Ultrasound-assisted synthesis of eight novel and highly functionalized 2-aminonitrile oxazoles via Ugi-3CR

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Abstract

Eight novel 2-aminonitrile oxazoles were synthesized efficiently and quickly via an Ugi reaction in its three-component version in moderate to good yields (61-79%) at room temperature or in good to excellent yields (73-90%) under ultrasound irradiation (USI) conditions. It is noteworthy that not only the yields were improved by using USI, also the reaction times decreased considerably, from 3 hours (at r.t.) to 1 hour (under USI), depending on the substituents in the final products, which are highly functionalized because have an amino group, a nitrile group, an oxazole group and a very reactive methylene-linked biaryl. In this context, they can be used for further condensations, cyclizations and/or functionalizations toward a variety of compounds with potential applications in several fields of knowledge like optics, material science and medicinal chemistry.

Keywords

Ugi-3CR, oxazoles, aminonitriles, ultrasound irradiation

Introduction

The oxazole ring is an oxygen and nitrogen-containing five-membered heterocyclic system of high interest in medicinal chemistry because it is the core of various natural and synthetic products exhibiting very valuable pharmacological activities, for example, the non-steroidal anti-inflammatory drug Oxaprozin (**1**),[1] and the antitubercular oxazole-based compound **2**,[2] **figure 1**. Thus, we herein communicate an ultrasound-assisted multicomponent-based method toward the synthesis of the eight novel and highly functionalized 2-aminonitrile oxazoles **3a-h**, which could be used for further *in vitro* SAR studies, as well as for further smart synthetic transformations.

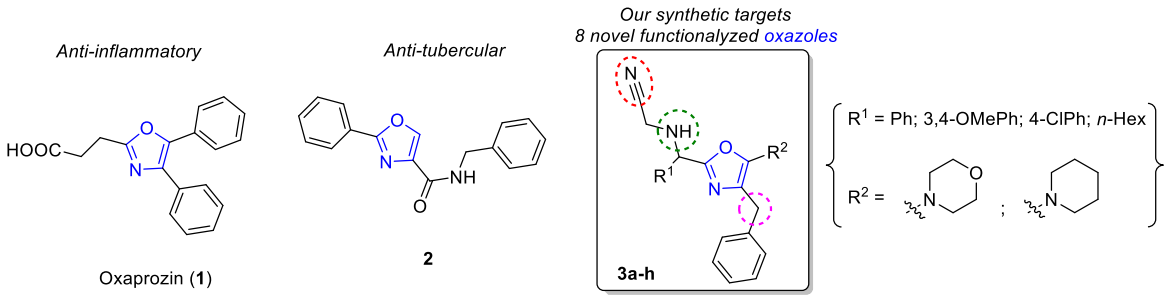
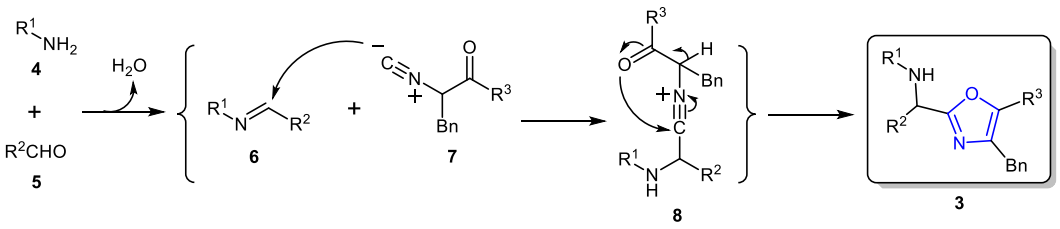


Figure 1. Selected oxazoles with pharmacological activity and our synthetic targets.

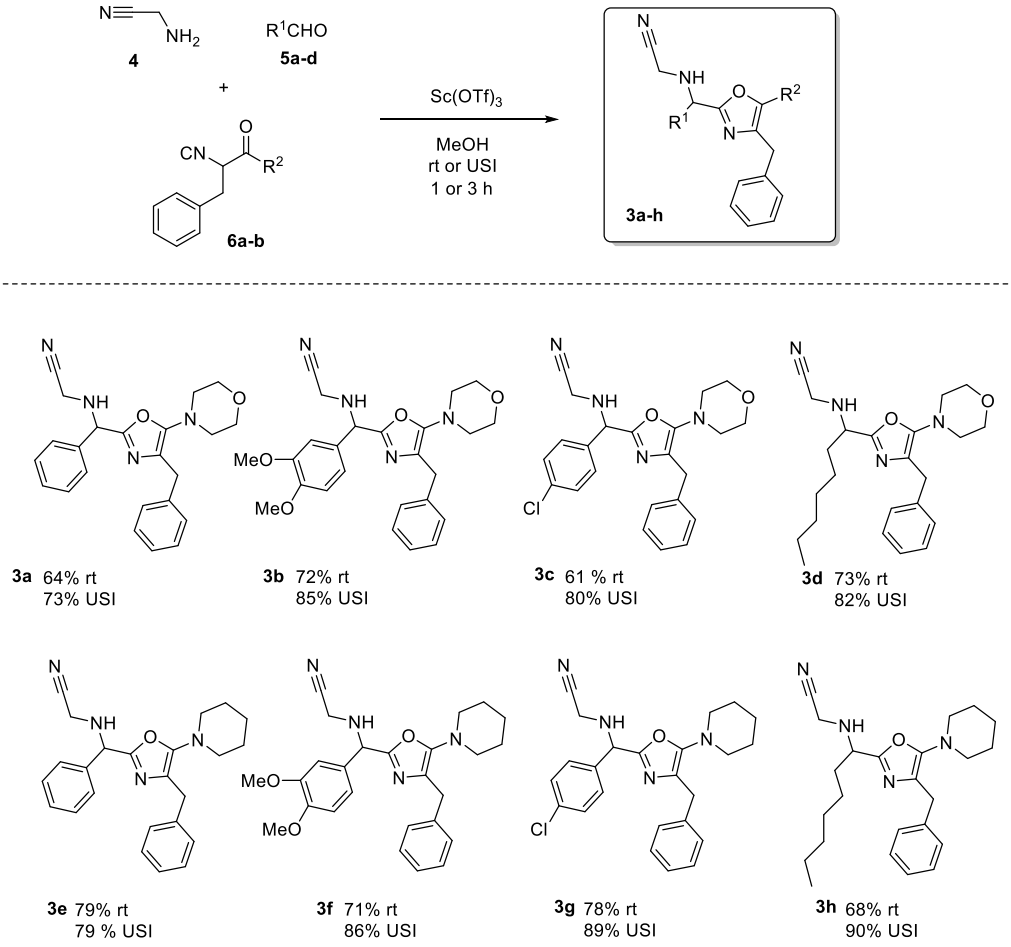
Poly-substituted oxazoles are commonly synthesized through a cyclization step involving the use of substrates prepared stepwise under harsh conditions. Thus, among all reported methods, those allowing the synthesis of highly functionalized oxazoles are via: *i)* visible-light photocatalysis of α-bromoketones with benzylamines,[3] *ii)* intramolecular oxidative cyclization of *N*-styrylbenzamides,[4] *iii)* Copper(II) triflate catalyzed coupling of α-diazoketones with amides (used to synthesize analogues of Balzoxin),[5] *iv)* [2+2+1] heteroannulation of alkynes, nitriles and *O*-atoms using triflic acid (harsh acidic conditions),[6] *v)* ring expansion of 2-carbonyl ketoaziridines (used to synthesize the Oxaprozin **1**),[7] and *vi)* via phenyl iodine diacetate (PIDA)-mediated intramolecular cyclization of enamides.[8] Besides, it has been reported some multicomponent-based synthetic strategies toward a variety of polysubstituted and highly functionalized oxazoles. It is noteworthy that Multicomponent reactions (MCR's) are privileged one pot processes in which sequential combinations of at least three reagents in the same pot are involved, reducing the use of harsh conditions and the atomic waste.[9] In this context, the general MCR-based method to synthesize functionalized oxazoles is the Van Leusen oxazole synthesis from aldehydes and the bifunctional TOSMIC.[10] However, particularly with respect to 5-amino oxazoles, pioneering works were performed by J. Zhu and H. Bienaymé via a sequential combination of amines, aldehydes and ring-chain tautomerizable isocyanides (aminoacid derivatives) via the Ugi-type MCR in its three component version.[11-13] Further works from J. Zhu's group were published toward 5-alcoxy oxazoles.[14-15] The more plausible reaction mechanism involves a condensation of the amines **4** with the aldehydes **5** to give the intermediate imines **6**, which by a further α-nucleophilic attack of the isocyanides **7** coupled to a ring-chain tautomerizable process of the nitrilium ion **8** results in the heterocycles **3**, **scheme 1**.



Scheme 1. Reaction mechanism involved in the Ugi-3CR toward 5-amino oxazoles

Results and discussion

Thus, inspired on the Zhu's work and after optimizing the reaction conditions, the series of novel 5-aminonitrile oxazoles **3a-h** were synthesized either, in moderate to good yields (61-79%) at room temperature or in good to excellent yields (73-90%) under ultrasound irradiation (USI) conditions. The aminoacetonitrile (**4**) was combined sequentially with the aliphatic or aromatic aldehydes **5a-d** (decorated with substituents having different stereoelectronic nature), and the isocyanides **6a-b** (morpholine or piperidine derivatives) in anhydrous MeOH [1M] using scandium(III) triflate as Lewis acid catalyst to promote the α-nucleophilic attack, **scheme 2**.



Scheme 2. Substrate scope

As seen, one more time the great usefulness of the green ultrasound irradiation (USI) was demonstrated, not only for reducing the reaction times (from 3 to 1 h), but also for increasing the yields (from 61-79 to 73-90%). It is noteworthy that no much variation in the yields were observed. This behavior may be understood in terms of the generality of this methodology. Moreover, all the synthesized products were characterized by typical spectroscopic techniques, even by mp and R_f.

The **figure 2** shows the ^{1}H and ^{13}C NMR spectra for the selected 5-aminoacetonitrile oxazole **3a**. As it can be seen, the C-H bonding the three starting reagents (amine, aldehyde and isocyanide) appear as singlet in the H NMR spectra approximately at 5.0 ppm and a peak in the C NMR spectra approximately at 60.0 ppm (depending on the oxazole **3a-h**). All the other key signals and peaks can be found easily from these spectra,

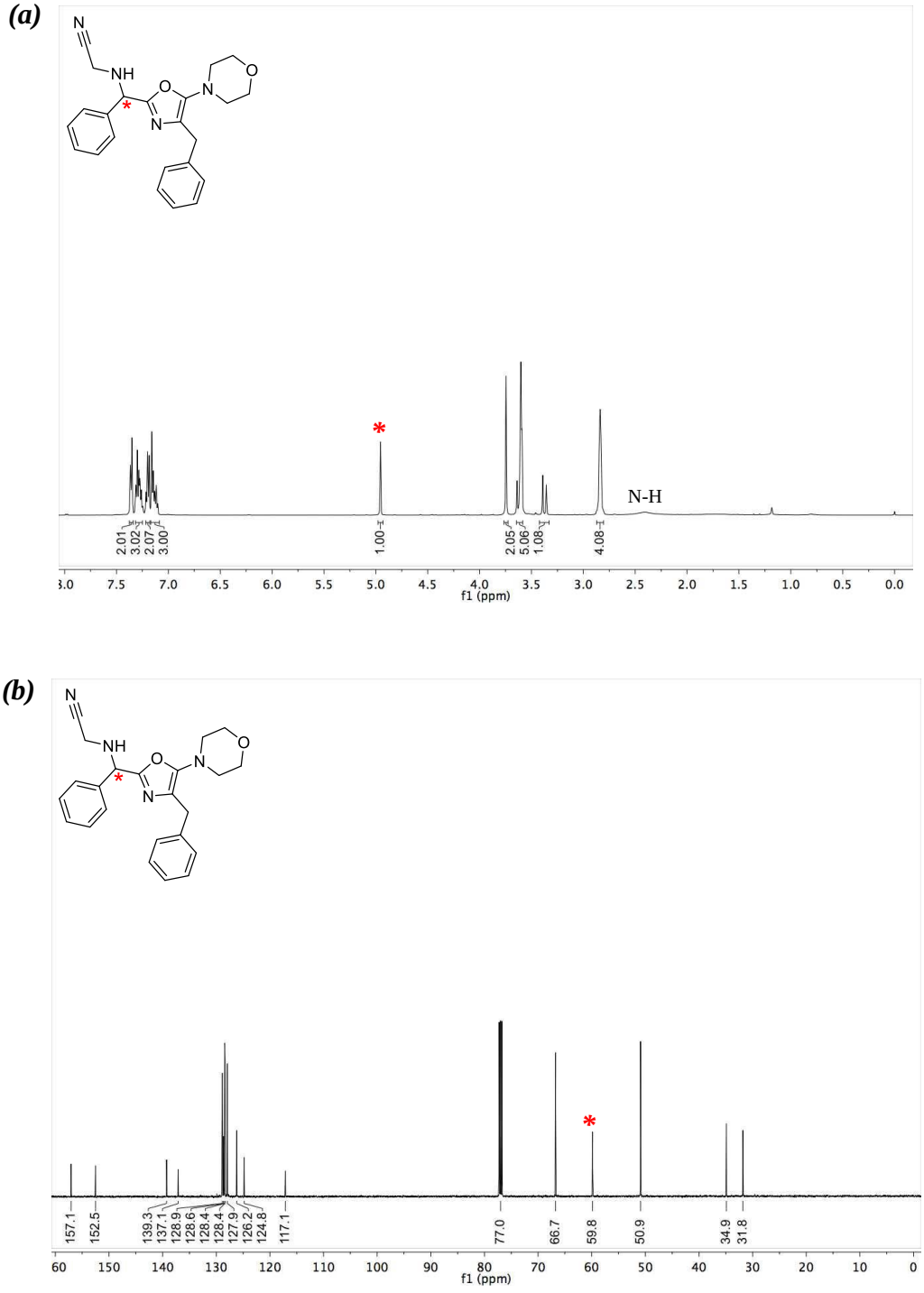


Figure 2. (a) ^{1}H and (b) ^{13}C NMR spectra for the selected 5-aminoacetonitrile oxazole **3a**.

The products **3a-h** are highly functionalized oxazole-containing products. In this context, they can be used for further condensations, cyclizations and/or functionalizations toward a variety of compounds with potential applications in several fields of knowledge like optics, material science and medicinal chemistry. For example, the nitrile moiety can be used to perform [3+2] dipolar cyclizations. The secondary amine can be used for *N*-acyl substitutions, S_N2, or for tandem-type condensations. The methylene-linked biaryl has a very short value of pKa. The oxazole ring can be used as aza-diene for Diels-Alder cycloadditions.[16-20] In the same way, our compounds can be taken also as starting points for future SAR studies, for example, toward anti-inflammatories or antitubercular because there are some reports describing the usefulness of polysubstituted and polyfunctionalized oxazoles from these approaches.

Acknowledgements

I.A.I. acknowledges PAPIIT-UNAM-Mexico (IN100415) for financial support. E.G.-Z. thanks CONACyT-México (236879) for financial support. R.G.-M is grateful for financial support from the DAIP (859/2016) and CONACYT (CB-2011-166747-Q) projects. A.I.-J. acknowledges QI-DQ-CBI-UAMI for his position as visiting professor (40966) and PRODEP for financial support (12413143).

Experimental part

General information, instrumentation, and chemicals

^{1}H and ^{13}C NMR spectra were acquired on either, Bruker Advance III spectrometers (500 or 400 MHz). The solvent used was deuterated chloroform ($CDCl_3$). Chemical shifts are reported in parts per million (δ/ppm). Internal reference for ^{1}H NMR spectra is respect to TMS at 0.0 ppm. Internal reference for ^{13}C NMR spectra is respect to $CDCl_3$ at 77.0 ppm. Coupling constants are reported in Hertz (*J*/Hz). Multiplicities of the signals are reported using the standard abbreviations: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). NMR spectra were analyzed using the MestreNova software version 10.0.1-14719. IR spectra were acquired on a Perkin Elmer 100 spectrometer. The absorbance peaks are reported in reciprocal centimeters (υ_{max}/cm^{-1}). US-irradiated reactions were performed in sealed vials placed in a water bath of a sonicator cleaner working at frequencies of 42 kHz ± 6%. Reaction progress was monitored by TLC on precoated Silica-gel 60 F_{254} plates and the spots were visualized under UV light at 254 or 365 nm. Mixtures of hexanes (Hex) with ethyl acetate (AcOEt) were used to run TLC and for measuring retention factors (R_f). Flash column chromatography was performed using silica gel (230-400 mesh) and mixtures of Hex with AcOEt in different proportions (v/v) as mobile phase. All starting materials were purchased from Sigma-Aldrich and were used without further purification. Chemical names and drawings were obtained using the ChemBioDraw Ultra 13.0.2.3020 software package. The purity for all the synthesized products (up to 99%) was assessed by NMR.

Synthesis and characterization of the 6-propargyl-pyrrolo[3,4-*b*]pyridin-5-ones **3a-h**

General procedure (GP): Aminoacetonitrile (**4**) (1.1 equiv.), the corresponding aldehyde **5** (1.0 equiv.) and the $Sc(OTf)_3$ (3% mol) were placed in a 10 mL sealed vial equipped with a magnetic stirring bar in methanol [1.0 M]. Then, the mixture was stirred at rt or under USI conditions for 30 min and the corresponding isocyanide **6** (1.2 equiv.) was added. The new mixture was stirred at rt for 3 h or under USI conditions for 1 h. Then, the solvent was removed to dryness under vacuum. The crude was diluted in dichloromethane (5.0 mL) and washed with a concentrated aq. solution of $NaHCO_3$ (3×15 mL) and brine (3×15 mL). The organic layer was dried using Na_2SO_4, filtered over celite pad and the solvent was removed to dryness under vacuum. The residue was purified via silica-gel chromatoflash using mixtures of Hex–EtOAc (v/v) in different proportions to afford the corresponding oxazoles **3a-h**.

2-(((4-benzyl-5-morpholinooxazol-2-yl)(phenyl)methyl)amino)acetonitrile **3a**

According to the GP, aminoacetonitrile (29.0 mg, 0.517 mmol), benzaldehyde (49.9 mg, 0.470 mmol), scandium(III) triflate (7.0 mg, 0.014 mmol), and the 2-isocyano-1-morpholino-3-phenylpropan-1-one (138.0 mg, 0.564 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3a** (118.0 mg, 64%, rt) or (135.0 mg, 73%, USI) as a white oil; R_f = 0.31 (Hex-AcOEt = 3/1 v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1697 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.38–7.34 (m, 2H), 7.32–7.25 (m, 3H), 7.22–7.18 (m, 2H), 7.17–7.09 (m, 3H), 4.96 (s, 1H), 3.75 (s, 2H), 3.65–3.58 (m, 5H), 3.37 (d, *J* = 17.5 Hz, 1H), 2.88–2.80 (m, 4H), 2.39 (bs, 1H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 157.1, 152.5, 139.3, 137.1, 128.9, 128.7, 128.5, 128.4, 128.0, 126.2, 124.8, 117.9, 66.8, 59.9, 50.9, 34.9, 31.8.

2-(((4-benzyl-5-morpholinooxazol-2-yl)(3,4-dimethoxyphenyl)methyl)amino)acetonitrile **3b**

According to the GP, aminoacetonitrile (30.0 mg, 0.535 mmol), 3,4-dimethoxybenzaldehyde (80.8 mg, 0.486 mmol), scandium(III) triflate (6.0 mg, 0.141 mmol), and the 2-isocyano-1-morpholino-3-phenylpropan-1-one (142.0 mg, 0.583 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3b** (158.0 mg, 72%, rt) or (188.0 mg, 85%, USI) as a yellow oil; R_f = 0.35 (Hex-AcOEt = 1/1 v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1699 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.20–7.09 (m, 5H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.87 (s, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 4.90 (s, 1H), 3.78 (s, 3H), 3.76–3.73 (m, 5H), 3.63–3.57 (m, 5H), 3.35 (d, *J* = 17.6 Hz, 1H), 2.87–2.81 (m, 4H), 2.35 (bs, 1H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 157.4, 152.4, 149.4, 149.3, 139.4, 129.4, 128.5, 128.4, 126.2, 124.9, 120.7, 117.2, 111.1, 110.5, 66.8, 59.5, 55.9, 51.0, 34.8, 31.8.

2-(((4-benzyl-5-morpholinooxazol-2-yl)(4-chlorophenyl)methyl)amino)acetonitrile **3c**

According to the GP, aminoacetonitrile (26.0 mg, 0.463 mmol), 4-chlorobenzaldehyde (59.2 mg, 0.421 mmol), scandium(III) triflate (6.0 mg, 0.012 mmol), and the 2-isocyano-1-morpholino-3-phenylpropan-1-one (123.0 mg, 0.505 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3c** (109.0 mg, 61%, rt) or (140.0 mg, 80%, USI) as a withe oil; R_f = 0.32 (Hex-AcOEt = 3/1 v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1696 (C=O); ^{1}H NMR (500

MHz, $CDCl_3$, 25 °C): δ 7.29 (d, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.20–7.16 (m, 2H), 7.15–7.08 (m, 3H), 4.91 (s, 1H), 3.73 (s, 2H), 3.62–3.57 (m, 5H), 3.32 (d, *J* = 17.6 Hz, 1H), 2.87–2.81 (m, 4H), 2.41 (bs, 1H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 156.7, 152.7, 139.2, 135.7, 134.6, 129.4, 129.1, 128.5, 128.4, 126.3, 124.9, 117.1, 66.8, 59.2, 50.9, 34.9, 31.8.

2-((1-(4-benzyl-5-morpholinooxazol-2-yl)heptyl)amino)acetonitrile **3d**

According to the GP, aminoacetonitrile (26.0 mg, 0.463 mmol), heptanaldehyde (0.060mL, 0.421 mmol), scandium(III) triflate (6.0 mg, 0.012 mmol), and the 2-isocyano-1-morpholino-3-phenylpropan-1-one (123.0 mg, 0.505 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3d** (123.0 mg, 73%, rt) or (138.0 mg, 82%, USI) as a white oil; R_f = 0.30 (Hex-AcOEt = 3/1 v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1694 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.22–7.10 (m, 5H), 3.77–3.70 (m, 3H), 3.67–3.63 (m, 4H), 3.54 (d, *J* = 17.6 Hz, 1H), 3.49 (d, *J* = 17.6 Hz, 1H), 2.96–2.87 (m, 4H), 1.81–1.67 (m, 3H), 1.30–1.17 (m, 8H), 0.79 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 158.8, 152.3, 139.4, 128.45 (2), 126.2, 124.9, 117.6, 66.9, 56.3, 51.1, 35.4, 34.0, 31.8, 31.6, 28.8, 25.6, 22.5, 14.0.

2-(((4-benzyl-5-(piperidin-1-yl)oxazol-2-yl)(phenyl)methyl)amino)acetonitrile **3e**

According to the GP, aminoacetonitrile (27.0 mg, 0.463 mmol), benzaldehyde (0.043 mL, 0.421 mmol), scandium(III) triflate (6.0 mg, 0.012 mmol), and the 2-isocyano-3-phenyl-1-(piperidin-1-yl)propan-1-one (122.0 mg, 0.505 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3e** (134.0 mg, 79%, rt) or (134.0 mg, 79%, USI) as a yellow oil; R_f = 0.30 (Hex-AcOEt = 4/1, v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1658 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.36–7.33 (m, 2H), 7.29–7.23 (m, 3H), 7.19–7.14 (m, 4H), 7.12–7.01 (m, 1H), 4.92 (s, 1H), 3.72 (s, 2H), 3.57 (d, *J* = 17.5 Hz, 1H), 3.34 (d, *J* = 17.6 Hz, 1H), 2.84–2.78 (m, 4H), 2.35 (bs, 1H), 1.51–1.46 (m, 4H), 1.42–1.39 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 156.5, 154.0, 139.7, 137.4, 128.6, 128.5, 128.4, 128.0, 126.1, 123.4, 117.3, 66.8, 59.9, 52.0, 34.9, 31.9, 25.8, 23.8.

2-(((4-benzyl-5-(piperidin-1-yl)oxazol-2-yl)(3,4-dimethoxyphenyl)methyl)amino) acetonitrile **3f**

According to the GP, aminoacetonitrile (27.0 mg, 0.463 mmol), 3,4-dimethoxybenzaldehyde (73 mg, 0.421 mmol), scandium(III) triflate (6.0 mg, 0.012 mmol), and the 2-isocyano-3-phenyl-1-(piperidin-1-yl)propan-1-one (127.0 mg, 0.505 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3f** (140.0 mg, 71%, rt) or (168.0 mg, 86%, USI) as a yellow oil; R_f = 0.36 (Hex-AcOEt = 1/1, v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1692 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.29–7.23 (m, 4H), 7.22–7.15 (m, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 4.98 (s, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 3.82 (s, 2H), 3.67 (d, *J* = 17.7 Hz, 1H), 3.44 (d, *J* = 17.5 Hz, 1H), 2.41 (bs, 1H), 2.94–2.88 (m, 4H), 1.62–1.56 (m, 4H), 1.53–1.48 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 156.8, 153.9, 149.3, 149.2, 139.8, 129.7, 128.5, 128.3, 126.0, 123.6, 117.3, 111.1, 110.6 66.8, 59.5, 55.9(2), 52.0, 34.8, 31.8, 25.8, 23.8.

2-(((4-benzyl-5-(piperidin-1-yl)oxazol-2-yl)(4-chlorophenyl)methyl)amino)acetonitrile **3g**

According to the GP, aminoacetonitrile (26.0 mg, 0.463 mmol), 4-chlorobenzaldehyde (59.0 mg, 0.421 mmol), scandium(III) triflate (6.0 mg, 0.013 mmol), and the 2-isocyano-3-phenyl-1-(piperidin-1-yl)propan-1-one (122.0 mg, 0.505 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3g** (139.0 mg, 78%, rt) or (158.0 mg, 89%, USI) as a yellow oil; R_f = 0.33 (Hex-AcOEt = 3/1, v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1696 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.29 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H),7.20–7.17 (m, 2H), 7.16–7.13 (m, 2H), 7.12–7.08 (m, 1H), 4.90 (s, 1H), 3.71 (s, 2H), 3.58 (d, *J* = 17.5 Hz, 1H), 3.32 (d, *J* = 17.3 Hz, 1H), 2.87–2.76 (m, 4H), 2.38 (bs, 1H), 1.50–1.46 (m, 4H), 1.43–1.38 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ 156.0, 154.1, 139.6, 134.5, 129.4, 129.1, 128.5, 128.4, 126.1, 123.5, 117.1, 59.2, 52.0, 34.9, 31.9, 25.8, 23.8.

2-((1-(4-benzyl-5-(piperidin-1-yl)oxazol-2-yl)heptyl)amino)acetonitrile **3h**

According to the GP, aminoacetonitrile (26.0 mg, 0.463 mmol), heptanaldehyde (0.060 mL, 0.421 mmol), scandium(III) triflate (6.0 mg, 0.013 mmol), and the 2-isocyano-3-phenyl-1-(piperidin-1-yl)propan-1-one (122.0 mg, 0.505 mmol) were reacted together in MeOH (0.5 mL) to afford the oxazole **3h** (113.0 mg, 68%, rt) or (150.0 mg, 90%, USI) as a yellow oil; R_f = 0.30 (Hex-AcOEt = 4/1, v/v); FT-IR (ATR) υ_{max}/cm^{-1} 1699 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): 7.29–7.09 (m, 5H), 4.49 (t, *J* = 7.1 Hz, 1H), 3.74–3.69 (m, 1H), 3.59–3.53 (m, 1H), 3.50 (s, 1H), 3.46–3.40 (m, 1H), 3.37–3.31 (m, 1H), 3.23–3.15 (m, 2H), 3.13–3.06 (m, 1H), 2.90–2.86 (m, 2H), 1.79–1.62 (m, 2H), 1.60–1.41 (m, 8H), 1.33–1.13 (m, 6H), 0.84–0.77 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 166.8, 161.6, 159.3, 149.1, 139.7, 128.9, 128.1, 123.9, 123.1, 77.9, 72.1, 60.2, 54.2, 39.7, 31.5, 29.6, 29.3, 29.1, 26.3, 23.9, 22.6, 22.5, 14.0.

The authors declare no competing financial interests. Samples of the products **3a-h** are available from the authors.

References

1.- Fernandes, E.; Costa, D.; Toste, S.A.; Lima, J.L.F.C.; Reis, L. *Free Rad. Biol. Med.* **2004**, *37*, 1895.

2.- Moraski, G.C.; Markley, L.D.; Chang, M.; Cho, S.; Franzblau, S.G.; Hwang, C.H.; Boshoff, H.; Miller, M.J. *Bioorg. Med. Chem.* **2012**, *20*, 2214.

3.- Chatterjee, T.; Cho, J.Y.; Cho, E.J. *J. Org. Chem.* **2016**, *81*, 6995.

4.- Hempel, C.; Nachtsheim, B.J. *Synlett* **2013**, *24*, 2119.

5.- Reddy, M.R.; Reddy, G.N.; Mehmood, U.; Hussein, I.A.; Rahman, S.U.; Harrabi, K.; Reddy, B.V.S. *Synthesis* **2015**, *47*, 3315.

6.- Saito, A.; Taniguchi, A.; Kambara, Y.; Hanzawa, Y. *Org. Lett.* **2013**, *15*, 2672.

7.- Samimi, H.A.; Mohammadi, S. *Synlett* **2013**, *24*, 223.

8.- Zheng, Y.; Li, X.; Ren, C.; Zhang-Negrerie, D.; Du, Y.; Zhao, K. *J. Org. Chem.* **2012**, *77*, 10353.

9.- Ramón D.J.; Yus, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 1602.

10.- Van Leusen, A. *Tetrahedron Lett.* **1972**, *13*, 3114.

11.- Sun, X.; Janvier, P.; Zhao, G.; Bienaymé, H.; Zhu, J. *Org. Lett.* **2001**, *3*, 877.

12.- Janvier, P.; Sun, X.; Bienaymé, H.; Zhu, J. *Am. Chem. Soc.* **2002**, *124*, 2560.

13.- Bughin, C.; Zhao, G.; Bienaymé, H.; Zhu, J. *Chem. Eur. J.* **2006**, *12*, 1174.

14.- Cuny, G.; Gámez-Montaño, R.; Zhu, J. *Tetrahedron* **2004**, *60*, 4879

15.- Bonne, D.; Dekhane, M.; Zhu, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 2485.

16.- Islas-Jácome, A.; González-Zamora, E.; Gámez-Montaño, R. *Tetrahedron Lett.* **2011**, *52*, 5245.

17.- Islas-Jácome, A.; Cárdenas-Galindo, L. E.; Jerezano, A. V.; Tamariz, J.; González-Zamora, E.; Gámez-Montaño, R. *Synlett* **2012**, *23*, 2951.

18.- Islas-Jácome, A.; Gutierrez-Carrillo, A.; García-Garibay, M. A.; González-Zamora, E. *Synlett* **2014**, *25*, 403.

19.- Islas-Jácome, A.; Rentería-Gómez, A.; Rentería-Gómez, M. A.; González-Zamora, E.; Jiménez-Halla, J.O.C.; Gámez-Montaño, R. *Tetrahedron Lett.* **2016**, *57*, 3496.

20.- Vázquez-Vera, O.; Sánchez-Badillo, J.S.; Islas-Jácome, A. Rentería-Gómez, M.A.; Pharande, S.G.; Cortes-García, C.J.; Rincón-Guevara, M.A.; Ibarra, I.A.; Gámez-Montaño, R.; González-Zamora, E. *Org. Biomol. Chem.* **2017**, *15*, 2363.