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

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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.

Keywords: Pterolactams, acid catalysis, N-acyliminiums, inter- and intra-α-amidoalkylation, cascade process.

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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.\textsuperscript{1-6} While the C–heteroatom bond formation proved to be scarce,\textsuperscript{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\textsuperscript{8} or exocyclic\textsuperscript{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.

\textbf{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\textsubscript{β} elimination (E). In the case of NAI of type (II), H\textsubscript{β} elimination can occur giving endocyclic enamidones C\textsuperscript{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\textsuperscript{12-14} we have already explored the reactivity of pterolactam derivatives of type 1 (R = H, Me, CH\textsubscript{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).\textsuperscript{15} In addition, via this reaction, compounds 5\textsubscript{a,b}, and the potential farnesyltransferase (FTase) inhibitors 6\textsubscript{A,B} could be synthesized (Scheme 2).\textsuperscript{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.

**Scheme 2.** $\alpha$-Aminoalkylation of cyclic NAI 2\textsubscript{a} into $N,N$-aminals 5-6 from pterolactams 1 under acid catalysis.

We began the study by re-examining the reaction of pterolactam 1\textsubscript{a} with $N$-trimethylsilylamine 4\textsubscript{a} 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\%.\textsuperscript{15} Thus after heating for 14 h at 50 °C, the $N,N$-aminal product 5\textsubscript{a}\textsuperscript{15} was isolated in only 10% yield after chromatography separation. The latter compound was accompanied by many new compounds identified as the quinolines 7\textsubscript{a}, 8\textsubscript{a} and 9\textsubscript{a} in 0.15% to 2% yields, in addition to the amine 10\textsubscript{a} (trance) and the azo-derivative 11\textsubscript{a} in 1% yield (Scheme 3).

**Scheme 3.** $\alpha$-Aminoalkylation of 1\textsubscript{a} under TMSOTf catalysis.

Considering the literature on slightly related transformations, the formation of compounds 5\textsubscript{a} and 7\textsubscript{a}-11\textsubscript{a} can be explained as described in Scheme 4. Thus, pterolactam 1\textsubscript{a} under acidic conditions can provide the NAI 2\textsubscript{a} which gave the enamide 12\textsubscript{a} by functional equilibration,\textsuperscript{19-23} and also $N,N$-aminal derivative 5\textsubscript{a} by $\alpha$-aminoalkylation\textsuperscript{15} when reacted with TMS aniline 4\textsubscript{a}. All the three compounds 2\textsubscript{a}, 5\textsubscript{a}, and 12\textsubscript{a} are in equilibrium in the acid medium. Ring opening of $N,N$-aminal derivative 5\textsubscript{a} furnished aromatic imine L, which under acid catalyzed Povarov type reaction (aza-Diels-Alder reaction)\textsuperscript{24-30} with enamide 12\textsubscript{a} provided tetrahydroquinoline intermediate M. The latter after lactam ring cleavage\textsuperscript{31-34} furnished dihydroquinoline N.
whose air oxidation provided the isolated quinoline product 9a (1%). Interestingly, no lactam cleavage was reported in related piperidinoquinolones. 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. 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.

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, 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, 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 (R2 = Ph) and 1c (R2 = 1,3-Cl2Ph) were chosen. These substrates 1b,c obtained by N-arylation of pterolactam (1a) under Buchwald type coupling reaction, 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; R2 = 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 Naryl-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 \(\alpha\)-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\(_2\)Cl\(_2\) 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 (\( R = \text{H} \)) as highlighted in Scheme 7.

Scheme 8. Transformation of pterolactams 1c-g without amines under acid catalysis. \textit{Reactions conditions}: Method A: TMSOTf (5 mol%), \( \text{CH}_2\text{Cl}_2 \), 20-50 °C, 2-4 days. Method B: TMSOTf (50 mol%), \( \text{CH}_2\text{Cl}_2 \), 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%\(^d\)     |    |    |      |    |    |    |    |
| SM: 1d       | 42% | -  | 90% | -  | -  | -  | -  |
| 52% (7%)\(^e\) | -  | -  | -  | -  | Traces | -  | -  |
| SM: 1e       | 35% | Traces | -  | -  | -  | 40% | -  |
| 60%         |    |    |      |    |    |    | 5%  |
| SM: 1f       | -  | -  | -  | 25% | 5% | -  | -  |
| SM: 1g       | -  | -  | -  | -  | -  | -  | 2%  |
| 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\(_2\)Cl\(_2\) at 20-50 °C for 2-4 days (Method A), or reactions in CH\(_2\)Cl\(_2\) 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 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)](image1)
![Part II (Stick drawing of 14e-β)](image2)

**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 H2, H3 and H4 (as outlined in Scheme 9) are in the same side for the isomer 14e-α while H4 in the opposite side to H2, H3 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 1H 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 (H2-4 and H3-4 all cis)55 and aglycon of Incargranine-B (H2-3 cis and H3-4 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 1D 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 pterolactams 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 1H NMR and at 100 MHz for 13C 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 Rf 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-Csp² 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 salt 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 filtrate was concentrated in vacuo and the residue was partitioned between distilled water and dichloromethane. The organic layer was dried over MgSO₄ and evaporated to dryness. The crude product was purified by flash chromatography on prepacked SiOH columns (40-63 μm) (elucent EtOAc/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-heptane) 181-182 °C; IR (KBr): ν 3329, 3068, 2956, 2886, 1691, 1610, 1545, 1498, 1435, 1389, 1255, 1201, 1128, 1075, 1010, 985, 839, 758 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.08-2.20 (m, 1H, CH₂CH₂CH₂), 2.47-2.65 (m, 2H, CH₂CH₂CH₂), 2.69-2.81 (m, 1H, CH₂CH₂CH₂), 3.76 (s, 3H, OCH₃), 3.79 (s, 6H, 2OCH₃), 3.86 (d, J 9.4 Hz, 1H, NH), 5.53-5.62 (m, 1H, CH₂CH₂CH₂), 5.82 (s, 2H, ArH), 7.17 (t, J 1.9 Hz, 1H, ArH), 7.46 (d, J 1.9 Hz, 2H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 26.7 (CH₂), 30.2 (CH₂), 56.1 (2CH₃), 61.0 (CH₃), 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⁺) (calcld for C₁₉H₂₀Cl₂N₂O₄: 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): ν 1696, 1593, 1513, 1452, 1172, 1117 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.99 (b dd, J 9.5, 9.2 Hz, 1H, CH₂CH₂CH₂), 2.09-2.21 (m, 1H, CH₂CH₂CH₂), 2.33 (ddd, J 17.6, 9.7, 2.2 Hz, 1H, CH₂CH₂CH₂), 2.59 (dt, J 17.4, 9.3 Hz, 1H, CH₂CH₂CH₂), 3.15 (s, 3H, CH₃), 3.73 (s, 3H, OCH₃), 3.74 (s, 3H, 2OCH₃), 5.13 (dd, J 6.1 Hz, 1H, CH₂CH₂CH₂), 6.74 (d, J 6.7 Hz, 2H, ArH), 6.84 (dd, J 6.1, 2.1 Hz, 1H, ArH), 7.02 (d, J 2.1 Hz, 1H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 24.4 (CH₂), 29.6 (CH₂), 53.8 (CH₃), 55.8 (CH₃), 59.9 (CH₃), 92.1 (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 C₁₉H₂₁NO₄: 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): ν 1708, 1585, 1503, 1453, 1126, 1075 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.11-2.19 (dddd, J 13.7, 9.4, 2.3, 1.0 Hz, 1H, CH₂CH₂CH), 2.25-2.36 (m, 1H, CH₂CH₂CH), 2.51 (dddd, J 17.4, 9.8, 2.5 Hz, 1H, CH₂CH₂CH), 2.76 (dt, J 17.4, 9.4 Hz, 1H, CH₂CH₂CH), 3.32 (s, 3H, CH₃), 3.84 (s, 3H, OCH₃), 3.86 (s, 6H, 2OCH₃), 5.26 (dd, J 6.1, 1.2 Hz, 1H, CH₂CH₂CH), 6.76 (s, 2H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 24.6 (CH₂), 29.8 (CH₂), 53.9 (CH₃), 56.2 (2CH₃), 60.9 (CH₃), 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 C₁₄H₁₉NO₅: 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): ν 1707, 1594, 1498, 1192, 1164, 1113 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.20-2.36 (m, 2H, CH₂CH₂CH), 2.56 (dddd, J 17.7, 9.2, 2.9 Hz, 1H, CH₂CH₂CH), 2.76 (dt, J 19.3, 9.6 Hz, 1H, CH₂CH₂CH), 3.37 (s, 3H, OCH₃), 5.42 (dd, J 5.6, 1.3 Hz, 1H, CH₂CH₂CH), 7.83 (d, J 9.6 Hz, 2H, ArH), 8.20 (d, J 9.6 Hz, 2H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 23.5 (CH₂), 30.1 (CH₂), 53.0 (CH₃), 90.9 (CH), 120.9 (2CH), 124.4 (2CH), 143.3 (C), 144.0 (C), 174.5 (C). Anal. Calcd for C₁₁H₁₂N₂O₄: 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-methoxy-pyrrolidin-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-biphenylpyrrolidin-2-one (1g) a white solid in 55% yield (2.10 g); mp (EtOAc/n-heptane) 75-76 °C; IR (KBr): ν 1709, 1609, 1520, 1485, 1456, 1192, 1166, 1129 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.13 (dddd, J 13.7, 9.3, 2.4, 1.1 Hz, 1H, CH₂CH₂CH), 2.20-2.30 (m, 1H, CH₂CH₂CH), 2.49 (m, J 17.3, 9.7, 2.4 Hz, 1H, CH₂CH₂CH), 2.76 (dt, J 17.4, 8.7 Hz, 1H, CH₂CH₂CH), 3.29 (s, 3H, OCH₃), 5.35 (dd, J 6.0, 1.2 Hz, 1H, CH₂CH₂CH), 7.34 (ddt, J 8.1, 6.7, 1.3 Hz, 1H, ArH), 7.42 (bt, J 7.6 Hz, 2H, ArH), 7.56 (bd, J 7.3 Hz, 2H, ArH), 7.60 (s, 4H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 24.3 (CH₂), 30.0 (CH₂), 53.5 (CH₃), 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 C₁₇H₁₉NO₂: 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 (MgSO₄). 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): ν 3312, 1685, 1598, 1530, 1508, 1467, 1447, 1191, 1114 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.85-1.96 (m, 1H, CH₂CH₂CH),
2.30-2.51 (m, 2H, CH₂CH₂CH₂), 2.52-2.63 (m, 1H, CH₂CH₂CH₂), 3.77 (s, 3H, OCH₃), 3.82 (s, 6H, 2OCH₃), 3.99 (d, J 9.6 Hz, 1H, NH), 5.20-5.27 (m, 1H, CH₂CH₂CH₂), 5.90 (s, 2H, ArH), 6.76 (s, 1H, NH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 28.9 (CH₂), 29.2 (CH₃), 56.0 (2CH₃), 61.1 (CH₃), 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 C₃₃H₁₈N₂O₆: 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 (MgSO₄). 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). 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-trimethoxyquinolin-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): v 3374, 3259, 1662, 1601, 1538, 1509, 1486, 1450, 1126 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 2.87 (t, J 7.4 Hz, 2H, CH₂), 3.19 (t, J 7.4 Hz, 2H, CH₂), 3.61 (s, 3H, OCH₃), 3.70 (s, 2H, CH₂), 3.72 (s, 6H, 2OCH₃), 3.85 (s, 3H, OCH₃), 3.91 (s, 3H, OCH₃), 3.97 (s, 3H, OCH₃), 7.02 (s, 2H, ArH), 7.03 (bs, 1H, NH₂), 7.11 (s, 1H, ArH), 7.66 (bs, 1H, NH₂), 8.10 (s, 1H, ArH), 9.97 (bs, 1H, NH) ppm; ¹³C NMR (DMSO-d₆, 100 MHz): δ 30.4 (CH₂), 34.7 (CH₂), 39.4 (CH₂), 56.1 (2CH₃), 56.3 (CH₃), 60.5 (CH₃), 61.3 (CH₃), 61.9 (CH₃), 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 C₂₆H₃₁N₃O₆: 513.55 g/mol).

3-(3-(Carbamoylmethyl)-5,6,7-trimethoxyquinolin-2-yl)-N-(3,4,5-trimethoxyphenyl)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): v 3405, 3257, 1664, 1602, 1537, 1510, 1452, 1131 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 2.87 (t, J 7.5 Hz, 2H, CH₂), 3.18 (s, 3H, OCH₃), 3.68 (s, 2H, CH₂), 3.72 (s, 6H, 2OCH₃), 3.84 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 3.97 (s, 3H, OCH₃), 7.02 (bs, 3H, 2ArH + NH₂), 7.11 (s, 1H, ArH), 7.59 (bs, 1H, NH₂), 8.09 (s, 1H, ArH), 9.96 (bs, 1H, NH) ppm; ¹³C NMR (DMSO-d₆, 100 MHz): δ 30.3 (CH₂), 34.7 (CH₂), 39.3 (CH₂), 56.1 (2CH₃), 56.2 (CH₃), 60.5 (CH₃), 61.3 (CH₃), 61.9 (CH₃), 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 C₂₆H₃₁N₃O₆: 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): v 3414, 3328, 1661, 1616, 1571, 1484, 1092 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 2.60 (t, J 7.8 Hz, 2H, CH₂), 3.07 (t, J 7.8 Hz, 2H, CH₂), 3.66 (s, 2H, CH₂), 3.85 (s, 3H, OCH₃), 3.94 (s, 3H, OCH₃), 3.97 (s, 3H, OCH₃), 6.75 (bs, 1H, NH₂), 7.00 (bs, 1H, NH₂), 7.13 (s, 1H, ArH), 7.34 (bs, 1H, NH₂), 7.56 (bs, 1H, NH₂), 8.07 (s, 1H, ArH) ppm; ¹³C NMR (DMSO-d₆, 100 MHz): δ 30.6 (CH₂), 33.5 (CH₂), 39.3 (CH₂), 56.3 (CH₃), 61.3 (CH₃), 61.9 (CH₃), 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 C₁₇H₁₂N₂O₅: 347.37 g/mol).

4-(3,4,5-Trimethoxyphenylamino)butanamide (10a). This product was obtained in traces as slightly brown oil; ¹H NMR (CDCl₃, 400 MHz): δ 1.93 (q, J 6.9 Hz 2H, CH₂), 2.33 (t, J 7.2 Hz, 2H, CH₂), 3.12 (t, J 6.39 Hz, 2H, CH₂),...
3.74 (s, 3H, OCH₃), 3.80 (s, 6H, 2OCH₂), 5.85 (s, 2H, ArH), 6.07 (s, 1H, NH), 6.21 (s, 1H, NH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 24.9 (CH₂), 33.0 (CH₂), 43.7 (CH₂), 55.9 (2CH₃), 61.0 (CH₃), 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 then dried (MgSO₄). The residue obtained upon evaporation was purified by flash chromatography (EtOAc/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/heptane) 202-204 °C; IR (KBr): v 3299, 1656, 1599, 1533, 1493, 1235, 1029 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 2.94 (t, J 7.5 Hz, 2H, CH₂), 3.24 (t, J 7.5 Hz, 2H, CH₂), 3.87 (s, 3H, OCH₃), 3.98 (s, 2H, CH₂), 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; ¹³C NMR (DMSO-d₆, 100 MHz): δ 29.6 (CH₂), 34.0 (CH₂), 38.8 (CH₂), 55.4 (CH₃), 105.2 (CH), 118.9 (2CH), 119.2 (2CH), 121.1 (CH), 122.7 (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⁺) (calcld for C₂₇H₂₅N₅O₃: 439.52 g/mol).

**4-(4-Methoxyphenylamino)-(N-phenylbutanamide (10b).** This product was obtained as white solid; 5% yield (0.075 g); mp (EtOH) 88-89 °C; IR (KBr): v 3335, 1650, 1597, 1512, 1441, 1233, 1030 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.95 (q, 2H, J 6.9 Hz, CH₂), 2.41 (t, J 7.2 Hz, 2H, CH₂), 3.09 (t, J 6.7 Hz, 2H, CH₂), 3.51-3.62 (m, 1H, NH), 3.71 (s, 3H, OCH₃), 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; ¹³C NMR (CDCl₃, 100 MHz): δ 25.2 (CH₂), 35.0 (CH₃), 44.3 (CH₃), 55.8 (CH₃), 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⁺) (calcld for C₁₇H₂₀N₂O₂: 284.36 g/mol).

**1,2-Bis(4-Methoxyphenyl)diadene (11b).** This product was obtained as yellow solid with the same physicochemical properties as described in the literature; ¹H NMR (CDCl₃, 400 MHz): δ 3.89 (s, 6H, 2OCH₃), 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 (MgSO₄). The residue obtained upon evaporation was purified by flash chromatography (EtOAc/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)propanamide (9c).** This product was obtained as white solid in 53% yield (0.65 g); mp (EtOAc/heptane) 257-259 °C.
(decomposition); IR (KBr): v 3292, 1680, 1583, 1520, 1443, 1099 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 2.92 (t, J 7.1 Hz, 2H, CH₂), 3.22 (t, J 7.1 Hz, 2H, CH₂), 3.85 (s, 3H, OCH₃), 3.91 (s, 3H, OCH₃), 3.98 (s, 3H, OCH₃), 4.01 (s, 2H, CH₂), 7.09 (s, 1H, ArH), 7.22 (t, J 1.8 Hz, 1H, ArH), 7.26 (t, J 1.8 Hz, 1H, ArH), 7.66 (d, J 1.8 Hz, 2H, ArH), 7.67 (d, J 1.8 Hz, 2H, ArH) 8.17 (s, 1H, ArH), 10.38 (s, 1H, NH), 10.62 (s, 1H, NH) ppm; ¹³C NMR (DMSO-d₆, 100 MHz): δ 30.0 (CH₂), 34.6 (CH₂), 40.4 (CH₂), 56.2 (CH₃), 61.3 (CH₃), 61.9 (CH₃), 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), 170.1 (C), 172.4 (C) ppm; LC/MS (APCI⁺) m/z 638.05 (MH⁺) (calcd for C₂₉H₂₅Cl₅N₅O₇; 637.35 g/mol).

4-(3,4,5-Trimethoxyphenylamino)-N-(3,5-dichlorophenylbutanamide (10c). This product was obtained as brown oil in traces; ¹H NMR (CDCl₃, 400 MHz): δ 1.97-2.06 (m, 2H, CH₂), 2.47 (t, J 7.0 Hz, 2H, CH₂), 3.17 (t, J 7.0 Hz, 2H, CH₂), 3.76 (s, 3H, OCH₃), 3.91 (s, 3H, OCH₃), 3.77 (s, 1H, NH), 3.79 (s, 6H, 2OCH₃), 5.84 (s, 2H, ArH), 7.07 (t, J 2.0 Hz, 1H, ArH), 7.45 (t, J 2.0 Hz, 2H, ArH), 7.85 (s, 1H, NH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 24.9 (CH₂), 34.9 (CH₂), 43.7 (CH₂), 55.9 (2CH₃), 61.1 (CH₃), 90.5 (2CH), 117.0 (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;¹⁸¹ 217-218 °C with the same physicochemical characteristics as previously described in reference.¹⁸¹

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 CH₂Cl₂ (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 (MgSO₄). 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 CH₂Cl₂ (5 mL) placed under nitrogen. The brownish, homogeneous solution was stirred for 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 (MgSO₄). 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 CH₂Cl₂ 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 CH₂Cl₂ were stirred at rt for 1.5 h.

9,11-Dichloro-1-(3,5-dichlorophenyl)-3a,4,5,11b-tetrahydro-1H-dipyrrrolo[1,2-a:3',2'-c]quinoline-2,6(3H,3bH)-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; ¹H NMR (DMSO-d₆, 400 MHz): δ 1.74 (quint, J 10.4 Hz, 1H, CH₂CH₂CH), 2.33 (d, J 16.5 Hz, 1H, CH₂CH₂CH), 2.53-2.58 (m, 2H, CH₂CH₂CH), 2.61-2.73 (m, 2H, CH₂CH₂CH), 3.02 (dd, J 16.5, 6.5 Hz, 1H, CH₂CH₂CH), 3.96-4.06 (sym m, J 6.7 Hz, 1H, CH), 5.36 (d, J 4.3 Hz, 1H, CH), 6.95 (d, J 2.1 Hz, 2H, ArH), 7.22 (d, J 1.9 Hz, 1H, ArH), 7.52 (t, J 9.1 Hz, 1H, ArH), 7.68 (d, J 9.1 Hz, 1H, ArH), 8.16 (s, 1H, ArH), 10.10 (s, 1H, NH), 10.69 (s, 1H, NH) ppm; LC/MS (APCI⁺) m/z 638.05 (MH⁺) (calcd for C₂₉H₂₅Cl₅N₅O₇; 637.35 g/mol).
5,5'-[1-(3,5-dichlorophenyl)-2-oxo-2,3-dihydro-1H-pyrrrole-3,4-diyl]bis(1-(3,5-dichlorophenyl)pypyrolidin-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): v 1703, 1600, 1445, 1168, 1123 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 0.88-0.95 (m, 1H, CH₂CH₂CH₂), 1.46-1.58 (m, 1H, CH₂CH₂CH₂), 1.70-1.84 (m, 1H, CH₂CH₂CH₂), 1.88-2.06 (m, 2H, CH₂CH₂CH₂), 2.42-2.58 (m, 5H, CH₂CH₂CH₂), 2.60-2.71 (m, 1H, CH₂CH₂CH₂), 4.56-4.62 (m, 1H, CH), 5.08 (dd, J 3.6, 1.8 Hz, 1H, CH), 5.33 (d, J 8.0 Hz, 1H, CH), 7.33 (t, J 1.8 Hz, 1H, ArH), 7.43 (t, J 1.8 Hz, 1H, ArH), 7.45 (s, 1H, ArH), 7.46 (d, J 1.8 Hz, 1H, ArH), 7.56 (d, J 1.8 Hz, 1H, ArH), 7.68 (d, J 1.8 Hz, 1H, ArH) ppm; ¹³C NMR (DMSO-d₆, 100 MHz): δ 16.7 (CH₂), 25.0 (CH₂), 30.2 (CH₂), 31.3 (2CH₂), 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 C₇₀H₂₁Cl₆N₃O₅: 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 CH₂Cl₂ 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 CH₂Cl₂ were stirred at rt for 1.5 h.

1-(3,4-Dimethoxyphenyl)-9,10-dimethoxy-3a,4,5,11b-tetrahydro-1H-dipyrrrole[1,2-a:3',2'-c]-quínoline-2,6(3H,3bH)-dione (14α,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): v 1694, 1666, 1591, 1511, 1455, 1153, 1133 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.72-1.89 (m, 1H, CH₂CH₂CH₂), 2.46 (d, J 17.2 Hz, 1H, CH₂CH₂CH₂), 2.45-2.77 (m, 4H, CH₂CH₂CH₂), 2.98 (dd, J 17.2, 7.2 Hz, 1H, CH₂CH₂CH₂), 3.35 (s, 3H, OCH₃), 3.75 (s, 3H, OCH₃), 3.86 (s, 3H, OCH₃), 3.84-3.91 (m, 1H, CH), 3.90 (s, 3H, OCH₃), 4.88 (d, J 5.2 Hz, 1H, CH), 5.90 (s, 1H, ArH), 6.46 (d, J 2.2 Hz, 1H, ArH), 6.49 (dd, J 8.4, 2.2 Hz, 1H, ArH), 6.83 (d, J 8.4 Hz, 1H, ArH), 8.38 (s, 1H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 23.1 (CH₂), 31.6 (CH₂), 34.2 (CH₂), 38.3 (CH), 55.5 (CH₃), 55.9 (CH₃), 56.0 (CH), 56.1 (CH₃), 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 C₂₄H₂₆NO₆: 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: Traces); IR (KBr): v 3347, 1668, 1594, 1512, 1452, 1199, 1168, 1109 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.90-1.97 (m, 1H, CH₂CH₂CH₂), 2.27-2.28 (m, 2H, CH₂CH₂CH₂), 2.59-2.69 (m, 1H, CH₂CH₂CH₂), 3.79 (s, 3H, OCH₃), 3.81 (s, 3H, OCH₃), 4.45 (d, J 7.1 Hz, 1H, OH), 5.45 (td, J 6.4, 2.0 Hz, 1H, CH₂CH₂CH₂), 6.78 (d, J 8.6 Hz, 1H, ArH), 6.90 (dd, J 8.6, 2.4 Hz, 1H, ArH), 7.04 (d, J 2.4 Hz, 1H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 28.1 (CH₃), 29.5 (CH₂), 55.9 (CH₃), 56.0 (CH₃), 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 C₁₂H₁₅NO₄: 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 CH₂Cl₂ 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 CH₂Cl₂ were stirred at rt for 1.5 h.
3a,4,5,11b-tetrahydro-1H-dipyrrrolo[1,2-a:3′,2′-c]quinoline-2,6(3H,3bH)-dione (15e). This product was obtained as yellow-brownish oil with Method A in 40% yield (0.380 g). 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; ¹H NMR (CDCl₃, 400 MHz): δ 1.99-2.09 (m, 1H, CH₂CH₂CH₂), 2.35-2.48 (m, 2H, CH₂CH₂CH₂), 2.67-2.76 (m, 1H, CH₂CH₂CH₂), 3.78 (s, 3H, OCH₃), 3.79 (s, 6H, 2OCH₃), 3.79 (bs, 1H, OH), 5.58 (dd, J 5.8, 1.6 Hz, 1H, CH₂CH₂CH₂), 6.66 (s, 2H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 27.9 (CH₂), 29.7 (CH₂), 56.1 (2CH₂), 60.8 (CH₃), 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 C₁₃H₁₇NO₅: 267.28 g/mol).

Reaction of N-(4-nitrophenyl)teroctlam 1f with TMSOTf. The following compounds were obtained by using Method B N-(4-nitrophenyl)teroctlam 1f (1.0 g, 4.23 mmol) and TMSOTf (0.5 mL, 0.61 g, 2.7 mmol) in 10 mL of CH₂Cl₂ 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 3171, 1610, 1597, 1589, 1527, 1406 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz): δ 2.15-2.26 (m, 1H, CH₂CH₂CH₂), 2.55-2.67 (m, 2H, CH₂CH₂CH₂), 2.72-2.85 (m, 1H, CH₂CH₂CH₂), 4.65 (dd, J 19.4, 1.6 Hz, 1H, CH₂), 4.90 (dd, J 19.4, 1.6 Hz, 1H, CH₂), 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; ¹³C NMR (DMSO-d₆, 100 MHz): δ 24.6 (CH₃), 31.2 (CH₂), 52.3 (CH), 57.9 (CH), 118.0 (2CH), 121.1 (2CH), 123.4 (CH), 125.0 (2CH), 124.3 (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 C₂₀H₁₆N₄O₅: C, 58.82; H, 3.95; N, 13.72. Found: C, 59.24; H, 4.31; N, 14.01%.
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 CH₂Cl₂ were stirred at rt for 1.5 h. Trimeres 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-1H-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): ν 1697, 1606, 1521, 1487, 1156, 1081 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.91-1.05 (m, 1H, CH₂CH₂CH₂), 1.20-1.29 (m, 3H, CH₂CH₂CH₂), 1.63-1.68 (m, 1H, CH₂CH₂CH₂), 1.94-2.01 (m, 2H, CH₂CH₂CH₂), 2.63-2.74 (m, 3H, CH₂CH₂CH₂), 4.56-4.62 (m, 1H, CH), 4.97 (d, J 2.4 Hz, 1H, CH), 5.46-5.51 (m, 1H, CH), 6.70 (d, J 1.2 Hz, 1H, CH), 7.35-7.49 (m, 12H, ArH), 7.59-7.62 (m, 6H, ArH), 7.65-7.72 (m, 7H, ArH) ppm; ¹³C NMR (CDCl₃, 400 MHz): δ 16.4 (CH₂), 25.5 (CH₂), 29.8 (CH₂), 31.2 (CH₂), 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-1H-pyrrole-2,4-diyl]bis[1-[(1,1'-biphenyl)-4-yl]pyrrolidin-2-one] (16g). This product was obtained as white solid; 8% yield (0.056 g); mp (EtOAc/n-heptane) 175-178 °C; IR (KBr): ν 1689, 1605, 1521, 1486, 1156, 1032 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.77-0.84 (m, 1H, CH₂CH₂CH₂), 1.61-1.67 (m, 1H, CH₂CH₂CH₂), 1.93-2.01 (m, 1H, CH₂CH₂CH₂), 2.18-2.23 (m, 3H, CH₂CH₂CH₂), 2.57-2.66 (m, 3H, CH₂CH₂CH₂), 2.90-3.01 (m, 1H, CH₂CH₂CH₂), 4.53-4.59 (m, 1H, CH), 4.93 (d, J 2.4 Hz, 1H, CH), 5.25-5.29 (m, 1H, CH), 6.86 (d, J 1.2 Hz, 1H, CH), 7.31-7.38 (m, 3H, ArH), 7.41-7.48 (m, 9H, ArH), 7.52-7.68 (m, 13H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 16.4 (CH₂), 23.5 (CH₂), 30.9 (CH₂), 31.6 (CH₂), 39.4 (CH₂), 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 (2CH), 129.7 (2CH), 129.9 (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-2H-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): ν 1677, 1609, 1523, 1485, 1151, 1091 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.14-2.21 (sym m, 1H, CH₂CH₂CH₂), 2.59-2.72 (m, 2H, CH₂CH₂CH₂), 2.72-2.80 (m, 1H, CH₂CH₂CH₂), 4.37 (t, J 1.8 Hz, 2H, CH₂), 5.33 (bd, J 5.7 Hz, 1H, CH), 6.79 (dd, J 3.3, 1.8 Hz, 1H, CH), 7.30-7.37 (m, 2H, ArH), 7.40-7.47 (m, 4H, ArH), 7.54-7.67 (m, 10H, ArH), 7.80 (d, J 8.8 Hz, 2H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 25.0 (CH₂), 31.1 (CH₂), 51.2 (CH₂), 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 C₃₂H₂₅N₂O₅: 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-hydroxyptyrroldin-2-one (19g). This product was obtained as white solid; 2% yield (0.015 g); mp (EtOAc/n-heptane) 278-180 °C; IR (KBr): ν 3218, 1661, 1607, 1522, 1485, 1452, 1166, 1123, 1093 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.00-2.09 (m, 1H, CH₂CH₂CH₂), 2.36-2.52 (m, 2H, CH₂CH₂CH₂), 2.71-2.83 (m, 1H, CH₂CH₂CH₂), 3.43 (d, J 6.9 Hz, 1H, OH), 5.67 (td, J 6.4, 1.8 Hz, 1H, CH), 7.33 (ddt, J 8.1, 6.6, 1.4 Hz, 1H, ArH), 7.41 (tt, J 7.5, 1.5 Hz, 2H, ArH), 7.52-7.56 (m, 2H, ArH), 7.58 (s, 4H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ
(ppm) 28.2 (CH₂), 29.7 (CH₂), 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 C₁₆H₁₅NO₂: 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-2H-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): ν 1672, 1601, 1525, 1488, 1453, 1147, 1073 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 4.64 (td, J 2.0, 0.8 Hz, 2H, CH₂), 6.27 (dt, J 6.1, 2.0 Hz, 1H, CH), 7.35 (t, J 7.4 Hz, 1H, CH), 7.46 (t, J 7.7 Hz, 2H, ArH), 7.49 (dt, J 6.1, 2.0 Hz, 1H, CH), 7.68 (dd, J 7.3, 0.9 Hz, 2H, ArH), 7.70 (dd, J 9.0, 0.7 Hz, 2H, ArH) ppm; ¹³C NMR (CDCl₃, 100 MHz): δ 53.6 (CH₂), 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 C₁₆H₁₃NO: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.73; H, 5.80; N, 6.08%.

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