EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Rh2(esp)2-catalysed coupling of α-diazo-γ-butyrolactams with aromatic amines

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201900565

Link to VoR: http://dx.doi.org/10.1002/ejoc.201900565

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$Rh_2(esp)_2$-catalysed coupling of α-diazo-γ-butyrolactams with aromatic amines

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ABSTRACT

Decomposition of α-diazo-γ-butyrolactams in the presence of aromatic and heteroaromatic amines, under $Rh_2(esp)_2$ catalysis, led to corresponding α-arylamino-γ-butyrolactams, which are of significant value for medicinal chemistry. The reaction scope encompasses primary as well as secondary, diversely substituted anilines and heteroaromatic amines. Insertion into the anilinic amino group was shown to be selective over amide and sulfonamide N-H insertion.

Introduction

The chemistry of α-diazocarbonyl compounds has attracted much attention from the synthetic organic and medicinal chemistry community,[1]–[5] as it offers a wealth of powerful synthetic transformations including those which involve generation of metal carbene species.[6][7] One such transformation, allowing for direct functionalization of a carbo- or heterocyclic core, is the formal insertion of metal carbenes into the N–H bond of aromatic[8]–[10] and aliphatic amines,[11]–[13] amides[14][15] as well as azaheterocycles.[16][17] However, quite a number of chemistries involving α-diazocarbonyl compounds remain unexplored for some medicinally useful cores, and thus has not been validated for use in drug design. One such class is α-diazo-γ-butyrolactams, which has only sporadically appeared in the literature.[18][19] In our recent work we reported the first general method for the synthesis of these compounds, we investigated their stability, and we proved them valid partners for metal-catalyzed O–H insertion and 1,2-hydride

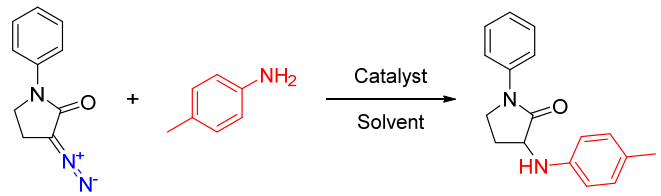
shift reactions.[20] Next, it came to our attention that the respective N–H insertion reactions have not been investigated for α-diazo-γ-butyrolactams. This is seemed like a significant methodology void considering the utility of the respective α-amino-γ-butyrolactams for medicinal chemistry. Indeed, compounds based on such cores have displayed various types of biological activity such as factor Xa inhibition,[21][22] selective inhibition of histone deacetylase 6 (HDAC6)[23] as well as modulation of the dopamine D_2 receptor.[24][25]

This motivated us to continue the synthetic exploration of α-diazo-γ-butyrolactams, especially in light of the N-H insertion reactions reported in the literature for 3-diazoindolin-2-ones.[26] Herein, we present the results of our investigation of the formal N–H insertion reactions of Rh(II) carbenes (generated from these diazo compounds) into various amines as a new way to access a vast diversity of druglike molecular scaffolds.

Results and discussion

The initial experiments were conducted with *N*-phenyl α-diazo-γ-butyrolactam (**1a**) and *p*-toluidine (**2a**) (Table 1). With $Rh_2(OAc)_4$[27][28] employed as the catalyst, 50% of the desired product (**3a**) was observed by ^{1}H NMR analysis of the crude mixture (entry 1). With more reactive $Rh_2(esp)_2$[29][30] employed in 5 mol% quantity (entry 2), the NH-insertion product **3a** NMR yield was raised to 62% and remained virtually identical when the catalyst amount was reduced 10-fold (entry 3). Notably, the latter reaction repeated on a preparative scale resulted in 69% isolated yield of **3a** (*vide infra*). Other Rh or Cu catalysts (entries 4-6) resulted in appreciable, albeit substantially lower ^{1}H NMR conversion while $Cu(OTf)_2$ (entry 7) proved ineffective. Attempted catalyst-free thermal generation of carbene[31] led to decomposiotion of **1a** an no product formation (entry 8).

Table 1. Condition finding experiments using **1a** and **2a** as reaction partners.



1a **2a** **3a**

Entry[a]	Catalyst	Quantity	Solvent	Temperature	Time	Yield[b]
1	$Rh_2(OAc)_4$	5 mol %	CH_2Cl_2	20 °C	10 min	50%
2	$Rh_2(esp)_2$	5 mol %	CH_2Cl_2	20 °C	10 min	62%
3	**$Rh_2(esp)_2$**	**0.5 mol %**	**CH_2Cl_2**	**20 °C**	**10 min**	**61%**
4	$Rh_2(TFA)_4$	5 mol %	CH_2Cl_2	20 °C	24 h	24%

5	$Rh_2(OPiv)_4$	5 mol %	CH_2Cl_2	20 °C	10 min	49%
6	$Cu(acac)_2$	5 mol %	CH_2Cl_2	20 °C	3 h	26%
7	$Cu(OTf)_2$	5 mol %	CH_2Cl_2	20 °C	10 min	trace
8	None	-	$PhCF_3$	80 °C	16 h	0%

[a]Reaction conditions: catalyst was added to a mixture of 0.025 mmol diazo lactam **1a** with 0.025 mmol of *p*-toluidine **2a** in CD_2Cl_2 (0.5 ml); and the solution was stirred for appropriate time

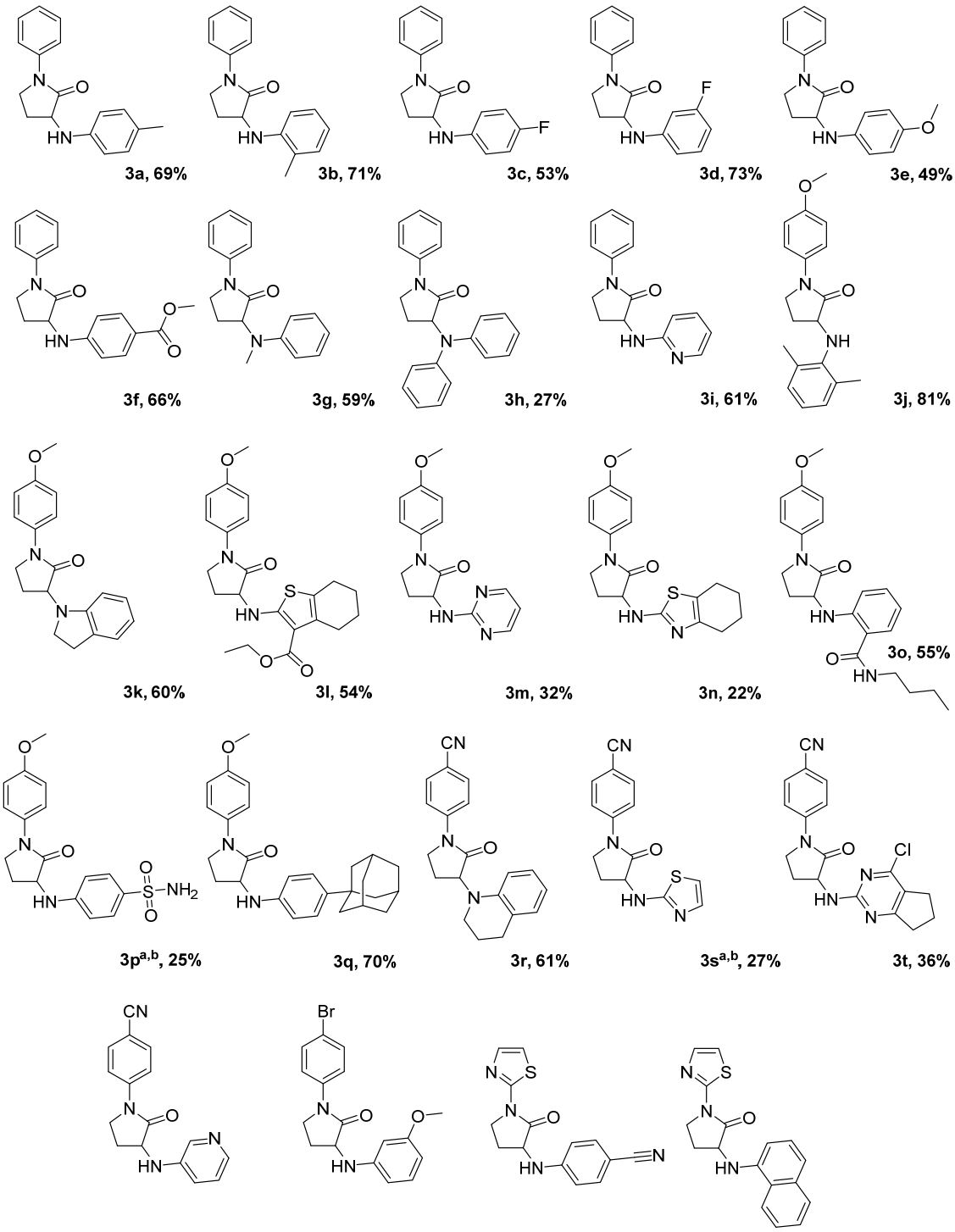
[b]Yields was determined by ^1H NMR with isoquinoline as internal standard

With the workable conditions in hand, we investigated a wider range of $Rh_2(esp)_2$-catalyzed N-H insertion reactions (Scheme 1).

Scheme 1. $Rh_2(esp)_2$-catalyzed N-H insertion reactions of α-diazo γ-butyrolactams.

10.1002/ejoc.201900565

1a-e **2a-x** **3a-x**



[a] Reaction was carried out in 1,4-dioxane

[b] Product was isolated by HPLC

In general, reactions were conducted in dichloromethane. However, for substrates displaying limited solubility (such as **3p** and **3s**), 1,4-dioxane was successfully employed as a solvent. Five α-diazo-γ-butyrolactams (**1a-e**) carrying different donor and acceptor aromatic substituents on nitrogen were employed as diazo component and no significant difference in their reactivity was observed.

The reaction was found somewhat insensitive sensitive to the steric hindrance at the aromatic amine. Thus, in the row of *p*-toluidine (**2a**) - *o*-toluidine (**2b**) - 2,6-xylidine (**2j**), no noticeable change in the product yield was observed. However, with a more sterically demanding diphenylamine (**2h**), the yield was markedly lower. At the same time, the reaction with secondary anilines (**2g**, **2k** and **2r**) worked similarly well compare to their primary counterparts. Unfortunately, the reaction displayed no selectivity toward primary *vs.* secondary aniline (or vice versa) as observed for the reaction of 6-aminoindoline delivering a mixture of insertion products including double insertion (data not shown).

In order to further explore the generality of this transformation, a wide range of anilines carrying different electron-donating (**2e** and **2q**) as well as electron-withdrawing (**2c**, **2d**, **2f**, **2v** and **2w**) substituents were examined and no particular correlation between the reaction yield and the electronic properties of the substituent was observed. Aminopyridines (**2i** and **2u**), as well as Gewald-type aminothiophene (**2l**) worked well while 2-aminothiazole (**2n**) and 2-aminopyrimidines (**2m** and **2t**) gave significantly lower yields. Notably, in the latter case, the labile 4-chloropyrimidine moiety remained intact in the product obtained (**3t**), offering an opportunity for further scaffold decoration.

Reassuringly, the N-H insertion into aromatic amino group under these conditions demonstrated selectivity over the insertion into amide or sulfonamide N-H bond. Thus, in the case of anthranilamide **2o** and sulfanilamide (**2p**), only the products of insertion into the aromatic amino group were obtained. Structure of **3p** was confirmed by HMBC and HSQC spectra (Figure 1).

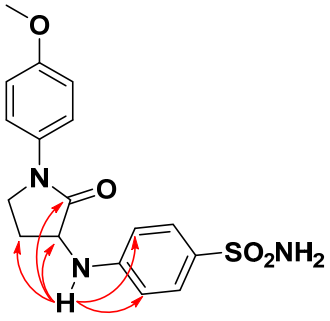
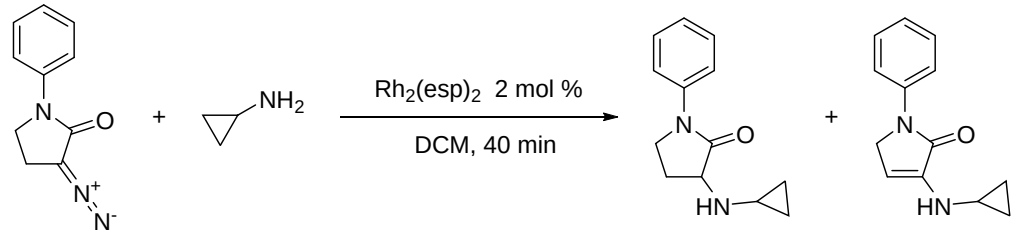


Figure 1. Key HMBC correlations confirmed the structure of **3p**

We also tried to carry out decomposition of diazo lactams in the presence of aliphatic amines. Unfortunately, the test experiment with cyclopropylamine **2y** provided N-H insertion product **3y** only in moderate yield. Moreover, it was contaminated with side product enamine **4** which is presumably formed by oxidation of diazo lactam **1a** (a process described in the literature for other α-dazocarbonyl compounds[31]) followed by nucleophilic attack (Scheme 2). Adding more catalyst in several portions (up to four times the initial amount) in order to drive the reaction to completion, only led to catalyst inactivation and incomplete conversion. This limitation seems to be general for aliphatic amines as a similar reaction with *n*-propylamine gave an even more complex mixture of unidentified by-products.

Scheme 2. $Rh_2(esp)_2$-catalyzed N-H insertion reaction into cyclopropylamine.



1a **2y** **3y, 37%** **4, 19%**

Some of the compounds obtained have particular value in medicinal chemistry, as documented in the literature. For instance, compound **3f** was employed as an advanced intermediate for HDAC 6 inhibitors[23] while compound **3v** has been reported as a precursor to Rho kinase inhibitors.[32] While being comparable to these syntheses in terms of the number of steps, our approach involves a mild Rh(II)-catalyzed N-H carbene insertion step and is likely to display a different functional group tolerance profile. Furthermore, the presence of a primary sulfonamide group in compound **3p** makes it a potential carbonic anhydrase inhibitor[33]–[35]. As already noted above, the active chlorine in compound **3t** could be easily substituted by different amines thus delivering the ubiquitous bioactive 2,4-diaminopyrimidine scaffold[36][37].

Conclusion

Thus, we reported $Rh_2(esp)_2$-catalyzed reaction of rare α-diazo γ-butyrolactams with aromatic amines. This transformation was found to be somewhat insensitive to steric hindrance and electronic properties of the amine partner and worked well for a wide range of primary and secondary anilines. Aminoheterocycles were also found employable in the reaction albeit they provided lower product yield. In addition, N-H insertion into aromatic amino group demonstrated selectivity over insertion into N-H bond of amide and sulfonamide groups. Along with dichloromethane, 1,4-dioxane was found suitable as a solvent and could be used to

overcome reagent solubility issues. The reaction provides a hitherto unexplored, one-step entry into medicinally relevant compounds.

Experimental part

General considerations. Diazo compounds were prepared according to our previously reported method,[20] other reagents were obtained from commercial sources and used without additional purification. 1,4-Dioxane, tetrahydrofuran, diethyl oxalate and dichloromethane were distilled over suitable drying agents. Mass spectra were recorded with a Bruker Maxis HRMS-ESI-qTOF spectrometer (electrospray ionization mode). NMR spectroscopic data were recorded with Bruker Avance 400 spectrometer (400.13 MHz for ^{1}H, 100.61 MHz for ^{13}C and 376.50 MHz for ^{19}F) and were referenced to residual solvent proton peaks and solvent carbon peaks. Melting points were determined with a Stuart SMP50 instrument in open capillary tubes. HPLC preparative chromatography was performed with Agilent PrepHT XDB-C18 preparative cartridge 21.2 × 150 mm 5 μm. Products **3p** and **3s** were purified by HPLC eluting with H_2O-MeCN with addition of 0.1% TFA (elution gradient MeCN: 40 → 60%); flow rate 12 mL/min, column temperature 40 °C.

General procedure for $Rh_2(esp)_2$-catalysed decomposition of α-diazo γ-butyrolactams in presence of aromatic amines (preparation of 3a-x). To a vigorous stirred solution of corresponding amine (0.3 mmol) and diazo lactam (0.3 mmol) in dichloromethane (5 ml) (1,4-dioxane for **3p** and **3s**) was added $Rh_2(esp)_2$ (1.1 mg, 0.0015 mmol, 0.5 mol %). After completion of nitrogen evolution the resulting cloudy mixture was evaporated to dryness and purified using column chromatography on silica gel. Compounds **3p** and **3s** were purified by HPLC using above described conditions.

1-Phenyl-3-(*p*-tolylamino)pyrrolidin-2-one (3a). Eluent ethyl acetate – *n*-hexane 1:3. Yield 55 mg, 69%. White solid, mp 143.2-144.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.58 (m, 2H), 7.58 – 7.38 (m, 2H), 7.26 – 7.14 (m, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.78 – 6.56 (m, 2H), 4.52 (s, 1H), 4.13 (ddd, *J* = 9.8, 7.6, 1.7 Hz, 1H), 3.99 – 3.75 (m, 2H), 2.88 (dddd, *J* = 14.0, 7.9, 3.8, 1.6 Hz, 1H), 2.29 (s, 3H), 2.14 – 1.98 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 145.1, 139.2, 129.9, 129.0, 127.8, 125.0, 119.8, 113.9, 56.7, 45.3, 29.3, 20.4. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_2O$ 267.1492; Found 267.1502.

1-Phenyl-3-(*o*-tolylamino)pyrrolidin-2-one (3b). Eluent ethyl acetate – *n*-hexane 1:3. Yield 57 mg, 69%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.69 (m, 2H), 7.54 – 7.39 (m, 2H), 7.27 – 7.18 (m, 2H), 7.18 – 7.12 (m, 1H), 6.81 (td, *J* = 7.4, 1.1 Hz, 1H), 6.69 (dd, *J* = 8.0, 1.1 Hz, 1H), 4.57 (s, 1H), 4.19 (ddd, *J* = 10.0, 7.8, 1.7 Hz, 1H), 3.99 – 3.84 (m, 2H), 2.93 (dddd, *J* =

12.4, 7.8, 6.1, 1.8 Hz, 1H), 2.31 (s, 3H), 2.18 – 2.00 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 145.5, 139.1, 130.4, 129.0, 127.0, 125.1, 123.5, 119.7, 118.3, 110.6, 56.4, 45.3, 29.4, 17.6. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_2O$ 267.1492; Found 267.1498.

3-((4-Fluorophenyl)amino)-1-phenylpyrrolidin-2-one (3c). Eluent ethyl acetate – *n*-hexane 1:3. Yield 43 mg, 53%. White solid, mp 144.8-146.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.59 (m, 2H), 7.51 – 7.37 (m, 2H), 7.26 – 7.18 (m, 1H), 7.03 – 6.89 (m, 2H), 6.77 – 6.63 (m, 2H), 4.51 (s, 1H), 4.10 (dd, *J* = 10.5, 7.8 Hz, 1H), 3.97 – 3.83 (m, 2H), 2.86 (dddd, *J* = 12.4, 7.9, 6.0, 1.9 Hz, 1H), 2.19 – 1.99 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 156.5 (d, *J* = 236.0 Hz), 143.8 (d, *J* = 2.2 Hz), 139.1, 129.0, 125.1, 119.8, 115.8 (d, *J* = 22.3 Hz), 114.7 (d, *J* = 7.6 Hz), 56.9, 45.2, 29.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -126.74. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}FN_2O$ 271.1241; Found 271.1245.

3-((3-Fluorophenyl)amino)-1-phenylpyrrolidin-2-one (3d). Eluent ethyl acetate – *n*-hexane 1:3. Yield 59 mg, 73%. Yellow solid, mp 100.9-101.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.63 (m, 2H), 7.51 – 7.39 (m, 2H), 7.26 – 7.20 (m, 1H), 7.20 – 7.12 (m, 1H), 6.56 – 6.47 (m, 2H), 6.46 – 6.35 (m, 1H), 4.76 (s, 1H), 4.13 (ddd, *J* = 10.7, 7.8, 3.0 Hz, 1H), 3.99 – 3.77 (m, 2H), 2.85 (dddd, *J* = 12.3, 7.8, 6.0, 1.7 Hz, 1H), 2.02 (dtd, *J* = 12.4, 10.4, 9.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 164.1 (d, *J* = 242.9 Hz), 149.2 (d, *J* = 10.7 Hz), 139.0, 130.5 (d, *J* = 10.1 Hz), 129.1, 125.2, 119.8, 109.6 (d, *J* = 2.3 Hz), 104.8 (d, *J* = 21.5 Hz), 100.4 (d, *J* = 25.0 Hz), 56.2, 45.2, 28.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ -112.57. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}FN_2O$ 271.1241; Found 271.1242.

3-((4-Methoxyphenyl)amino)-1-phenylpyrrolidin-2-one (3e). Eluent ethyl acetate – *n*-hexane 1:3. Yield 43 mg, 49%. White solid, mp 148.9-150.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.64 (m, 2H), 7.50 – 7.37 (m, 2H), 7.25 – 7.14 (m, 1H), 6.96 – 6.80 (m, 2H), 6.77 – 6.69 (m, 2H), 4.36 (s, 1H), 4.09 (dd, *J* = 10.4, 7.8 Hz, 1H), 3.96 – 3.84 (m, 2H), 3.79 (s, 3H), 2.85 (dddd, *J* = 12.3, 7.8, 6.0, 1.9 Hz, 1H), 2.07 (dtd, *J* = 12.3, 10.2, 9.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 153.0, 141.5, 139.2, 129.0, 125.0, 119.8, 115.2, 115.0, 57.3, 55.8, 45.3, 29.2. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_2O_2$ 283.1441; Found 283.1443.

Methyl 4-((2-oxo-1-phenylpyrrolidin-3-yl)amino)benzoate (3f). Eluent ethyl acetate – *n*-hexane 1:2. Yield 61 mg, 66%. Yellow solid, mp 129.ii6-131.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.74 – 7.67 (m, 2H), 7.49 – 7.39 (m, 2H), 7.27 – 7.20 (m, 1H), 6.82 – 6.68 (m, 2H), 4.98 (d, *J* = 3.3 Hz, 1H), 4.26 (ddd, *J* = 11.0, 7.8, 3.4 Hz, 1H), 4.01 – 3.86 (m, 2H), 3.89 (s, 3H), 2.94 (dddd, *J* = 12.4, 7.7, 6.0, 1.5 Hz, 1H), 2.07 (dtd, *J* = 12.4, 10.4, 9.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 167.2, 151.1, 138.9, 131.6, 129.1, 125.2, 119.8, 119.7, 112.5,

55.7, 51.6, 45.2, 28.8. HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{18}N_2O_3$ 333.1210; Found 333.1210.

3-(Methyl(phenyl)amino)-1-phenylpyrrolidin-2-one (3g). Eluent ethyl acetate – *n*-hexane 1:3. Yield 47 mg, 59%. White solid, mp 113.4-114.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.69 (m, 2H), 7.48 – 7.38 (m, 2H), 7.32 – 7.25 (m, 2H), 7.24 – 7.18 (m, 1H), 6.94 – 6.87 (m, 2H), 6.85 – 6.74 (m, 1H), 4.80 (dd, *J* = 10.4, 8.6 Hz, 1H), 3.94 – 3.78 (m, 2H), 2.97 (s, 3H), 2.51 (dddd, *J* = 12.9, 8.8, 6.1, 2.8 Hz, 1H), 2.21 (ddt, *J* = 12.9, 10.5, 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 149.8, 139.4, 129.2, 129.0, 124.9, 119.7, 118.0, 113.9, 62.4, 44.8, 34.1, 21.6. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_2O$ 267.1492; Found 267.1485.

3-(Diphenylamino)-1-phenylpyrrolidin-2-one (3h). Eluent ethyl acetate – *n*-hexane 1:3. Yield 27 mg, 27%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.58 (m, 2H), 7.50 – 7.36 (m, 2H), 7.34 – 7.25 (m, 4H), 7.24 – 7.16 (m, 1H), 7.12 – 7.00 (m, 6H), 4.99 (t, *J* = 9.2 Hz, 1H), 3.79 (ddd, *J* = 9.6, 8.4, 7.5 Hz, 1H), 3.63 (ddd, *J* = 9.7, 8.9, 2.9 Hz, 1H), 2.50 (dddd, *J* = 12.9, 8.9, 7.5, 2.9 Hz, 1H), 2.39 (ddt, *J* = 12.9, 9.6, 8.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 147.1, 139.4, 129.3, 128.9, 124.8, 123.0, 122.6, 119.7, 62.2, 45.0, 22.7. HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{20}N_2O$ 351.1468; Found 351.1458.

1-Phenyl-3-(pyridin-2-ylamino)pyrrolidin-2-one (3i). Eluent ethyl acetate – *n*-hexane 1:1. Yield 46 mg, 61%. White solid, mp 103.8-105.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 5.4, 1.9 Hz, 1H), 7.80 – 7.65 (m, 2H), 7.55 – 7.37 (m, 3H), 7.24 – 7.16 (m, 1H), 6.75 – 6.63 (m, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 5.17 (s, 1H), 4.63 (ddd, *J* = 11.4, 7.9, 3.9 Hz, 1H), 4.02 – 3.75 (m, 2H), 3.05 (dddd, *J* = 12.4, 7.7, 6.1, 1.4 Hz, 1H), 2.02 (dtd, *J* = 12.4, 10.6, 8.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 158.0, 147.8, 139.3, 137.1, 128.9, 124.9, 119.7, 113.7, 109.4, 54.7, 45.4, 28.8. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{15}N_3O$ 254.1288; Found 254.1297.

3-((2,6-Dimethylphenyl)amino)-1-(4-methoxyphenyl)pyrrolidin-2-one (3j). Eluent ethyl acetate – *n*-hexane 1:3. Yield 75 mg, 81%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.52 (m, 2H), 7.05 (d, *J* = 7.4 Hz, 2H), 6.99 – 6.92 (m, 2H), 6.89 (t, *J* = 7.5 Hz, 1H), 3.98 (dd, *J* = 10.9, 7.9 Hz, 1H), 3.87 – 3.80 (m, 4H), 3.80 – 3.64 (m, 2H), 2.62 (dddd, *J* = 12.4, 7.8, 6.0, 1.7 Hz, 1H), 2.43 (s, 6H), 2.18 – 2.02 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 156.7, 145.3, 132.6, 130.5, 128.9, 122.6, 121.3, 114.1, 60.8, 55.5, 45.1, 29.3, 19.0. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{22}N_2O_2$ 311.1754; Found 311.1767.

3-(Indolin-1-yl)-1-(4-methoxyphenyl)pyrrolidin-2-one (3k). Eluent ethyl acetate – *n*-hexane 1:2. Yield 55 mg, 60%. White solid, mp 129.3-130.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.55 (m, 2H), 7.19 – 7.10 (m, 1H), 7.07 (td, *J* = 7.6, 1.2 Hz, 1H), 7.00 – 6.90 (m, 2H), 6.75 –

6.67 (m, 1H), 6.52 (d, *J* = 7.8 Hz, 1H), 4.56 (dd, *J* = 9.9, 8.7 Hz, 1H), 3.95 – 3.76 (m, 5H), 3.61 – 3.44 (m, 2H), 3.15 – 2.96 (m, 2H), 2.56 – 2.35 (m, 1H), 2.30 – 2.16 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 156.8, 150.6, 132.6, 130.2, 127.2, 124.7, 121.4, 118.1, 114.1, 107.4, 58.7, 55.5, 49.0, 45.5, 28.4, 20.1. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{20}N_2O_2$ 309.1598; Found 309.1610.

Ethyl 2-((1-(4-methoxyphenyl)-2-oxopyrrolidin-3-yl)amino)-4,5,6,7-tetrahydrobenzo[b]thiop-hene-3-carboxylate (3l). Eluent ethyl acetate – *n*-hexane 1:3. Yield 67 mg, 54%. White solid, mp 135.5-136.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 5.4 Hz, 1H), 7.63 – 7.52 (m, 2H), 7.03 – 6.86 (m, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.20 (ddd, *J* = 10.4, 8.1, 5.4 Hz, 1H), 3.91 – 3.74 (m, 2H), 3.81 (s, 3H), 2.82 (dddd, *J* = 12.5, 8.1, 6.3, 1.7 Hz, 1H), 2.78 – 2.74 (m, 2H), 2.59 – 2.52 (m, 2H), 2.16 – 1.98 (m, 1H), 1.86 – 1.69 (m, 4H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 166.1, 162.6, 156.8, 133.4, 132.3, 121.3, 117.4, 114.1, 104.7, 59.4, 58.7, 55.5, 45.3, 27.5, 26.9, 24.6, 23.3, 22.9, 14.5. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{26}N_2O_4S$ 415.1686; Found 415.1693.

1-(4-Methoxyphenyl)-3-(pyrimidin-2-ylamino)pyrrolidin-2-one (3m). Eluent ethyl acetate. Yield 27 mg, 32%. White solid, mp 160.1-161.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 4.8 Hz, 2H), 7.68 – 7.51 (m, 2H), 7.03 – 6.85 (m, 2H), 6.62 (t, *J* = 4.8 Hz, 1H), 5.96 (s, 1H), 4.70 (ddd, *J* = 10.8, 8.1, 5.3 Hz, 1H), 3.92 – 3.74 (m, 2H), 3.82 (s, 3H), 2.92 (dddd, *J* = 12.4, 7.9, 6.1, 1.5 Hz, 1H), 2.05 (dtd, *J* = 12.2, 10.4, 9.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 162.2, 158.0, 156.8, 132.5, 121.4, 114.1, 111.5, 55.5, 54.2, 45.6, 28.0. HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{16}N_4O_2$ 307.1165; Found 307.1166.

1-(4-Methoxyphenyl)-3-((4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)amino)pyrrolidin-2-one (3n). Eluent ethyl acetate – *n*-hexane 3:1. Yield 27 mg, 22%. Pale pink solid, mp 164.3-165.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.40 (m, 2H), 7.08 – 6.77 (m, 2H), 5.64 (s, 1H), 4.45 (dd, *J* = 10.7, 7.9 Hz, 1H), 3.82 (s, 3H), 4.09 – 3.58 (m, 2H), 2.99 (dddd, *J* = 12.6, 7.8, 6.2, 1.3 Hz, 1H), 2.77 – 2.48 (m, 4H), 2.22 – 1.97 (m, 1H), 1.92 – 1.59 (m, *J* = 5.1, 4.6 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 165.5, 156.9, 145.8, 132.3, 121.5, 117.6, 114.2, 56.8, 55.5, 45.8, 28.4, 26.8, 23.5, 23.2, 23.1. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{21}N_3O_2S$ 344.1427; Found 344.1432.

***N*-Butyl-2-((1-(4-methoxyphenyl)-2-oxopyrrolidin-3-yl)amino)benzamide (3o).** Eluent ethyl acetate – *n*-hexane 1:1. Yield 63 mg, 55%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 5.5 Hz, 1H), 7.71 – 7.52 (m, 2H), 7.37 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.33 – 7.14 (m, 1H), 6.96 – 6.89 (m, 2H), 6.83 (d, *J* = 8.3 Hz, 1H), 6.63 (t, *J* = 7.5 Hz, 1H), 6.39 – 6.29 (m, 1H), 4.29 (ddd, *J*

= 9.9, 8.1, 5.5 Hz, 1H), 3.94 – 3.71 (m, 2H), 3.81 (s, 3H), 3.55 – 3.26 (m, 2H), 2.74 (dddd, *J* = 12.5, 8.5, 6.7, 2.2 Hz, 1H), 2.32 – 1.99 (m, 1H), 1.73 – 1.52 (m, 2H), 1.52 – 1.34 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.5, 156.7, 148.5, 132.6, 132.4, 127.4, 121.3, 116.7, 115.9, 114.1, 112.6, 55.5, 55.3, 45.4, 39.5, 31.7, 27.8, 20.2, 13.8. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{27}N_3O_3$ 382.2125; Found 382.2141.

4-((1-(4-Methoxyphenyl)-2-oxopyrrolidin-3-yl)amino)benzenesulfonamide (3p). HPLC R_t = 16.7 min. Yield 27 mg, 25%. White solid, mp 230.9-232.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 – 7.57 (m, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.08 – 6.96 (m, 2H), 6.94 (s, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 6.68 (d, *J* = 7.5 Hz, 1H), 4.73 – 4.34 (m, 1H), 3.97 – 3.62 (m, 2H), 3.76 (s, 3H), 2.74 – 2.56 (m, 1H), 2.03 – 1.81 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.1, 156.5, 151.3, 133.2, 131.2, 127.7, 121.5, 114.4, 112.0, 55.7, 54.8, 45.3, 26.6. HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{19}N_3O_4S$ 384.0988; Found 384.0987.

3-((4-(Adamantan-1-yl)phenyl)amino)-1-(4-methoxyphenyl)pyrrolidin-2-one (3q). Eluent ethyl acetate – *n*-hexane 1:1. Yield 88 mg, 70%. White solid, mp 143.2-144.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.1 Hz, 2H), 4.56 (s, 1H), 4.12 (t, *J* = 9.1 Hz, 1H), 3.95 – 3.71 (m, 2H), 3.84 (s, 3H), 2.87 (dt, *J* = 13.4, 7.1 Hz, 1H), 2.22 – 2.00 (m, 4H), 1.98 – 1.88 (m, 6H), 1.87 – 1.71 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 156.9, 145.2, 141.8, 132.4, 125.7, 121.5, 114.2, 113.5, 56.4, 55.5, 45.7, 43.4, 36.9, 35.4, 29.5, 29.1. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{32}N_2O_2$ 417.2537; Found 417.2551.

4-(3-(3,4-Dihydroquinolin-1(2*H*)-yl)-2-oxopyrrolidin-1-yl)benzonitrile (3r). Eluent ethyl acetate – *n*-hexane 1:3. Yield 58 mg, 61%. White solid, mp 198.7-200.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.9 Hz, 2H), 7.78 – 7.49 (m, 2H), 7.07 (td, *J* = 7.8, 1.6 Hz, 1H), 7.03 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.82 – 6.53 (m, 2H), 4.82 (dd, *J* = 10.6, 8.7 Hz, 1H), 4.13 – 3.69 (m, 2H), 3.35 (ddd, *J* = 11.0, 6.9, 4.0 Hz, 1H), 3.22 (ddd, *J* = 11.2, 8.0, 3.8 Hz, 1H), 2.83 (t, *J* = 6.5 Hz, 2H), 2.55 (dddd, *J* = 12.9, 8.9, 7.0, 2.0 Hz, 1H), 2.38 – 2.20 (m, 1H), 2.18 – 2.05 (m, 1H), 2.04 – 1.90 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 144.7, 143.1, 133.1, 129.6, ij127.0, 124.0, 119.2, 118.8, 117.2, 111.1, 107.6, 60.9, 44.7, 44.5, 28.0, 22.4, 20.8. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}N_3O$ 318.1601; Found 318.1609.

4-(2-Oxo-3-(thiazol-2-ylamino)pyrrolidin-1-yl)benzonitrile (3s). HPLC R_t = 18.5 min. Yield 23 mg, 27%. White solid, mp 169.9-171.0 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.05 – 7.95 (m, 2H), 7.89 – 7.75 (m, 2H), 7.35 (d, *J* = 4.1 Hz, 1H), 6.92 (d, *J* = 4.1 Hz, 1H), 6.41 (s, 1H), 4.71 (dd, *J* = 10.7, 8.4 Hz, 1H), 4.18 – 3.94 (m, 2H), 2.89 (dddd, *J* = 12.5, 8.4, 6.4, 1.8 Hz, 1H), 2.47

– 2.23 (m, 1H). ^{13}C NMR (101 MHz, acetone-d_6) δ 171.0, 170.9, 143.4, 132.9, 131.2, 119.2, 118.4, 108.0, 107.2, 58.6, 44.4, 25.0. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}N_4OS$ 285.0805; Found 285.0811.

4-(3-((4-Chloro-6,7-dihydro-5H-cyclopenta[d]pyrimidin-2-yl)amino)-2-oxopyrrolidin-1-yl)ben-zonitrile (3t). Eluent ethyl acetate – *n*-hexane 3:1. Yield 38 mg, 36%. White solid, mp 218.2-219.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.79 (m, 2H), 7.74 – 7.57 (m, 2H), 6.17 (s, 1H), 4.76 (ddd, *J* = 10.9, 8.5, 5.8 Hz, 1H), 4.00 – 3.76 (m, 2H), 3.03 – 2.73 (m, 5H), 2.27 – 1.97 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 172.4, 160.9, 157.3, 142.9, 133.1, 123.0, 119.2, 118.7, 107.6, 54.5, 44.9, 34.6, 28.2, 26.8, 21.6. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}ClN_5O$ 354.1116; Found 354.1120.

4-(2-Oxo-3-(pyridin-3-ylamino)pyrrolidin-1-yl)benzonitrile (3u). Eluent ethyl acetate – *n*-hexane 3:1. Yield 48 mg, 58%. Brown semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 2.9 Hz, 1H), 8.06 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.90 – 7.78 (m, 2H), 7.74 – 7.62 (m, 2H), 7.13 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.02 (ddd, *J* = 8.2, 2.9, 1.4 Hz, 1H), 4.65 (s, 1H), 4.22 (ddd, *J* = 10.6, 7.9, 2.6 Hz, 1H), 3.91 (dd, *J* = 9.7, 3.9 Hz, 2H), 2.90 (ddt, *J* = 12.1, 7.9, 3.9 Hz, 1H), 2.32 – 1.94 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 143.0, 142.6, 140.2, 136.3, 133.1, 123.8, 120.1, 119.3, 118.6, 108.0, 56.0, 44.8, 28.2. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{14}N_4O$ 279.1240; Found 279.1234.

1-(4-Bromophenyl)-3-((3-methoxyphenyl)amino)pyrrolidin-2-one (3v). Eluent ethyl acetate – *n*-hexane 1:3. Yield 52 mg, 48%. Beige solid, mp 111.0-112.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.58 (m, 2H), 7.57 – 7.46 (m, 2H), 7.15 (t, *J* = 8.1 Hz, 1H), 6.39 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.35 (dd, *J* = 7.9, 2.2 Hz, 1H), 6.29 (t, *J* = 2.3 Hz, 1H), 4.60 (s, 1H), 4.14 (dd, *J* = 10.5, 7.8 Hz, 1H), 3.95 – 3.76 (m, 2H), 3.81 (s, 3H), 2.88 (dddd, *J* = 12.4, 7.8, 5.9, 1.9 Hz, 1H), 2.19 – 1.94 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 160.9, 148.7, 138.1, 132.0, 130.2, 121.1, 117.9, 106.8, 103.6, 100.0, 56.4, 55.2, 45.1, 29.0. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{17}BrN_2O_2$ 361.0546; Found 361.0537.

4-((2-Oxo-1-(thiazol-2-yl)pyrrolidin-3-yl)amino)benzonitrile (3w). Eluent ethyl acetate – *n*-hexane 3:1. Yield 60 mg, 70%. White solid, mp 206.8-207.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6 - $CDCl_3$) δ 7.43 (d, *J* = 3.5 Hz, 1H), 7.38 – 7.26 (m, 2H), 7.05 (d, *J* = 3.5 Hz, 1H), 6.80 – 6.68 (m, 2H), 6.54 (d, *J* = 7.1 Hz, 1H), 4.52 (ddd, *J* = 9.6, 8.3, 7.1 Hz, 1H), 4.25 (ddd, *J* = 11.1, 9.0, 2.3 Hz, 1H), 3.97 (ddd, *J* = 10.9, 9.3, 7.1 Hz, 1H), 2.71 (dddd, *J* = 12.8, 8.4, 7.2, 2.3 Hz, 1H), 2.21 – 2.04 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6 - $CDCl_3$) δ 171.5, 157.4, 151.2, 137.8,

133.4, 120.4, 114.2, 113.0, 98.5, 54.4, 44.8, 26.8. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{12}N_4OS$ 285.0805; Found 285.0814.

3-(Naphthalen-1-ylamino)-1-(thiazol-2-yl)pyrrolidin-2-one (3x). Eluent ethyl acetate – *n*-hexane 1:2. Yield 61 mg, 66%. White solid, mp 184.3-185.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.93 (m, 1H), 7.88 – 7.79 (m, 1H), 7.56 (d, *J* = 3.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.42 – 7.34 (m, 2H), 7.11 (d, *J* = 3.5 Hz, 1H), 6.68 (dd, *J* = 5.9, 2.7 Hz, 1H), 5.11 (s, 1H), 4.46 (dd, *J* = 10.0, 8.0 Hz, 1H), 4.39 (ddd, *J* = 10.9, 9.3, 1.5 Hz, 1H), 4.08 (ddd, *J* = 11.0, 10.0, 6.9 Hz, 1H), 3.10 – 2.89 (m, 1H), 2.28 – 2.05 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 157.5, 142.0, 137.9, 134.3, 128.6, 126.2, 126.1, 125.3, 124.1, 120.3, 119.2, 114.4, 105.7, 55.9, 45.1, 28.8. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}N_3OS$ 310.1009; Found 310.1006.

$Rh_2(esp)_2$-catalysed decomposition of *N*-phenyl α-diazo γ-butyrolactam (1a) in presence of cyclopropylamine. To a vigorous stirred solution of cyclopropylamine (17 mg, 0.3 mmol) and *N*-phenyl α-diazo γ-butyrolactam (56 mg, 0.3 mmol) in dichloromethane (5 ml) was added $Rh_2(esp)_2$ (4.4 mg, 0.006 mmol, 2 mol %) in several portions during 20 minutes and the resulting mixture was stirred for another 20 minutes. The suspension obtained was evaporated to dryness and the residue was subjected to column chromatography on silica gel.

3-(Cyclopropylamino)-1-phenylpyrrolidin-2-one (3y). Eluent ethyl acetate – *n*-hexane 1:3. Yield 24 mg, 37%. White solid, mp 89.8-90.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.60 (m, 2H), 7.45 – 7.34 (m, 2H), 7.22 – 7.13 (m, 1H), 3.80 (dd, *J* = 9.5, 4.5 Hz, 2H), 3.72 (dd, *J* = 10.2, 8.0 Hz, 1H), 2.78 – 2.46 (m, 2H), 2.29 (tt, *J* = 6.6, 3.7 Hz, 1H), 2.17 – 1.93 (m, 1H), 0.87 – 0.48 (m, 2H), 0.47 – 0.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 139.3, 128.9, 124.7, 119.7, 60.6, 45.5, 29.0, 27.1, 6.6, 5.9. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{16}N_2O$ 217.1335; Found 217.1333.

3-(Cyclopropylamino)-1-phenyl-1,5-dihydro-2H-pyrrol-2-one (4). Eluent ethyl acetate – *n*-hexane 1:3. Yield 12 mg, 19%. Brown amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.70 (m, 2H), 7.51 – 7.35 (m, 2H), 7.24 – 7.05 (m, 1H), 5.59 (t, *J* = 2.5 Hz, 1H), 4.51 (s, 1H), 4.32 (dd, *J* = 2.6, 0.8 Hz, 2H), 2.82 – 2.37 (m, 1H), 0.80 – 0.64 (m, 2H), 0.62 – 0.44 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 140.9, 139.5, 129.1, 124.0, 118.6, 98.3, 49.4, 25.2, 6.5. HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{14}N_2O$ 215.1179; Found 215.1177.

ASSOCIATED CONTENT

Supporting Information

Synthetic procedures, analytical data, copies of the ^{1}H, ^{13}C and ^{19}F NMR spectra.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

This research was supported by the Russian Foundation for Basic Research (project grant 19-03-00775). We thank Research Centre for Magnetic Resonance and the Center for Chemical Analysis and Materials Research of Saint Petersburg State University Research Park for obtaining the analytical data.

KEYWORDS: α-diazo lactams; α-amino lactams; N-H insertion; rhodium (II) catalysis; γ-butyrolactams

REFERENCES

[1] S.E. Cleary, X. Li, L.-C. Yang, K.N. Houk, X. Hong, M. Brewer, *J. Am. Chem. Soc.* **2019**, *141*, 3558.

[2] D.P. Hari, J. Waser, *J. Am. Chem. Soc.* **2016**, *138*, 2190.

[3] B. Shen, B. Wan, X. Li, *Angew. Chem. Int. Ed.* **2018**, *57*, 15534.

[4] J.D. Neuhaus, A. Bauer, A. Pinto, N. Maulide, *Angew. Chem. Int. Ed.* **2018**, *57*, 16215.

[5] X. Lin, Y. Tang, W. Yang, F. Tan, L. Lin, X. Liu, X. Feng, *J. Am. Chem. Soc.* **2018**, *140*, 3299.

[6] A. Ford, H. Miel, A. Ring, C.N. Slattery, A.R. Maguire, M.A. McKervey, *Chem. Rev.* **2015**, *115*, 9981. (b) M.P. Doyle, M.A. McKervey, T. Ye, Modern Catalytic Methods for Organic Synthesis with Diazo Compounds, John Wiley & Sons, Inc., New York, NY, 1998.

[7] T. Ye, M.A. McKervey, *Chem. Rev.* **1994**, *94*, 1091.

[8] J. Ueda, S. Harada, H. Nakayama, T. Nemoto, *Org. Biomol. Chem.* **2018**, *16*, 4675.

[9] H. Yang, A.M. Swartz, H.J. Park, P. Srivastava, K. Ellis-Guardiola, D.M. Upp, G. Lee, K. Belsare, Y. Gu, C. Zhang, R.E. Moellering, J.C. Lewis, *Nat. Chem.* **2018**, *10*, 318.

[10] Z. Wang, A.G. Herraiz, A.M. del Hoyo, M.G. Suero, *Nature* **2018**, *554*, 86.

[11] I.D. Jurberg, H.M.L. Davies, *Chem. Sci.* **2018**, *9*, 5112.

[12] L. Chen, H. Cui, Y. Wang, X. Liang, L. Zhang, C.-Y. Su, *Dalton Trans.* **2018**, *47*, 3940.

[13] N.L. Loskutova, N.V. Shvydkiy, Y.V. Nelyubina, D.S. Perekalin, *J. Organomet. Chem.* **2018**, *867*, 86.

[14] J. Kang, L. Chen, H. Cui, L. Zhang, C.-Y. Su, *Chin. J. Chem.* **2017**, *35*, 964.

[15] S.M. Nicolle, C.J. Hayes, C.J. Moody, *Chem. - Eur. J.* **2015**, *21*, 4576.

[16] K. Wang, P. Chen, D. Ji, X. Zhang, G. Xu, J. Sun, *Angew. Chem. Int. Ed.* **2018**, *57*, 12489.

[17] V. Arredondo, S.C. Hiew, E.S. Gutman, I.D.U.A. Premachandra, D.L. Van Vranken, *Angew. Chem. Int. Ed.* **2017**, *56*, 4156.

[18] A. DeAngelis, O. Dmitrenko, J.M. Fox, *J. Am. Chem. Soc.* **2012**, *134*, 11035.

[19] R.M. Sultanova, A.N. Lobov, L.V. Spirikhin, *Chem. Heterocycl. Compd.* **2015**, *51*, 1048.

[20] D. Zhukovsky, D. Dar'in, G. Kantin, M. Krasavin, *Eur. J. Org. Chem.* **2019**, *2019*, 2397.

[21] W.R. Ewing, M.R. Becker, V.E. Manetta, R.S. Davis, H.W. Pauls, H. Mason, Y.M. Choi-Sledeski, D. Green, D. Cha, A.P. Spada, D.L. Cheney, J.S. Mason, S. Maignan, J.-P. Guilloteau, K. Brown, D. Colussi, R. Bentley, J. Bostwick, C.J. Kasiewski, S.R. Morgan, R.J. Leadley, C.T. Dunwiddie, M.H. Perrone, V. Chu, *J. Med. Chem.* **1999**, *42*, 3557.

[22] Y.M. Choi-Sledeski, D.G. McGarry, D.M. Green, H.J. Mason, M.R. Becker, R.S. Davis, W.R. Ewing, W.P. Dankulich, V.E. Manetta, R.L. Morris, A.P. Spada, D.L. Cheney, K.D. Brown, D.J. Colussi, V. Chu, C.L. Heran, S.R. Morgan, R.G. Bentley, R.J. Leadley, S. Maignan, J.-P. Guilloteau, C.T. Dunwiddie, H.W. Pauls, *J. Med. Chem.* **1999**, *42*, 3572.

[23] X. Lin, W. Chen, Z. Qiu, L. Guo, W. Zhu, W. Li, Z. Wang, W. Zhang, Z. Zhang, Y. Rong, M. Zhang, L. Yu, S. Zhong, R. Zhao, X. Wu, J.C. Wong, G. Tang, *J. Med. Chem.* **2015**, *58*, 2809.

[24] M.G.R. Beyaert, R.P. Daya, B.A. Dyck, R.L. Johnson, R.K. Mishra, *Eur. Neuropsychopharmacol.* **2013**, *23*, 253.

[25] D. Basu, Y. Tian, J. Bhandari, J.R. Jiang, P. Hui, R.L. Johnson, R.K. Mishra, *PLoS ONE* **2013**, *8*, e70736.

[26] S. Muthusamy, T. Karikalan, *Org Biomol Chem* **2014**, *12*, 9243.

[27] H. Huang, Y. Wang, Z. Chen, W. Hu, *Adv. Synth. Catal.* **2005**, *347*, 531.

[28] R. Dada, Z. Wei, R. Gui, R.J. Lundgren, *Angew. Chem. Int. Ed.* **2018**, *57*, 3981.

[29] S. Jansone-Popova, J.A. May, *J. Am. Chem. Soc.* **2012**, *134*, 17877.

[30] A.C. Hunter, K. Chinthapally, I. Sharma, *Eur. J. Org. Chem.* **2016**, *2016*, 2260.

[31] S.R. Hansen, J.E. Spangler, J.H. Hansen, H.M.L. Davies, *Org. Lett.* **2012**, *14*, 4626.

[32] P.W. Glunz, D.F. Sitkoff, M.S. Bodas, N.D. Yadav, S. Patil, P.S.M. Rao, K. Thiyagarajan, T.K. Maishal, PCT Int Appl WO2016144936; *Chem Abstr* **2016**, *165*, 416522.

[33] C.T. Supuran, J.-Y. Winum, *Future Med. Chem.* **2015**, *7*, 1407.

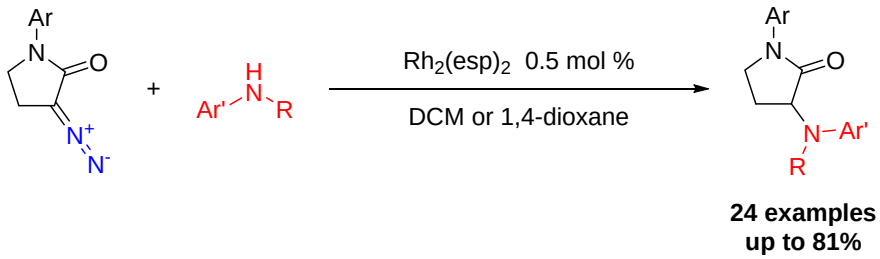
[34] C.T. Supuran, V. Alterio, A. Di Fiore, K. D' Ambrosio, F. Carta, S.M. Monti, G. De Simone, *Med. Res. Rev.* **2018**, *38*, 1799.

[35] M. Krasavin, A. Shetnev, S. Baykov, S. Kalinin, A. Nocentini, V. Sharoyko, G. Poli, T. Tuccinardi, M. Korsakov, T.B. Tennikova, C.T. Supuran, *Eur. J. Med. Chem.* **2019**, *168*, 301.

[36] A.V. Galkin, J.S. Melnick, S. Kim, T.L. Hood, N. Li, L. Li, G. Xia, R. Steensma, G. Chopiuk, J. Jiang, Y. Wan, P. Ding, Y. Liu, F. Sun, P.G. Schultz, N.S. Gray, M. Warmuth, *Proc. Natl. Acad. Sci.* **2007**, *104*, 270.

[37] E.D. Deeks, *Target. Oncol.* **2016**, *11*, 693.

Graphical abstract



TOC text

α-Arylamino-γ-butyrolactams are valuable scaffolds in medicinal chemistry. Their assembly has been achieved via NH-insertion into an anilinic amino group of metal carbene species generated,

10.1002/ejoc.201900565

via the use of $Rh_2(esp)_2$ catalyst, from the hitherto poorly explored α-diazo-γ-butyrolactams. The reaction works well for aromatic and heteroaromatic (but not aliphatic) amines.

Key topic

Diazo compounds