d, *J* 8.8 Hz, 2H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 25.0 (CH$_2$), 31.1 (CH$_2$), 51.2 (CH$_2$), 56.3 (CH), 118.8 (2CH), 121.5 (2CH), 126.8 (2CH), 126.9 (2CH), 127.2 (CH), 127.5 (CH), 127.6 (2CH), 127.7 (2CH), 128.8 (2CH), 128.9 (2CH), 135.8 (2C), 137.1 (CH), 137.3 (C), 137.7 (C), 138.0 (C), 140.0 (C), 140.2 (C), 168.3 (C), 174.5 (C) ppm; Anal. Calcd for C$_{32}$H$_{26}$N$_2$O$_2$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.81; H, 5.72; N, 6.30%.

1-(1,1'-Biphenyl-4-yl)-5-hydroxypyrrolidin-2-one (19g). This product was obtained as white solid; 2% yield (0.015 g); mp (EtOAc/*n*-heptane) 278-180 °C; IR (KBr): v 3218, 1661, 1607, 1522, 1485, 1452, 1166, 1123, 1093 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.00-2.09 (m, 1H, C*H*$_2$CH$_2$C*H*), 2.36-2.52 (m, 2H, C*H*$_2$CH$_2$CH), 2.71-2.83 (m, 1H, C*H*$_2$CH$_2$CH), 3.43 (d, *J* 6.9 Hz, 1H, O*H*), 5.67 (td, *J* 6.4, 1.8 Hz, 1H, C*H*), 7.33 (ddt, *J* 8.1, 6.6, 1.4 Hz, 1H, Ar*H*), 7.41 (tt, *J* 7.5, 1.5 Hz, 2H, Ar*H*), 7.52-7.56 (m, 2H, Ar*H*), 7.58 (s, 4H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz) δ

(ppm) 28.2 (CH$_2$), 29.7 (CH$_2$), 85.1 (CH), 123.6 (2CH), 127.0 (2CH), 127.4 (CH), 127.8 (2CH), 128.8 (2CH), 136.3 (C), 139.0 (C), 140.3 (C), 174.4 (C) ppm; Anal. Calcd for C$_{16}$H$_{15}$NO$_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.02; H, 6.11; N, 5.90%.

1-(1,1'-Biphenyl-4-yl)-1,5-dihydro-2*H*-pyrrol-2-one (20g). This product was obtained as white solid; 2% yield (0.014 g); mp (EtOAc/*n*-heptane) 278-180 °C; IR (KBr): v 1672, 1601, 1525, 1488, 1453, 1147, 1073 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 4.64 (td, *J* 2.0, 0.8 Hz, 2H, C*H$_2$*), 6.27 (dt, *J* 6.1, 2.0 Hz, 1H, C*H*), 7.35 (t, *J* 7.4 Hz, 1H, C*H*), 7.46 (t, *J* 7.7 Hz, 2H, Ar*H*), 7.49 (dt, *J* 6.1, 2.0 Hz, 1H, C*H*), 7.68 (dd, *J* 7.3, 0.9 Hz, 2H, Ar*H*), 7.70 (dd, *J* 9.0, 0.7 Hz, 2H, Ar*H*), 7.88 (dd, *J* 9.0, 0.7 Hz, 2H, Ar*H*) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz): δ 53.6 (CH$_2$), 119.1 (2CH), 126.8 (2CH), 127.5 (3CH), 128.0 (CH), 129.4 (2CH), 135.6 (C), 139.2 (C), 140.0 (C), 145.7 (CH), 170.3 (C) ppm; Anal. Calcd for C$_{16}$H$_{13}$NO: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.73; H, 5.80; N, 6.08%.

Acknowledgements

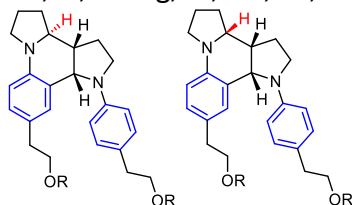## References

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