Synthesis of 1,5-disubstituted-1H-tetrazole methane-linked bis-heterocycles via Ugi-azide

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Abstract

A series of twelve new 1,5-disubstituted-1*H*-tetrazoles (1,5-DS-T) were synthesized by a MCR Ugi-azide. The Ugi-azide products were obtained in moderate to excellent yields (50 - 96%). The 1,5-DS-T have in their structure a furan ring in linked manner. Both heterocycles are present in many biologically active products. 1,5-DS-T act like *cis*-amide bond bioisosters, while furan is used to optimize the solubility parameters and bioavailability of poorly soluble molecules.

Keywords: Multicomponent Reactions, Ugi-azide, bis-heterocycles, tetrazoles, furan.

Introduction

Multicomponent reactions[1] (MCR) are convergent processes, in which at least three different substrates react in the same flask to give compounds where converge most of the atoms present in the starting materials. Among them, isocyanide-based multicomponent reactions (I-MCR) are one of the most powerful and efficient tools for the synthesis of compounds with high complexity.[2] The most useful I-MCR is the Ugi reaction, in which amines, aldehydes, carboxylic acids and an isocyanides react toward *N*-substituted aminoamides.[3] A variant of the Ugi reaction is the Ugi-azide, in which carboxylic acid is replaced by hydrazoic acid to give 1,5-disubstituted-1*H*-tetrazoles (1,5-DS-T).[4] However, direct use of hydrazoic acid may result in lower yields due to its volatility. Azidotrimethylsilane ($TMSN_3$) has been used instead sodium azide (NaN_3) to generate the HN_3 required in Ugi-azide reaction .[5]

Tetrazoles are an important class of nitrogen heterocycles formed by a five-membered ring with one carbon and four nitrogen atoms. This privileged class of heterocycles can be classified by their substitution pattern as: a) tetrazole, b) monosubstituted tetrazoles (2- or 5- substituted), c) disubstituted (1,5- or 2,5- disubstituted) and d) bicyclic fused tetrazoles.[6] Tetrazoles are present in various molecules of great interest in medicinal chemistry because them contribute to pharmacological properties of bioactive products.[7] 1,5-DS-T are bioisosters of the *cis*-amide bonds of peptides due to some similarities in their physicochemical properties.[8] In the other hand, furan is not found in animal metabolism, but it is abundantly available in secondary metabolites of plants such as furanolactones and furanocoumarins.[9] Several furan metabolites have exhibited therapeutic properties as antimicrobial, antihypertensive, relaxants and antidiuretic.[10]

Several reports describe the synthesis of compounds with 1,5-DS-T system. However, the most important are those based on click reactions of organic azides with cyanides[11] and the Ugi-azide reaction.[12]

Actually, the synthesis of *bis*-heterocycles has taken relevance due to their applications in many fields of knowledge like agrochemistry, [13] optics[14] and medicinal chemistry.[15] The majority of their properties lie in medicinal chemistry.[16] In this context, the integration of two heterocyclic moieties in

a single molecule usually creates unexpected interactions with biological targets enabling discovery of new kind of potent modulators with therapeutic activities enhanced.[17]

There are many reports in the literature describing the synthesis of new 1,5-DS-T, which are linked to other heterocycles,[18] but only a few reports of them are via one pot Ugi-azide process, which obtained 1,5-DS-T linked with other heterocyclic.[19] It is noteworthy that only two reports described for the synthesis of 1,5-DS-T linked with furans.[20]

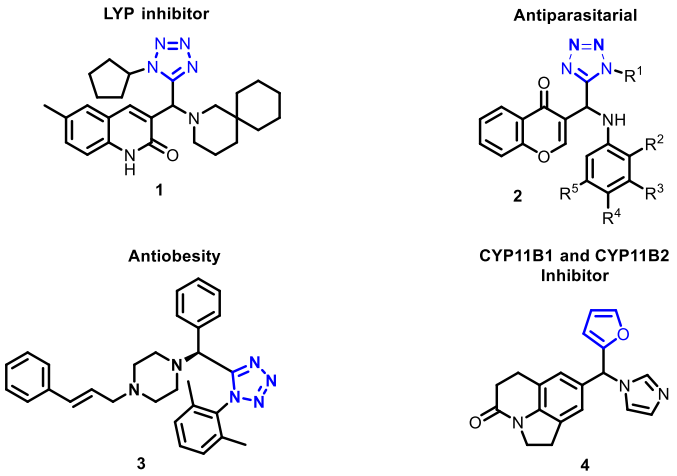
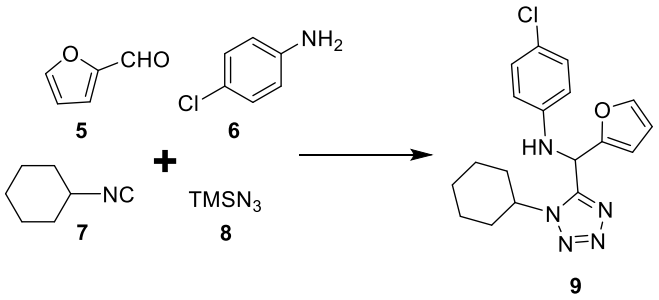


Figure 1. linked-type *bis* heterocycles containing 1,5-DS-T or furan moieties.

Results and Discussion

To optimize reaction conditions, we took the 1,5-DS-T **9a** as model. Thus, furaldehyde **5**, 4-methoxyaniline **6**, *tert*-butyl isocyanide **7** and azidotrimethylsilane **8** were reacted together (Table 1). As seen, the first experiment was done in water (entry 1), but the yield was low due to poor solubility of starting materials. Experiments in which acetonitrile (entry 2), a polar aprotic nature favors the RMC Ugi. However, as shown in the entry 3, the yield is considerably increased using methanol as solvent compared to other solvents. The results in Table 1 regarding the use of solvents of a different nature match reports in the literature: as the solvent polarity increases, decreases the reaction time and increase yields. For the reactions at room temperature and heating at 65 ° C gave lower yields compared to those obtained at room temperature. This one can be attributed to the boiling point of hydrazoic acid, which is generated from the azidotrimethylsilane. This one can lead to significant losses of this component due to its disintegration on these temperature conditions. It should be noted that the yields obtained in microwave and ultrasound are not negligible because, although the yields are lower in comparison with the reaction time at room temperature, this is drastically reduced. Further, is noteworthy that anilines, which are not good nucleophiles were used as amino component in the Ugi-azide reaction. It has been reported that Lewis acids favor the condensation between anilines with aldehydes or ketones.[21] In this context, $InCl_3$ was used because compared to other Lewis acids has advantages such as being less toxic and hygroscopic and easy handling. However, yields were low probably due to the formation of a complex with the metal and the isocyanide.[22]



Entry	Temperature	Solvent	time	Catal.	Yield (%)[c]
1	r.t[a]	H_2O (1M)	24 h	------	45
2	r.t	CH_3CN (1M)	24 h	------	70
3	**r.t**	**MeOH (1M)**	**24 h**	-----	**90**
4	r.t	EtOH (1M)	24 h	------	80%
5	r.t	*i*PrOH (1M)	24 h	------	79%
6	r.t	MeOH (1M)	6 h	$InCl_3$	24
7	r.t	----------	24 h	------	20
8	65°C	MeOH (1M)	1.5 h	------	80
9	65°C (MW)[b]	MeOH (1M)	1 h	------	82
10	r.t. US	MeOH (1M)	1 h	------	83

[a] rt = Room temperature
[b] 150 W
[c] Isolated yields.

A reaction mechanism proposed is shown in **Figure 2**.

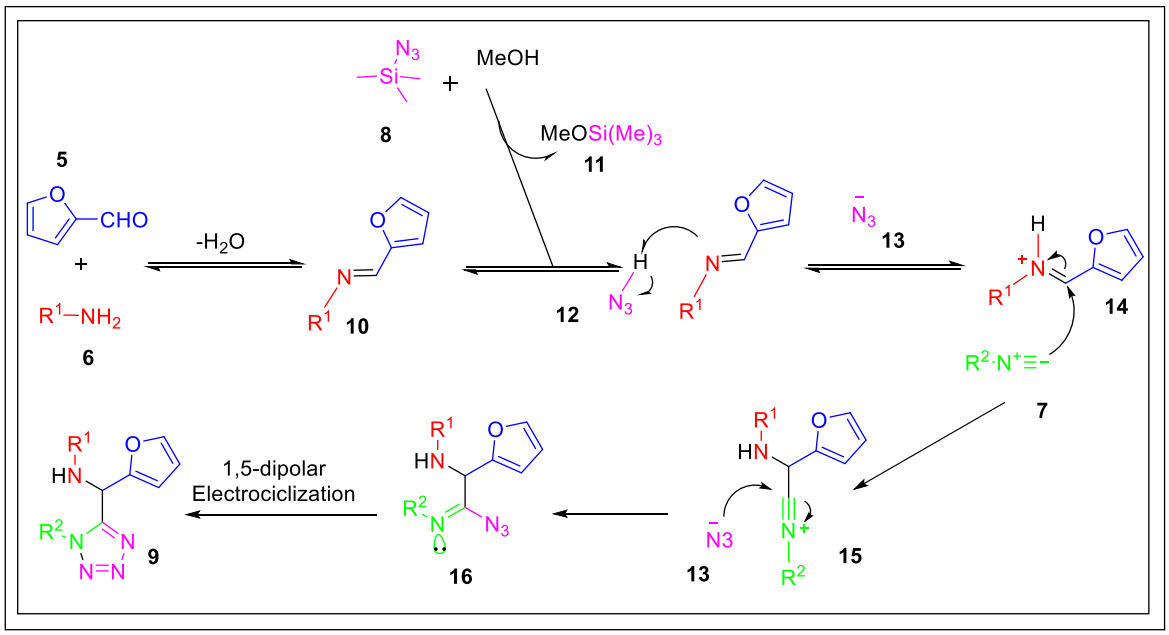


Figure 2. Reaction mechanism

After finding optimal conditions, a series of *bis* heterocycles linked-type (1,5-DS-T with furan) were successfully synthesized in good to excellent yields (50-96%) (Table 2).

Table 2. Substrate scope

9	R^1	R^2	Yield[a] (%)
9a	*4*-ClPh	Cy	90
9b	*4*-OMePh	Cy	70
9c	Ph	Cy	96
9d	*t*-Bu	Cy	90
9e	*4*-ClPh	*t*-Bu	50[b]
9f	*4*-OMePh	*t*-Bu	56[b]
9g	Ph	*t*-Bu	93
9h	*t*-Bu	*t*-Bu	83
9i	*4*-ClPh	2,6-diMePh	85
9j	4-OMePh	2,6-diMePh	70
9k	Ph	2,6-diMePh	92
9l	*t*-Bu	2,6-diMePh	90

[a] Measured after purification by chromatoflash
[b.] After crystallization

Condensation between amine and aldehyde is the key step in the MCR. There are reports in which low yields are observed in the use of little nucleophilic amines in Ugi azide adducts. 4-methoxyaniline was used, where the methoxy group is an electron donor increasing the poor nucleophilicity of the anilines. However, yields are lower in comparison with those obtained from other substituents. This is because the carbon of imine 14 needs to be electrophilic, and the effect of the methoxy group confers low electrophilicity against isocyanide attack due to mesomeric effect. Another important effect observed is the use of amines with *tert*-butyl group, which due to a steric effect, it would have been expected lower yields. However, the electronic effect influenced more than the steric effect, so their performance is not affected. Moreover, the nature of the isocyanide does not affect the reaction yield, as might be expected that an isocyanide with electronic effect, like 2,6-dimethylphenyl, which is little nucleophilic, resulting in yields decreasing.

Conclusions

A series of new linked-type *bis*-heterocycles containing 1,5-DS-T and furan in their structures were synthesized in good to excellent yields via Ugi-azide reaction. This work means a contribution to the one pot synthesis of bis-heterocycles. These products may find application in MedChem because they are formed by two scaffolds present in a wide variety of bioactive products and drugs.

Experimental section

General Information, instrumentation and chemicals.

Commercially available starting materials were purchased from Sigma–Aldrich and were used without further purification. The solvents were distilled and dried using common procedures. IR spectra were recorded on a Perkin Elmer 100 FT-IR spectrometer (ν in cm^{-1}). ^1H and ^{13}C NMR

spectra were acquired in Bruker (500 MHz) spectrometers. CDCl3 was used as solvent and chemical shifts were reported in ppm. Coupling constants were reported in Hz. Internal reference for 1H NMR spectra is respect to TMS at 0.0 ppm. Internal reference for ^{13}C NMR spectra is respect to $CDCl_3$ at 77.00 ppm.

General Procedure (GP): In a room flask equipped with a magnetic stirring bar, to a 1.0 M solution of aldehyde (1.0 equiv.) in anhydrous methanol [1 M], amine (1.0 equiv.), isocyanide (1.0 equiv.), and azidotrimethylsilane (1.0 equiv.) were sequentially added and the reaction mixture was stirrer to room temperature for 24 h. Then, the solvent was removed until dryness and the crude was immediately purified by silica gel column chromatography using a mixture of hexanes with ethyl acetate (4/1; *v/v*) to afford the corresponding products 9a-l.

4-chloro-*N*-((1-cyclohexyl-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)aniline (9a). Ambar solid; yield 90%; mp = 108- 110 °C; R_f = 0.20 (Hex-AcOEt= 9:1; v/v). *Spectral data*: ^1H NMR (500 MHz, $CDCl_3$, 25°C, TMS), δ 7.40 (s, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.64 (d, *J* = 8.5 Hz, 2H), 6.37 (m, 1H), 6.32 (t, *J* = 3.0 Hz, 1H), 6.02 (d, *J* = 5.8 Hz, 1H), 4.98 (d, *J* = 6.3 Hz, 1H), 4.44 (m, 1H), 2.05 (m, 1H), 1.95 (m, 2H), 1.86 (m, 2H), 1.73 (m, 1H), 1.61 (m, 1H), 1.29 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS): δ 152.4, 149.4, 143.9, 143.1, 129.3, 124.4, 115.1, 111.1, 108.9, 58.7, 48.3, 32.9, 32.8, 25.4, 25.3, 24.7 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3386 (N-H), 1295 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{18}H_{21}ClN_5O$: 358.1429; found: 358.1426.

***N*-((1-cyclohexyl-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)-4-methoxyaniline (9b).** White solid; yield: 70%; mp= 85 - 87 °C; R_f = 0.20 (Hex-AcOEt= 4:1; v/v). *Spectral data*: ^1H NMR (500 MHz; $CDCl_3$; 25°C, TMS): δ 7.33(d, *J* = 1.7 Hz, 1H), 6.68 (d, *J* = 9.0 Hz, 2H), 6.60 (d, *J* = 9.0 Hz, 2H), 6.29 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.24 (d, *J* = 3.3 Hz, 1H), 5.93 (d, *J* = 4.5 Hz, 1H), 4.44 (m, 2H), 3.65 (s, 3H), 1.97 – 1.91 (m, 1H), 1.86 – 1.77 (m, 4H), 1.67 – 1.63 (m, 1H), 1.60 – 1.57 (m, 1H), 1.32 – 1.26 (m, 1H), 1.25 – 1.19 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS): δ 153.7, 152.8, 150.1, 143.0, 139.3, 116.1, 114.0, 111.0, 108.6, 58.6, 55.6, 49.6, 32.9, 32.8, 25.4, 25.3, 24.8 ppm. FT-IR (ATR)ν_{max}/cm^{-1} 3344 (N-H), 1237 (N-N=N). HRMS $[M+H]^+$: m/z calcd for$C_{19}H_{24}N_5O_2$: 354.1924; found: 354.1927.

***N*-((1-cyclohexyl-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)aniline (9c).** Yellow solid; yield: 80%; mp=108 -110°C; R_f = 0.50 (Hex-AcOEt= 9:1; v/v). *Spectral data*: ^1H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.40 (s, 1H), 7.18 (m, 2H), 6.81 (m, 1H), 6.70 (d, *J* = 8.1 Hz, 2H), 6.37 (m, 1H), 6.33 (d, *J* = 2.9 Hz, 1H), 6.08 (d, *J* = 5.9 Hz, 1H), 4.85 (d, *J* = 5.7 Hz, 1H), 4.53 – 4.47 (m, 1H), 2.07 – 2.01 (m, 1H), 1.96 – 1.92 (m, 2H), 1.89 – 1.83 (m, 2H), 1.75 – 1.72 (m, 1H), 1.64 - 1.60 (m, 1H), 1.37 – 1.26 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ. 152.7, 149.8, 145.4, 143.0, 129.5, 119.7, 114.0, 111.1, 108.7, 58.7, 48.4, 32.9, 32.8, 25.4, 25.3, 24.8 ppm. FT-IR $(ATR)_{\nu max}/cm^{-1}$ 3280 (N-H), 1290 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{18}H_{22}N_5O$: 324.1819; found: 324.1838.

***N*-((1-cyclohexyl-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)-2-methylpropan-2-amine (9d).** ambar solid; yield: 90%; mp=85 -87°C; R_f = 0.20 (Hex-AcOEt= 4:1; v/v). *Spectral data*: ^1H NMR (500 MHz, $CDCl_3$, 25°C, TMS): δ 7. 7.37 (s, 1H), 6.33 (m, 1H), 6.13 (d, *J* = 2.7 Hz, 1H), 5.63 (s, 1H), 4.77 – 4.69 (m, 1H), 2.00 – 1.97 (m, 2H),1.93 – 1.88 (m, 2H),1.83 – 1.80 (m, 1H), 1.76 – 1.72 (m, 1H), 1.37 – 1.30 (m, 3H), 1.07 (s, 9H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 154.7, 152.0, 142.4, 110.8, 107.3, 58.2, 51.7, 47.0, 32.7, 32.6, 29.2, 25.4, 25.3, 24.9 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3303 (N-H), 1310 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{16}H_{26}N_5O$: 304.2132; found: 304.2132.

***N*-((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)-4-chloroaniline (9e).** White powder; yield 58%; mp = 118 - 120 °C; R_f = 0.30 (Hex-AcOEt= 4:1; v/v). *Spectral data*: ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ 7.37 (s, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.1 Hz, 2H), 6.33 (s, 1H), 6.24 (s, 1H), 6.19 (d, *J* = 9.6 Hz, 1H), 5.03 (d, *J* = 8.2 Hz, 1H), 1.72 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$, 25°C, TMS): δ 153.3, 150.5, 143.9, 142.9, 129.3, 124.2, 115.6, 110.9, 109.0, 62.0, 48.9, 29.9 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3280 (N-H), 1290 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{16}H_{19}ClN_5O$: 332.1273; found: 332.1268.

***N*-((1-*tert*-butyl-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)-4-methoxyaniline (9f)**. Light-brown powder; yield: 56%; mp = 152 - 154°C; R_f = 0.40 (Hex-AcOEt= 4:1; v/v); Spectral data: ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.37 (s, 1H), 6.77 – 6.72 (m, 4H), 6.33 – 6.31 (m, 1H), 6.22 (d, *J* = 2.8 Hz, 1H), 6.12 (d, *J* = 4.5 Hz, 1H), 4.62 (s, 1H), 3.72 (s, 3H), 1.69 (s, 9H).ppm. ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 153.9, 151.2, 142.8, 139.3, 117.2, 114.8, 110.8, 108.8, 61.7, 55.5, 50.7, 29.9 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3303 (N-H), 1291 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{17}H_{22}N_5O_2$: 328.1768; found: 328.1770.

***N*-((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)aniline (9g).** Yellow solid; yield: 93%; mp = 112 – 114°C; R_f = 0.25 (Hex-AcOEt= 4:1; v/v); *Spectral data*: ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ 7.35 (s, 1H), 7.18 (t, *J* = 6.8 Hz, 2H), 6.83 (s, 3H), 6.31 (s, 1H), 6.27 (m, 2H), 5.22 (s, 1H), 1.72 (s, 9H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$, 25°C, TMS) δ 153.6, 150.8, 145.3, 142.8, 129.4, 119.6, 114.4, 110.8, 108.8, 61.9, 48.8, 29.9 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3307 (N-H), 1230 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{16}H_{20}N_5O$: 298.1662; found: 298.1656.

***N*-((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)(furan-3-yl)methyl)-2-methylpropan-2-amine (9h).** Ambar oil; yield: 83%; R_f = 0.4 (Hex-AcOEt= 4:1; v/v); *Spectral data*: ^{1}H NMR (500 MHz, $CDCl_3$, 25|°C, TMS) δ 7.33 (s, 1H), 6.26 (dd, J = 2.9, 1.9 Hz 1H), 5.98 (d, J = 3.2 Hz, 1H), 5.50 (s, 1H), 2.43 (s, 1H), 1.66 (s, 9H), 1.04 (s, 9H).ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 156.0, 144.4, 142.1, 110.8, 107.9, 61.6, 51.4, 47.5, 29.8, 29.5 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3340 (N-H), 1230 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{14}H_{24}N_5O$: 278.1975; found: 278.1977.

4-chloro-*N*-((1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)aniline (9i). light-brown solid; yield: 85%; R_f = 0.30 (Hex-AcOEt= 95:5; v/v) m.p. 94 – 96°C. *Spectral data*: ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.37 (m, 1H), 7.24 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.18 (m, 2H), 7.03 (m, 2H), 6.54 (d, *J* = 8.9 Hz, 2H), 6.22 (dd, *J* = 3.4, 1.6 Hz, 1H), 6.20 (d, *J* = 3.3 Hz, 1H), 5.65 (d, *J* = 9.0 Hz, 1H), 5.25 (m, 1H), 1.81 (s, 3H), 1.67 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 154.4, 148.7, 143.7, 142.8, 136.1, 135.4, 131.0, 130.9, 128.9, 128.7, 128.6, 123.7, 115.1, 110.5, 108.8, 47.0, 16.8, 16.6 ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3358 (N-H), 1270 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{20}H_{19}ClN_5O$: 380.1273; found: 380.1270.

***N*-((1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)-4-methoxyaniline (9j).** light-brown oil; yield: 70%; R_f = 0.30 (Hex-AcOEt= 4:1; v/v). *Spectral data*: ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.39 (m, 1H), 7.29 (s, 1H), 7.19 (m, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.57 (d, *J* = 8.9 Hz, 2H), 6.27 (dd, *J* = 3.1, 1.7 Hz, 1H), 6.19 (d, *J* = 3.2 Hz, 1H), 5.51 (d, *J* = 9.8 Hz, 1H), 4.54 (d, *J* = 9.9 Hz, 1H), 3.71 (s, 3H), 1.76 (s, 3H), 1.68 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 155.1, 153.8, 149.7, 143.0, 139.1, 136.5, 136.0, 131.3, 131.1, 128.8, 128.8, 116.8, 114.8, 110.7, 108.8, 55.6, 48.9, 17.0 ppm; FT-IR (ATR) ν_{max}/cm^{-1} 3355 (N-H), 1237 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{21}H_{22}N_5O_2$: 376.1768; found: 376.1749.

***N*-((1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-yl)(furan-2-yl)methyl)aniline (9k).** Light-brown oil; yield 92%: R_f = 0.30 (Hex-AcOEt= 4:1; v/v). *Spectral data*: ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS)

δ 7.38 (m, 1H), 7.26 (d, *J* = 0.8 Hz, 1H), 7.19 (m, 2H), 7.10 (m, 2H), 6.75 (m, 1H), 6.58 (d, *J* = 7.7 Hz, 2H), 6.25 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.19 (d, *J* = 3.3 Hz, 1H), 5.67 (s, 1H), 4.91 (s, 1H), 1.79 (s, 3H), 1.68 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 154.8, 149.3, 145.1, 142.9, 136.4, 135.7, 131.2, 131.1, 129.2, 128.7, 128.7, 119.5, 114.1, 110.6, 108.7, 47.2, 16.9, 16.8.ppm. FT-IR (ATR) ν_{max}/cm^{-1} 3362 (N-H), 1276 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{20}H_{19}N_5O$: 346.1662; found: 346.1670.

***N*-((1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-yl)(furan-3-yl)methyl)-2-methylpropan-2-amine (9l).** Light-brown oil; yield: 80%; R_f = 0.40 (Hex-AcOEt= 4:1; v/v). *Spectral data*: ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.37 (dd, *J* = 9.6, 5.7 Hz, 1H), 7.32 (d, *J* = 1.2 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 6.28 (dd, *J* = 3.1, 1.9 Hz, 1H), 6.08 (d, *J* = 3.2 Hz, 1H), 5.00 (s, 1H), 2.07 (s, 1H), 1.96 (s, 3H), 1.73 (s, 3H), 0.89 (s, 9H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ 156.2, 152.0, 142.1, 136., 136., 131.8, 130.8, 128.6, 128.5, 110.7, 107.6, 51.2, 45.6, 29.1, 17.4, 17.0 ppm; FT-IR (ATR) ν_{max}/cm^{-1} 3386 (N-H), 1295 (N-N=N). HRMS $[M+H]^+$: m/z calcd for $C_{18}H_{24}N_5O$: 326.1975; found: 326.1976.

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