# UPDATES

# Selective Intramolecular Palladium(II)-Catalyzed Aminooxygenation *vs.* Diamination of Alkenylureas: Efficient Microwave-Assisted Reactions to Bicyclic Piperazinones

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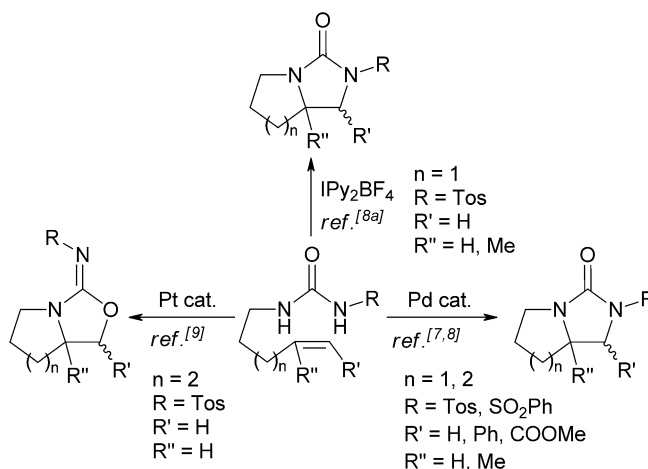
**Abstract:** Alkenylureas arising from glycine allylamides were proven to be suitable substrates for the synthesis of bicyclic five-membered ring-fused piperazinones. The reported intramolecular domino processes, performed under oxidative conditions with bis(acetonitrile)palladium dichloride as catalyst and copper(II) chloride in a stoichiometric amount by microwave activation, were completely selective, involving either diamination or aminooxygenation. While the latter process is determined by the direct intervention of the urea oxygen on the σ-alkylpalladium intermediate, the diamination reaction can in principle derive from a direct attack of the second nitrogen atom on the palladium complex or on the first formed chloromethylpiperazinone. Indeed, this latter species was isolated and proved to be capable of conversion solely into the imidazopiperazinone.

**Keywords:** domino reactions; heterocycles; homogeneous catalysis; microwave chemistry; palladium

## Introduction

The difunctionalization of alkenes under oxidative conditions is a fruitful strategy for the synthesis of various organic compounds.[1] Recent investigations of palladium-catalyzed oxidative reactions have evidenced that domino processes such as aminooxygenations,[2] diaminations,[3] dioxygenations,[4] carboaminations,[5] and aminohalogenations[6] of alkenes can be efficiently used to achieve (poly)functionalized compounds or bicyclic systems.

Alkenylureas have been extensively explored in double intramolecular domino processes providing the formation of oxazole and imidazole bicyclic products either by transition metal-catalyzed reactions,[7,8] or by using iodonium reagents[8a] (Figure 1). These transformations involve an initial carbon-nitrogen bond formation, followed by the intervention of the oxygen or the second nitrogen atom of the urea group on the intermediate to generate the final structure. Among the cyclizations of alkenylureas promoted by transition metals, Muñiz and co-workers have recently reported a palladium-catalyzed reaction which gives selectively the diamination products working with PhI(OAc)$_2$[7] or a Cu(II) salt[8] as oxidants. Conversely, the aminooxygenation process was only occasionally operative when terminally substituted allyl substrates were used.[8a] A totally selective aminooxygenation was obtained in the presence of a catalytic system based on platinum chloride.[9] *N*-Iodosuccinimide-



**Figure 1.** State of the art for the cyclization of alkenylureas.
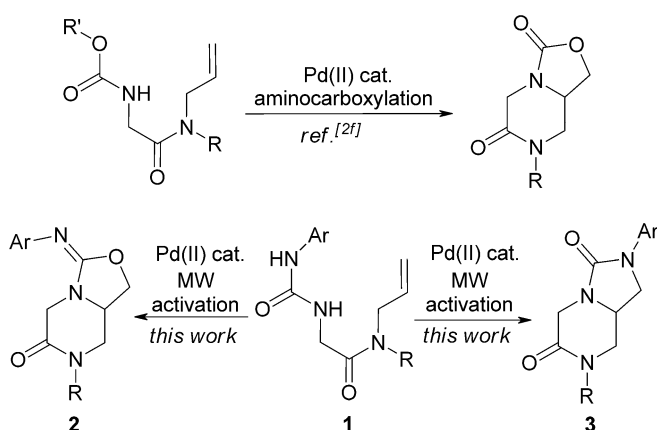
**Scheme 1.** Palladium-catalyzed double intramolecular difunctionalization of alkenylureas.

mediated reactions were proven to be effective to perform diaminations and aminoalkoxylations of *N*-sulfonyl ureas.[10]

As a part of our ongoing interest in constructing hetero-polycyclic compounds by palladium catalysis,[11] we have recently reported the intramolecular aminocarboxylation of *tert*-butoxycarbonyl-protected aminoalkenes catalyzed by palladium in the presence of copper chloride to produce piperazinone derivatives fused to an oxazolidinone ring (Scheme 1).[2f] Herein we describe a selective synthesis of oxazolo- and imidazo-piperazinones (**2** and **3**, respectively) by selective and straightforward Pd(II)-catalyzed microwave-activated aminooxygenation and diamination re-

actions of alkenylureas **1** arising from glycine allylamides.

## Results and Discussion

Initially, we examined the double intramolecular domino reaction on the *N*-phenylurea **1a**, deriving from *N*-allyl-*N*-cyclohexylglycine amide which was chosen as the model. The conditions that successfully promoted the aminocarboxylation process of *N*-Boc-protected allylic amides of α-amino acids, i.e., PdCl$_2$ (MeCN)$_2$ 5 mol% and CuCl$_2$ in a stoichiometric amount in DMF at 100 °C,[2f] resulted in a scarcely selective process, giving a mixture of three products in 39%, 32% and 11% yields, respectively, following the order of chromatographic elution (Table 1, entry 1). Analytical and spectroscopic data allowed us to identify the aminochlorination product **4a** and the bicyclic ring-fused compounds **2a** and **3a**. The distinction between the isomeric oxazolo- and imidazo-piperazine structures **2a** and **3a** was achieved on the basis of the $^{13}$C NMR chemical shifts of the methylene group of the five-membered ring, which resulted to be less shielded for the oxazole ring compared with the imidazole one (67.9 ppm *vs.* 44.4 ppm), in agreement with the literature data.[12]

The outcome of the reaction, although occurring with low selectivity, gave these clues: (i) the PdCl$_2$ (MeCN)$_2$/CuCl$_2$ catalytic system was proven to be suitable for the cyclization of alkenylureas, furnishing piperazinone products by domino processes; (ii) both

**Table 1.** Optimization of selective reaction conditions.
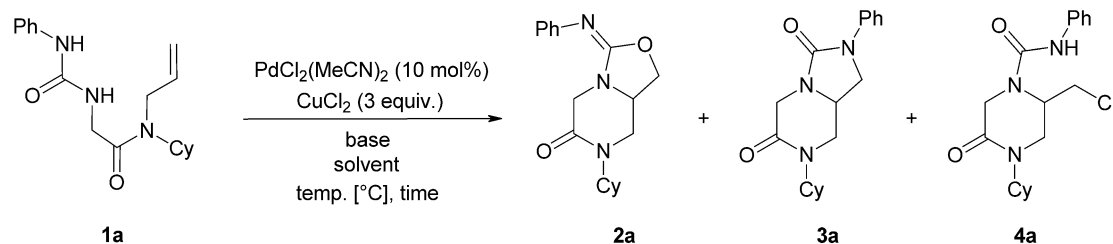


| Entry | Base | Solvent | Temperature [°C] | Time | **2a** [%] | **3a** [%] | **4a** [%] |
|-------|------|---------|------------------|------|------------|------------|------------|
| 1 | – | DMF | 100 | 24 h | 32 | 11 | 39 |
| 2 | – | THF | 60 | 24 h | 83 | – | – |
| 3 | K$_2$CO$_3$ | DMF | 100 | 24 h | 65 | 17 | – |
| 4 | K$_2$CO$_3$ | MeCN | reflux | 24 h | 42 | 9 | – |
| 5 | AcONa | DMF | 100 | 24 h | 27 | 13 | – |
| 6 | DBU | DMF | 100 | 24 h | – | – | – |
| 7 | DIPEA | DMF | 100 | 24 h | – | – | – |
| 8 | DIPEA | CH$_2$Cl$_2$ | 40 | 24 h | – | – | – |
| 9 | K$_2$CO$_3$ | DMF | 150[a] | 15 min | – | 78 | – |
| 10 | K$_2$CO$_3$ | DMF | 60[a] | 30 min | 85 | – | – |
| 11 | – | DMF | 60[a] | 30 min | 85 | – | – |
| 12 | – | DMF | 60 | 24 h | 76 | – | – |

[a] MW activation.

oxygen and nitrogen atoms of the urea group can promote the second step of the process giving the divergent formation of a five-membered ring fused to the piperazine moiety; (iii) besides aminooxygenation reactions analogous to those observed with carbamate derivatives, alkenylureas can undergo aminochlorination and diamination processes.

Both PdCl$_2$(MeCN)$_2$ and CuCl$_2$ were proven to be essential for the conversion of **1a** to bicyclic products.[2f] In order to obtain more selective processes, different parameters including base, solvent and temperature were screened in combination with the established PdCl$_2$(MeCN)$_2$/CuCl$_2$ catalytic system. The most significant results are collected in Table 1. The use of THF at 60 °C gave the aminooxygenation product **2a** in 83% yield (entry 2). Due to the satisfactory behaviour of these conditions to involve the oxygen atom in the domino process, we tested new conditions in the presence of a base to favour the diamination reaction. Although in a few cases the formation of the imidazo[1,5-*a*]pyrazine product **3a** was observed, the use of various bases such as K$_2$CO$_3$, AcONa, DIPEA and DBU in different solvents did not provide a satisfactory outcome of the diamination process (Table 1, entries 3–8). Conversely, the activation by microwave irradiation highlighted the determinant role of temperature to improve the selectivity in the aminooxygenation and diamination pathways. Firstly, the exposure to the microwaves of a DMF solution of **1a** in the presence of K$_2$CO$_3$ at 150 °C for 15 min led to the diamination product **3a** as the sole product, isolated in 78% yield (Table 1, entry 9). Working under the same conditions at lower temperature (60 *vs.* 150 °C) for 30 min, only the aminooxygenation compound **2a** was observed (Table 1, entry 10). Further investigations revealed that the selectivity in this process is preserved on working in the absence of the base at 60 °C, also by conventional heating (Table 1, entries 11 and 12).

Comparing the outcomes of the cyclizations reported in Table 1, in particular the conditions of entries 9 and 10, temperature seems to be determinant for the formation of oxazolyl and imidazolyl compounds. This feature can justify the total selectivity of the diamination product obtained by microwave irradiation working at 150 °C (entry 10), plausibly due to the rapid heating achieved by this activation technique that avoids the alternative product. On the other hand, the possibility that the oxazolo-piperazine **2a** may convert into **3a** by a progressive heating was excluded by the treatment of the former at 150 °C in DMF, either in the absence or in the presence of the catalytic system.

Based on these results, we verified the scope of the reaction on a wide range of alkenylureas, in all cases by microwave irradiation and preferring the presence of K$_2$CO$_3$ in the aminooxygenation reactions (entry 10

of Table 1) to shorten the reaction times. Ureas **1b–j**, easily prepared by removal of the *tert*-butoxycarbonyl group from Boc-glycine allylic amides and subsequent reaction with the appropriate isocyanate, were envisaged as substrates suitable to warrant a satisfactory survey of substituents on the aryl moiety. Aminooxygenation and diamination processes evidenced similar outcomes for all alkenylureas, leading to the bicyclic products **2** and **3** with the yields described in Table 2. It is worth noting that both domino reactions are inhibited by the presence of a substituent such as methyl, phenyl or methoxycarbonyl group on the terminal position of the allylic moiety. The domino processes performed on optically active substrates, such as the *N,N*-allylcyclohexylamide of L-valine and L-phenylalanine, gave in both cases inseparable mixtures of diastereoisomeric bicyclic products.

It should be remarked that the molecular structure of the oxazolo-piperazinone **2d**, obtained from the 2-

**Table 2.** Scope of aminooxygenation and diamination reactions.
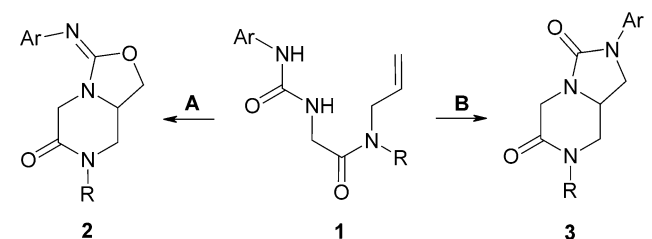


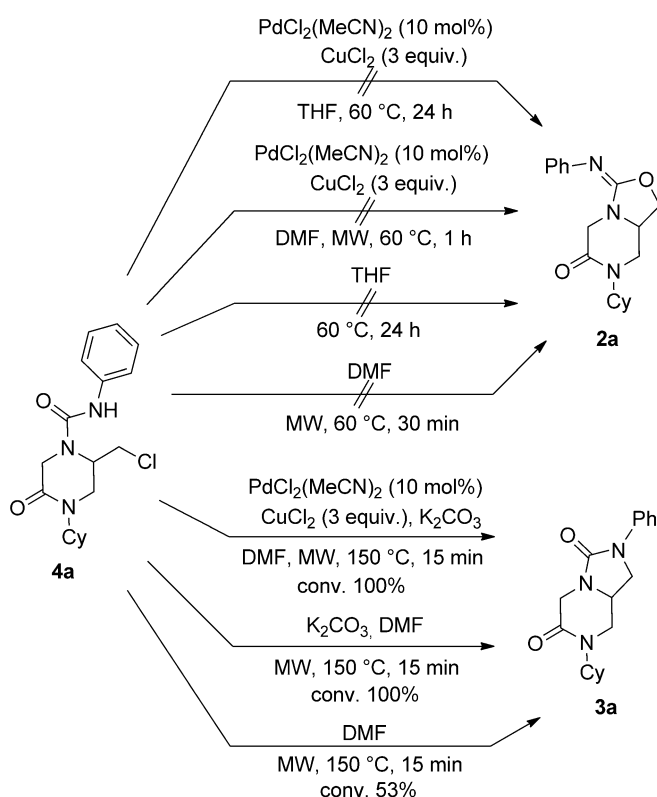| Substrate | R | Ar | Conditions[a] | 2 [%] | 3 [%] |
|---|---|---|---|---|---|
| **1b** | Cy | 4-Cl-C$_6$H$_4$ | **A** | 75 | |
| **1b** | Cy | 4-Cl-C$_6$H$_4$ | **B** | | 73 |
| **1c** | Cy | 4-NO$_2$-C$_6$H$_4$ | **A** | 71 | |
| **1c** | Cy | 4-NO$_2$-C$_6$H$_4$ | **B** | | 78 |
| **1d** | Cy | 2-NO$_2$-C$_6$H$_4$ | **A** | 77 | |
| **1d** | Cy | 2-NO$_2$-C$_6$H$_4$ | **B** | | 80 |
| **1e** | Cy | 4-MeO-C$_6$H$_4$ | **A** | 78 | |
| **1e** | Cy | 4-MeO-C$_6$H$_4$ | **B** | | 79 |
| **1f** | Bn | C$_6$H$_5$ | **C** | 79 | |
| **1f** | Bn | C$_6$H$_5$ | **B** | | 74 |
| **1g** | Bn | 4-Cl-C$_6$H$_4$ | **A** | 76 | |
| **1g** | Bn | 4-Cl-C$_6$H$_4$ | **B** | | 72 |
| **1h** | Bn | 4-NO$_2$-C$_6$H$_4$ | **A** | 72 | |
| **1h** | Bn | 4-NO$_2$-C$_6$H$_4$ | **B** | | 76 |
| **1i** | Bn | 2-NO$_2$-C$_6$H$_4$ | **A** | 74 | |
| **1i** | Bn | 2-NO$_2$-C$_6$H$_4$ | **B** | | 78 |
| **1j** | Bn | 4-MeO-C$_6$H$_4$ | **A** | 77 | |
| **1j** | Bn | 4-MeO-C$_6$H$_4$ | **B** | | 73 |

[a] *Conditions* **A**: PdCl$_2$(MeCN)$_2$ (10 mol%), CuCl$_2$ (3 mmol) and urea (1 mmol), DMF, 60 °C, MW irradiation, 30 min; *conditions* **B**: PdCl$_2$(MeCN)$_2$ (10 mol%), CuCl$_2$ (3 mmol), K$_2$CO$_3$ (3 mmol), and urea (1 mmol), DMF, 150 °C, MW irradiation, 15 min; *conditions* **C**: PdCl$_2$(MeCN)$_2$ (10 mol%), CuCl$_2$ (3 mmol) and urea (1 mmol), THF, 60 °C, 24 h.
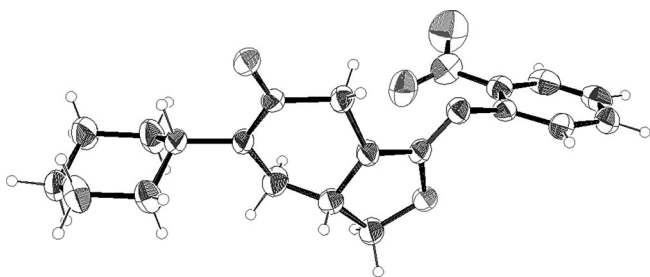
**Figure 2.** Ortep drawing, at 30% probability level, of the molecular structure of species **2d**.

nitrophenyl-substituted urea **1d** by performing the reaction at 60 °C under microwave activation, was confirmed by a single crystal X-ray diffraction study (Figure 2).[13]

Having in hand the aminochlorination product **4a**, we planned some experiments to find indications on its possible role as the precursor for the oxazole and imidazole bicyclic products **2** and **3**.[14] Firstly, chloromethylpiperazinone **4a** was treated under the conditions which were successful in the aminooxygenation process [i.e., PdCl₂(MeCN)₂/CuCl₂ as the catalytic system in THF at 60 °C with conventional heating, or in DMF at 60 °C for 30 min under microwave activation], but no reaction was observed (Scheme 2). The

conversion of compound **4a** was unsuccessful also on heating in THF or by treatment under microwave irradiation in DMF in the absence of the couple PdCl₂(MeCN)₂/CuCl₂. Conversely, on performing the reaction with the catalytic system in DMF at 150 °C under microwave activation, the chloro derivative **4a** was quantitatively converted into the imidazo-piperazinone product **3a**. The transformation into the diamination product was achievable also without Pd catalyst and CuCl₂, even if the presence of K₂CO₃ was required to have a quantitative yield.

This behaviour was confirmed by submitting different chloromethylpiperazinones to aminooxygenation and diamination reactions, as described in Table 3. Compounds **4f**, **h**, **j** were converted solely into the imidazo-fused products **3f**, **h**, **j**, isolated in all cases in high yields.

This investigation on the reactivity of the chloromethylpiperazinones furnished new insights on the mechanism of the double intramolecular domino processes. Even if the conversion of the compound **1** into the imidazole bicyclic product **3** can involve the chloro intermediate **4** or a direct intervention of the nitrogen atom on the σ-alkyl-complex **A**, the aminooxygenation process can only arise from an intramolecular nucleophilic attack by the oxygen atom of the urea on the σ-alkyl-complex **A'** (Figure 3). In both pathways, CuCl₂ would inhibit the common palladium β-hydride elimination favouring the loss of the Pd species through a transient palladium oxidation[15] or by formation of a heterobimetallic σ-Pd/Cu complex.[16] The



**Scheme 2.** Attempts to promote oxygenation and amination reactions from the chloromethyl derivative **4a**.

**Table 3.** Control experiments proving the role of chloromethyl derivatives as possible intermediates toward derivatives **3**.
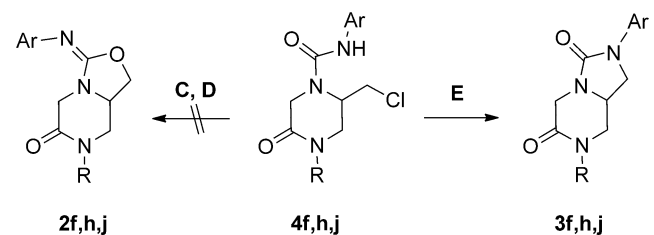


| Substrate | R | Ar | Conditions[a] | 2 [%] | 3 [%] |
|-----------|-----|-----------------------------|---------------|-------|-------|
| **4f** | Bn | C₆H₅ | **E** | – | 92 |
| **4f** | Bn | C₆H₅ | **C, D** | – | – |
| **4h** | Bn | 4-NO₂-C₆H₄ | **E** | – | 97 |
| **4h** | Bn | 4-NO₂-C₆H₄ | **C, D** | – | – |
| **4j** | Bn | 4-MeO-C₆H₄ | **E** | – | 89 |
| **4j** | Bn | 4-MeO-C₆H₄ | **C, D** | – | – |

[a] *Conditions* **C**: PdCl₂(MeCN)₂ (10 mol%), CuCl₂ (3 mmol) and urea (1 mmol), THF, 60 °C, 24 h; *conditions* **D**: PdCl₂(MeCN)₂ (10 mol%), CuCl₂ (3 mmol), and urea (1 mmol), DMF, 60 °C, MW irradiation, 1 h; *conditions* **E**: K₂CO₃ (3 mmol) and urea (1 mmol), DMF, 150 °C, MW irradiation, 15 min.
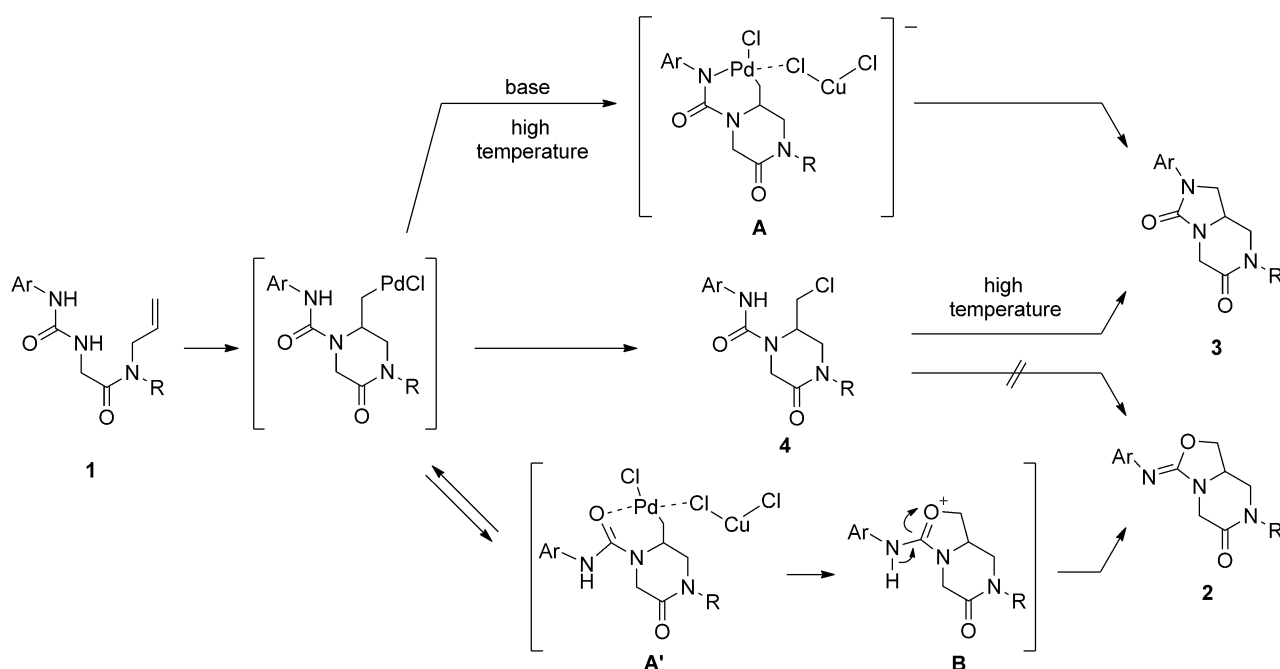
**Figure 3.** Proposed mechanism for the Pd(II)/CuCl₂-mediated aminooxygenation and diamination reactions.

aminooxygenation process generates the intermediate **B** and the elimination of H⁺ furnishes the product **2**. The domino processes plausibly occur by a selective *trans*-amino-palladation, as proven by studies conducted on deuterated unfunctionalized aminoalkenes.[7a]

In the attempt to convert the chloro derivatives into the bicyclic products, the results observed matched the hypothesis proposed about the cyclization of the analogous alkenyl carbamates,[2f] where chloromethyl-substituted products were never detected, making plausible a direct attack of the oxygen atom of the *tert*-butoxycarbonyl group on the palladium intermediate.

## Conclusions

In conclusion, we have developed selective double intramolecular aminooxygenation and diamination reactions of alkenylureas to yield bicyclic products containing a piperazinone ring. These Pd(II)-catalyzed transformations under microwave irradiation provide efficient and selective synthetic protocols for the construction of 3-arylimino-oxazolo[3,4-*a*]pyrazin-6-one and 2-aryl-imidazo[1,5-*a*]pyrazin-3,6-dione derivatives in few steps from readily available precursors. The aminooxygenation process can also be carried out in satisfactory yield by conventional heating, even if the reaction times are longer. From the mechanistic point of view, the reactions performed on the chloromethyl-piperazinones allowed us to exclude their involve-

ment as intermediates in the aminooxygenation pathway.

## Experimental Section

### General Remarks

Reagents and solvents were used as received from commercial sources. Flash column chromatography was performed employing 230–400 mesh silica gel. Analytical thin layer chromatography was performed on silica gel 60 F254. Melting points were measured with a Büchi B-540 apparatus and are uncorrected. IR spectra were recorded on a 550 Nicolet FT-IR spectrophotometer. Nuclear magnetic resonance spectra were acquired on an AVANCE 400 Bruker spectrometer operating at 400 MHz for ¹H NMR and 100 MHz for ¹³C NMR. ¹³C spectra were ¹H decoupled and multiplicities were determined by the APT pulse sequence. Mass spectra were determined on an HPLC-MS LCQ-Advantage Thermo Finnigan instrument. Elemental analyses were executed on a PerkinElmer CHN Analyzer Series II 2400.

Detailed procedures for the preparation of alkenylureas and details on the X-ray diffraction measurement and analysis are available as Supporting Information.

### General Procedure for the Aminooxygenation Reactions

A mixture of PdCl₂(MeCN)₂ (0.1 mmol), CuCl₂ (3 mmol) and urea **1** (1 mmol) in DMF (10 mL) was heated at 60 °C for 30 min under microwave irradiation. Brine (15 mL) was added and the mixture was extracted with CH₂Cl₂ (3× 15 mL). The organic phase was dried over Na₂SO₄ and the solvent removed under reduced pressure. The crude mixture

was purified by silica gel column chromatography (petroleum ether/AcOEt 3:7).

**7-Cyclohexyl-3-(phenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2a):** Yield: 85%; white solid; mp 156 °C. IR: $\nu = 1757$, 1585 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.25$–1.82 [m, 10 H, (CH$_2$)$_5$], 3.15 (dd, 1 H, $J = 11.1$, 9.8 Hz, NCHH), 3.28 (dd, 1 H, $J = 11.1$, 3.8 Hz, NCHH), 3.82–3.87 (m, 1 H, NCH), 3.88 (d, $J = 17.8$ Hz, 1 H, CHH), 4.02 (dd, 1 H, $J = 8.6$, 4.4 Hz, OCHH), 4.43 (dd, 1 H, $J = 8.6$, 7.4 Hz, OCHH), 4.46–4.52 [m, 1 H, NCH(CH$_2$)$_5$], 4.53 (d, 1 H, $J = 17.8$ Hz, CHH) 6.89–6.98 (m, 1 H, ArH), 7.05 (d, 2 H, $J = 7.6$ Hz, ArH), 7.20–7.24 (m, 2 H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.6 (t), 29.3 (t), 29.6 (t), 43.6 (t), 46.4 (t), 51.6 (d), 52.6 (d), 67.9 (t), 122.5 (d), 124.4 (d), 128.5 (d), 146.6 (s), 150.9 (s), 164.3 (s); MS: $m/z = 313$ (M$^+$); anal. calcd. for C$_{18}$H$_{23}$N$_3$O$_2$: C 68.98, H 7.40, N 13.41; found: C 69.17, H 7.14, N 13.50.

**7-Cyclohexyl-3-(4-chlorophenylimino),1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2b):** Yield: 75%; white solid; mp 103 °C. IR: $\nu = 1755$, 1588, 1089 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.33$–1.84 [m, 10 H, (CH$_2$)$_5$], 3.23 (dd, 1 H, $J = 11.1$, 9.2 Hz, NCHH), 3.35 (dd, 1 H, $J = 11.1$, 3.8 Hz, NCHH), 3.95 (d, 1 H, $J = 18.2$ Hz, CHH), 3.95–4.02 (m, 1 H, NCH), 4.11 (dd, 1 H, $J = 8.4$, 4.3 Hz, OCHH), 4.51–5.56 (m, 3 H, OCHH, NCH(CH$_2$)$_5$, CHH), 7.01 (d, 2 H, $J = 8.6$ Hz, ArH), 7.19 (d, 2 H, $J = 8.7$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.7 (t), 43.7 (t), 46.3 (t), 51.7 (d), 52.6 (d), 68.0 (t), 124.7 (d), 128.7 (d), 145.0 (s), 147.2 (s), 151.1 (s), 164.2 (s); MS: $m/z = 347$ (M$^+$); anal. calcd. for C$_{18}$H$_{22}$ClN$_3$O$_2$: C 62.15, H 6.37, N 12.08; found: C 61.91, H 6.61, N 12.31.

**7-Cyclohexyl-3-(4-nitrophenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2c):** Yield: 71%; yellow solid; mp 118 °C. IR: $\nu = 1750$, 1581, 1522, 1349 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.17$–1.83 [m, 10 H, (CH$_2$)$_5$], 3.26 (dd, 1 H, $J = 11.0$, 9.2 Hz, NCHH), 3.43 (dd, 1 H, $J = 11.0$, 3.8 Hz, NCHH), 3.97 (d, 1 H, $J = 18.3$ Hz, CHH), 3.98–4.11 (m, 1 H, NCH), 4.20 (dd, 1 H, $J = 8.6$, 4.5 Hz, OCHH), 4.57 (d, 1 H, $J = 18.3$ Hz, CHH), 4.61–4.65 (m, 2 H, OCHH, NCH(CH$_2$)$_5$), 7.16 (d, 2 H, $J = 9.0$ Hz, ArH), 8.11 (d, 2 H, $J = 8.9$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.7 (t), 43.8 (t), 46.1 (t), 51.7 (d), 52.6 (d), 68.4 (t), 123.8 (d), 125.0 (d), 142.6 (s), 151.9 (s), 153.4 (s), 164.2 (s); MS: $m/z = 358$ (M$^+$); anal. calcd. for C$_{18}$H$_{22}$N$_4$O$_4$: C 60.32, H 6.19, N 15.63; found: C 60.39, H 6.32, N 15.49.

**7-Cyclohexyl-3-(2-nitrophenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2d):** Yield: 77%; yellow solid; mp 126 °C. IR: $\nu = 1754$, 1579, 1492, 1333 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.18$–1.84 [m, 10 H, (CH$_2$)$_5$], 3.35–3.38 (m, 2 H, NCHH, NCHH), 3.98 (d, 1 H, $J = 18.2$ Hz, CHH), 4.01–4.05 (m, 1 H, NCH), 4.08 (dd, 1 H, $J = 8.6$, 3.8 Hz, OCHH), 4.46 (dd, 1 H, $J = 8.6$, 7.2 Hz, OCHH), 4.53–4.55 (m, 1 H, NCH(CH$_2$)$_5$), 4,56 (d, 1 H, $J = 18.2$ Hz, CHH) 7.04–7.12 (m, 2 H, ArH), 7.42–7.46 (m, 1 H, ArH), 7.87(dd, 1 H, $J = 8.4$, 1.4 Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.7 (t), 43.9 (t), 46.3 (t), 52.4 (d), 52.6 (d), 67.8 (t), 122.4 (d), 124.9 (d), 126.6 (d), 133.3 (d), 142.4 (s), 142.8 (s), 152.5 (s), 163.8 (s); MS: $m/z = 358$ (M$^+$); anal. calcd. for C$_{18}$H$_{22}$N$_4$O$_4$: C 60.32, H 6.19, N 15.63; found: C 60.09, H 6.41, N 15.70.

**7-Cyclohexyl-3-(4-methoxyphenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2e):** Yield: 78%; white solid; mp 129 °C. IR: $\nu = 1749$, 1589, 1260 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.25$–1.83 [m, 10 H, (CH$_2$)$_5$], 3.22 (dd, 1 H, $J = 11.1$, 9.3 Hz, NCHH), 3.34 (dd, 1 H, $J = 11.1$, 3.8 Hz, NCHH), 3.76 (s, 3 H, OCH$_3$), 3.89–3.93 (m, 1 H, NCH), 3.91 (d, 1 H, $J = 18.2$ Hz, CHH), 4.06 (dd, 1 H, $J = 8.6$, 4.5 Hz, OCHH), 4.47 (dd, 1 H, $J = 8.6$, 7.3 Hz, OCHH), 4.49–4.51 (m, 1 H, NCH(CH$_2$)$_5$), 4.54 (d, 1 H, $J = 18.2$ Hz, CHH), 6.80 (d, 2 H, $J = 8.9$ Hz, ArH), 7.02 (d, 2 H, $J = 8.9$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.5 (t), 25.5 (t), 29.3 (t), 29.7 (t), 43.6 (t), 46.5 (t), 51.7 (d), 52.5 (d), 55.4 (q), 67.8 (t), 113.9 (d), 124.1 (d), 139.6 (s), 150.7 (s), 155.2 (s), 164.4 (s); MS: $m/z = 343$ (M$^+$); anal. calcd. for C$_{19}$H$_{25}$N$_3$O$_3$: C 66.45, H 7.34, N 12.24; found: C 66.38, H 7.62, N 12.47.

**7-Benzyl-3-(phenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2f):** Yield: 79%; colourless oil. IR: $\nu = 1758$, 1587 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.26$ (dd, 1 H, $J = 10.9$, 4.0 Hz, NCHH), 3.36 (dd, 1 H, $J = 10.9$, 9.4 Hz, NCHH), 3.95–4.03 (m, 3 H, OCHH, CHH, NCH), 4.41–4.46 (m, 1 H, OCHH), 4.46 (d, 1 H, $J = 14.2$ Hz, CHHPh), 4.67 (d, 1 H, $J = 18.3$ Hz, CHH), 4.88 (d, 1 H, $J = 14.2$ Hz, CHHPh), 7.00–7.07 (m, 2 H, ArH) 7.50–7.23 (m, 8 H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 46.1$ (t), 48.4 (t), 50.4 (t), 51.3 (d), 67.7 (t), 122.7 (d), 124.0 (d), 128.0 (d), 128.2 (d), 128.6 (d), 128.9 (d), 139.7 (s), 146.4(s), 150.7 (s), 165.1 (s); MS: $m/z = 321$ (M$^+$); anal. calcd. for C$_{19}$H$_{19}$N$_3$O$_2$: C 71.01, H 5.96, N 13.08; found: C 70.83, H 6.25, N 13.21.

**7-Benzyl-3-(4-chlorophenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2g):** Yield: 76%; white solid; mp 107 °C. IR: $\nu = 1748$, 1584, 1098 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.26$ (dd, 1 H, $J = 11.3$, 3.8 Hz, NCHH), 3.48 (dd, 1 H, $J = 11.3$, 9.1 Hz, NCHH), 4.00 (d, 1 H, $J = 18.6$ Hz, CHH), 4.01–4.02 (m, 2 H, OCHH, NCH), 4.44–4.48 (m, 1 H, OCHH), 4.47 (d, 1 H, $J = 14.4$ Hz, CHHPh), 4.64 (d, 1 H, $J = 18.2$ Hz, CHH), 4.88 (d, 1 H, $J = 14.4$ Hz, CHHPh), 7.00 (d, 2 H, $J = 8.7$ Hz, ArH), 7.19 (d, 2 H, $J = 8.6$ Hz, ArH) 7.27–7.32 (m, 6 H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 44.5$ (t), 48.4 (t), 50.4 (t), 51.2 (d), 67.8 (t), 118.5 (s), 124.7 (d), 127.7 (d), 128.0 (d), 128.3 (d), 128.5 (d), 128.9 (d), 135.8 (s), 144.9 (s), 150.9 (s), 164.9 (s); MS: $m/z = 335$ (M$^+$); anal. calcd. for C$_{19}$H$_{18}$ClN$_3$O$_2$: C 64.13, H 5.10, N 11.81; found: C 64.20, H 4.85, N 11.51.

**7-Benzyl-3-(4-nitrophenylimino)-1,7,8,8a-tetrahydro-3*H*-oxazolo[3,4-*a*]pyrazine-6(5*H*)-one (2h):** Yield: 72%; pale yellow solid; mp 124 °C. IR: $\nu = 1760$, 1588, 1519, 1340 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.32$ (dd, 1 H, $J = 11.2$, 4.0 Hz, NCHH), 3.39 (dd, 1 H, $J = 11.2$, 9.2 Hz, NCHH), 4.00 (d, 1 H, $J = 18.4$ Hz, CHH), 4.06–4.13 (m, 2 H, OCHH, NCH), 4.47 (d, 1 H, $J = 14.6$ Hz, CHHPh), 4.54 (dd, 1 H, $J = 8.4$, 2.2 Hz, OCHH), 4.67 (d, 1 H, $J = 18.4$ Hz, CHH), 4.88 (d, 1 H, $J = 14.6$ Hz, CHHPh), 7.14–7.26 (m, 2 H, ArH), 7.27–7.37 (m, 5 H, ArH), 8.01–8.12 (m, 2 H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 45.9$ (t), 48.5 (t), 50.5 (t), 51.2 (d), 68.3 (t), 123.8 (d), 124.6 (d), 128.1 (d), 128.3 (d), 128.4 (d), 128.9 (d), 135.7 (s), 142.7 (s), 151.8 (s), 155.3 (s), 164.5 (s); MS: $m/z = 366$ (M$^+$); anal. calcd. for C$_{19}$H$_{18}$N$_4$O$_4$: C 62.29, H 4.95, N 15.29; found: C 62.51, H 5.22, N 15.37.

**7-Benzyl-3-(2-nitrophenylimino)-1,7,8,8a-tetrahydro-3H-oxazolo[3,4-a]pyrazine-6(5H)-one (2i):** Yield: 74%; pale yellow solid; mp 132 °C. IR: $\nu = 1757$, 1585, 1511, 1356 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.26$ (dd, 1H, $J = 11.5$, 4.0 Hz, NCHH), 3.48 (dd, 1H, $J = 11.5$, 9.4 Hz, NCHH), 3.98 (dd, 1H, $J = 8.7$, 3.8 Hz, OCHH), 4.06 (d, 1H, $J = 18.4$ Hz, CHH), 4.01–4.08 (m, 1H, NCH), 4.39 (dd, 1H, $J = 8.7$, 7.1 Hz, OCHH), 4.43 (d, 1H, $J = 14.1$ Hz, CHHPh), 4.66 (d, 1H, $J = 18.3$ Hz, CHH), 4.96 (d, 1H, $J = 14.5$ Hz, CHHPh), 7.07–7.12 (m, 2H, ArH), 7.27–7.45 (m, 6H, ArH), 7.87 (d, 1H, $J = 7.5$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 46.0$ (t), 48.5 (t), 50.4 (t), 51.9 (d), 67.7 (t), 122.5 (d), 124.9 (d), 126.6 (d), 128.0 (d), 128.2 (d), 128.9 (d), 133.3 (d), 135.7 (s), 142.3 (s), 143.6 (s), 152.3 (s), 164.6 (s); MS: $m/z = 366$ (M$^+$); anal. calcd. for C$_{19}$H$_{18}$N$_4$O$_4$: C 62.29, H 4.95, N 15.29; found: C 62.16, H 5.09, N 15.51.

**7-Benzyl-3-(4-methoxyphenylimino)-1,7,8,8a-tetrahydro-3H-oxazolo[3,4-a]pyrazine-6(5H)-one (2j):** Yield: 77%; white solid; mp 136 °C. IR: $\nu = 1761$, 1586, 1253 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.26$ (dd, 1H, $J = 11.7$, 3.6 Hz, NCHH), 3.36 (dd, 1H, $J = 11.1$, 10.4 Hz, NCHH), 3.75–3.80 (m, 4H, OCHH, OCH$_3$), 3.95–4.03 (m, 2H, CHH, NCH), 4.26–4.46 (m, 1H, OCHH), 4.47 (d, 1H, $J = 14.7$ Hz, CHHPh), 4.67 (d, 1H, $J = 18.4$ Hz, CHH), 4.87 (d, 1H, $J = 14.6$ Hz, CHHPh), 6.80 (d, 2H, $J = 8.8$ Hz, ArH), 7.03 (d, 2H, $J = 8.7$ Hz, ArH) 7.27–7.36 (m, 6H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 46.2$ (t), 48.4 (t), 50.3 (t), 51.2 (d), 55.4 (q), 67.7 (t), 113.9 (d), 122.7 (d), 127.9 (d), 128.5 (d), 129.4 (d), 135.6 (s), 139.5 (s), 150.5 (s), 155.3 (s), 165.2 (s); MS: $m/z = 351$ (M$^+$); anal. calcd. for C$_{20}$H$_{21}$N$_3$O$_3$: C 68.36, H 6.02, N 11.96; found: C 68.07, H 6.12, N 12.11.

## General Procedure for the Diamination Reactions

A mixture of PdCl$_2$(MeCN)$_2$ (0.1 mmol), CuCl$_2$ (3 mmol), K$_2$CO$_3$ (3 mmol), and urea **1** (1 mmol) in DMF (10 mL) was heated at 150 °C for 15 min under microwave irradiation. Brine (15 mL) was added and the mixture was extracted with CH$_2$Cl$_2$ (3 × 15 mL). The organic phase was dried over Na$_2$SO$_4$ and the solvent removed under reduced pressure. The crude mixture was purified by silica gel column chromatography (petroleum ether/AcOEt 3:7).

**7-Cyclohexyl-2-(phenyl)-1,7,8,8a-tetrahydroimidazo[1,5-a]pyrazine-3,6(2H,5H)-dione (3a):** Yield: 78%; beige solid; mp 147 °C. IR: $\nu = 1753$, 1722 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.25$–1.82 [m, 10H, (CH$_2$)$_5$], 3.23 (dd, 1H, $J = 11.2$, 9.4 Hz, NCHH), 3.34 (dd, 1H, $J = 11.2$, 3.8 Hz, NCHH), 3.55 (dd, 1H, $J = 9.1$, 2.6 Hz, NCHH), 3.82 (d, $J = 18.3$ Hz, 1H, CHH), 3.91–3.98 (m, 1H, NCH), 4.01 (dd, 1H, $J = 9.1$, 7.6 Hz, NCHH), 4.49 (d, 1H, $J = 18.4$ Hz, CHH), 4.50–4.56 [m, 1H, NCH(CH$_2$)$_5$], 7.04–7.09 (m, 1H, ArH), 7.27–7.35 (m, 2H, ArH), 7.53 (d, 2H, $J = 8.8$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.6 (t), 44.3 (t), 44.7 (t), 46.2 (t), 47.3 (d), 52.4 (d), 117.43 (d), 123.1 (d), 128.9 (d), 139.7 (s), 155.8 (s), 164.5 (s); MS: $m/z = 313$ (M$^+$); anal. calcd. for C$_{18}$H$_{23}$N$_3$O$_2$: C 68.98, H 7.40, N 13.41; found: C 69.27, H 7.17, N 13.60.

**7-Cyclohexyl-2-(4-chlorophenyl)-1,7,8,8a-tetrahydro-imidazo[1,5-a]pyrazine-3,6(2H,5H)-dione (3b):** Yield: 73%; beige solid; mp 161 °C. IR: $\nu = 1750$, 1724, 1085 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.26$–1.83 [m, 10H, (CH$_2$)$_5$], 3.19–3.25 (m, 1H, NCHH), 3.37 (d, 1H, $J = 9.4$,

3.2 Hz, NCHH), 3.54 (dd, 1H, $J = 9.4$, 2.6 Hz, NCHH), 3.85 (d, 1H, $J = 18.6$ Hz, CHH), 3.97–4.03 (m, 2H, NCHH, NCH), 4.50 (d, 1H, $J = 18.6$ Hz, CHH), 4.50–4.56 [m, 1H, NCH(CH$_2$)$_5$], 7.24 (d, 2H, $J = 8.4$ Hz, ArH), 7.34 (d, 2H, $J = 8.6$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.7 (t), 44.5 (t), 44.7 (t), 46.1 (t), 47.7 (d), 52.5 (d), 121.1 (d), 127.9 (s), 128.9 (d), 137.7 (s), 155.5 (s), 164.3 (s); MS: $m/z = 347$ (M$^+$); anal. calcd. for C$_{18}$H$_{22}$ClN$_3$O$_2$: C 62.15, H 6.37, N 12.08; found: C 61.99, H 6.61, N 12.29.

**7-Cyclohexyl-2-(4-nitrophenyl)-1,7,8,8a-tetrahydro-imidazo[1,5-a]pyrazine-3,6(2H,5H)-dione (3c):** Yield: 78%; brown solid; mp 162 °C. IR: $\nu = 1757$, 1726, 1536, 1361 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.12$–1.81 [m, 10H, (CH$_2$)$_5$], 3.26 (dd, 1H, $J = 11.5$, 9.6 Hz, NCHH), 3.44 (dd, 1H, $J = 11.5$, 3.1 Hz, NCHH), 3.64 (dd, 1H, $J = 9.2$, 2.6 Hz, NCHH), 3.87 (d, 1H, $J = 18.3$ Hz, CHH), 4.04–4.10 (m, 2H, NCHH, NCH), 4.50 (d, 1H, $J = 18.3$ Hz, CHH), 4.48–4.54 [m, 1H, NCH(CH$_2$)$_5$], 7.71 (d, 2H, $J = 9.0$ Hz, ArH), 7.20 (d, 2H, $J = 9.0$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.7 (t), 44.6 (t), 44.8 (t), 46.0 (t), 47.5 (d), 52.6 (d), 116.2 (d), 125.0 (d), 142.3 (s), 145.4 (s), 154.8 (s), 163.8 (s); MS: $m/z = 358$ (M$^+$); anal. calcd. for C$_{18}$H$_{22}$N$_4$O$_4$: C 60.32, H 6.19, N 15.63; found: C 60.06, H 6.37, N 15.70.

**7-Cyclohexyl-2-(2-nitrophenyl)-1,7,8,8a-tetrahydro-imidazo[1,5-a]pyrazine-3,6(2H,5H)-dione (3d):** Yield: 80%; white solid; mp 141 °C. IR: $\nu = 1751$, 1729, 1513, 1356 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.11$–1.80 [m, 10H, (CH$_2$)$_5$], 3.37 (dd, 1H, $J = 12.1$, 3.8 Hz, NCHH), 3.46–3.49 (m, 1H, NCHH), 3.63 (dd, 1H, $J = 9.1$, 2.3 Hz, NCHH), 3.64 (dd, 1H, $J = 9.1$, 2.6 Hz, NCHH), 3.83 (d, 1H, $J = 18.3$ Hz, CHH), 3.95–3.05 (m, 1H, NCH), 4.07–4.11 (m, 1H, NCHH), 4.43 (d, 1H, $J = 18.4$ Hz, CHH), 4.48–4.59 [m, 1H, NCH(CH$_2$)$_5$], 7.34–7.39 (m, 2H, ArH), 7.61–7.66 (m, 1H, ArH), 7.93 (dd, 1H, $J = 8.1$, 1.4 Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.6 (t), 29.3 (t), 29.7 (t), 43.9 (t), 44.9 (t), 48.2 (t), 48.9 (d), 52.6 (d), 125.7 (d), 126.9 (d), 127.0 (d), 132.4 (s), 133.7 (d), 145.6 (s), 156.1 (s), 164.2 (s); MS: $m/z = 358$ (M$^+$); anal. calcd. for C$_{18}$H$_{22}$N$_4$O$_4$: C 60.32, H 6.19, N 15.63; found: C 60.45, H 5.90, N 15.44.

**7-Cyclohexyl-2-(4-methoxyphenyl)-1,7,8,8a-tetrahydro-imidazo[1,5-a]pyrazine-3,6(2H,5H)-dione (3e):** Yield: 79%; pale yellow solid; mp 196 °C. IR: $\nu = 1755$, 1728, 1253 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.09$–1.80 [m, 10H, (CH$_2$)$_5$], 3.24–3.30 (m, 1H, NCHH), 3.33 (dd, 1H, $J = 10.9$, 4.0 Hz, NCHH), 3.52 (dd, 1H, $J = 10.9$, 2.5 Hz, NCHH), 3.80 (s, 3H, OCH$_3$), 3.83 (d, 1H, $J = 18.5$ Hz, CHH), 3.90–4.02 (m, 2H, NCHH, NCH), 4.50 (d, 1H, $J = 18.5$ Hz, CHH), 4.51–4.56 [m, 1H, NCH(CH$_2$)$_5$], 6.89 (d, 2H, $J = 9.1$ Hz, ArH), 7.43 (d, 2H, $J = 9.1$ Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 25.3$ (t), 25.4 (t), 25.5 (t), 29.3 (t), 29.7 (t), 44.2 (t), 44.8 (t), 46.7 (t), 47.8 (d), 52.4 (d), 55.5 (q), 114.2 (d), 119.6 (d), 133.0 (s), 155.7 (s), 156.2 (s), 164.6 (s); MS: $m/z = 343$ (M$^+$); anal. calcd. for C$_{19}$H$_{25}$N$_3$O$_3$: C 66.45, H 7.34, N 12.24; found: C 66.46, H 7.04, N 12.02.

**7-Benzyl-2-(phenyl)-1,7,8,8a-tetrahydroimidazo[1,5-a]pyrazine-3,6(2H,5H)-dione (3f):** Yield: 74%; white solid; mp 158 °C. IR: $\nu = 1759$, 1720 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.25$ (dd, 1H, $J = 11.8$, 3.8 Hz, NCHH), 3.35–3.45 (m, 1H, NCHH), 3.47 (dd, 1H, $J = 8.6$, 2.4 Hz, NCHH), 3.93 (d, $J = 18.5$ Hz, 1H, CHH), 3.96–4.03 (m, 2H, NCHH,

NC*H*), 4.49 (d, *J* = 14.6 Hz, 1H, C*H*HPh), 4.62 (d, 1H, *J* = 18.5 Hz, CH*H*), 4.82 (d, 1 H, *J* = 14.6 Hz, CH*H*Ph), 7.07–7.09 (m, 1 H, Ar*H*), 7.26–7.36 (m, 7 H, Ar*H*), 7.51 (dd, 2 H, *J* = 8.8, 1.1 Hz, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 44.5 (t), 46.0 (t), 47.3 (d), 49.3 (t), 50.4 (t), 117.5 (d), 123.1 (d), 123.1 (d), 128.0 (d), 128.2 (d), 128.5 (d), 128.6 (d), 128.9 (d), 129.0 (d), 135.8 (s), 139.6 (s), 155.8 (s), 165.3 (s); MS: *m/z* = 321 (M$^+$); anal. calcd. for C$_{19}$H$_{19}$N$_3$O$_2$: C 71.01m, H 5.96, N 13.08; found: C 70.88, H 6.19, N, 12.76.

**7-Benzyl-2-(4-chlorophenyl)-1,7,8,8a-tetrahydroimidazo-[1,5-*a*]pyrazine-3,6(2*H*,5*H*)-dione (3g):** Yield: 72%; pale yellow solid; mp 167 °C. IR: $\nu$ = 1757, 1725, 1102 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.27 (dd, 1 H, *J* = 11.9, 4.1 Hz, NC*H*H), 3.34–3.40 (m, 1 H, NCH*H*), 3.44 (dd, 1 H, *J* = 8.9, 2.8 Hz, NC*H*H), 3.93 (d, *J* = 18.5 Hz, 1 H, C*H*H), 3.95–3.99 (m, 2 H, NCH*H*, NC*H*), 4.49 (d, *J* = 14.6 Hz, 1 H, C*H*HPh), 4.62 (d, 1 H, *J* = 18.5 Hz, CH*H*), 4.82 (d, 1 H, *J* = 14.6 Hz, CH*H*Ph), 7.25–7.36 (m, 7 H, Ar*H*), 7.46 (dd, 2 H, *J* = 7.0, 2.0 Hz, Ar*H*); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 44.5 (t), 46.0 (t), 47.3 (d), 49.3 (t), 50.4 (t), 118.5 (d), 128.0 (d), 128.3 (d), 128.8 (d), 128.9 (d), 133.8 (s), 135.8 (s), 138.2 (s), 155.5 (s), 165.1 (s); MS: *m/z* = 335 (M$^+$); anal. calcd. for C$_{19}$H$_{18}$ClN$_3$O$_2$: C 64.13, H 5.10, N 11.81; found: C 64.08, H 4.82, N 12.09.

**7-Benzyl-2-(4-nitrophenyl)-1,7,8,8a-tetrahydroimidazo-[1,5-*a*]pyrazine-3,6(2*H*,5*H*)-dione (3h):** Yield: 76%; pale yellow solid; mp 186 °C. IR: $\nu$ = 1758, 1729. 1524, 1348 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.27- 3.28 (m, 2 H, NCH*H*), 3.56 (dd, 1 H, *J* = 11.8, 3.8 Hz, NC*H*H), 3.96 (d, *J* = 18.5 Hz, 1 H, C*H*H), 4.02–4.10 (m, 2 H, NCH*H*, NC*H*), 4.53 (d, *J* = 14.5 Hz, 1 H, C*H*HPh), 4.62 (d, 1 H, *J* = 18.5 Hz, CH*H*), 4.81 (d, 1 H, *J* = 14.5 Hz, CH*H*Ph), 7.27–7.37 (m, 5 H, Ar*H*), 7.68 (d, 2 H, *J* = 9.3 Hz, Ar*H*), 8.21 (d, 2 H, *J* = 9.4 Hz, Ar*H*); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 44.4 (t), 45.8 (t), 47.0 (d), 49.6 (t), 50.5 (t), 116.3 (d), 125.0 (d), 128.1 (d), 128.3 (d), 129.1 (d), 135.6 (s), 145.2 (s), 152.7 (s), 154.7 (s), 164.6 (s); MS: *m/z* = 366 (M$^+$); anal. calcd. for C$_{19}$H$_{18}$N$_4$O$_4$: C 62.29, H 4.95, N 15.29; found: C 62.44, H 4.72, N 15.42.

**7-Benzyl-2-(2-nitrophenyl)-1,7,8,8a-tetrahydroimidazo-[1,5-*a*]pyrazine-3,6(2*H*,5*H*)-dione (3i):** Yield: 78%; white solid; mp 163 °C. IR: $\nu$ = 1754, 1721, 1514, 1355 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.26 (dd, 1 H, *J* = 9.3, 3.6 Hz, NC*H*H), 3.53–3.63 (m, 2 H, NC*H*H, NCH*H*), 3.93 (d, *J* = 18.5 Hz, 1 H, C*H*H), 4.00–4.10 (m, 2 H, NCH*H*, NC*H*), 4.41 (d, *J* = 14.7 Hz, 1 H, C*H*HPh), 4.56 (d, 1 H, *J* = 18.5 Hz, CH*H*), 4.96 (d, 1 H, *J* = 14.7 Hz, CH*H*Ph), 7.28–7.38 (m, 7 H, Ar*H*), 7.61–7.66 (m, 1 H, Ar*H*), 7.93 (dd, 1 H, *J* = 8.1, 1.4 Hz, Ar*H*); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 44.7 (t), 48.0 (t), 48.5 (d), 48.8 (t), 50.3 (t), 122.5 (d), 126.9 (d), 127.0 (d), 127.9 (d), 128.2 (d), 128.9 (d), 132.4 (s), 133.3 (d), 133.6 (d), 135.9 (s), 145.6 (s), 156.0 (s), 164.9 (s); MS: *m/z* = 366 (M$^+$); anal. calcd. for C$_{19}$H$_{18}$N$_4$O$_4$: C 62.29, H 4.95, N 15.29; found: C 62.07, H 5.12, N 15.22.

**7-Benzyl-2-(4-methoxyphenyl)-1,7,8,8a-tetrahydroimidazo-[1,5-*a*]pyrazine-3,6(2*H*,5*H*)-dione (3j):** Yield: 73%; beige solid; mp 225 °C. IR: $\nu$ = 1755, 1724, 1261 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.24 (dd, 1 H, *J* = 11.8, 4.0 Hz, NC*H*H), 3.37–3.44 (m, 2 H, NCH*H*, NC*H*H), 3.79 (s, 3 H, OC*H$_3$*), 3.91 (d, *J* = 18.5 Hz, 1 H, C*H*H), 3.92–3.98 (m, 2 H, NCH*H*, NC*H*), 4.50 (d, *J* = 14.6 Hz, 1 H, C*H*HPh), 4.61 (d, 1 H, *J* = 18.5 Hz, CH*H*), 4.82 (d, 1 H, *J* = 14.6 Hz, CH*H*Ph), 6.88 (d, 1 H, *J* = 9.1 Hz, Ar*H*), 7.28–7.41 (m, 7 H, Ar*H*);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 44.6 (t), 46.6 (t), 47.5 (d), 49.2 (t), 50.4 (t), 55.5 (q), 114.2 (d), 119.6 (d), 127.9 (d), 128.3 (d), 129.9 (d), 132.9 (s), 138.7 (s), 155.8 (s), 147.1 (s), 165.4(s); MS: *m/z* = 351 (M$^+$); anal. calcd. for C$_{20}$H$_{21}$N$_3$O$_3$: C 68.36, H 6.02, N 11.96; found: C 68.11, H 5.76, N 12.25.

# Acknowledgements

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