EurJOC
European Journal of Organic Chemistry
A Journal of ChemPubSoc Europe

Accepted Article

Title: Monohydrochloride Assisted Synthesis of Functionalised Isoxazoles and Pyrazoles from Allenic Ketones - First Synthesis of (Z)-2-methyl -7H benzo[b]pyrazolo[5,1-d][1,5]oxazocines

Authors: Debayan Sarkar and Sushree Ranjan Sahoo

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201900008

Link to VoR: http://dx.doi.org/10.1002/ejoc.201900008

Supported by ACES Asian Chemical Editorial Society

WILEY-VCH

Monohydrochloride Assisted Synthesis of Functionalised Isoxazoles and Pyrazoles from Allenic Ketones – First Synthesis of (*Z*)-2-methyl - 7H benzo[b]pyrazolo[5,1-d][1,5]oxazocines

Prof. Dr. Debayan Sarkar[a]* and Sushree Ranjan Sahoo[a]

Abstract: A facile hydrochloride promoted regioslective synthesis of isoxazoles and pyrazoles from 1,2-allenic ketones is reported. The reaction has been scaled upto grams. A direct 8-*endo dig* ring annulations towards the first synthesis of (*Z*)-2-methyl -7H benzo[b]pyrazolo[5,1-d][1,5]oxazocine has been developed

Introduction

Isoxazoles, Pyrazoles and their derivatives, are highly privileged five-membered nitrogen and oxygen containing heterocycles usually found in a number of natural products, drugs and are known to carry a wide range of pharmacological activities and agricultural importance.[1] Some of these important isoxazoles and pyrazoles are enlisted below in **Fig. 1**.[2] Celecoxib (Celebrax) and sildenafil (Viagra) are billion dollar medicines which enclose pyrazoles as central core.[3]

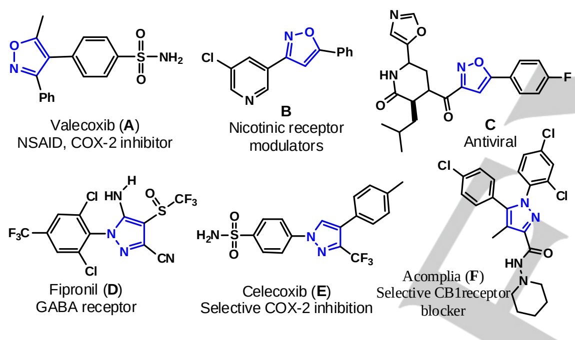


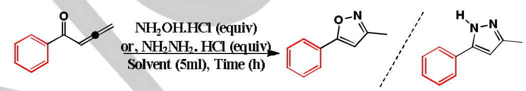
Fig. 1 Biologically Important Isoxazoles and Pyrazoles

The direct addition of nucleophilic hydrazine and hydroxylamine to 1,3-diketones and α,β-unsaturated carbonyls are by far the most accessible pathways to synthesise these nitrogen heterocycles.[4] Other protocols comprise of a typical [3 + 2]-cycloaddition reaction of diazo derivatives with alkynes.[5] Albeit, simultaneous formation of two regioisomers and usage of toxic and explosive diazo compounds pause the biggest hindrance towards the bulk scale production of the isoxazole and pyrazole derivatives till now. Thus, a mild and regioselective method for the formation of isoxazoles and pyrazoles is a desired transformation.

Herein, we report a direct regioselective synthesis of disubstituted isoxazoles and trisubstituted pyrazoles employing 1,2 allenic ketones as primary substrate and isoxazole and hydrazine hydrochlorides as reactants. The manuscript also discloses the first synthesis of fused benzoxacylcle (*Z*)-2-methyl -7H benzo[b]pyrazolo[5,1-d][1,5]oxazocine by 8-*endo-dig* cyclization from the synthesized pyrazoles in an environmental benign reaction conditions using employing water as the solvent of choice.

Results and Discussion

To start with, Phenyl allenyl ketone (**1a**) was taken as the substrate and hydrochlorides of hydroxyl amine and hydrazine were added in different flasks to deliver the isoxazoles and pyrazoles in appreciable yields. Ethanol was the best solvent and the formation of pyrazoles happened faster than the isoxazoles (**Table-1**).



1a 2a 3a

Table-1 Optimization reaction conditions of 1a with $NH_2OH.HCl$[a] & $NH_2NH_2.HCl$[a]

Entry No.	Solvent	$NH_2OH.HCl$ (A) or, NH_2NH_2. HCl (B) in equiv.	Time in (h)	Product	Yield (%)[b]
1	CH_3CN	A-1.2	5	2a	78
2	THF	A-1.2	4.5	2a	75
3	DCM	A-1.2	5	2a	81
4	DCE	A-1.2	5	2a	80
5	MeOH	A-1.2	4.5	2a	83
6	EtOH	A-1.2	4.5	2a	87
7	**EtOH**	**A-1.0**	**4.5**	**2a**	**87**
8	CH_3CN	B-1.2	3	3a	87
9	THF	B-1.2	2.5	3a	85
10	DCM	B-1.2	3	3a	87
11	DCE	B-1.2	3	3a	86
12	MeOH	B-1.2	2	3a	90
13	EtOH	B-1.2	2	3a	94
14	**EtOH**	**B-1.0**	**2**	**3a**	**94**

[a]All the reactions were carried out at r.t on 0.5 mmol scale in open air condition. [b]isolated yield.

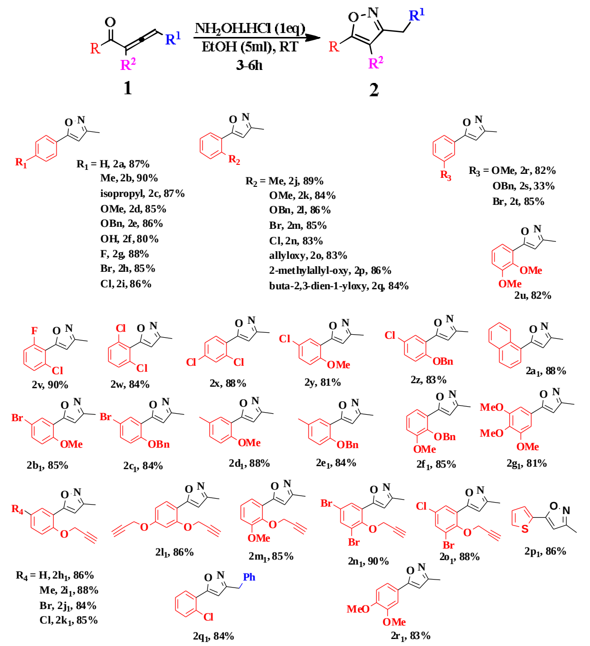
A variety of allenic ketones underwent the transformation which illustrated a wider substrate scope. Even the yields were quite impressive with allenic ketones with halide substitutions (**Table-2**, entries 2v, 2w, 2x) or alkyne substituents (**Table-2**, entry $2l_1$). The reaction preceded remarkably well delivering 88-90% yield with allenic ketones possessing two halide and one alkyne substitutions (**Table-2**, entries $2n_1$, $2o_1$). Interesting heterocycles like thiophenyl isoxazoles could also be synthesized with fantastic yields (**Table-2**, entry $2p_1$), which is delivers a wide substrate scope towards isoxazoles and has been absent in earlier reports.

[a] Organic Synthesis and Molecular Engineering Laboratory, National Institute Of Technology, Department of Chemistry, Rourkela, Odisha, India, Pin-769008, e-mail: sarkard@nitrkl.ac.in
http://www.nitrkl.ac.in/CY/~sarkard/

 10.1002/ejoc.201900008

 WILEY-VCH

Table-2 3,5-disubstituted Isoxazoles from 1,2-allenic Ketones with $NH_2OH.HCl$



After having a wide substrate scope of isoxazoles, we decided to validate the developed protocol to synthesise disubstituted and trisubstituted pyrazoles. The substrate scope was equally impressive with pyrazoles including multiple halides, alkynes and sulphur heterocycles (**Table-3**, entries 3v, 3w, 3x, $3h_1$, $3j_1$, $3p_1$). Interestingly, designed *bis*-pyrazoles (**Table- 4**, entries 5a, 5b) were also synthesized employing the same protocol however; the methodology failed to deliver *bis*-isoxazoles rather delivered only vinyl chloro isoxazoles (**Table-4**, entries 4a, 4b).

Table-3 3,5-disubstituted & 3,4,5-trisubstituted Pyrazoles Prepared from 1,2-allenic Ketones with $NH_2NH_2.HCl$

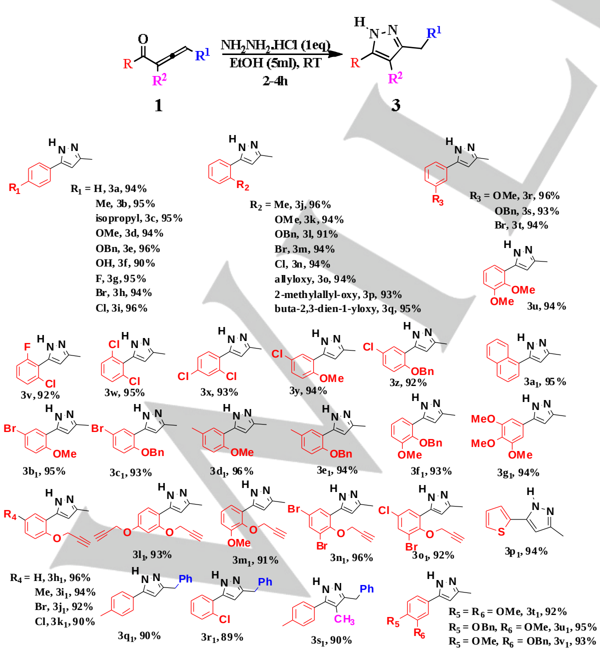
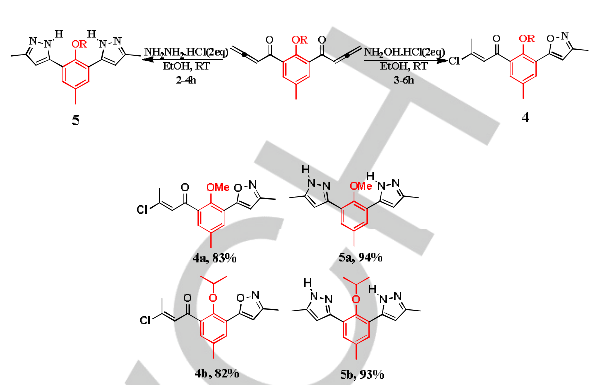
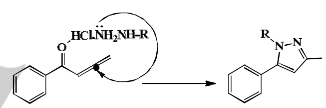


Table-4 Isoxazoles and Pyrazoles Prepared from 1,1'-(5-methyl-1,3-phenylene)bis(buta-2,3-dien-1-one) with $NH_2OH.HCl$ & $NH_2NH_2.HCl$



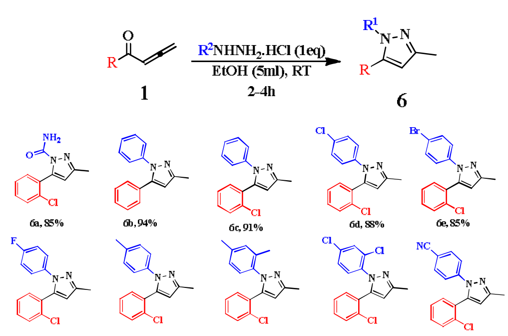
Employing of 1,2 allenic ketones for synthesis of pyrazoles has already been reported by Fan *et. al.*[6] but the group received a mixture of isomeric pyrazoles. It was interesting to find that monohydrochloride form of the hydrazine on reaction with allenyl ketones delivered only a single trisubstituted 1,3,5-pyrazoles in quantitative yields . This may be attributed to the protic activation of the allenyl ketones which delivered the thermodynamically controlled synthesis of the pyrazole (**Scheme-1**).



Scheme-1 Protic activation of the allenyl ketones

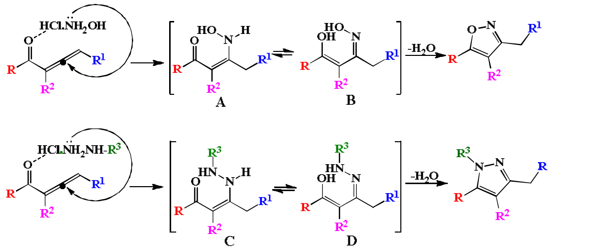
The reaction proceeded well in presence of functional groups like amide, fluoride, cyanide and thus exhibited a rich substrate scope of 1,3,5 trisubstituted pyrazoles (**Table-5**, entries 6a, 6f, 6j). Electron withdrawing substituents did not pose any retarding effect in the reaction.

Table-5 1,3,5 trisubstuted Pyrazoles Prepared from 1,2-allenic Ketones with $R^2NHNH_2.HCl$



As we believe, the reaction mechanism proceeds with the protic activation of the allenyl ketones by hydrochloride molecules of hydroxyl amine and hydrazine respectively followed by nucleophilic attack of nitrogen to the ketone giving rise intermediate **A** and **C** (**Scheme-2**) and furthers converts to the intermediates **B** and **D** followed by dehydration leading to isoxazoles and pyrazoles respectively.

10.1002/ejoc.201900008



Scheme-2 Proton assisted dehydration Mechanism of formation of Isoxazole & Pyrazole

Ring annulations strategies to develop eight membered benzoxacycles have been a challenging reaction.[7] Particularly, it appeared to us that pyrazolo benzoxacines[8] can be an interesting heterocyclic targets because of their telomerase and BuChE inhibitors. Interestingly, heating of the propyloxy-phenyl pyrazoles in a solution of H_2O:EtOH (10:2) at 120^0 C underwent 8-*endo dig* ring annulations delivered the targeted benzoxacines (**7**) in good yields. The reaction was well tolerated by halides and additional alkynes and thus supports the generalisability of the transformation. Soon after the purification by column chromatography, the benzoxacines represented high emissive tendencies in the solution which were then put under the ultra-violet chamber **fig. 2**.

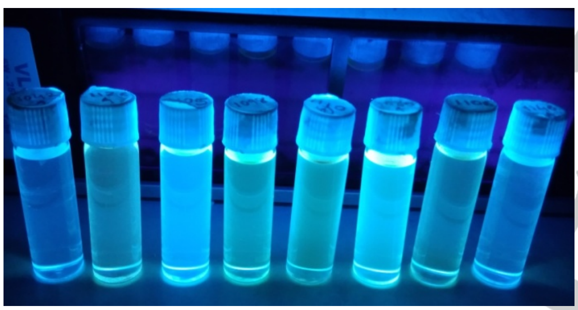
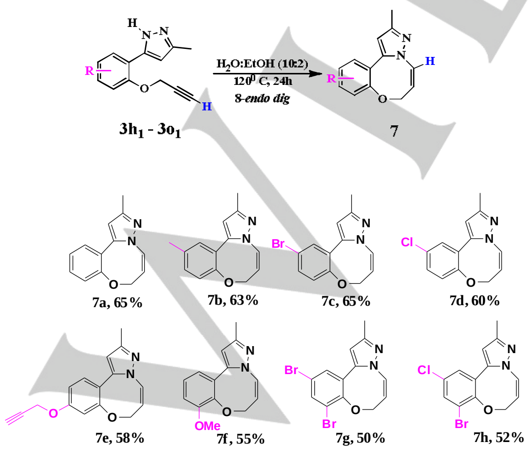


Fig. 2 Benxoxacine solutions under the UV chamber

Table-6 Substituted (*Z*)-2-methyl 7H benzo[b]pyrazolo[5,1-d][1,5]oxazocine from substituted 3-methyl-5-(2-(prop-2-yn-1-yloxy)phenyl)-1H-pyrazole



Photophysical properties

Fig. 3 shows the UV-Visible absorption spectroscopy of all the compounds **7a**-**7h**. The absorption peaks around 230-350 nm were corresponds to $\pi \rightarrow \pi$ transitions of the materials. Based on the absorption bands of the materials, emission spectra were performed. Form the emission spectra, it is concluded that there is an emission variation observed form the compounds. It is clearly evident that **7e** exhibited higher intensive emission as compared to others thus highlighting the effect of an alkyne substitution in such benzoxacines **fig. 4**. From the normalized spectrum, it is further concluded that there is a red shift observed in the emission spectra from unsubstituted 7a to other compounds (**7b-7h**). In addition, compared to all, **7e** and **7f** resembled higher wavelength emissions, which may be attributed to electron donating groups on the molecular core.

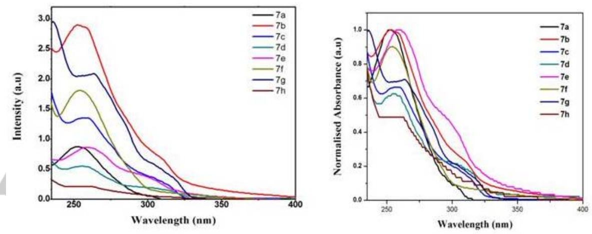


Fig. 3. UV-Visible spectroscopy of 7a-7h

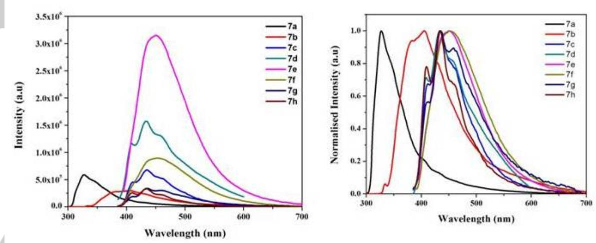
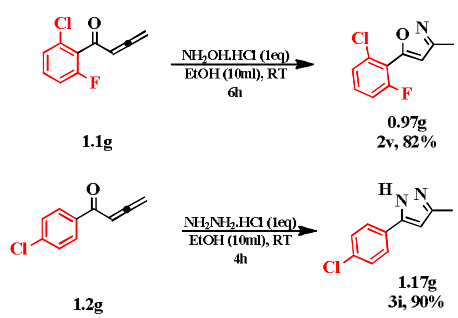


Fig. 4. Emission spectroscopy of 7a-7h

Now it was also important for us to check, whether the protocol worked good on scaling up. So two reactions were set up with the challenging halo-aryl allenyl ketones as substrates as shown in **Scheme-3**. The molar yields as shown was 82% and 90% for the isoxazoles and pyrazoles respectively when the reactions were performed in grams scale. This makes the protocol more sustainable and best of the available lot.



Scheme-3 Gram Scale Synthesis of Isoxazole and Pyrazole

Conclusions

To conclude, we have developed a direct synthesis of isoxazoles and pyrazoles from 1,2-allenic ketones mediated by hydrochlorides of hydrazine and hydroxylamine. The developed procedure was proton activated and the synthesized 1,3,5-pyrazoles were regioselective and yields were overwhelming. Both the isoxazoles and pyrazoles were scaled upto grams with fantastic yields without any side products. The propyloxy-phenyl pyrazoles were transformed to (*Z*)-2-methyl 7H benzo[b]pyrazolo[5,1-d][1,5]oxazocine which turned out to be important emissive compounds based on the attached substituents and thus can be further tuned. Thus, the related merits attached to the procedure designate it as the best practical way out to synthesise these heterocycles in the most benign fashion. The employability of the developed aryl *bis*-pyrazoles as important ligands in coupling reactions is presently being studied in our laboratories.

Experimental Section

All reactions were performed open air condition using oven dried glass wares. Anhydrous sodium sulphate was used for drying reaction mixture after aqueous workup. TLC was performed with 0.25mm coated commercial silica gel plates (DC-kiesel gel 60 F254) and stained by Iodine, vanillin solution. Chromatographic separation was done by using (200-400 and 100-200 mesh) silica gel. ^{1}H was recorded on 400 MHz & ^{13}C NMR was recorded on 100 MHz at 21^0 C. NMR chemical shift (δ) value is reported in ppm. TMS taken as internal standard in $CDCl_3$ solution. Multiplicity was reported as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); td (triplet of doublets); dq (doublet of quartets); qd (quartet of doublets); br s (broad singlet) etc. Coupling constants are given in Hz. HRMS (High resolution Mass Spectra) was measured in a QTOF I (quadrupolehexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface on micro (YA-263) mass spectrometer. IR spectra were recorded by using thin film deposit on NaCl & absorption frequency reported in cm^{-1}.

General procedure for synthesis of Isoxazoles (2a as Example): $NH_2OH.HCl$ (48mg, 0.69mmol) was added to a well stirred mixture of allenic ketones (**1a**) (100mg, 0.69mmol) and EtOH (5ml) under open air condition. After the completion of reaction, the solvent of reaction mixture was evaporated under reduced pressure. The crude mass was then purified by column chromatography using silica gel in specified solvent combination to deliver the desired compounds **2a** (95mg, 0.6mmol) with expected purity.

5-(4-isopropylphenyl)-3-methylisoxazole (2c): Yellow oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 95mg, yield: 87% (R_f = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.28 (d, J = 6.8 Hz, 6H), 2.35 (s, 3H), 2.92 (p, J = 6.8 Hz, 1H), 6.32 (s, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.68-7.70 (m, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.38, 23.64, 33.96, 99.49, 113.45, 125.71, 126.88, 150.99, 160.15, 169.73 ppm. **IR** (Neat Film, NaCl): 2850, 1623, 1468, 1441, 1249 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{15}NONa$ [M+Na]$^+$: 224.1051, Found: 224.1055.

5-(4-(benzyloxy)phenyl)-3-methylisoxazole (2e): White solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 90mg, yield: 86% (R_f = 0.7; 15% EtOAc in hexane). **MP**: 106-109 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 5.12 (s, 2H), 6.25 (s, 1H), 7.04 (d, J = 8.8 Hz, 2H), 7.36-7.47 (m, 5H), 7.70 (dd, J = 6.8, 2.0 Hz, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.44, 69.98, 98.81, 115.12, 120.58, 128.03, 128.07, 128.57, 129.04, 136.34, 160.00, 160.23, 169.45 ppm. **IR** (Neat Film, NaCl): 2960, 1620, 1448, 1445, 1250 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{15}NO_2$ [M]$^+$: 265.1103, Found: 265.1103.

4-(3-methylisoxazol-5-yl)phenol (2f): Red semisolid, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 88mg, yield: 80% (R_f = 0.6; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.42 (s, 3H), 6.23 (s, 1H), 6.92-6.96 (m, 2H), 7.59 (d, J = 8.8 Hz, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.32, 100.05, 116.18, 120.40, 128.47, 158.28, 162.51, 170.10 ppm. **IR** (Neat Film, NaCl): 3538, 2866, 1630, 1433, 1404, 1260 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_9NO_2Na$ [M+Na]$^+$: 198.0531, Found: 198.0544.

5-(4-fluorophenyl)-3-methylisoxazole (2g): Red oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 97mg, yield: 88% (R_f = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.46 (s, 3H), 6.25 (s, 1H), 7.10-7.14 (m, 2H), 7.74-7.78 (m, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.19, 99.47, 113.49, 115.70, 128.45, 161.48, 164.78, 170.00 ppm. **^{19}F NMR** (377 MHz, CDCl3): δ = -110.96 ppm. **IR** (Neat Film, NaCl): 2936, 1654, 1450, 1434, 1244, 1150 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8FNONa$ [M+Na]$^+$: 200.0488, Found: 200.0498.

5-(2-(benzyloxy)phenyl)-3-methylisoxazole (2l): Yellow oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 90mg, yield: 86% (R_f = 0.7; 15% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.32 (s, 3H), 5.22 (s, 2H), 6.61 (s, 1H), 7.06-7.11 (m, 2H), 7.36-7.49 (m, 6H), 8.01 (dd, J = 7.6, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.46, 70.48, 104.39, 112.41, 121.04, 121.16, 127.51, 127.79, 128.18, 128.63, 130.82, 136.25, 155.17, 160.27, 165.36 ppm. **IR** (Neat Film, NaCl): 2866, 1633, 1455, 1444, 1250 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{15}NO_2$ [M]$^+$: 265.1103, Found: 265.1113.

5-(2-bromophenyl)-3-methylisoxazole (2m): Yellow oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 90mg, yield: 85% (R_f = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.38 (s, 3H), 6.81 (s, 1H), 7.23-7.28 (m, 1H), 7.38-7.42 (m, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.48, 101.52, 120.88, 127.53, 129.91, 130.71, 131.41, 134.01, 159.89, 167.04 ppm. **IR** (Neat Film, NaCl): 2935, 1663, 1445, 1435, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8BrNO$ [M]$^+$: 236.9789, Found: 236.9780.

5-(2-chlorophenyl)-3-methylisoxazole (2n): Yellow oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 89mg, yield: 83% (R_f = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.39 (s, 3H), 6.79 (s, 1H), 7.32-7.39 (m, 2H), 7.47-7.49 (m, 1H), 7.92-7.94 (m, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.46, 105.05, 126.30, 127.03, 129.24, 130.50, 130.64, 131.49, 160.14, 165.68 ppm. **IR** (Neat Film, NaCl): 2910, 1660, 1450, 1440, 755 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8{}^{35}ClNO$ [M]$^+$: 193.0294, Found: 193.0294.

5-(2-(allyloxy)phenyl)-3-methylisoxazole (2o): White solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 90mg, yield: 83% (R_f = 0.6; 10% EtOAc in hexane). **MP**: 116-118 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.37 (s, 3H), 4.67 (d, J = 5.2 Hz, 2H), 5.35 (dd, J = 10.8, 1.2 Hz, 1H), 5.44-5.48 (m, 1H), 6.09-6.18 (m, 1H), 6.67 (s, 1H), 6.97 (d, J = 8.4 Hz, 1H), 7.02-7.09 (m, 1H), 7.34-7.40 (m, 1H), 7.98 (d, J =

1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.52, 69.24, 104.28, 112.25, 112.63, 118.39, 120.90, 127.74, 130.76, 132.61, 155.00, 160.27, 165.40 ppm. **IR** (Neat Film, NaCl): 2950, 1654, 1455, 1435, 745 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{13}NO_2Na$ [M+Na]$^+$: 238.0844, Found: 238.0844.

3-methyl-5-(2-((2-methylallyl)oxy) phenyl) isoxazole (2p): Yellow oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 92mg, yield: 86% (***R****f* = 0.6; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 1.86 (s, 3H), 2.35 (s, 3H), 4.55 (s, 2H), 5.04 (s, 1H), 5.11 (s, 1H), 6.66 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 7.01 (td, *J* = 7.6, 0.8 Hz, 1H), 7.30 (td, *J* = 8.4, 1.6 Hz, 1H), 7.94 (dd, *J* = 7.6, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.51, 19.49, 72.06, 104.18, 112.27, 113.60, 120.79, 127.67, 129.39, 130.80, 140.09, 155.08, 160.24, 165.50 ppm. **IR** (Neat Film, NaCl): 2915, 1660, 1440, 1428, 750 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{15}NO_2Na$ [M+Na]$^+$: 252.1000, Found: 252.1002.

5-(2-(buta-2,3-dien-1-yloxy) phenyl)-3-methylisoxazole (2q): Yellow oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 87mg, yield: 84% (***R****f* = 0.7; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.38 (s, 3H), 4.70-4.73 (m, 2H), 4.93-4.96 (m, 2H), 5.44-5.51 (m, 1H), 6.73 (s, 1H), 7.00-7.11 (m, 2H), 7.36-7.41 (m, 1H), 7.98 (dd, *J* = 8.0, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.51, 66.12, 76.76, 86.72, 104.42, 112.29, 112.79, 127.75, 129.42, 130.69, 154.79, 160.26, 168.39, 209.28 ppm. **IR** (Neat Film, NaCl): 2945, 1643, 1485, 1465, 780 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{13}NO_2Na$ [M+Na]$^+$: 250.0844, Found: 250.0836.

5-(3-methoxyphenyl)-3-methyl isoxazole (2r): Yellow oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 89mg, yield: 82% (***R****f* = 0.6; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.31 (s, 3H), 3.81 (s, 3H), 6.32 (s, 1H), 6.91-6.94 (m, 1H), 7.26 (d, *J* = 2.4 Hz, 1H), 7.28-7.32 (m, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.36, 55.19, 100.33, 110.70, 115.75, 118.06, 128.58, 129.91, 159.76, 160.26, 169.30 ppm. **IR** (Neat Film, NaCl): 2860, 1623, 1442, 1415, 1239 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{11}NO_2$ [M]$^+$: 189.0790, Found: 189.0780.

5-(3-(benzyloxy)phenyl)-3-methylisoxazole (2s): White solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 88mg, yield: 83% (***R****f* = 0.7; 15% EtOAc in hexane). **MP**: 116-119 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.37 (s, 3H), 5.14 (s, 2H), 6.36 (s, 1H), 7.04-7.09 (m, 1H), 7.37-7.49 (m, 8H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 12.27, 69.99, 100.37, 163.63, 119.43, 127.46, 127.97, 128.04, 128.57, 129.87, 130.01, 136.85, 160.30, 162.33, 169.84 ppm. **IR** (Neat Film, NaCl): 2860, 1628, 1458, 1440, 1249 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{15}NO_2$ [M]$^+$: 265.1103, Found: 265.1101.

5-(3-bromophenyl)-3-methylisoxazole (2t): Colorless oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 90mg, yield: 85% (***R****f* = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.37 (s, 3H), 6.39 (s, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.54-7.57 (m, 1H), 7.68-7.70 (m, 1H), 7.90-7.91 (m, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.41, 100.87, 122.88, 124.15, 128.57, 130.39, 130.20, 132.77, 160.35, 168.20 ppm. **IR** (Neat Film, NaCl): 2826, 1654, 1430, 1425, 755 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8BrNO$ [M]$^+$: 236.9789, Found: 236.9799.

5-(2,3-dimethoxyphenyl)-3-methylisoxazole (2u): Red oil, purified by silica gel column chromatography (elution with 5% EtOAc in hexane), 88mg, yield: 82% (***R****f* = 0.3; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.31 (s, 3H), 3.89 (s, 3H), 3.91 (s, 3H), 6.24 (s, 1H), 6.81-6.89 (m, 1H), 7.21 (dd, *J* = 9.2, 1.6 Hz, 1H), 7.27 (dd, *J* = 8.0, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.39, 55.76, 55.82, 99.00, 108.40, 110.83, 111.04, 118.86, 150.27, 150.37, 160.30, 169.42 ppm. **IR** (Neat Film, NaCl): 2966, 1638, 1445, 1435, 1250 cm^{-1}. **HRMS** (ESI) calc'd for $C_{12}H_{13}NO_3Na$ [M+Na]$^+$: 242.0793, Found: 242.0793.

5-(2-chloro-6-fluorophenyl)-3-methyl isoxazole (2v): Colorless oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 97mg, yield: 90% (***R****f* = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.40 (s, 3H), 6.44 (s, 1H), 7.08 (td, *J* = 9.2, 0.8 Hz, 1H), 7.30 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.34-7.40 (m, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.38, 107.16, 114.44, 114.66, 126.02, 131.59, 131.69, 159.60, 161.45, 170.00 ppm. **^{19}F NMR** (377 MHz, CDCl3): *δ* = -108.23 ppm. **IR** (Neat Film, NaCl): 2866, 1654, 1450, 1438, 1224, 1151,750 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_7{}^{35}ClFNONa$ [M+Na]$^+$: 234.0098, Found: 234.0088.

5-(2,6-dichlorophenyl)-3-methylisoxazole (2w): Yellow oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 89mg, yield: 84% (***R****f* = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.42 (s, 3H), 6.31 (s, 1H), 7.32-7.36 (m, 1H), 7.41-7.43 (m, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.46, 106.58, 127.13, 128.19, 131.51, 135.71, 159.56, 164.34 ppm. **IR** (Neat Film, NaCl): 2935, 1660, 1447, 1430, 735 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_7{}^{35}Cl_2NONa$ [M+Na]$^+$: 249.9802, Found: 249.9802.

5-(5-chloro-2-methoxyphenyl)-3-methyl isoxazole (2y): Yellow oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 87mg, yield: 81% (***R****f* = 0.6; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.34 (s, 3H), 3.91 (s, 3H), 6.63 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 7.27-7.32 (m, 1H), 7.87 (d, *J* = 2.8 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 12.16, 55.85, 104.93, 112.36, 112.59, 128.82, 130.38, 132.23, 154.49, 160.39, 168.94 ppm. **IR** (Neat Film, NaCl): 2930, 1663, 1448, 1430, 770 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{10}{}^{35}ClNO_2$ [M]$^+$: 223.0400, Found: 223.0402.

5-(2-(benzyloxy)-5-chlorophenyl)-3-methyl isoxazole (2z): Yellow oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 87mg, yield: 83% (***R****f* = 0.6; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.32 (s, 3H), 5.20 (s, 2H), 6.60 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 7.29 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.41-7.45 (m, 5H), 7.96 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.42, 70.87, 105.03, 113.74, 118.17, 126.24, 127.42, 127.46, 128.35, 128.69, 130.26, 135.74, 153.60, 160.35, 164.02 ppm. **IR** (Neat Film, NaCl): 2920, 1654, 1444, 1433, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{14}{}^{35}ClNO_2$ [M]$^+$: 299.0713, Found: 299.0723.

3-methyl-5-(naphthalen-1-yl)isoxazole (2a$_1$): Red oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 94mg, yield: 88% (***R****f* = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.45 (s, 3H), 6.46 (s, 1H), 7.52-7.59 (m, 3H), 7.79 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.91-7.96 (m, 2H), 8.32-8.34 (m, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.52, 104.25, 124.95, 125.03, 125.26, 126.27, 127.18, 127.42, 128.54, 130.19, 130.60, 133.66, 160.01, 169.56 ppm. **IR** (Neat Film, NaCl): 2955, 1653, 1455, 1430, 770 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{11}NONa$ [M+Na]$^+$: 232.0738, Found: 232.0736.

5-(5-bromo-2-methoxyphenyl)-3-methyl isoxazole (2b$_1$): Colorless oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 91mg, yield: 85% (***R****f* = 0.5; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.36 (s, 3H), 3.93 (s, 3H), 6.64 (s, 1H), 6.85 (d, *J* = 9.2 Hz, 1H), 7.44 (dd, *J* = 8.8, 2.4 Hz, 1H), 8.04 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C**

NMR ($CDCl_3$, 100 MHz): δ = 11.46, 55.71, 104.94, 112.80, 130.06, 131.76, 133.27, 133.34, 154.98, 160.37, 163.89 ppm. **IR** (Neat Film, NaCl): 2937, 1667, 1450, 1432, 766 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{10}BrNO_2Na$ $[M+Na]^+$: 289.9793, Found: 289.9799.

5-(2-(benzyloxy)-5-bromophenyl)-3-methyl isoxazole (2c$_1$): White solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 86mg, yield: 84% (R_f = 0.6; 10% EtOAc in hexane). **MP**: 133-136 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.32 (s, 3H), 4.93 (s, 2H), 6.61 (s, 1H), 7.40-7.45 (m, 4H), 7.49-7.51 (m, 2H), 7.81 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.45, 74.88, 105.27, 114.87, 117.97, 127.26, 128.16, 128.56, 128.60, 130.01, 135.71, 136.90, 151.73, 160.62, 163.41 ppm. **IR** (Neat Film, NaCl): 2945, 1653, 1455, 1445, 765 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{14}BrNO_2$ $[M]^+$: 343.0208, Found: 343.0218.

5-(2-methoxy-5-methylphenyl)-3-methyl isoxazole (2d$_1$): Red oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 96mg, yield: 88% (R_f = 0.5; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.32 (s, 3H), 2.34 (s, 3H), 3.88 (s, 3H), 6.62 (s, 1H), 6.84 (d, J = 8.8 Hz, 1H), 7.14 (dd, J = 8.4, 1.6 Hz, 1H), 7.75 (d, J = 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.46, 20.32, 55.38, 104.12, 111.27, 111.42, 127.87, 129.63, 131.36, 154.02, 160.24, 168.45 ppm. **IR** (Neat Film, NaCl): 2910, 1700, 1445, 1420, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{12}H_{13}NO_2$ $[M]^+$: 203.0946, Found: 203.0941.

5-(2-(benzyloxy)-5-methylphenyl)-3-methylisoxazole (2e$_1$): Yellow oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 89mg, yield: 84% (R_f = 0.6; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 2.38 (s, 3H), 5.19 (s, 2H), 6.61 (s, 1H), 6.92-6.97 (m, 1H), 7.16-7.20 (m, 1H), 7.36 (m, 5H), 7.83 (d, J = 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.64, 20.53, 70.61, 104.44, 112.49, 116.53, 127.59, 127.99, 128.69, 128.79, 130.55, 131.44, 136.56, 153.28, 160.28, 165.65 ppm. **IR** (Neat Film, NaCl): 2955, 1655, 1455, 1435, 765 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{17}NO_2Na$ $[M+Na]^+$: 302.1157, Found: 302.1167.

5-(2-(benzyloxy)-3-methoxyphenyl)-3-methylisoxazole (2f$_1$): Yellow oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 92mg, yield: 85% (R_f = 0.5; 15% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.30 (s, 3H), 3.93 (s, 3H), 5.06 (s, 2H), 6.58 (s, 1H), 7.01 (dd, J = 8.4, 1.2 Hz, 1H), 7.16 (t, J = 8.4 Hz, 1H), 7.36-7.43 (m, 3H), 7.47-7.49 (m, 2H), 7.52 (dd, J = 8.0, 1.2 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.47, 55.88, 74.55, 104.35, 113.63, 119.28, 124.50, 128.21, 128.29, 128.35, 128.47, 137.09, 145.01, 153.03, 160.37, 165.58 ppm. **IR** (Neat Film, NaCl): 2938, 1660, 1470, 1440, 780 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{17}NO_3$ $[M]^+$: 295.1208, Found: 295.1208.

3-methyl-5-(3,4,5-trimethoxyphenyl)isoxazole (2g$_1$): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 87mg, yield: 81% (R_f = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.36 (s, 3H), 3.93 (s, 9H), 6.33 (s, 1H), 6.98 (s, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.46, 56.21, 60.88, 99.81, 102.91, 122.90, 153.46, 160.37, 162.08, 170.08 ppm. **IR** (Neat Film, NaCl): 2867, 1632, 1455, 1444, 1250 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{15}NO_4$ $[M]^+$: 249.1001, Found: 249.1011.

3-methyl-5-(2-(prop-2-yn-1-yloxy)phenyl)isoxazole (2h$_1$): Yellow oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 92mg, yield: 86% (R_f = 0.7; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.36 (s, 3H), 2.58 (t, J = 2.4 Hz, 1H), 4.81 (d, J = 2.4 Hz, 2H), 6.68 (s, 1H), 7.08-7.12 (m, 2H), 7.36-7.40 (m, 1H), 7.96 (dd, J = 7.6, 1.2 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.44, 56.06, 76.05, 77.84, 104.48, 112.47, 121.67, 127.82, 129.52, 130.67, 153.94, 160.27, 165.02 ppm. **IR** (Neat Film, NaCl): 2955, 1665, 1455, 1435, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{11}NO_2Na$ $[M+Na]^+$: 236.0687, Found: 236.0677.

3-methyl-5-(5-methyl-2-(prop-2-yn-1-yloxy) phenyl) isoxazole (2i$_1$): Red oil, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 93mg, yield: 88% (R_f = 0.7; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.36 (s, 3H), 2.37 (s, 3H), 2.57 (t, J = 2.4 Hz, 1H), 4.80 (d, J = 2.4 Hz, 2H), 6.68 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.18 (dd, J = 8.4, 2.4 Hz, 1H), 7.79 (d, J = 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.53, 20.43, 56.11, 75.89, 78.01, 104.41, 112.44, 128.20, 129.88, 131.09, 131.17, 151.90, 160.34, 165.14 ppm. **IR** (Neat Film, NaCl): 2925, 1673, 1475, 1435, 750 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{13}NO_2$ $[M]^+$: 227.0946, Found: 227.0950.

5-(5-bromo-2-(prop-2-yn-1-yloxy)phenyl)-3-methylisoxazole (2j$_1$): Yellow solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 88mg, yield: 84% (R_f = 0.7; 10% EtOAc in hexane). **MP**: 136-139 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.38 (s, 3H), 2.60 (t, J = 2.4 Hz, 1H), 4.83 (d, J = 2.4 Hz, 2H), 6.70 (s, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.48 (dd, J = 9.2, 2.4 Hz, 1H), 8.10 (d, J = 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.50, 56.42, 76.28, 76.51, 105.22, 114.20, 129.15, 130.41, 133.15, 144.95, 152.83, 160.45, 164.45 ppm. **IR** (Neat Film, NaCl): 2920, 1660, 1447, 1435, 780 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{10}BrNO_2Na$ $[M+Na]^+$: 313.9793, Found: 313.9799.

5-(5-chloro-2-(prop-2-yn-1-yloxy)phenyl)-3-methylisoxazole (2k$_1$): Gray solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 92mg, yield: 85% (R_f = 0.7; 10% EtOAc in hexane). **MP**: 146-148 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.38 (s, 3H), 2.60 (t, J = 2.4 Hz, 1H), 4.84 (d, J = 2.4 Hz, 2H), 6.71 (s, 1H), 7.05 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 9.2, 2.4 Hz, 1H), 7.96 (d, J = 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.50, 56.37, 76.24, 77.37, 105.20, 113.80, 116.58, 127.54, 130.22, 130.41, 152.63, 160.88, 164.00 ppm. **IR** (Neat Film, NaCl): 2933, 1633, 1444, 1433, 766 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{10}{}^{35}ClNO_2Na$ $[M+Na]^+$: 270.0298, Found: 270.0298.

5-(2,4-bis(prop-2-yn-1-yloxy)phenyl)-3-methyl isoxazole (2l$_1$): White solid, purified by silica gel column chromatography (elution with 3% EtOAc in hexane), 91mg, yield: 86% (R_f = 0.7; 10% EtOAc in hexane). **MP**: 129-132 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.59-2.60 (m, 5H), 4.73-4.75 (m, 4H), 6.56 (s, 1H), 6.70 (d, J = 2.4 Hz, 1H), 7.10 (d, J = 1.6 Hz, 1H), 7.71 (d, J = 9.2 Hz, 1H) ppm. **IR** (Neat Film, NaCl): 2945, 1643, 1475, 1465, 780 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{13}NO_3Na$ $[M+Na]^+$: 290.0793, Found: 290.0793.

5-(3-methoxy-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl isoxazole (2m$_1$): Yellow oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 90mg, yield: 85% (R_f = 0.6; 15% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.43 (t, J = 2.4 Hz, 1H), 2.49 (s, 3H), 3.89 (s, 3H), 4.71 (d, J = 2.8 Hz, 2H), 6.62 (s, 1H), 6.99-7.09 (m, 2H), 7.47 (dd, J = 7.6, 1.2 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.24, 55.95, 60.59, 76.24, 76.86, 102.96, 115.02, 115.49, 120.70, 121.03, 152.76, 152.98, 159.91, 168.86 ppm. **IR** (Neat Film, NaCl): 2965, 1663, 1455, 1445, 770 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{13}NO_3$ $[M]^+$: 243.0895, Found: 243.0895.

10.1002/ejoc.201900008

WILEY-VCH

5-(3,5-dibromo-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl isoxazole ($2n_1$): White solid, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 93mg, yield: 90% (***R**$_f$* = 0.8; 10% EtOAc in hexane). **MP**: 140-142 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.39 (s, 3H), 2.53 (t, *J* = 2.4 Hz, 1H), 4.68 (d, *J* = 2.8 Hz, 2H), 6.82 (s, 1H), 7.76 (d, *J* = 1.6 Hz, 1H), 8.01 (d, *J* = 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.50, 60.22, 76.76, 77.25, 105.57, 118.57, 119.14, 125.13, 129.88, 136.76, 150.43, 160.69, 163.11 ppm. **IR** (Neat Film, NaCl): 2960, 1653, 1440, 1435, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_9Br_2NO_2Na$ [M+Na]$^+$: 391.8898, Found: 391.8888.

5-(3-bromo-5-chloro-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl isoxazole ($2o_1$): White solid, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 91mg, yield: 88% (***R**$_f$* = 0.8; 10% EtOAc in hexane). **MP**: 133-136 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.39 (s, 3H), 2.53 (t, *J* = 2.4 Hz, 1H), 4.67 (d, *J* = 2.4 Hz, 2H), 6.82 (s, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.85 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.62, 60.40, 76.87, 77.28, 105.67, 118.95, 124.79, 127.05, 131.38, 134.11, 150.06, 160.83, 163.32 ppm. **IR** (Neat Film, NaCl): 2928, 1658, 1448, 1438, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_9Br^{35}ClNO_2$ [M]$^+$: 324.9505, Found: 324.9500.

3-benzyl-5-(2-chlorophenyl)isoxazole ($2q_1$): Yellow oil, purified by silica gel column chromatography (elution with 2% EtOAc in hexane), 89mg, yield: 84% (***R**$_f$* = 0.8; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 3.75 (s, 2H), 6.05 (s, 1H), 7.26-7.48 (m, 8H), 7.55 (d, *J* = 8.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 45.69, 101.54, 127.20, 127.97, 128.86, 129.37, 129.50, 130.12, 130.73, 131.72, 134.84, 135.29, 163.53, 166.15 ppm. **IR** (Neat Film, NaCl): 2925, 1643, 1455, 1444, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{12}{}^{35}ClNONa$ [M+Na]$^+$: 292.0505, Found: 292.0515.

5-(3,4-dimethoxyphenyl)-3-methylisoxazole ($2r_1$): Yellow oil, purified by silica gel column chromatography (elution with 5% EtOAc in hexane), 90mg, yield: 83% (***R**$_f$* = 0.3; 10% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.35 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 6.66 (s, 1H), 6.95 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.48 (dd, *J* = 8.0, 1.2 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.46, 55.79, 59.99, 103.98, 113.63, 119.09, 120.94, 124.37, 152.95, 153.01, 160.46, 165.46 ppm. **IR** (Neat Film, NaCl): 2850, 1638, 1440, 1435, 1250 cm^{-1}. **HRMS** (ESI) calc'd for $C_{12}H_{13}NO_3Na$ [M+Na]$^+$: 242.0793, Found: 242.0799.

(*E*)-3-chloro-1-(2-methoxy-5-methyl-3-(3-methylisoxazol-5-yl)phenyl)but-2-en-1-one (4a): Yellow oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 98mg, yield: 83% (***R**$_f$* = 0.7; 15% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.39 (s, 3H), 2.40 (s, 3H), 2.69 (s, 3H), 3.72 (s, 3H), 6.68 (s, 1H), 7.12 (d, *J* = 0.8 Hz, 1H), 7.44 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.48, 20.60, 24.53, 62.72, 104.33, 121.77, 126.34, 131.91, 132.07, 134.29, 134.48, 152.93 153.93, 160.59, 164.75, 189.77 ppm. **IR** (Neat Film, NaCl): 2924, 1685, 1445, 1430, 770 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{16}{}^{35}ClNO_3Na$ [M+Na]$^+$: 328.0716, Found: 328.0716.

(*E*)-3-chloro-1-(2-isopropoxy-5-methyl-3-(3-methylisoxazol-5-yl)phenyl)but-2-en-1-one (4b): Red oil, purified by silica gel column chromatography (elution with 4% EtOAc in hexane), 97mg, yield: 82% (***R**$_f$* = 0.7; 15% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 1.17 (d, *J* = 6.0 Hz, 6H), 2.39 (s, 3H), 2.40 (s, 3H), 2.69 (s, 3H), 3.99 (p, *J* = 6.4 Hz, 1H), 6.71 (s, 1H), 7.15 (d, *J* = 1.2 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.83 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.51, 20.53, 21.70, 24.50, 79.63, 104.70, 122.96, 126.72, 131.89, 132.25, 133.88, 135.03, 151.45, 152.43, 160.20, 165.75, 190.25 ppm. **IR** (Neat Film, NaCl): 2975, 1665, 1455, 1435, 755 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{20}{}^{35}ClNO_3$ [M]$^+$: 333.1132, Found: 333.1133.

General procedure for synthesis of Pyrazoles (3a as Example) : NH_2NH_2.HCl (47mg, 0.69mmol) or $RNHNH_2$.HCl (0.069mmol) was added to a well stirred mixture of allenic ketones (**1a**) (100mg, 0.69mmol) and EtOH (5ml) under open air condition. After the completion of reaction, the solvent of reaction mixture was evaporated under reduced pressure. The crude mass was then purified by column chromatography using silica gel in specified solvent combination to deliver the desired compounds **3a** (103mg, 0.65mmol) with expected purity.

5-(4-isopropylphenyl)-3-methyl-1H-pyrazole (3c): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 102mg, yield: 95% (***R**$_f$* = 0.2; 20% EtOAc in hexane). **MP**: 196-198 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 1.30 (d, *J* = 6.8 Hz, 6H), 2.27 (s, 3H), 2.92 (p, *J* = 6.8 Hz, 1H), 6.33 (s, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 10.79 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.63, 23.83, 33.79, 101.73, 125.73, 126.60, 129.94, 143.45, 148.39, 149.41 ppm. **IR** (Neat Film, NaCl): 2935, 1675, 1448, 1435, 785 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{16}N_2Na$ [M+Na]$^+$: 223.1211, Found: 223.1211.

3-methyl-5-(*o*-tolyl)-1H-pyrazole (3j): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 95mg, yield: 96% (***R**$_f$* = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.19 (s, 3H), 2.45 (s, 3H), 6.19 (s, 1H), 7.20 (dd, *J* = 7.6, 4.0 Hz, 1H), 7.26-7.28 (m, 2H), 7.48 (d, *J* = 7.6 Hz, 1H), 11.33 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.48, 20.72, 104.93, 125.71, 127.83, 129.24, 130.54, 132.20, 135.99, 143.21, 148.43 ppm. **IR** (Neat Film, NaCl): 2960, 1660, 1450, 1430, 775 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{12}N_2$ [M]$^+$: 172.1000, Found: 172.1001.

5-(2-methoxyphenyl)-3-methyl-1H-pyrazole (3k): Red oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 102mg, yield: 94% (***R**$_f$* = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.36 (s, 3H), 3.94 (d, *J* = 2.4 Hz, 3H), 6.45 (s, 1H), 6.98-7.04 (m, 2H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.65 (dd, *J* = 7.6, 1.6 Hz, 1H), 9.43 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 13.13, 55.54, 102.74, 111.41, 118.25, 121.15, 127.86, 128.93, 141.84, 147.37, 155.82 ppm. **IR** (Neat Film, NaCl): 2926, 1700, 1465, 1453, 740 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{12}N_2O$ [M]$^+$: 188.0950, Found: 188.0945.

5-(2-(benzyloxy)phenyl)-3-methyl-1H-pyrazole (3l): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 95mg, yield: 91% (***R**$_f$* = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.36 (s, 3H), 5.19 (s, 2H), 6.50 (s, 1H), 7.04-7.08 (m, 2H), 7.26-7.30 (m, 1H), 7.36-7.48 (m, 5H), 7.71 (dd, *J* = 7.6, 1.6 Hz, 1H), 9.69 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 13.17, 70.81, 102.82, 112.85, 118.57, 121.54, 127.65, 127.99, 128.10, 128.42, 128.88, 129.84, 136.01, 141.82, 147.56, 155.01 ppm. **IR** (Neat Film, NaCl): 2977, 1666, 1455, 1430, 755 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{16}N_2ONa$ [M+Na]$^+$: 287.1160, Found: 287.1177.

5-(2-(allyloxy)phenyl)-3-methyl-1H-pyrazole (3o): Red oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 94% (***R**$_f$* = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.36 (s, 3H), 4.66 (dd, *J* = 3.2, 1.6 Hz, 2H), 5.34 (d, *J* = 10.8 Hz, 1H), 5.43 (d, *J* = 17.2

10.1002/ejoc.201900008

Hz, 1H), 6.08-6.15 (m, 1H), 6.47 (s, 1H), 6.96-7.04 (m, 2H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.67-7.69 (m, 1H), 9.31 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.17, 69.46, 102.81, 112.80, 118.84, 120.97, 121.40, 127.97, 128.83, 132.50, 142.04, 147.73, 154.84 ppm. **IR** (Neat Film, NaCl): 2944, 1665, 1444, 1435, 788 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{14}N_2ONa$ $[M+Na]^+$: 237.1004, Found: 237.1005.

3-methyl-5-(2-((2-methylallyl)oxy)phenyl)-1H-pyrazole (3p): Red oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 93% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.87 (s, 3H), 2.36 (s, 3H), 4.60 (s, 3H), 5.07 (s, 1H), .14 (s, 1H), 6.47 (s, 1H), 6.98-7.05 (m, 2H), 7.24 (m, 1H), 7.66 (dd, *J* = 8.0, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.26, 19.57, 72.42, 102.62, 112.79, 114.04, 118.35, 121.39, 127.93, 128.79, 139.97, 141.77, 147.82, 154.90 ppm. **IR** (Neat Film, NaCl): 2915, 1655, 1455, 1445, 778 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{16}N_2ONa$ $[M+Na]^+$: 251.1160, Found: 251.1169.

5-(2-(buta-2,3-dien-1-yloxy)phenyl)-3-methyl-1H-pyrazole (3q): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 102mg, yield: 95% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 106-108 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.36 (s, 3H), 4.69-4.71 (m, 2H), 5.07 (p, *J* = 3.2 Hz, 2H), 5.47-5.50 (m, 1H), 6.46 (s, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 7.25-7.29 (m, 1H), 7.67 (dd, *J* = 7.6, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.35, 65.65, 78.01, 86.90, 102.39, 112.48, 180.20, 121.54, 127.87, 128.75, 141.31, 148.07, 154.48, 208.94 ppm. **IR** (Neat Film, NaCl): 2925, 1715, 1484, 1475, 788 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{14}N_2ONa$ $[M+Na]^+$: 249.1004, Found: 249.1006.

5-(3-(benzyloxy)phenyl)-3-methyl-1H-pyrazole (3s): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 98mg, yield: 93% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.27 (s, 3H), 5.01 (s, 2H), 6.35 (s, 1H), 6.93-6.95 (m, 1H), 7.27-7.31 (m, 1H), 7.34-7.45 (m, 7H), 10.31 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.52, 69.77, 102.13, 111.73, 114.55, 118.47, 127.45, 127.84, 128.46, 129.68, 133.79, 136.90, 143.08, 149.65, 159.02 ppm. **IR** (Neat Film, NaCl): 2970, 1690, 1455, 1430, 772 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{16}N_2ONa$ $[M+Na]^+$: 287.1160, Found: 287.1155.

5-(3-bromophenyl)-3-methyl-1H-pyrazole (3t): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 94% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.25 (s, 3H), 6.32 (s, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.88-7.89 (m, 1H), 10.83 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.24, 102.20, 122.72, 124.20, 128.66, 130.10, 130.49, 134.84, 142.53, 149.07 ppm. **IR** (Neat Film, NaCl): 2954, 1665, 1453, 1442, 774 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_9BrN_2$ $[M]^+$: 235.9949, Found: 235.9940.

5-(2,3-dimethoxyphenyl)-3-methyl-1H-pyrazole (3u): Red oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 100mg, yield: 94% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.28 (s, 3H), 3.84 (s, 3H), 3.88 (s, 2H), 6.27 (s, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.26 (d, *J* = 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.55, 55.65, 55.75, 101.49, 108.61, 111.03, 118.11, 121.35, 125.29, 142.87, 148.70, 148.89, 149.57 ppm. **IR** (Neat Film, NaCl): 2920, 1648, 1442, 1435, 774 cm^{-1}. **HRMS** (ESI) calc'd for $C_{12}H_{14}N_2O_2Na$ $[M+Na]^+$: 241.0953, Found: 241.0953.

5-(2-chloro-6-fluorophenyl)-3-methyl-1H-pyrazole (3v): Red oil, purified by silica gel column chromatography (elution with 28% EtOAc in hexane), 99mg, yield: 92% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.19 (s, 3H), 6.27 (s, 1H), 7.01-7.06 (m, 1H), 7.22-7.26 (m, 2H), 11.03 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 10.97, 106.50, 114.07, 121.40, 125.54, 129.61, 134.74, 140.60, 141.64, 162.01 ppm. **^{19}F NMR** (377 MHz, CDCl3): δ = -109.99 ppm. **IR** (Neat Film, NaCl): 2977, 1668, 1458, 1436, 777 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8{}^{35}ClFN_2Na$ $[M+Na]^+$: 233.0258, Found: 233.0250.

5-(2,6-dichlorophenyl)-3-methyl-1H-pyrazole (3w): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 102mg, yield: 95% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 135-139 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 6.16 (s, 1H), 7.23-7.27 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.49, 106.12, 127.98, 129.68, 131.74, 135.88, 142.00, 149.00 ppm. **IR** (Neat Film, NaCl): 2933, 1688, 1455, 1448, 773 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8{}^{35}Cl_2N_2Na$ $[M+Na]^+$: 248.9962, Found: 248.9960.

5-(2,4-dichlorophenyl)-3-methyl-1H-pyrazole (3x): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 93% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.27 (s, 3H), 6.47 (s, 1H), 7.18-7.21 (m, 1H), 7.45 (d, *J* = 2.0 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 9.47 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.36, 105.70, 127.01, 129.87, 130.09, 131.05, 132.69, 133.94, 142.06, 146.22 ppm. **IR** (Neat Film, NaCl): 2928, 1668, 1466, 1455, 766 cm^{-1}. **HRMS** (ESI) calc'd for $C_{10}H_8{}^{35}Cl_2N_2Na$ $[M+Na]^+$: 248.9962, Found: 248.9966.

5-(5-chloro-2-methoxyphenyl)-3-methyl-1H-pyrazole (3y): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 100mg, yield: 94% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **MP**: 133-135 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.32 (s, 3H), 3.84 (s, 3H), 6.43 (s, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 7.14 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 10.08 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.61, 55.73, 103.75, 112.54, 120.59, 125.86, 127.51, 128.17, 141.75, 145.96, 154.48 ppm. **IR** (Neat Film, NaCl): 2938, 1678, 1467, 1459, 766 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{11}{}^{35}ClN_2ONa$ $[M+Na]^+$: 245.0458, Found: 245.0460.

5-(2-(benzyloxy)-5-chlorophenyl)-3-methyl-1H-pyrazole (3z): Red oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 96mg, yield: 92% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 5.15 (s, 2H), 6.46 (s, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 7.20 (dd, *J* = 8.8, 2.8 Hz, 1H) 7.38-7.44 (m, 5H), 7.67 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.02, 71.26, 103.24, 114.11, 126.57, 127.58, 127.64, 128.22, 128.61, 128.94, 135.48, 140.92, 147.45, 153.48 ppm. **IR** (Neat Film, NaCl): 2948, 1677, 1457, 1449, 776 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{15}{}^{35}ClN_2ONa$ $[M+Na]^+$: 321.0771, Found: 321.0777.

3-methyl-5-(naphthalen-1-yl)-1H-pyrazole (3a$_1$): Red oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 95% (***R$_f$*** = 0.2; 20% EtOAc in hexane).**^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.06 (s, 3H), 6.31 (s, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.48-7.53 (m, 2H), 7.59 (dd, *J* = 6.8, 0.8 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.88-7.90 (m, 1H), 8.36-8.38 (m, 1H), 9.87 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.21, 105.73, 125.17, 125.77, 125.82, 126.21, 126.95, 128.15, 128.30, 130.62, 131.41, 133.67, 142.69, 148.27 ppm. **IR** (Neat Film, NaCl): 2945, 1665, 1454, 1445, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{12}N_2Na$ [M+Na]$^+$: 231.0898, Found: 231.0889.

5-(5-bromo-2-methoxyphenyl)-3-methyl-1H-pyrazole (3b$_1$): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 102mg, yield: 95% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **MP**: 137-139 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 3.97 (s, 3H), 6.44 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 7.35 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.74 (d, *J* = 2.4 Hz, 1H), 9.36 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.65, 55.82, 103.51, 113.12, 130.39, 131.65, 133.71, 138.72, 140.66, 146.18, 155.02 ppm. **IR** (Neat Film, NaCl): 2928, 1688, 1477, 1469, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{11}BrN_2ONa$ [M+Na]$^+$: 288.9952, Found: 288.9955.

5-(2-(benzyloxy)-5-bromophenyl)-3-methyl-1H-pyrazole (3c$_1$): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 96mg, yield: 93% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **MP**: 141-144 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.34 (s, 3H), 4.82 (s, 2H), 6.48 (s, 1H), 7.34-7.47 (m, 6H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.81 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.26, 75.11, 104.83, 114.49, 127.64, 128.57, 128.64, 128.95, 130.48, 130.63, 131.21, 134.78, 135.56, 151.50, 153.95 ppm. **IR** (Neat Film, NaCl): 2953, 1677, 1457, 1439, 767cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{15}BrN_2ONa$ [M+Na]$^+$: 365.0265, Found: 365.0255.

5-(2-methoxy-5-methylphenyl)-3-methyl-1H-pyrazole (3d$_1$): Yellow oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 103mg, yield: 96% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 2.36 (s, 3H), 3.92 (s, 3H), 6.45 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 7.07 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.18, 20.37, 55.64, 102.50, 111.38, 117.75, 128.30, 129.36, 130.34, 141.87, 147.55, 153.84 ppm. **IR** (Neat Film, NaCl): 2948, 1666, 1444, 1434, 764 cm^{-1}. **HRMS** (ESI) calc'd for $C_{12}H_{14}N_2ONa$ [M+Na]$^+$: 225.1004, Found: 225.1010.

5-(2-(benzyloxy)-5-methylphenyl)-3-methyl-1H-pyrazole (3e$_1$): Yellow oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 100mg, yield: 94% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.34 (s, 3H), 2.35 (s, 3H), 5.24 (s, 2H), 6.48 (s, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.33-7.49 (m, 6H), 8.64 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.05, 20.54, 70.81, 102.97, 113.10, 117.97, 127.55, 128.29, 128.56, 128.85, 129.71, 130.77, 136.45, 141.90, 147.15, 153.08 ppm. **IR** (Neat Film, NaCl): 2978, 1656, 1445, 1434, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{18}N_2ONa$ [M+Na]$^+$: 301.1317, Found: 301.1318.

5-(2-(benzyloxy)-3-methoxyphenyl)-3-methyl-1H-pyrazole (3f$_1$): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 97mg, yield: 93% (***R$_f$*** = 0.4; 30% EtOAc in hexane). **MP**: 106-108 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 3.93 (s, 3H), 5.03 (s, 2H), 6.43 (s, 1H), 6.90 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 7.22 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.36-7.38 (m, 3H), 7.43-7.45 (m, 2H), 7.91 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.02, 55.82, 75.03, 103.56, 111.79, 119.71, 121.62, 123.88, 124.68, 128.48, 128.58, 128.63, 136.56, 138.87, 144.46, 153.14 ppm. **IR** (Neat Film, NaCl): 2938, 1676, 1464, 1444, 765 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{18}N_2O_2$ [M]$^+$: 294.1368, Found: 294.1366.

3-methyl-5-(3,4,5-trimethoxyphenyl)-1H-pyrazole (3g$_1$): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 99mg, yield: 94% (***R$_f$*** = 0.2; 30% EtOAc in hexane). **MP**: 96-98 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.29 (s, 3H), 3.85 (s, 9H), 6.30 (s, 1H), 6.95 (s, 2H), 8.06 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.36, 55.95, 60.78, 101.80, 102.84, 106.33, 128.25, 142.46, 150.11, 153.32 ppm. **IR** (Neat Film, NaCl): 2935, 1625, 1455, 1445, 750 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{16}N_2O_3$ [M]$^+$: 248.1161, Found: 248.1165.

3-methyl-5-(2-(prop-2-yn-1-yloxy)phenyl)-1H-pyrazole (3h$_1$): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 102mg, yield: 96% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 124-126 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.36 (s, 3H), 2.59 (t, *J* = 2.4Hz, 1H), 4.85 (d, *J* = 2.0 Hz, 2H), 6.46 (s, 1H), 7.07-7.12 (m, 2H), 7.28-7.33 (m, 1H), 7.68 (dd, *J* = 6.8, 1.6 Hz, 1H), 9.00 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.16, 56.48, 76.35, 77.68, 102.93, 113.03, 118.93, 122.19, 128.13, 128.75, 141.47, 147.69, 153.84 ppm. **IR** (Neat Film, NaCl): 2910, 1664, 1452, 1442, 777 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{12}N_2O$ [M]$^+$: 212.0950, Found: 212.0958.

3-methyl-5-(5-methyl-2-(prop-2-yn-1-yloxy)phenyl)-1H-pyrazole (3i$_1$): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 94% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 126-128 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.29 (s, 3H), 2.34 (s, 3H), 2.54 (t, *J* = 2.4 Hz, 1H), 4.71 (d, *J* = 2.4 Hz, 2H), 6.47 (s, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.03 (dd, *J* = 8.8, 1.6 Hz, 1 H), 7.49 (d, *J* = 1.6 Hz, 1H), 9.64 (s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.92, 20.41, 56.34, 76.12, 78.19, 103.33, 113.06, 119.09, 128.65, 129.18, 131.28, 142.19, 146.69, 151.87 ppm. **IR** (Neat Film, NaCl): 2945, 1675, 1459, 1455, 788 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{14}N_2O$ [M]$^+$: 226.1106, Found: 226.1117.

5-(5-bromo-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl-1H-pyrazole (3j$_1$): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 96mg, yield: 92% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 135-137 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 2.57 (t, *J* = 2.4 Hz, 1H), 4.78 (d, *J* = 2.4 Hz, 2H), 6.47 (s, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.81 (d, *J* = 2.8 Hz, 1H), 8.98 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.65, 56.51, 76.61, 76.67, 104.03, 114.75, 131.14, 131.19, 132.78, 134.56, 141.43, 146.12, 152.91 ppm. **IR** (Neat Film, NaCl): 2922, 1658, 1457, 1442, 764 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{11}BrN_2O$ [M]$^+$: 290.0055, Found: 290.0056.

5-(5-chloro-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl-1H-pyrazole (3k$_1$): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 96mg, yield: 90% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 141-144 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 2.59 (t, *J* = 2.4 Hz, 1H), 4.82 (d. *J* = 2.0 Hz, 2H), 6.49 (s, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 7.23 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.68 (d, *J* = 1.6 Hz, 1H), 8.81 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.91, 56.74, 76.60, 77.24, 103.80, 114.38, 120.98, 127.24, 127.84, 128.18, 141.18, 147.14, 152.35ppm. **IR** (Neat Film, NaCl): 2932, 1655, 1458, 1435, 782 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{11}{}^{35}ClN_2ONa$ [M+Na]$^+$: 269.0458, Found: 269.0446.

5-(2,4-bis(prop-2-yn-1-yloxy)phenyl)-3-methyl-1H-pyrazole (3l$_1$): Gray solid, purified by silica gel column chromatography (elution with 9% EtOAc in hexane), 98mg, yield: 93% (***R$_f$*** = 0.2; 20% EtOAc in hexane). **MP**: 125-128 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.34 (s, 1H), 2.57 (t, *J* = 2.4 Hz, 1H), 2.60 (t, *J* = 2.4 Hz, 1H), 4.74 (d, *J* = 2.4 Hz, 1H), 4.82 (d, *J* = 2.4 Hz, 1H), 6.37 (s, 1H), 6.69 (dd, *J* = 8.8, 1.6 Hz, 1H), 6.75 (d, *J* = 1.6 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ =

10.1002/ejoc.201900008

13.17, 55.92, 56.50, 75.87, 76.61, 76.92, 78.00, 101.17, 102.23, 107.40, 113.09, 128.89, 141.63, 147.81, 154.86, 158.13 ppm. **IR** (Neat Film, NaCl): 2935, 1665, 1464, 1454, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{14}N_2O_2Na$ $[M+Na]^+$: 289.0953, Found: 289.0954.

5-(3-methoxy-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl-1H-pyrazole (3m₁): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 97mg, yield: 91% (***R**_f* = 0.3; 30% EtOAc in hexane). **MP**: 126-129 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.32 (s, 3H), 2.49 (t, *J* = 2.4 Hz, 1H), 3.85 (s, 3H), 4.73 (d, *J* = 2.4 Hz, 2H), 6.47 (s, 1H), 6.82 (dd, *J* = 8.4, 12 Hz, 1H), 7.05 (t, *J* = 8.0Hz, 1H), 7.23 (dd, *J* = 8.0, 1.2 Hz, 1H), 9.01 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 12.86, 55.75, 60.12, 76.17, 78.53, 103.93, 111.56, 119.66, 124.35, 125.02, 138.72, 141.93, 146.73, 152.88 ppm. **IR** (Neat Film, NaCl): 2955, 1655, 1455, 1444, 766 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{14}N_2O_2Na$ $[M+Na]^+$: 265.0953, Found: 265.0948.

5-(3,5-dibromo-2-(prop-2-yn-1-yloxy)phenyl)-3-methyl-1H-pyrazole (3n₁): White solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 100mg, yield: 96% (***R**_f* = 0.2; 20% EtOAc in hexane). **MP**: 135-139 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.34 (s, 3H), 2.48 (t, *J* = 2.4 Hz, 1H), 4.55 (d, *J* = 2.4 Hz, 2H), 6.55 (s, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.82 (d, *J* = 1.6 Hz, 1H), 9.11 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.90, 60.44, 76.34, 76.65, 104.95, 115.71, 118.26, 129.05, 130.68, 134.65, 143.15, 143.94, 150.76 ppm. **IR** (Neat Film, NaCl): 2915, 1645, 1455, 1434, 786 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{10}Br_2N_2O$ $[M]^+$: 367.9160, Found: 367.9166.

5-(3-bromo-5-chloro-2-(prop-2-yn-1-yloxy) phenyl)-3-methyl-1H-pyrazole (3o₁): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 94mg, yield: 92% (R_f = 0.2; 20% EtOAc in hexane). **MP**: 140-143 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.37 (s, 3H), 2.50 (t, *J* = 2.4 Hz, 1H), 4.58 (d, *J* = 2.4 Hz, 1H), 6.55 (s, 1H), 7.51 (d, *J* = 2.4 Hz, 1H), 7.66 (d, *J* = 2.4 Hz, 1H) ppm. **IR** (Neat Film, NaCl): 2925, 1665, 1462, 1445, 764 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{10}Br^{35}ClN_2O$ $[M]^+$: 323.9665, Found: 323.9666.

3-methyl-5-(thiophen-2-yl)-1H-pyrazole (3p₁): White solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 103mg, yield: 94% (***R**_f* = 0.2; 20% EtOAc in hexane). **MP**: 125-128 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.26 (s, 3H), 6.25 (s, 1H), 7.03-7.05 (m, 1H), 7.22 (d, *J* = 4.8 Hz, 1H), 7.29 (d, *J* = 3.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.03, 101.90, 123.61, 124.24, 127.33, 136.18, 141.76, 145.87 ppm. **IR** (Neat Film, NaCl): 2925, 1675, 1453, 1435, 748 cm^{-1}. **HRMS** (ESI) calc'd for $C_8H_8N_2SNa$ $[M+Na]^+$: 187.0306, Found: 187.0306.

3-benzyl-5-(*p*-tolyl)-1H-pyrazole (3q₁): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 97mg, yield: 90% (***R**_f* = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.37 (s, 3H), 4.01 (s, 2H), 6.32 (s, 1H), 7.17-7.23 (m, 2H), 7.24-7.34 (m, 5H), 7.56 (dd, *J* = 13.6, 8.0 Hz, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 21.02, 33.17, 101.64, 125.38, 126.43, 127.03, 128.51, 128.64, 129.29, 137.66, 138.56, 147.65, 148.66 ppm. **IR** (Neat Film, NaCl): 2950, 1650, 1450, 1440, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{16}N_2Na$ $[M+Na]^+$: 271.1211, Found: 271.1212.

3-benzyl-5-(2-chlorophenyl)-1H-pyrazole (3r₁): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 94mg, yield: 89% (***R**_f* = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 4.03 (s, 2H), 6.51 (s, 1H), 7.24-7.35 (m, 7H), 7.43 (dd, *J* = 5.6, 3.6 Hz, 1H), 7.61-7.64 (m, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 33.28, 105.59, 126.58, 126.98, 128.66, 128.78, 129.10, 130.36, 130.47, 130.53, 131.86, 138.64, 145.58, 147.28 ppm. **IR** (Neat Film, NaCl): 2905, 1605, 1450, 1440, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{13}{}^{35}ClN_2Na$ $[M+Na]^+$: 291.0665, Found: 291.0665.

3-benzyl-4-methyl-5-(*p*-tolyl)-1H-pyrazole (3s₁): Yellow solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 94mg, yield: 90% (***R**_f* = 0.2; 20% EtOAc in hexane). **MP**: 199-202 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.10 (s, 3H), 2.39 (s, 3H), 3.98 (s, 2H), 7.20-7.24 (m, 5H), 7.28 (d, *J* = 6.8 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 8.94, 21.28, 32.21, 110.62, 125.62, 126.28, 126.35, 127.28, 128.54, 128.58, 129.35, 137.51, 138.80, 144.80, 146.94 ppm. **IR** (Neat Film, NaCl): 2934, 1654, 1454, 1444, 764 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{18}N_2$ $[M]^+$: 262.1470, Found: 262.1470.

5-(3,4-dimethoxyphenyl)-3-methyl-1H-pyrazole (3t₁): Red oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 98mg, yield: 92% (***R**_f* = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.34 (s, 3H), 3.85 (s, 3H), 3.89 (s, 3H), 6.44 (s, 1H), 6.86 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 7.22 (dd, *J* = 8.0, 1.2 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 13.07, 55.75, 60.52, 103.47, 111.65, 118.35, 119.55, 124.59, 141.71, 145.74, 147.46, 153.05 ppm. **IR** (Neat Film, NaCl): 2975, 1655, 1455, 1435, 785 cm^{-1}. **HRMS** (ESI) calc'd for $C_{12}H_{14}N_2O_2Na$ $[M+Na]^+$: 241.0953, Found: 241.0954.

5-(4-(benzyloxy)-3-methoxyphenyl)-3-methyl-1H-pyrazole (3u₁): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 100mg, yield: 95% (***R**_f* = 0.4; 30% EtOAc in hexane). **MP**: 110-112 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.27 (s, 3H), 3.86 (s, 3H), 5.17 (s, 2H), 6.27 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.29-7.39 (m, 4H), 7.44-7.48 (m, 2H), 9.10 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.52, 55.78, 70.91, 101.59, 109.27, 113.96, 118.13, 125.80, 127.20, 127.75, 128.70, 136.94, 142.95, 147.95, 149.60, 149.68 ppm. **IR** (Neat Film, NaCl): 2925, 1652, 1452, 1447, 764 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{18}N_2O_2$ $[M]^+$: 294.1368, Found: 294.1369.

5-(3-(benzyloxy)-4-methoxyphenyl)-3-methyl-1H-pyrazole (3v₁): Red oil, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 97mg, yield: 93% (***R**_f* = 0.4; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.27 (s, 3H), 3.88 (s, 3H), 5.11 (s, 2H), 6.22 (s, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 7.24-7.37 (m, 6H), 7.44 (d, *J* = 7.2 Hz, 1H), 9.78 (br s, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 11.49, 55.89, 70.80, 101.62, 111.36, 111.82, 118.75, 124.92, 127.49, 127.75, 128.39, 136.88, 142.92, 148.23, 149.05, 149.54 ppm. **IR** (Neat Film, NaCl): 2945, 1656, 1454, 1444, 788 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{18}N_2O_2$ $[M]^+$: 294.1368, Found: 294.1368.

5,5'-(2-methoxy-5-methyl-1,3-phenylene)bis(3-methyl-1H-pyrazole) (5a): Yellow solid, purified by silica gel column chromatography (elution with 10% EtOAc in hexane), 104mg, yield: 94% (***R**_f* = 0.3; 30% EtOAc in hexane). **MP**: 97-99 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): *δ* = 2.33 (s, 3H), 2.36 (s, 6H), 3.54 (s, 3H), 6.45 (s, 2H), 7.38 (s, 2H), 10.35 (br s, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): *δ* = 12.70, 20.68, 60.81, 103.96, 124.22, 127.60, 134.60, 142.14, 146.44, 151.72 ppm. **IR** (Neat Film, NaCl): 2932, 1652, 1454, 1442, 762 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{18}N_4ONa$ $[M+Na]^+$: 305.1378, Found: 305.1370.

5,5'-(2-isopropoxy-5-methyl-1,3-phenylene)bis(3-methyl-1H-pyrazole) (5b): Red oil, purified by silica gel column

10.1002/ejoc.201900008

chromatography (elution with 10% EtOAc in hexane), 102mg, yield: 93% (***R**$_f$* = 0.2; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.02 (d, *J* = 7.2 Hz, 6H), 2.33 (s, 3H), 2.35 (s, 6H), 3.85 (p, *J* = 6.4 Hz, 1H), 6.40 (s, 2H), 7.32 (s, 2H), 8.98 (br s, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.77, 20.64, 21.44, 76.57, 103.72, 125.24, 129.17, 134.43, 143.14, 146.97, 149.41 ppm. **IR** (Neat Film, NaCl): 2950, 1655, 1450, 1444, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{22}N_4O$ $[M]^+$: 310.1794, Found: 310.1794.

5-(2-chlorophenyl)-3-methyl-1H-pyrazole-1-carboxamide (6a): Yellow solid, purified by silica gel column chromatography (elution with 80% EtOAc in hexane), 113mg, yield: 85% (**R$_f$** = 0.2; 50% EtOAc in hexane). **MP**: 140-143 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.39 (s, 3H), 6.54 (s, 1H), 7.29-7.39 (m, 2H), 7.41-7.48 (m, 1H), 7.64 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.97 (br s, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ =11.77, 105.99, 126.44, 126.50, 126.92, 130.22, 130.99, 132.39, 142.79, 153.24, 169.40 ppm. **IR** (Neat Film, NaCl): 2945, 1650, 1465, 1454, 786 cm^{-1}. **HRMS** (ESI) calc'd for $C_{11}H_{10}{}^{35}ClN_3ONa$ $[M+Na]^+$: 258.0410, Found: 258.0416.

3-methyl-1,5-diphenyl-1H-pyrazole (6b): Yellow oil, purified by silica gel column chromatography (elution with 7% EtOAc in hexane), 152mg, yield: 94% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.44 (s, 3H), 6.35 (s, 1H), 7.25-7.27 (m, 2H), 7.28-7.33 (m, 8H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.53, 107.72, 125.07, 127.06, 128.03, 128.35, 128.56, 128.79, 130.61, 140.03, 143.63, 149.39 ppm. **IR** (Neat Film, NaCl): 2925, 1655, 1475, 1444, 776 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{14}N_2$ $[M]^+$: 234.1157, Found: 234.1162.

5-(2-chlorophenyl)-3-methyl-1-phenyl-1H-pyrazole (6c): Red oil, purified by silica gel column chromatography (elution with 7% EtOAc in hexane), 137mg, yield: 91% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.43 (s, 3H), 6.34 (s, 1H), 7.21-7.29 (m, 8H), 7.39 (d, *J* = 8.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.53, 109.22, 123.76, 124.98, 126.54, 126.66, 128.61, 128.98, 129.81, 129.87, 131.92, 133.87, 140.10, 149.10 ppm. **IR** (Neat Film, NaCl): 2942, 1652, 1465, 1454, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{13}{}^{35}ClN_2$ $[M]^+$: 268.0767, Found: 268.0768.

5-(2-chlorophenyl)-1-(4-chlorophenyl)-3-methyl-1H-pyrazole (6d): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 148mg, yield: 88% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.42 (s, 3H), 6.33 (s, 1H), 7.15-7.18 (m, 2H), 7.22-7.24 (m, 2H), 7.26-7.28 (m, 2H), 7.31-7.36 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.52, 109.53, 124.74, 126.73, 128.79, 128.94, 129.94, 130.15, 131.82, 132.48, 133.73, 138.53, 140.28, 149.48 ppm. **IR** (Neat Film, NaCl): 2955, 1675, 1487, 1464, 755 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{12}{}^{35}Cl_2N_2Na$ $[M+Na]^+$: 325.0275, Found: 325.0277.

1-(4-bromophenyl)-5-(2-chlorophenyl)-3-methyl-1H-pyrazole (6e): Red oil, purified by silica gel column chromatography (elution with 7% EtOAc in hexane), 169mg, yield: 85% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.42 (s, 3H), 6.33 (s, 1H), 7.10 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.26-7.28 (m, 2H), 7.31-7.42 (m, 4H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.52, 109.61, 114.26, 120.17, 125.00, 126.75, 129.27, 130.12, 130.16, 131.75, 133.70, 139.04, 140.25, 149.54 ppm. **IR** (Neat Film, NaCl): 2945, 1645, 1447, 1434, 765 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{12}Br{}^{35}ClN_2Na$ $[M+Na]^+$: 368.9770, Found: 368.9770.

5-(2-chlorophenyl)-1-(4-fluorophenyl)-3-methyl-1H-pyrazole (6f): Red oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 135mg, yield: 84% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.42 (s, 3H), 6.32 (s, 1H), 6.93-6.98 (m, 2H), 7.18-7.22 (m, 2H), 7.25-7.27 (m, 2H), 7.30-7.37 (m, 1H), 7.39 (d, *J* = 8.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.49, 109.13, 115.39, 115.62, 125.50, 125.58, 126.63, 126.94, 128.80, 129.28, 129.87, 130.05, 131.88, 140.39, 148.97, 162.34 ppm. **^{19}F NMR** (377 MHz, CDCl3): δ = -114.63 ppm. **IR** (Neat Film, NaCl): 2950, 1645, 1457, 1433, 776 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{12}{}^{35}ClFN_2Na$ $[M+Na]^+$: 309.0571, Found: 309.0565.

5-(2-chlorophenyl)-3-methyl-1-(p-tolyl)-1H-pyrazole (6g): Red oil, purified by silica gel column chromatography (elution with 7% EtOAc in hexane), 130mg, yield: 83% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.40 (s, 3H), 2.43 (s, 3H), 6.76 (s, 1H), 7.28-7.31 (m, 3H), 7.41-7.47 (m, 4H), 7.89 (dd, *J* = 7.6, 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.38, 21.01, 107.88, 112.73, 114.02, 126.74, 126.78, 128.72, 129.86, 130.12, 130.55, 130.63, 131.43, 136.92, 137.74, 139.27, 148.72 ppm. **IR** (Neat Film, NaCl): 2915, 1685, 1485, 1465, 775 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{15}{}^{35}ClN_2Na$ $[M+Na]^+$: 305.0821, Found: 305.0822.

5-(2-chlorophenyl)-1-(2,4-dimethylphenyl)-3-methyl-1H-pyrazole (6h): Red oil, purified by silica gel column chromatography (elution with 7% EtOAc in hexane), 142mg, yield: 85% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.09 (s, 3H), 2.17 (s, 3H), 2.40 (s, 3H), 6.75 (s, 1H), 7.10-7.52 (m, 6H), 7.88 (dd, *J* = 7.6, 2.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.41, 17.15, 21.09, 106.29, 117.08, 126.81, 126.88, 127.05, 127.41, 128.48, 129.87, 130.54, 131.78, 133.47, 135.77, 139.04, 139.97, 148.63 ppm. **IR** (Neat Film, NaCl): 2928, 1678, 1488, 1464, 785 cm^{-1}. **HRMS** (ESI) calc'd for $C_{18}H_{17}{}^{35}ClN_2$ $[M]^+$: 296.1080, Found: 296.1081.

5-(2-chlorophenyl)-1-(2,4-dichlorophenyl)-3-methyl-1H-pyrazole (6i): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 155mg, yield: 82% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.42 (s, 3H), 6.39 (s, 1H), 7.15 (d, *J* = 4.0 Hz, 2H), 7.21-7.27 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.37-7.39 (m, 2H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.63, 108.58, 126.37, 127.40, 129.20, 129.81, 129.93, 129.98, 130.45, 131.56, 132.71, 133.53, 134.84, 136.21, 142.12, 149.83 ppm. **IR** (Neat Film, NaCl): 2965, 1665, 1467, 1444, 775 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{11}{}^{35}Cl_3N_2$ $[M]^+$: 335.9988, Found: 335.9988.

4-(5-(2-chlorophenyl)-3-methyl-1H-pyrazol-1-yl)benzonitrile (6j): White solid, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 147mg, yield: 90% (***R**$_f$* = 0.5; 20% EtOAc in hexane). **MP**: 146-148 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.43 (s, 3H), 6.36 (s, 1H), 7.14 (d, *J* = 8.8 Hz, 2H), 7.26-7.44 (m, 3H), 7.53-7.56 (m, 2H), 8.05 (dd, *J* = 7.6, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.54, 110.77, 112.63, 123.01, 126.67, 126.94, 127.05, 129.74, 129.96, 130.13, 131.63, 132.80, 133.64, 136.47, 143.40, 147.43, 150.62 ppm. **IR** (Neat Film, NaCl): 2975, 1675, 1477, 1457, 768 cm^{-1}. **HRMS** (ESI) calc'd for $C_{17}H_{12}{}^{35}ClN_3$ $[M]^+$: 293.0720, Found: 293.0722.

General procedure for synthesis of substituted (*Z*)-2-methyl -7H benzo[b]pyrazolo[5,1-d][1,5]oxazocine (7a as Example): To a well stirred mixture of 3-methyl-5-(2-(prop-2-yn-1-yloxy)phenyl)-1H-pyrazole **3h$_1$** (80mg, 0.38mmol) in H_2O:EtOH (10:2, 5ml) in a pressure tube was heated at 120^0 C.

The reaction mixture was allowed to heat for 24h continuously. The reaction mixture was allowed to cool and then quenched with distilled water and extracted with ethyl acetate (3x40ml). The organic part was washed with brine solution and dried over anhydrous sodium sulphate. Then the solvent was evaporated under reduced pressure. The mass was then purified by column chromatography using silica gel in specified solvent combination to deliver the desired compounds substituted **7a** (52mg, 0.24mmol) with expected purity.

(*Z*)-2-methyl-7H-benzo[b]pyrazolo[5,1-d][1,5] oxazocine (7a): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 52mg, yield: 65% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 4.83 (dd, *J* = 3.6, 2.0 Hz, 2H), 5.30 (dt, *J* = 10.0, 3.6 Hz, 1H), 6.15 (s, 1H), 6.93 (dt, *J* = 9.6, 1.6 Hz, 1H), 7.16 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.19 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.32 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.40 (td, *J* = 8.0, 1.6 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.45, 72.14, 106.87, 117.67, 121.79, 124.18, 128.53, 129.09, 130.78, 130.93, 142.79, 150.41, 156.01 ppm. **IR** (Neat Film, NaCl): 2950, 1670, 1480, 1464, 750 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{12}N_2ONa$ $[M+Na]^+$: 235.0847, Found: 235.0847.

(*Z*)-2,11-dimethyl-7H-benzo[b]pyrazolo[5,1-d][1,5] oxazocine (7b): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 50mg, yield: 63% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 2.36 (s, 3H), 4.81 (dd, *J* = 3.6, 2.4 Hz, 2H), 5.26 (dt, *J* = 10.0, 3.2 Hz, 1H), 6.14 (s, 1H), 6.91 (dd, *J* = 10.4, 2.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 7.14 (d, *J* = 2.0 Hz, 1H), 7.21 (dd, *J* = 8.4, 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.46, 20.62, 72.56, 106.69, 117.72, 121.55, 128.07, 130.95, 131.03, 131.51, 133.94, 142.85, 150.31, 153.92 ppm. **IR** (Neat Film, NaCl): 2948, 1665, 1467, 1444, 758 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{14}N_2ONa$ $[M+Na]^+$: 249.1004, Found: 249.1005.

(*Z*)-11-bromo-2-methyl-7H-benzo[b]pyrazolo[5,1-d][1,5] oxazocine (7c): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 52mg, yield: 65% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.34 (s, 3H), 4.80 (dd, *J* = 4.0, 2.0 Hz, 2H), 5.34 (dt, *J* = 10.0, 3.6 Hz, 1H), 6.17 (s, 1H), 6.93 (dt, *J* = 9.6, 1.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.49 (dd, *J* = 8.8, 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.44, 71.73, 107.27, 117.62, 123.57, 125.64, 127.73, 128.89, 132.78, 133.57, 140.84, 150.71, 155.00 ppm. **IR** (Neat Film, NaCl): 2944, 1665, 1477, 1464, 785 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{11}BrN_2O$ $[M]^+$: 290.0055, Found: 290.0056.

(*Z*)-11-chloro-2-methyl-7H-benzo[b]pyrazolo[5,1-d][1,5] oxazocine (7d): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 47mg, yield: 60% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 4.80 (dd, *J* = 5.6, 2.0 Hz, 2H), 5.32 (dt, *J* = 9.6, 3.6 Hz, 1H), 6.17 (s, 1H), 6.93-6.97 (m, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 7.30 (d, *J* = 2.8 Hz, 1H), 7.35 (dd, *J* = 2.8 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.43, 71.97, 107.22, 117.63, 123.23, 128.54, 128.70, 129.17, 130.54, 130.66, 140.94, 150.68, 154.51 ppm. **IR** (Neat Film, NaCl): 2965, 1665, 1477, 1464, 766 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{11}{}^{35}ClN_2ONa$ $[M+Na]^+$: 269.0458, Found: 269.0455.

(*Z*)-2-methyl-10-(prop-2-yn-1-yloxy)-7H-benzo[b]pyrazolo [5,1-d][1,5]oxazocine (7e): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 24mg, yield: 58% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.34 (s, 3H), 2.57 (t, *J* = 2.4 Hz, 1H), 4.73 (d, *J* = 2.8 Hz, 2H), 4.81 (dd, *J* = 4.0 Hz, 2H), 5.36 (dt, *J* = 9.6, 4.0 Hz, 1H), 6.11 (s, 1H), 6.76-6.781 (m, 1H), 6.80 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.96 (d, *J* = 9.6 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.49, 55.82, 71.27, 76.21, 76.99, 101.16, 106.70, 107.61, 111.01, 116.55, 117.61, 129.09, 132.17, 150.53, 156.80, 159.34 ppm. **IR** (Neat Film, NaCl): 2950, 1675, 1480, 1464, 750 cm^{-1}. **HRMS** (ESI) calc'd for $C_{16}H_{14}N_2O_2Na$ $[M+Na]^+$: 289.0953, Found: 289.0954.

(*Z*)-9-methoxy-2-methyl-7H-benzo[b]pyrazolo[5,1-d][1,5] oxazocine (7f): Yellow oil, purified by silica gel column chromatography (elution with 8% EtOAc in hexane), 22mg, yield: 55% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.35 (s, 3H), 3.92 (s, 3H), 4.86 (t, *J* = 2.4 Hz, 2H), 5.26 (dt, *J* = 10.4, 3.2 Hz, 1H), 6.15 (s, 1H), 6.86 (dt, *J* = 10.4, 2.0 Hz, 1H), 6.92 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.98 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.44, 55.79, 70.72, 106.67, 112.62, 118.28, 121.81, 124.88, 126.41, 127.18, 141.72, 144.59, 150.14, 152.44 ppm. **IR** (Neat Film, NaCl): 2935, 1670, 1480, 1464, 765 cm^{-1}. **HRMS** (ESI) calc'd for $C_{14}H_{14}N_2O_2Na$ $[M+Na]^+$: 265.0953, Found: 265.0953.

(*Z*)-9,11-dibromo-2-methyl-7H-benzo[b]pyrazolo[5,1-d][1,5] oxazocine (7g): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 22mg, yield: 50% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.33 (s, 3H), 4.88 (t, *J* = 2.4 Hz, 2H), 5.29 (dt, *J* = 10.4, 3.6 Hz, 1H), 6.14 (s, 1H), 6.90 (dt, *J* = 10.0, 1.6 Hz, 1H), 7.42 (d, *J* = 2.4 Hz, 1H), 7.76 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 12.01, 70.88, 107.76, 117.39, 130.20, 132.46, 133.94, 134.67, 136.36, 138.09, 140.09, 150.65, 151.61 ppm. **IR** (Neat Film, NaCl): 2946, 1676, 1486, 1464, 760 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{10}Br_2N_2O$ $[M]^+$: 367.9160, Found: 367.9161.

(*Z*)-9-bromo-11-chloro-2-methyl-7H-benzo[b]pyrazolo[5,1-d][1,5]oxazocine (7h): Yellow oil, purified by silica gel column chromatography (elution with 6% EtOAc in hexane), 20mg, yield: 52% (R_f = 0.5; 30% EtOAc in hexane). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.34 (s, 3H), 4.90-4.91 (m, 2H), 5.29 (dt, *J* = 10.0, 3.2 Hz, 1H), 6.15 (s, 1H), 6.91 (d, *J* = 10.0 Hz, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 13.53, 71.09, 107.83, 117.39, 117.81, 127.85, 128.82, 129.66, 130.90, 132.84, 133.72, 148.85, 150.76 ppm. **IR** (Neat Film, NaCl): 2936, 1676, 1467, 1454, 762 cm^{-1}. **HRMS** (ESI) calc'd for $C_{13}H_{10}Br^{35}ClN_2ONa$ $[M+Na]^+$: 346.9563, Found: 346.9564.

Acknowledgements

We sincerely acknowledge Department of Science and Technology (DST), Govt. of India (Grant no. SB/FT/CS-076/2012) and INSPIRE-DST, Govt. of India (Grant No.04/2013/000751). SRS thanks to DST-Inspire for fellowship. We acknowledge P Behera for NMR studies.

References

[1] (a) Y. Li, H.-Q. Zhang, J. Liu, X.-P. Yang, Z.-J. Liu, *J. Agric. Food Chem.* **2006**, *54*, 3636. (b) H. Chen, Z. Li, Y. J. Han, *J.Agric. Food Chem.* **2000**, *48*, 5312. (c) D. N. Gandhale, A. S. Patil, B. G. Awate, L. M. Naik, *Pesticides* **1982**, *16*, 27.
[2] (a) Y. Al-Abed, D. Dabideen, B. Aljabari, A. Valster, D. Messmer, M. Ochani, M. Tanovic, K. Ochani, M. Bacher, F. Nicoletti, C. Metz, V. A. Pavlov, E. J. Miller, K. J. Tracey, *J. Biol.Chem.* **2005**, *280*, 36541–36544. (b) R. Kakarla, J. Liu, D.

Naduthambi, W. Chang, R. T. Mosley, D. Bao, H. M. Micolochick Steuer, M. Keilman, S. Bansal, A. M. Lam, W. Seibel, S. Neilson, P. A. Furman, M. J. Sofia, *J. Med.Chem.* **2014**, *57*, 2136–2160. (c) A. P. Kozikowski, *Acc. Chem. Res.* **1984**, *17*, 410–416. (d) V. Nair, T. D. Suja, *Tetrahedron* **2007**, *63*, 12247–12275. (e) K. Takenaka, T. Nagano, S. Takizawa, H. Sasai, *Tetrahedron Asymmetry* **2010**, *21*, 379–381. (f) S. Tapadar, R. He, D. N. Luchini, D. D. Billadeau, A. P. Kozikowski, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3023–3026. (g) K. A. El Sayed, P. Bartyzel, X. Shen, T. L. Perry, J. K. Zjawiony, M. T. Hamann, *Tetrahedron* **2000**, *56*, 949–953. (h) M. Gopalakrishnan, J. Ji, C.-H. Lee, T. Li, K. B. Sippy, WO2009/149135A1 (Abbott Laboratories), **2009**. (i) P. Proksch, A. Putz, S. Ortlepp, J. Kjerand M. Bayer, *Phytochem. Rev.* **2010**, *9*, 475–489.

[3] (a) J. Elguero, In Comprehensive Heterocyclic Chemistry II; A. R. Katritzky, C. W. Rees, E. F. V. Scriven, Eds., Pergamon: Oxford **1996**, *Vol. 3*, p1. (b) C. Lamberth, *Heterocycles* **2007**, *71*, 1467. (c) T. Eicher, S. Hauptmann, A. Speicher, the Chemistry of Heterocycles, 2nd ed., Wiley & Sons: New York, **2004**; pp 179−184.

[4] V. K. Rao, R. Tiwari, B. S. Chhikara, A. N. Shirazi, K. Parangand, A. Kumar, *RSC Adv.* **2013**, 3, 15396.

[5] D. Vuluga, J. Legros, B. Crousse, D. Bonnet-Delpon, *Green Chem.* **2009**, 11, 156.

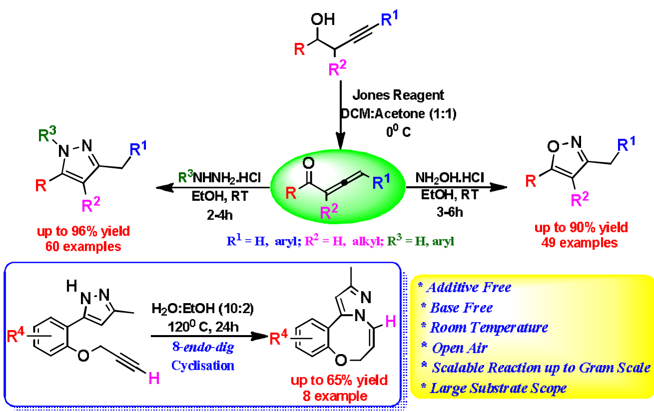
[6] S. Guo, J. Wang, D. Guo, X. Zhang, X. Fan, *RSC Adv.* **2012**, *2*, 3772-3777.

[7] (a) F. Lecornue, J. Ollivier, *Org. Biomol. Chem.* **2003**, *1*, 3600–3604. (b) S. K. Mandal, S. C. Roy, *Tetrahedron* **2007**, *63*, 11341-11348. (c) F. Quartieri, L. E. Mesiano, D. Borghi, V. Desperati, C. Gennari, G. Papeo, *Eur. J. Org. Chem.* **2011**, 6794–6801. (d) S. Sabui, S. Ghosh, D. Sarkar, R. V. Venkateswaran, *Tetrahedron Lett.* **2009**, *50*, 4683-4684.

[8] (a) X.-H. Liu, Y.-M. Jia, B.-A. Song, Z.-x. Pang, S. Yang, *Bioorg. Med. Chem. Lett.* **2013**, *23*, 720–723. (b) S.-C. Chen, G.-L. Qiu, B. Li, J.-B. Shi, X.-H. Liu, W.-J. Tang, *Eur. J. Med. Chem.* **2018**, *147*, 194-204.

Layout 1:

FULL PAPER



Sustainable Synthesis

A straight forward synthesis of substituted isoxazoles and pyrazoles from 1,2-allenic ketones assisted by hydrochlorides of hydrazine and hydroxylamine is presented. In the process, the propyloxy-phenyl pyrazoles were transformed to (*Z*)-2-methyl 7H benzo[b]pyrazolo[5,1-d][1,5]oxazocine which arised as important emissive compounds

Key Topic* Regioslective, Protic activation, annulation, Synthesis design, Benzoxacine, Emission Spectroscopy

Prof. Dr. Debayan Sarkar[a]* and Sushree Ranjan Sahoo[a]

Page No. – Page No.

Title: Monohydrochloride Assisted Synthesis of Functionalised Isoxazoles and Pyrazoles from Allenic Ketones – First Synthesis of (*Z*)-2-methyl -7H benzo[b]pyrazolo[5,1-d][1,5]oxazocines