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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02124 • Publication Date (Web): 18 Sep 2017

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Regioselective Synthesis of 2, 4, 5-Trisubstituted-Oxazoles and Ketene Aminals via Hydroamidation, and Iodo-imidation of Ynamides

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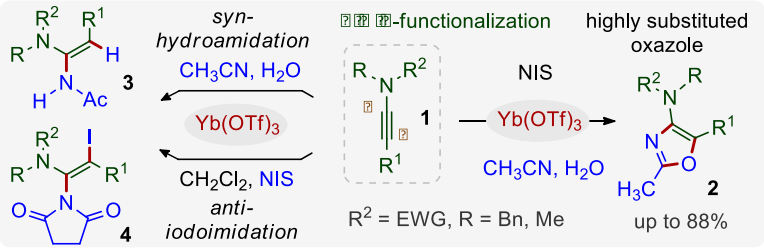


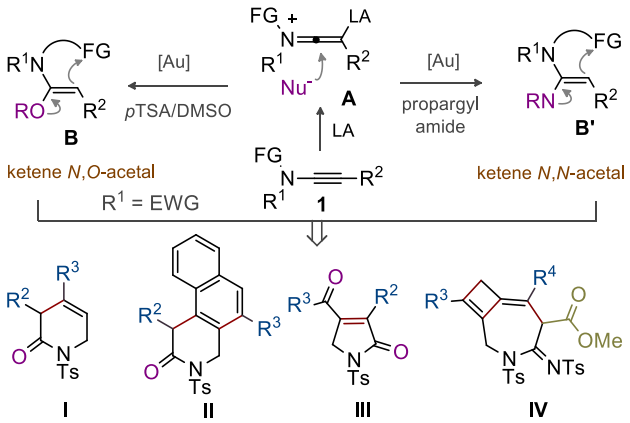
A novel and straightforward protocol is demonstrated for the synthesis of highly substituted oxazole from readily accessible ynamides in the presence of ytterbium(III) trifluoromethanesulfonate [$Yb(OTf)_3$], *N*-iodosuccinimide (NIS), and acetonitrile. Multiple

oxazole skeletons in the aryl-periphery are constructed in a single operation for the first time. The hydroamidation and iodo-imidation of ynamides to tri- and tetra-substituted ketene aminals is exemplified. An isotope labeling experiment is used to identify the oxygen source in this transformation. The reactions are scalable to the gram scale, testifying the robustness of the transformations.

INTRODUCTION

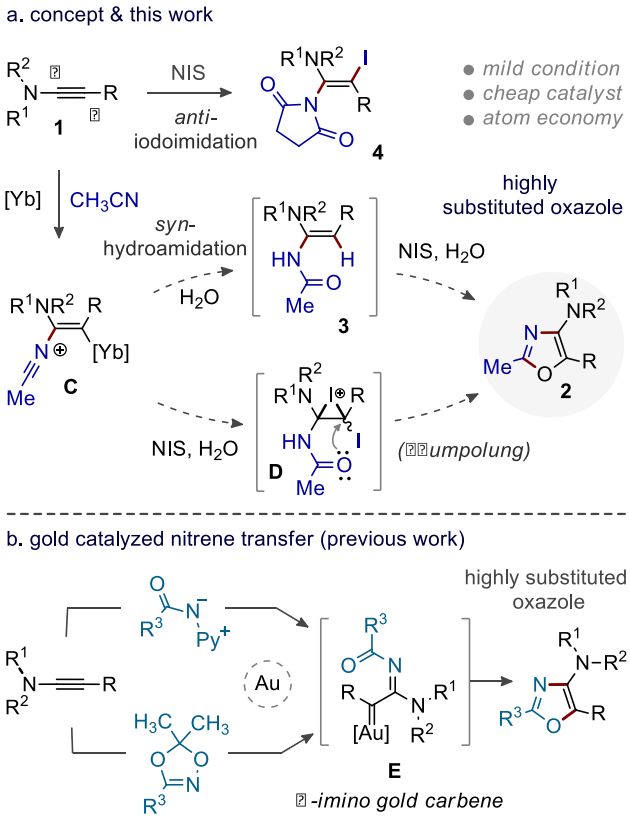
Ynamides, the nitrogen-substituted alkynes, have extensively been used in the conceptual development of novel synthetic transformations.[1] The polarized triple bond of ynamide under Brønsted/Lewis acid catalysis coherently allows *in situ* formation of reactive keteniminium species (**A**). Trapping of the reactive keteniminium species with nucleophiles offer novel pathways for the construction of complex *N*-heterocycles.[2] Eventually, the regioselective α-attack of *O*- and *N*-bearing nucleophiles to the activated ynamide **1** directly accesses ketene *N*,*O*-/*N*,*N*-acetal (**B**/**B′**; Scheme 1).[3] Thus, the intramolecular cyclization and cycloisomerization of π-tethered acetals fabricate diverse molecular scaffolds.[3b] We have recently showcased the use of ketene *N*,*O*- and *N*,*N*-acetal, obtained from yne-tethered-ynamides by the attack of *p*-toluenesulfonic acid, dimethyl sulfoxide, or amide moieties to construct dihydropyridine (**I**), benzo[*f*]dihydroisoquinolone (**II**), pyrrolidone (**III**), and cyclobutene-fused-azepine (**IV**) derivatives (Scheme 1).[4]

Scheme 1: Significance of Ketene *N,O*- and *N,N*-Acetal from Ynamides



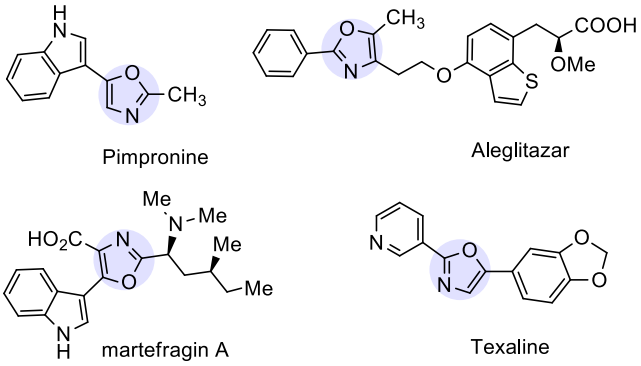
Intrigued by these results, we envisage the Lewis acid mediated regioselective attack of nitrile at the α-position of ynamide to yield a reactive nitrilium intermediate **C**, which eventually undergoes hydration to provide ketene-aminal **3** (Scheme 2a). Next, the intramolecular cyclization of ketene-aminal **3** (formed *in situ*) in the presence of an activator possibly constructs peripherally decorated and highly selective 4-amino-2,5-disubstituted oxazole (**2**) (Scheme 2a). This is possible when the nucleophilic β-position of the aminal becomes electrophilic (i.e., "*β-umpolung*"), which remains challenging. Thus, NIS is considered facilitating ketene aminal (**3**/**D**) for intramolecular 5-*endo*-trig cyclization of the pendant amide to yield oxazole **2** (Scheme 2a). As such, the Au(I)-catalyzed [2+2+1] annulation of a terminal alkyne, nitrile, and oxygen has been successfully used for the synthesis of 2,5-disubstituted oxazole.[5] The fabrication of 2,4,5-trisubstituted oxazoles from ynamides involving Au(I)-catalyzed [3+2] cycloaddition with nitrene transfer reagents are reliably deliberated (Scheme 2b); the transformation involves α-imino-β-Au-carbene making the β-position of ynamide electrophilic.[6]

Scheme 2: Previous Work and Current Hypothesis



The oxazole motifs are potential building blocks that are widely present in various natural products and bioactive molecules (Figure 1),[7] and are useful in many synthetic transformations.[8] Of course, a modular paradigm to build a highly substituted oxazole skeleton is exceedingly desirable.[9,10]

Figure 1. Oxazole Containing Bioactive Molecules



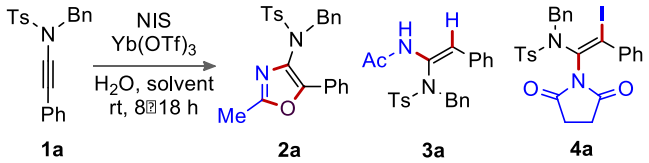
Despite the progress, we herein discussed the development of a modular synthetic protocol for 4-amino-2,5-disubstituted oxazole from readily accessible ynamides in the presence of a $Yb(OTf)_3$ catalyst, NIS promoter, and H_2O in acetonitrile (masked amide equivalent) at room temperature (rt). In addition, we demonstrate the regio and stereoselective hydroamidation[11] and iodo-imidation of ynamides to yield ketene aminals (**3;** *syn*-selectivity) and β-iodo ketene aminals (**4**; *anti*-selectivity) by independently exposing ynamides to $Yb(OTf)_3$, H_2O in CH_3CN and $Yb(OTf)_3$, NIS in CH_2Cl_2 (Scheme 2a).

RESULTS AND DISCUSSION

As envisaged, the investigation was commenced for the synthesis of oxazole **2** from ynamide **1** (Table 1). To begin with, ynamide **1a** was subjected to NIS (2.2 equiv), $Cu(OTf)_2$ (20 mol %), H_2O (2.0 equiv) in CH_3CN for 8 h at rt. To our delight, the oxazole product **2a** was isolated in 38% yield (entry 1) and the structure of **2a** was elucidated by X-ray analysis (Table 1). The reaction in the presence of $Yb(OTf)_3$ was found effective producing **2a** (88%); while other Lewis acids $Sc(OTf)_3$, $Fe(OTf)_3$ were found inferior (entries 2–4). Disappointingly, the reaction mediated by triflic acid turned complex (entry 5). The use of molecular iodine instead of NIS did not produce **2a** (entry 6); preferably NIS is better electrophilic iodinating agent over iodine.[12] Formation of **2a** was hampered in the absence of $Yb(OTf)_3$ (entry 7), demonstrating the importance of Lewis acid in this transformation. The additives NBS and NCS were not beneficial (entries 8–9). The use of less amount catalyst and/or NIS impacted the reaction outcome (entries 10 and 11). Predictably, the absence of H_2O led to 2a (<10%, entry 12). To our surprise, the reaction in the absence of NIS underwent *syn*-hydroamidation, explicitly delivering tri-substituted aminal **3a** in 57% yield (entry 13); X-ray crystallographic studies confirmed the

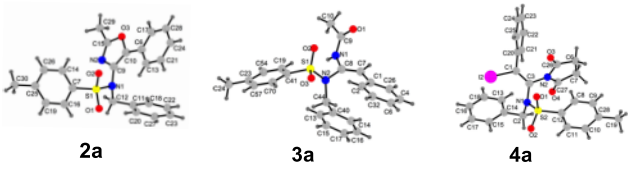
structure **3a** (Table 1). The co-ordination of nitrogen in CH_3CN to Yb-activated keteniminium species preferably builds the product **3a** with Z–olefin selectivity. Pleasingly, enhanced yield of **3a** (70%) was noticed, when the reaction continued for 18 h (entry 14). A trace of **3a** was formed when the reaction conducted in presence of molecular sieves (4Å) (entry 15); thus H_2O is indispensable in this transformation. Not surprisingly, reaction failed in the absence of $Yb(OTf)_3$ and NIS (entry 16). The reaction with CH_3CN (2.0 equiv) in $ClCH_2CH_2Cl$/toluene turned complex (entries 17 and 18); in contrast the identical reaction in CH_2Cl_2 yielded 67% of *anti*-iodo-imidation product **4a** and a trace of **2a** (entry 19); structure **4a** was further characterized by X-ray analysis (Table 1). The reaction in the absence of CH_3CN and H_2O was equally effective (entry 20). The use of either less amount of NIS or without $Yb(OTf)_3$ affected the reaction (entries 21 and 22). From these studies, it appears that ynamides undergo several transformations under the influence of $Yb(OTf)_3$ delivering oxazole (**2a**), and tri-/ tetra-sustituted ketene aminals (**3a** and **4a**) in a single step.

Table 1: Optimization of Reaction Conditions[a]



entry	catalyst (20 mol%)	additive (equiv)	solvent (1.5 mL)	time (h)	yield (%) **2a/3a/4a**
1	$Cu(OTf)_2$	NIS (2.2)	CH_3CN	8	38 (**2a**)
2[b]	$Sc(OTf)_3$	NIS (2.2)	CH_3CN	8	65 (**2a**)
3	**$Yb(OTf)_3$**	**NIS (2.2)**	**CH_3CN**	**8**	**88 (2a)**
4[b]	$Fe(OTf)_3$	NIS (2.2)	CH_3CN	8	10 (**2a**)

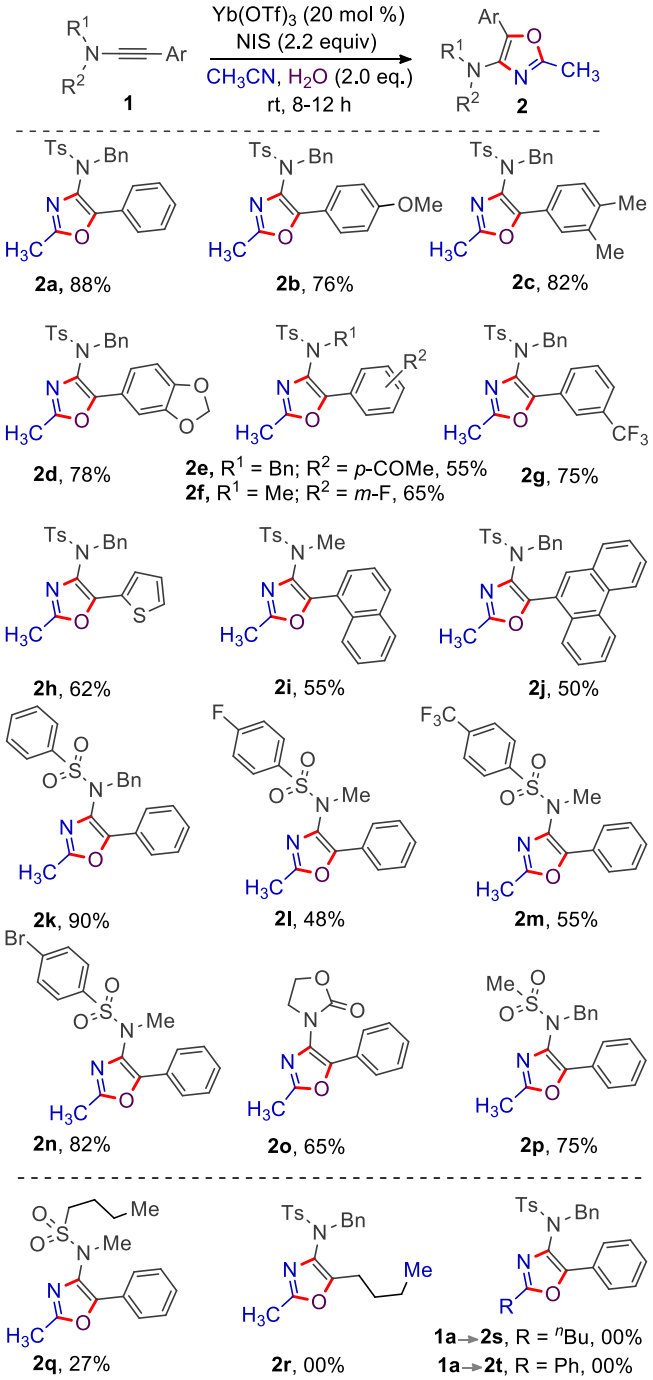
5[c]	HOTf	NIS (2.2)	CH_3CN	8	complex
6[d]	$Yb(OTf)_3$	I_2 (2.2)	CH_3CN	8	–
7	–	NIS (2.2)	CH_3CN	8	31 (**2a**)
8	$Yb(OTf)_3$	NBS (2.2)	CH_3CN	8	complex
9	$Yb(OTf)_3$	NCS (2.2)	CH_3CN	8	complex
10[e]	$Yb(OTf)_3$	NIS (2.2)	CH_3CN	8	62 (**2a**)
11[e]	$Yb(OTf)_3$	NIS (1.2)	CH_3CN	8	<20 (**2a**)
12[f]	$Yb(OTf)_3$	NIS (2.2)	CH_3CN	8	<10 (**2a**)
13[b]	$Yb(OTf)_3$	–	CH_3CN	8	57 (**3a**)
14	**$Yb(OTf)_3$**	**–**	**CH_3CN**	**18**	**70 (3a)**
15	$Yb(OTf)_3$	4Å MS	CH_3CN	18	<5 (**3a**)
16	–	–	CH_3CN	18	NR
17[g]	$Yb(OTf)_3$	NIS (2.2)	$ClCH_2CH_2Cl$	8	complex
18[g]	$Yb(OTf)_3$	NIS (2.2)	toluene	8	complex
19[b,g]	$Yb(OTf)_3$	NIS (2.2)	CH_2Cl_2	8	67 (**4a**)
20[f]	**$Yb(OTf)_3$**	**NIS (2.2)**	**CH_2Cl_2**	**8**	**69 (4a)**
21[f]	$Yb(OTf)_3$	NIS (1.2)	CH_2Cl_2	8	56 (**4a**)
22[f]	–	NIS (1.2)	CH_2Cl_2	8	40 (**4a**)



[a]Reactions were carried out using **1** (0.2 mmol), catalyst (20 mol %), H_2O (2.0 equiv.) in solvent at rt; [b]Crude NMR yield; [c]HOTf (1.2 equiv.) was used; [d]**2a** was not formed; [e]$Yb(OTf)_3$ (10 mol %) was used; [f]without H_2O; [g]CH_3CN (2.0 equiv) was used.

We then probed the reaction generality for the synthesis of trisubstituted oxazoles under the optimized conditions in entry 3, Table 1 (Scheme 3). The ynamide **1a** was effectively reacted with CH_3CN furnishing oxazole **2a** in 88% yield. Likewise, the ynamides **1b–d** with electron rich arenes in the alkyne-terminus successfully yielded the corresponding oxazoles **2b–d** [76–82%]. The electron-poor arene bearing ynamides delivered **2e–g** [*p*-COMe-**2e** (55%), *m*–F-**2f** (65%), and *m*–CF_3-**2g** (75%)]. Gratifyingly, the heteroaryl substituted ynamide **1h** was not exception, providing **2h** in 62% yield. The sterically encumbered napthyl and phenanthryl enabled oxazoles **2i** and **2j** were reliably accessed albeit in moderate yield. Instead of N-Ts, the neutral N-benzenesulfonyl protected ynamide **1k** furnished the desired product **2k** in excellent yield (90%). Likewise, various N-arenesulfonyl protected ynamides [*p*–F-C_6H_4 (**1l**), *p*–CF_3-C_6H_4 (**1m**), and *p*–Br-C_6H_4 (**1n**)] were effectively tolerated under the optimized conditions, yielding the corresponding highly substituted oxazoles **2l–2n** in good yields. Gratifyingly, the modifiable oxazolidinone protected ynamide delivered 65% of **2o**. To our delight, the alkyl-enabled N-sulfonyl protected oxazoles were reliably constructed (**2p**; 75% and **2q**; 27%). However, the ynamide (having alkyl moiety in the alkyne terminus) provided complex mixture, without forming the desired product **2r**. Disappointingly, repeated attempts condensing other nitriles (benzonitriles, butyronitrile, valeronitrile) with ynamide were failed (**2s** and **2t**); probably the absence of acidic α–H and the steric bulkiness of nitriles obstruct the cyclization (see Int **I** and **I′** in Scheme 10).

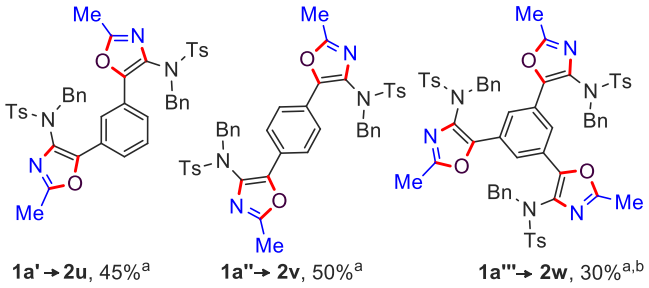
Scheme 3. Scope of 2,4,5-Trisubstituted-Oxazole[a]



[a]Reactions were carried out using 1 (0.5 mmol), NIS (1.1 mmol), $Yb(OTf)_3$ (0.1 mmol), H_2O (1.0 mmol) in CH_3CN (3.0 mL) at rt for 8–12 h.

A programmed synthetic manifestation for the $Yb(OTf)_3$ and NIS mediated amidation and cyclization sequence of large number of ynamides within a molecule would directly erect many oxazole motifs in a single operation. Pleasingly, this complexity driven notion eventually allows the construction of 1,3- and 1,4-bis-oxazoles **2u** (45%) and **2v** (50%), forming six bonds (two C–N and four C–O) in a single operation, from easily accessible precursors **1a′** and **1a″**. To our delight, a complex tri-substituted 1,3,5-tris-oxazole **2w** was successfully built from 1,3,5-triynamide precursor **1a‴** (Scheme 4).

Scheme 4: Construction of Poly-Oxazoles on Arene[a]

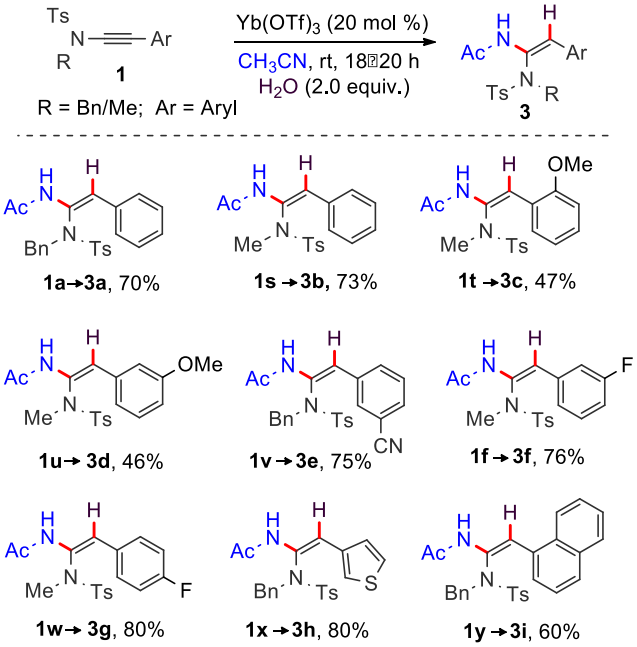


[a]Reactions were carried out using **1a′–1a‴** (0.3 mmol), NIS (1.32 mmol), $Yb(OTf)_3$ (0.12 mmol), H_2O (1.2 mmol), in CH_3CN (3.0 mL) at rt for 16 h; [b]NIS (1.98 mmol), $Yb(OTf)_3$ (0.18 mmol), H_2O (1.8 mmol), rt for 24 h.

Next, the $Yb(OTf)_3$ mediated hydroamidation of ynamide with CH_3CN in presence of H_2O (entry 14, Table 1) for the synthesis of ketene aminals **3** was surveyed (Scheme 5). The N-benzyl and N-methyl protected ketene aminals **3a** and **3b** were obtained in 70% and 73% yield, respectively. The electron rich ynamides successfully delivered **3c–d** [*o*-OMe-**3c** (47%) and *m*-OMe-**3d** (46%)] in moderate yield. Whereas the desired products **3e–g** [*m*-CN-**3e** (75%), *m*–F-**3f** (76%), and *p*–F-**3g** (80%)] were proficiently accessed from the electron-poor arene bearing

ynamides. The 3-thienyl and 1-naphthyl enabled products **3h** (80%) and **3i** (60%) were reliably isolated.

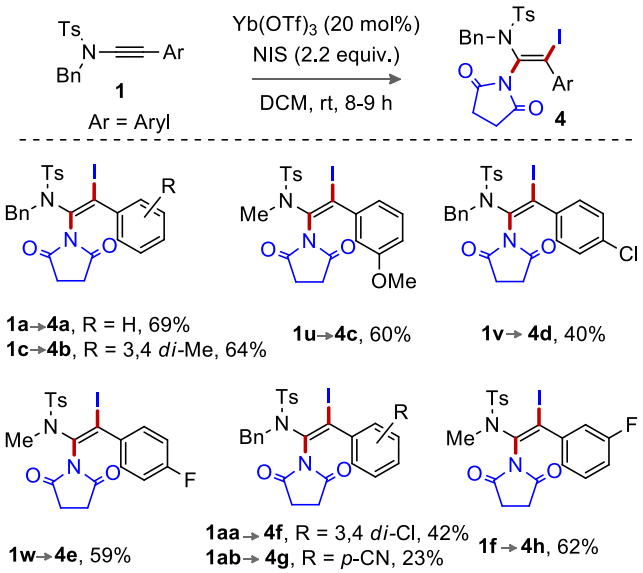
Scheme 5. Scope for *syn*-Hydroamidation of Ynamides[a]



[a]Reactions were carried out using **1** (0.5 mmol), $Yb(OTf)_3$ (0.1 mmol), H_2O (1.0 mmol) in CH_3CN (3.0 mL) at rt for 18–20 h.

The synthetic importance of β-halo ketene aminals motivated us scrutinizing the scope of **4a** under the optimized conditions shown in entry 20, Table 1 (Scheme 6). The ynamide **1a** afforded *Z*-β-iodo ketene aminal **4a** in 69% yield. The iodo-imidation was fruitfully exhibited for N-Bn/Me-protected ynamides having electron-rich/-poor arenes in the alkyne-terminus to yield the products **4b–h** [*m,p-di*Me-**4b** (64%), *m*-OMe-**4c** (60%), *p*-Cl-**4d** (40%), *p*-F-**4e** (59%), *m,p-di*Cl-**4f** (42%), *p*-CN-**4g** (23%), and *m*-F-**4h** (62%)] (Scheme 6).

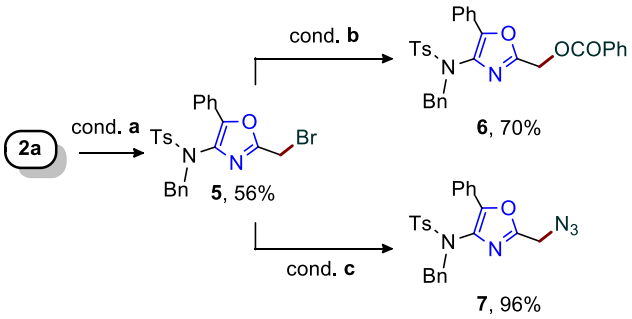
Scheme 6: Scope for *anti*-Iodo-Imidation of Ynamides[a]



[a]Reactions were carried out using **1** (0.5 mmol), NIS (1.1 mmol), $Yb(OTf)_3$ (0.1 mmol) in CH_2Cl_2 (3.0 mL) at rt for 8–9 h.

As deliberated in Table 1, Schemes 3 and 4, the reaction of large varieties of ynamides with CH_3CN in the presence of $Yb(OTf)_3$, NIS, and H_2O has reliably been demonstrated for the construction of 2-methyl-bearing peripheral decorated oxazoles **2**. The exclusive participation of CH_3CN significantly undermines broad synthetic importance of this demonstration. As the 2-Me group of oxazole skeleton is acidic, further functionalization of the active-methyl moiety is therefore possible. As expected, the bromination of methyl-moiety of **2a** with NBS in presence of AIBN smoothly occurred providing the desired bromination product **5** in 56% yield (Scheme 7). Next, the nucleophilic displacement of the bromo group in **5** with carboxylate and azide moieties constructed C–O (**6**, 70%) and C–N (**7**, 96%) bonds (Scheme 7). We therefore believe the 2-methyl oxazole motifs, fabricated from ynamides and acetonitrile, would be capable of showing broad synthetic potential.

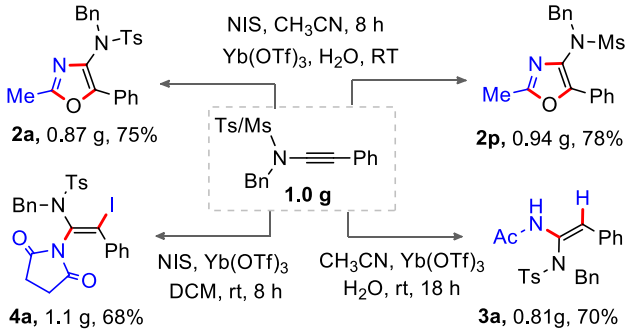
Scheme 7: **Functionalization of Methyl Group**



Condition **a**: **2a** (0.2 mmol), AIBN (0.01 mmol), NBS (0.22 mmol) in CCl_4 (2.0 mL) at 60 °C for 9 h. Condition **b**: **5** (0.1 mmol), PhCOOH (0.15 mmol), Et_3N (0.3 mmol) in CH_3CN (2.0 mL) at 80 °C for 1 h. Condition **c**: **5** (0.1 mmol), NaN_3 (0.5 mmol), in $(CH_3)_2CO$:H_2O (3:1; 2.0 mL) at rt for 1 h.

Finally, the robustness of the reaction was tested for gram scale (Scheme 8). Exposing **1a** and **1p** (1.0 g) to the mixture of NIS, $Yb(OTf)_3$, and CH_3CN yielded **2a** (0.87 g, 75%), and **2p** (0.94 g, 78%), respectively. Likewise, compounds **3a** (0.81 g, 70%) and **4a** (1.1 g, 68%) were obtained from **1a** (1.0 g) under the respective optimized conditions of hydroamidation and iodo-imidation of ynamides (Scheme 8). These results attest the scalability of the transformations.

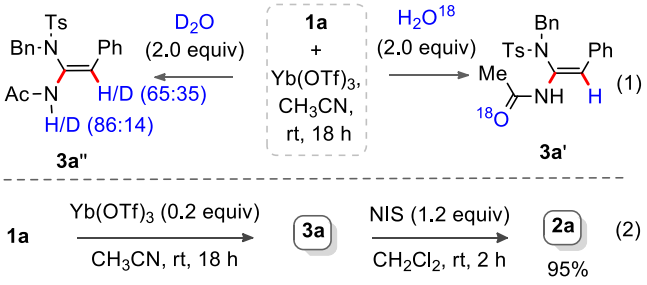
Scheme 8: Gram Scale Synthesis



To realize the source of water in this study, a set of isotope labeling experiments were independently carried out between **1a** and ^{18}O-labelled H_2O or D_2O (eq 1, Scheme 9). The

incorporation of ^{18}O in the amide and D-insertion in the vinyl position in the hydroamidation product (**3a′** and **3a″**; observed by HRMS and ^{1}H NMR analysis) clearly expresses the critical role of H_2O in this study (eq 1, Scheme 9). Next, the conversion of **1a** to **2a** was planned using $Yb(OTf)_3$ mediated hydroamidation and NIS-assisted cyclization in a stepwise manner to acquire preliminary insight into the mechanism and the necessity of NIS in these transformations. As envisaged, **3a** (obtained from **1a**) was efficiently converted to **2a** (95%), when subjected to NIS in CH_2Cl_2 at rt (eq 2, Scheme 9). Thus, the activation of **3a** with NIS helps the attack of the amide-oxygen of N-acetyl group at the β-position of enamide followed by elimination of HI to afford **2a** (eq 2, Scheme 9).

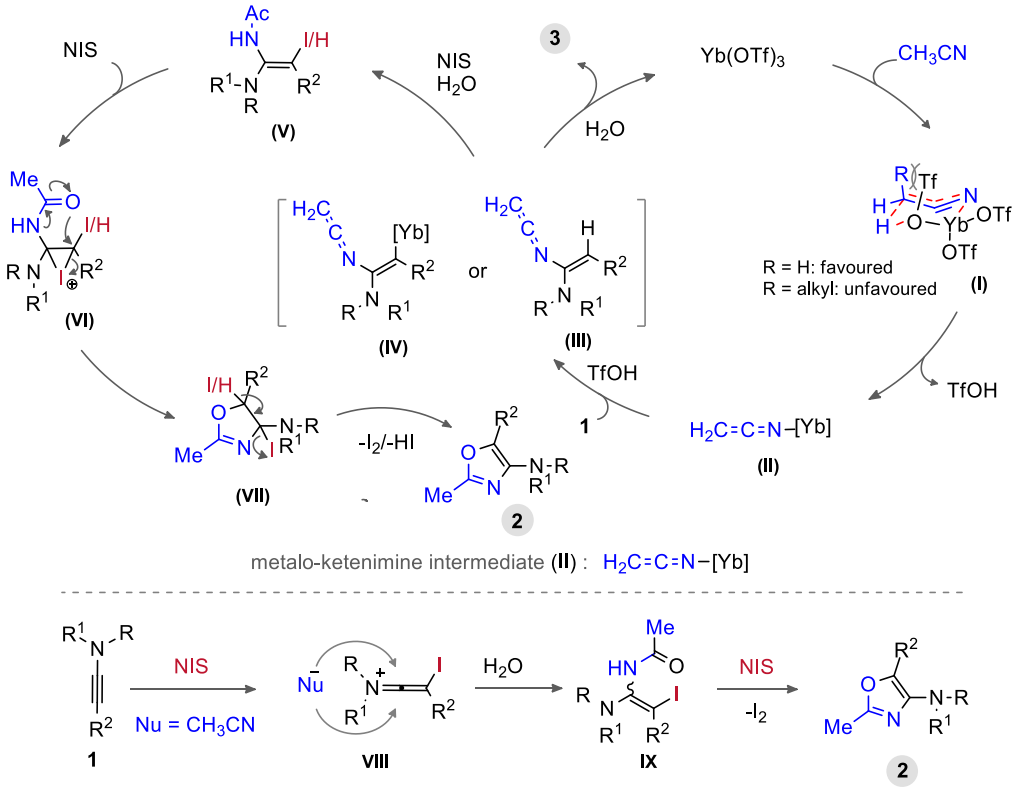
Scheme 9: Control Experiments



Although the mechanistic details are yet to be established, a plausible mechanism is displayed in Scheme 10. The transient metalo-ketenininium intermediate **II** is in-situ generated from acetonitrile with $Yb(OTf)_3$ possibly involving through Int-**I** along with the release of TfOH.[13] The direct attack of metalo-ketenininium species-**II** to ynamide (**1**) results Int-**IV**; alternatively, TfOH mediated protonation of ynamide forms the keteniminum species in-situ, which rapidly reacts with **II** to generate Int-**III** (*anti* to the substituent of the alkyne terminus and *syn* to the β-H). Next, the hydration of Int-**III** produces hydroamidation product (**3**) with *syn*-selectivity, justifying the participation of the Int-**III** in this transformation.[14] In the presence of NIS and

H_2O, Int-**IV** undergoes Yb-iodo exchange/protodemetalation and hydration to give Int-**V**.[15] Simultaneously, activation of the olefin-moiety in the ketene-aminal **V** with NIS produces **VI**. Finally, S_N2-type 5-*endo*-trig cyclization of the amide-oxygen of the N-acetyl group with the β-position of enamide followed by elimination of I_2/HI to produce highly substituted oxazole **2**, validating the requirements of 2.0 equivalents of NIS for reaction productivity. While the reaction of ynamide with NIS initially forms an active β-iodo-keteneiminium intermediate **VIII**, which subsequently undergoes the nitrile attack followed by hydration to form Int-**IX** (Scheme 10). Finally, NIS promoted activation of the olefin-moiety of **IX** followed by the intramolecular cyclization and elimination of I_2 affords **2** albeit in poor yield (entry 7, Table 1). These results reveal that $Yb(OTf)_3$ facilitates enhancing the reaction outcome.

Scheme 10: Plausible Mechanism



Conclusion

In summary, we reveal a convenient and reliable approach for the synthesis of highly peripheral decorated 4-amino-2,5-disubstituted oxazoles from ynamides in the presence of $Yb(OTf)_3$, NIS, and H_2O in CH_3CN at rt. Two and three oxazole skeletons on the arene periphery are erected by building the molecular complexity. Regio and stereoselective hydroamidation and iodo-imidation of ynamides reliably provides highly substituted ketene aminals. The robustness of the catalytic conditions is tested for gram scale synthesis. The H_2O^{18} labelling experiments and sequential reaction studies shed light on the underlying plausible mechanistic cycle that is involved.

Experimental Section

General Information

All the reactions were performed in an oven-dried reaction vials. Commercial grade solvents were distilled prior to use. Column chromatography was performed using silica gel (100–200 Mesh) and neutral alumina eluting with hexanes and ethyl acetate mixture. Thin layer chromatography (TLC) was performed on silica gel GF254 plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber.

Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR and ^{19}F NMR) were recorded on a 400 MHz (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) spectrometer and 500 MHz (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) spectrometer having solvent resonance as internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s = broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet), coupling constants *J*, in (Hz). IR spectra were recorded

on FT/IR spectrometer and are reported in cm^{-1}. High resolution mass spectra (HRMS) were obtained by using TOF analyzer in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. X–ray data was collected at 298K on a Bruker D8 Quest CCD diffractometer using Mo-Kα radiation (0.71073 Å).

Materials: Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Acetone, dichloromethane (CH_2Cl_2), toluene, acetonitrile, ethyl acetate and hexane were distilled over CaH_2. THF was freshly distilled over sodium/benzophenone ketyl under dry nitrogen. $Yb(OTf)_3$, CuI, K_3PO_4, $PdCl_2(PPh_3)_2$, $CuSO_4 \cdot 5H_2O$, trimethylsilane, 1,10–phenanthroline, and aryl iodides were purchased and used as received.

Following the known literature procedure,[16,17,18] compounds **1a–1c**, **1e**, **1f**, **1h**, **1i**, **1k**, **1m–1t**, **1v–1z** and **1ab** are prepared. The analytical and experimental data are exactly matching with reported values.

General Procedure for the Synthesis of Ynamide 1 (GP–1):[16,17,18] Mixture of sulfonamide (1.0 mmol), $CuSO_4 \cdot 5H_2O$ (0.10 mmol, 25 mg), 1,10-phenanthroline (0.20 mmol, 36 mg) and K_3PO_4 (2.0 mmol, 425 mg) in dry toluene (5.0 mL) was taken in a Schlenk tube. Subsequently 1-bromo-2-arylacetylene was introduced and the resulting mixture was heated up to 80 ^oC under the nitrogen atmosphere for 6–8 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature and diluted with dichloromethane (10 mL). The crude mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to provide **1**.

N-(Benzo[d][1,3]dioxol-5-ylethynyl)-N-benzyl-4-methylbenzenesulfonamide (1d): Following the general procedure GP−1, compound **1d** (316 mg) was obtained in 78% yield as yellow solid; mp = 120−122 °C; R_f = 0.64 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 2H), 7.36−7.30 (m, 7H), 6.78 (dd, J = 8.4, 1.6 Hz, 1H), 6.72−6.65 (m, 2H), 5.93 (s, 2H), 4.56 (s, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 147.6, 147.2, 144.6, 134.6, 134.4, 129.6, 128.8, 128.4, 128.2, 127.7, 126.1, 115.8, 111.6, 108.3, 101.2, 80.9, 71.0, 55.6, 21.6; IR (Neat)ν_{max} 3034, 2899, 2237, 1598, 1493, 1446, 1364, 1249 cm^{-1}; HRMS (ESI) for $C_{23}H_{19}NNaO_4S$ $(M+Na)^+$: calcd 428.0932, found 428.0931

N-benzyl-4-methyl-N-((3-(trifluoromethyl)phenyl)ethynyl)benzenesulfonamide (1g): Following the general procedure GP−1, compound **1g** (279 mg) was obtained in 65% yield as pale brown semi solid; R_f = 0.45 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 8.4 Hz, 2H), 7.50−7.45 (m, 1H), 7.43 (br s, 1H), 7.40−7.32 (m, 9H), 4.60 (s, 2H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.9, 134.6, 134.2, 133.9, 129.9, 128.9, 128.7, 128.6, 128.5, 128.2 (q, J = 242 Hz 1C), 127.8, 127.6 (q, J = 15 Hz, 1C), 124.1 (q, J = 15 Hz, 1C), 123.8, 84.3, 70.5, 55.6, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.7; IR (Neat)ν_{max} 3034, 2936, 2238, 1702, 1597, 1494, 1365, 1330 cm^{-1}; HRMS (ESI) for $C_{23}H_{19}F_3NO_2S$ $(M+H)^+$: calcd 430.1089, found 430.1089.

N-Benzyl-4-methyl-N-(phenanthren-9-ylethynyl)benzenesulfonamide (1j): Following the general procedure GP−1, compound **1j** (323 mg) was obtained in 70% yield as pale yellow semi solid; R_f = 0.52 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (t, J = 9.2 Hz, 2H), 7.92 (d, J = 8.4 Hz, 3H), 7.83−7.75 (m, 2H), 7.68−7.50 (m, 4H), 7.48−7.37 (m, 5H), 7.35 (d, J = 8.0 Hz, 2H), 4.72 (s, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ

144.9, 134.7, 134.5, 131.2, 131.0, 130.5, 130.0, 129.9, 129.1, 128.7, 128.5, 128.3, 127.9, 127.2, 126.9, 122.64, 122.59, 119.3, 86.8, 70.3, 55.7, 21.7; IR (Neat)ν_{max} 3064, 2925, 2231, 1596, 1493, 1365 cm^{-1}; HRMS (ESI) for $C_{30}H_{24}NO_2S$ $(M+H)^+$: calcd 462.1528, found 462.1528.

4-Fluoro-N-methyl-N-(phenylethynyl)benzenesulfonamide (1l): Following the general procedure GP−1, compound **1l** (249 mg) was obtained in 86% yield as yellow solid; mp = 93−95 °C; R_f = 0.72 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08−7.95 (m, 2H), 7.43−7.36 (m, 2H), 7.35−7.25 (m, 5H), 3.19 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8 (d, J = 258 Hz, 1C), 132.1, 131.4, 130.5 (d, J = 9.1 Hz, 1C), 128.3, 128.0, 122.3, 116.5 (d, J = 23.2 Hz, 1C), 83.4, 69.2, 39.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.1; IR (Neat)ν_{max} 3106, 3075, 2936, 2234, 1696, 1593, 1495, 1454 cm^{-1}; HRMS (ESI) for $C_{15}H_{12}FNNaO_2S$ $(M+Na)^+$: calcd 312.0470, found 312.0470.

N-((3-Methoxyphenyl)ethynyl)-N,4-dimethylbenzenesulfonamide (1u): Following the general procedure GP−1, compound **1u** (282 mg) was obtained in 72% yield as yellow semi solid; R_f = 0.67 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H), 6.97−6.93 (m, 1H), 6.91−6.88 (m, 1H), 6.86−6.82 (m, 1H), 3.79 (s, 3H), 3.15 (s, 3H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 144.8, 133.1, 129.8, 129.3, 127.8, 123.8, 123.6, 116.2, 114.2, 83.7, 68.9, 55.2, 39.2, 21.6; IR (Neat)ν_{max} 2939, 2838, 2238, 1699, 1599, 1490, 1460, 1364 cm^{-1}; HRMS (ESI) for $C_{17}H_{18}NO_3S$ $(M+H)^+$: calcd 316.1007, found 316.1007.

N-Benzyl-N-((3,4-dichlorophenyl)ethynyl)-4-methylbenzenesulfonamide (1aa): Following the general procedure GP−1, compound **1aa** (357 mg) was obtained in 83% yield as yellow solid; mp = 117−119 °C; R_f = 0.75 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz,

$CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 2H), 7.37–7.27 (m, 9H), 7.03 (dd, J = 8.4, 2.0 Hz, 1H), 4.58 (s, 2H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.9, 134.5, 134.1, 132.4, 132.3, 131.7, 130.14, 130.02, 129.8, 128.8, 128.6, 128.5, 127.6, 122.8, 84.5, 69.6, 55.5, 21.6; IR (Neat)ν_{max} 3061, 3034, 2924, 2868, 2247, 1925, 1593, 1451 cm^{-1}; HRMS (ESI) for $C_{22}H_{17}Cl_2NNaO_2S$ $(M+Na)^+$: calcd 452.0255, found 452.0256.

General Procedure for the Preparation of 1a′ and 1a′′ (GP–1A):[18f] A solution of bis(bromoethynyl)benzene (1.0 mmol), sulfonamide (2.0 mmol), $CuSO_4 \cdot 5H_2O$ (0.2 mmol, 50 mg), 1,10-phenanthroline (0.4 mmol, 72 mg) and K_3PO_4 (4.0 mmol, 849 mg) in dry toluene (5.0 mL) was stirred independently in a Schlenk tube at 80 ^oC for overnight under the nitrogen atmosphere. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature and diluted with dichloromethane (10 mL). The reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude residue was purified by using column chromatography on silica gel to provide arene tethered bis ynamide (1a' and 1a") in quantitative yields.

N,N'-(1,3-phenylenebis(ethyne-2,1-diyl))bis(N-benzyl-4-methylbenzenesulfonamide) (1a′): Following the general procedure GP–1A, compound **1a′** (574 mg) was obtained in 89% yield as yellow semi solid; R_f = 0.43 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.0 Hz, 4H), 7.39–7.32 (m, 14H), 7.17–7.08 (m, 4H), 4.60 (s, 4H), 2.47 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.7, 134.5, 134.3, 133.3, 130.0, 129.7, 128.8, 128.5, 128.3, 128.1, 127.6, 122.9, 83.1, 70.7, 55.6, 21.6; IR (KBr)ν_{max} 3065, 3034, 2925, 2362, 2236, 1596, 1495, 1302 cm^{-1}; HRMS (ESI) for $C_{38}H_{32}N_2NaO_4S_2$ $(M+Na)^+$: calcd 667.1701, found 667.1706.

N,N'-(1,4-phenylenebis(ethyne-2,1-diyl))bis(N-benzyl-4-methylbenzenesulfonamide) (1a′′): Following the general procedure GP−1A, compound **1a′′** (516 mg) was obtained in 80% yield as yellow solid; mp = 160−162 °C; R_f = 0.45 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 4H), 7.38−7.31 (m, 14H), 7.10 (s, 4H), 4.58 (s, 4H), 2.45 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.7, 134.5, 134.2, 130.7, 129.7, 128.8, 128.5, 128.3, 127.7, 121.9, 84.2, 71.3, 55.6, 21.6; IR (Neat)ν_{max} 3032, 2977, 2926, 2225, 1593, 1493, 1452, 1172 cm^{-1}; HRMS (ESI) for $C_{38}H_{32}N_2NaO_4S_2$ $(M+Na)^+$: calcd 667.1701, found 667.1700.

N,N',N''-(benzene-1,3,5-triyltris(ethyne-2,1-diyl))tris(N-benzyl-4-methylbenzene Sulfonamide) (1a′′′):[18f] A solution of tris(bromoethynyl)benzene (1.0 mmol), sulfonamide (3.0 mmol), $CuSO_4 \cdot 5H_2O$ (0.3 mmol, 75 mg), 1,10-phenanthroline (0.6 mmol, 108 mg) and K_3PO_4 (6.0 mmol, 1.27 g) in dry toluene (5.0 mL) was stirred in a Schlenk tube at 80 ^oC for overnight under the nitrogen atmosphere. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature and diluted with dichloromethane (10 mL). The reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude residue was purified by using column chromatography on silica gel to provide **1a′′′** in 94% yield (872 mg) as yellow solid; mp = 156−158 °C; R_f = 0.26 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 6.0 Hz, 6H), 7.36−7.28 (m, 21H), 6.93 (s, 3H), 4.56 (s, 6H), 2.45 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.8, 134.5, 134.2, 132.0, 129.8, 128.7, 128.5, 128.4, 127.6, 123.1, 83.6, 70.1, 55.5, 21.6; IR (Neat)ν_{max} 3065, 3034, 2926, 2235, 1583, 1495, 1454, 1366 cm^{-1}; HRMS (ESI) for $C_{54}H_{45}N_3NaO_6S_3$ $(M+Na)^+$: calcd 950.2368, found 950.2368.

General Procedure for the Synthesis of 2,4,5-Trisubstituted Oxazoles (2) (GP−2): A mixture of ynamide **1** (0.5 mmol), N-iodosuccinimide (NIS; 1.1 mmol, 247 mg), $Yb(OTf)_3$ (0.1 mmol, 62 mg) and H_2O (1.0 mmol, 18 μL) in freshly distilled acetonitrile (3.0 mL) was stirred at room temperature for 8−12 h. The progress of the reaction was monitered by TLC. After completion, the reaction mixture was quenched with saturated aqueous sodium thiosulfate. The organic layer was separated and the aqeous layer was extracted with ethylacetate (2 × 15 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under the reduced pressure. The crude mixture was purified by silica gel column chromatography to give the product **2**.

4-(N-Benzyl-N-tosyl)-2-methyl-5-phenyloxazole (2a): Following the general procedure GP−2, compound **2a** (184 mg) was obtained in 88% yield as colorless solid; mp = 196−198 °C; R_f = 0.48 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 7.2 Hz, 2H), 7.39−7.28 (m, 5H), 7.21 (dd, J = 5.6, 2.0 Hz, 2H), 7.12 (dd, J = 5.2, 1.6 Hz, 3H), 4.60 (s, 2H), 2.48 (s, 3H), 2.44 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.2, 147.4, 144.0, 135.4, 134.7, 130.9, 129.5, 129.0, 128.4, 128.2, 128.1, 127.8, 126.8, 125.3, 53.7, 21.6, 14.2; IR (Neat)ν_{max} 3063, 2926, 2361, 1594, 1446, 1347, 1210 cm^{-1}; HRMS (ESI) for $C_{24}H_{23}N_2O_3S$ $(M+H)^+$: calcd 419.1429, found 419.1429.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(4-methoxyphenyl)oxazole (2b): Following the general procedure GP−2, compound **2b** (170 mg) was obtained in 76% yield as pale yellow solid; mp = 189−191 °C; R_f = 0.48 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.18 (dd, J = 5.6, 2.0 Hz, 2H) 7.13−7.07 (m, 3H), 6.85 (d, J = 8.8 Hz, 2H)) 4.55 (s, 2H), 3.81 (s, 3H), 2.45 (s, 3H),

2.39 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.8, 157.5, 147.6, 144.0, 135.5, 135.0, 129.60, 129.57, 129.1, 128.5, 128.1, 127.8, 126.9, 119.7, 113.8, 55.3, 53.8, 21.7, 14.2; IR (Neat)ν_{max} 2931, 2838, 1589, 1642, 1243, 1150, 1035 cm^{-1}; HRMS (ESI) for $C_{25}H_{25}N_2O_4S$ $(M+H)^+$: calcd 449.1535, found 449.1537.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(3,4-dimethylphenyl)oxazole (2c): Following the general procedure GP–2, compound **2c** (183 mg) was obtained in 82% yield as pale yellow solid; mp = 144–147 °C; R_f = 0.42 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 2H), 7.44 (dd, J = 8.0, 1.2 Hz, 1H), 7.37 (s, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.24–7.18 (m, 2H), 7.16–7.10 (m, 3H), 7.07 (d, J = 8.0 Hz, 1H), 4.58 (s, 2H); 2.45 (s, 3H), 2.41 (s, 3H), 2.24 (s, 3H), 2.22 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 157.8, 147.6, 143.8, 137.2, 136.3, 135.63, 135.60, 135.0, 130.2, 129.5, 129.1, 128.4, 128.1, 127.7, 126.3, 124.4, 122.8, 53.6, 21.6, 19.7, 19.6, 14.2; IR (Neat)ν_{max} 2920, 1589, 1495, 1446, 1265, 1090, 821 cm^{-1}; HRMS (ESI) for $C_{26}H_{27}N_2O_3S$ $(M+H)^+$: calcd 447.1742, found 447.1745.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(benzo[d][1,3]dioxol-5-yl)oxazole (2d): Following the general procedure GP–2, compound **2d** (180 mg) was obtained in 78% yield as pale yellow solid; mp = 203–205 °C; R_f = 0.52 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.22 (dd, J = 8.0, 1.6 Hz, 1H), 7.20–7.16 (m, 2H), 7.15–7.10 (m, 4H), 6.75 (d, J = 8.4 Hz, 1H), 5.95 (s, 2H), 4.55 (s, 2H), 2.45 (s, 3H), 2.39 (s, 3H), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 157.6, 147.8, 147.5, 147.4, 144.0, 135.5, 134.9, 129.9, 129.6, 129.2, 128.5, 128.2, 127.9, 121.0, 119.9, 108.3, 106.0, 101.2, 53.8, 21.7, 14.2; IR (Neat)ν_{max} 3068, 2904, 2361, 1594, 1490, 1238, 1046, 882 cm^{-1}; HRMS (ESI) for $C_{25}H_{22}N_2NaO_5S$ $(M+Na)^+$: calcd 485.1147, found 485.1147.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(4-acetylphenyl)oxazole (2e): Following the general procedure GP–2, compound **2e** (127 mg) was obtained in 55% yield as pale yellow solid; mp = 182–184 °C; R_f = 0.35 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92–7.87 (m, 2H), 7.84–7.76 (m, 4H), 7.35 (d, J = 8.0 Hz, 2H), 7.19 (dd, J = 5.6, 2.4 Hz, 2H), 7.12–7.07 (m, 3H), 4.57 (br s, 2H), 2.59 (s, 3H), 2.45 (s, 3H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 197.5, 159.3, 146.4, 144.3, 136.3, 135.2, 134.7, 133.0, 131.0, 129.7, 129.1, 128.5, 128.4, 128.3, 128.0, 125.1, 53.8, 26.6, 21.7, 14.3; IR (Neat)ν_{max} 3024, 1682, 1605, 1578, 1358, 1260, 1156 cm^{-1}; HRMS (ESI) for $C_{26}H_{24}N_2NaO_4S$ $(M+Na)^+$: calcd 483.1354, found 483.1349.

4-(N-Methyl-N-tosyl)-2-methyl-5-(3-Fluorophenyl)-oxazole (2f): Following the general procedure GP–2, compound **2f** (114 mg) was obtained in 65% yield as colorless solid; mp = 178–180 °C; R_f = 0.42 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78–7.72 (m, 3H), 7.62–7.57 (m, 1H), 7.44–7.37 (m, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.08–7.0 (m, 1H), 3.10 (s, 3H), 2.45 (s, 3H), 2.44 (s, 3H), ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.9 (d, J = 246 Hz, 1C), 158.8, 144.4 (d, J = 3.0 Hz, 1C), 144.1, 134.2 (d, J = 8.0 Hz, 1C), 130.4 (d, J = 9.1 Hz, 1C), 129.6, 129.1 (d, J = 9.1 Hz, 1C), 128.6, 120.89, 120.86, 115.5 (d, J = 21.2 Hz, 1C), 112.1 (d, J = 24.2 Hz, 1C), 37.1, 21.6, 14.3; ^{19}F NMR (471 MHz, $CDCl_3$) δ –112.1; IR (Neat)ν_{max} 1578, 1484, 1347, 1265, 1024, 882 cm^{-1}; HRMS (ESI) for $C_{18}H_{18}FN_2O_3S$ $(M+H)^+$: calcd 361.1022, found 361.1020.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(3-(trifluoromethyl)phenyl)oxazole (2g): Following the general procedure GP–2, compound **2g** (182 mg) was obtained in 75% yield as colorless solid; mp = 152–155 °C; R_f = 0.46 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz,

$CDCl_3$): δ 7.93 (d, J = 8.0 Hz, 1H), 7.85 (s, 1H), 7.79 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.17 (dd, J = 5.6, 2.0 Hz, 2H), 7.12 – 6.07 (m, 3H), 4.57 (s, 2H), 2.46 (s, 3H), 2.45 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.0, 146.1, 144.2, 135.3, 134.6, 132.1, 130.7 (q, J = 33.3 Hz, 1C), 129.7, 129.2, 128.8, 128.5, 128.4, 128.3, 128.0, 127.6, 126.5 (q, J = 253 Hz, 1C), 124.9 (q, J = 4.0 Hz, 1C), 122.0 (q, J = 3.0 Hz, 1C), 53.7, 21.7, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8; IR (Neat)ν_{max} 3073, 1638, 1583, 1452, 1254, 1167, 904 cm^{-1}; HRMS (ESI) for $C_{25}H_{22}F_3N_2O_3S$ $(M+H)^+$: calcd 487.1303, found 487.1302.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(thiophen-2-yl)oxazole (2h): Following the general procedure GP−2, compound **2h** (132 mg) was obtained in 62% yield as brown color solid; mp = 152−155 °C; R_f = 0.51 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 2H), 7.42 (dd, J = 3.6, 1.2 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.28 (dd, J = 5.2, 1.2 Hz, 1H), 7.21 (dd, J = 6.0, 2.0 Hz, 2H), 7.14−7.09 (m, 3H), 7.0 (dd, J = 5.2, 4.0 Hz, 1H), 4.54 (s, 2H), 2.46 (s, 3H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.9, 144.3, 144.1, 135.4, 134.8, 129.9, 129.7, 129.0, 128.4, 128.1, 127.8, 127.2, 126.3, 125.9, 53.6, 21.7, 14.2; IR (Neat)ν_{max} 3073, 1583, 1495, 1435, 1353, 1172, 1084, 1052 cm^{-1}; HRMS (ESI) for $C_{22}H_{20}N_2NaO_3S_2$ $(M+Na)^+$: calcd 447.0813, found 447.0818.

4-(N-Methyl-N-tosyl)-2-methyl-5-(naphthalen-1-yl)oxazole (2i): Following the general procedure GP−2, compound **2i** (108 mg) was obtained in 55% yield as light brown solid; mp = 195−197 °C; R_f = 0.50 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94−7.87 (m, 3H), 7.79 (d, J = 7.2 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.55−7.49 (m, 3H), 7.14 (d, J = 8.0 Hz, 2H), 3.10 (s, 3H); 2.54 (s, 3H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ

159.4, 145.4, 143.6, 135.5, 134.8, 133.6, 131.1, 130.1, 129.2, 128.6, 128.4, 128.2, 126.7, 126.1, 125.23, 125.19, 124.2, 37.3, 21.5, 14.4; IR (Neat)ν_{max} 3046, 1715, 1589, 1506, 1364, 1156, 1084, cm^{-1}; HRMS (ESI) for $C_{22}H_{20}N_2NaO_3S$ $(M+Na)^+$: calcd 415.1092, found 415.1094.

4-(N-Benzyl-N-tosyl)-2-methyl-5-(phenanthren-9-yl)oxazole (2j): Following the general procedure GP–2, compound **2j** (130 mg) was obtained in 50% yield as pale brown solid; mp = 200–202 °C; R_f = 0.45 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, J = 8.0 Hz, 2H), 7.81–7.67 (m, 4H), 7.65–7.58 (m, 2H), 7.48 (s, 1H), 7.44–7.34 (m, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.04 (br t, J = 7.2 Hz, 3H), 6.98–6.92 (m, 2H), 4.60 (s, 2H), 2.54 (s, 3H), 2.31 (s, 3H), $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.5, 147.9, 143.7, 135.8, 135.2, 133.5, 130.88, 130.85, 130.6, 130.2, 130.1, 129.5, 129.4, 129.3, 128.3, 128.2, 127.8, 127.7, 126.8, 126.6, 126.5, 126.2, 122.7, 122.5, 122.4, 53.4, 21.6, 14.6; IR (Neat)ν_{max} 3073, 1589, 1446, 1353, 1161, 1046, 816 cm^{-1}; HRMS (ESI) for $C_{32}H_{27}N_2O_3S$ $(M+H)^+$: calcd 519.1742, found 519.1748.

N-Benzyl-N-(2-methyl-5-phenyloxazol-4-yl)benzenesulfonamide (2k): Following the general procedure GP–2, compound **2k** (182 mg) was obtained in 90% yield as colorless solid; mp = 189–190 °C; R_f = 0.51 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 2H), 7.72 (dd, J = 7.2, 1.6 Hz, 2H), 7.69–7.63 (m, 1H), 7.61–7.54 (m, 2H), 7.36–7.28 (m, 3H), 7.20 (dd, J = 6.0, 2.0 Hz, 2H), 7.15–7.08 (m, 3H), 4.61 (s, 2H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.2, 147.4, 138.4, 134.6, 133.1, 130.8, 129.1, 128.9, 128.5 128.4, 128.2, 128.1, 127.8, 126.7, 125.3, 53.8, 14.2; IR (Neat)ν_{max} 2926, 2853, 1583, 1495, 1448, 1350, 1268, 1159 cm^{-1}; HRMS (ESI) for $C_{23}H_{20}N_2NaO_3S$ $(M+Na)^+$: calcd 427.1092, found 427.1092.

4-Fluoro-N-methyl-N-(2-methyl-5-phenyloxazol-4-yl)benzenesulfonamide (2l): Following the general procedure GP–2, compound **2l** (83 mg) was obtained in 48% yield as colorless thick liquid; R_f = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95–7.89 (m, 4H), 7.44 (t, J = 7.2 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.24–7.17 (m, 2H), 3.11 (s, 3H), 2.44 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.4 (d, J = 257 Hz, 1C), 158.4, 145.5, 133.5, 133.4, 132.9, 131.3 (d, J = 9.1 Hz, 1C), 128.7, 126.9, 125.0, 116.1 (d, J = 22.2 Hz, 1C), 27.2, 14.2; ^{19}F NMR (376.4 MHz) δ -104.7; IR (Neat)ν_{max} 3060, 2926, 2848, 1629, 1588, 1495, 1366, 1159 cm^{-1}; HRMS (ESI) for $C_{17}H_{15}FN_2NaO_3S$ $(M+Na)^+$: calcd 369.0685, found 369.0687.

N-Methyl-N-(2-methyl-5-phenyloxazol-4-yl)-4-(trifluoromethyl)benzenesulfonamide (2m): Following the general procedure GP–2, compound **2m** (109 mg) was obtained in 55% as pale yellow solid; mp = 180–182 °C; R_f = 0.50 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0, 2H), 7.94–7.88 (m, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.49–7.42 (m, 2H), 7.41–7.33 (m, 1H), 3.15 (s, 3H), 2.46 (s, 3H), ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6, 145.8, 141.2, 134.7 (q, J = 33 Hz, 1C), 132.7, 126.8 (q, J = 263 Hz, 1C), 129.1, 128.9, 128.8, 126.9, 126.2–125.9 (m, 1C), 125.1, 124.7, 122.0, 37.4, 14.3; ^{19}F NMR (471 MHz) δ -63.1; IR (Neat)ν_{max} 2920, 1593, 1448, 1365, 1319, 1128, 1061, 622 cm^{-1}; HRMS (ESI) for $C_{18}H_{16}F_3N_2O_3S$ $(M+H)^+$: calcd 397.0834, found 397.0839.

4-Bromo-N-methyl-N-(2-methyl-5-phenyloxazol-4-yl)benzenesulfonamide (2n): Following the general procedure GP–2, compound **2n** (166 mg) was obtained in 82% as pale brown solid; mp = 172–174 °C; R_f = 0.35 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–7.89 (m, 2H), 7.78–7.74 (m, 2H), 7.68–7.64 (m, 2H), 7.47–7.41 (m, 2H), 7.38–7.33 (m, 1H), 3.11 (s, 3H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 145.7,

136.6, 132.9, 132.2, 130.1, 128.8, 128.4, 126.9, 125.1, 37.3, 14.3; IR (Neat)ν_{max} 3090, 1634, 1572, 1386, 1267, 1071, 859 cm^{-1}; HRMS (ESI) for $C_{17}H_{16}BrN_2O_3S$ $(M+H)^+$: calcd 407.0065, found 407.0068.

3-(2-Methyl-5-phenyloxazol-4-yl)oxazolidin-2-one (2o): Following the general procedure GP–2, compound **2o** (79 mg) was obtained in 65% yield as yellow color gummy liquid; R_f = 0.41 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64–7.59 (m, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.36–7.32 (m, 1H), 4.59–4.51 (m, 2H), 4.04–3.98 (m, 2H), 2.50 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.1, 156.4, 143.5, 129.7, 128.8, 128.5, 127.1, 125.0, 62.8, 46.0, 14.2; IR (Neat)ν_{max} 2921, 1758, 1634, 1583, 1418, 1257, 1211 cm^{-1}; HRMS (ESI) for $C_{13}H_{12}N_2NaO_3$ $(M+Na)^+$: calcd 267.0746, found 267.0746.

4-(N-Benzyl-N-mesyl)-2-methyl-5-phenyloxazole (2p): Following the general procedure GP–2, compound **2p** (128 mg) was obtained in 75% yield as yellow solid; mp = 190–192 °C; R_f = 0.50 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68–7.64 (m, 2H), 7.33–7.27 (m, 3H), 7.24 (dd, J = 4.8, 2.0 Hz, 2H), 7.16–7.13 (m, 3H), 4.76 (s, 2H), 3.15 (s, 3H), 2.50 (s, 3H), $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.7, 147.2, 134.7, 131.1, 129.3, 128.7, 128.31, 128.26, 128.1, 126.6, 125.3, 54.6, 38.5, 14.3; IR (Neat)ν_{max} 2910, 1329, 1593, 1494, 1448, 1340, 1267, 1169 cm^{-1}; HRMS (ESI) for $C_{18}H_{18}N_2NaO_3S$ $(M+Na)^+$: calcd 365.0936, found 365.0930.

N-Methyl-N-(2-methyl-5-phenyloxazol-4-yl)butane-1-sulfonamide (2q): Following the general procedure GP–2, compound **2q** (52 mg) was obtained in 27% yield as colorless gummy liquid; R_f = 0.64 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91–7.87 (m, 2H), 7.44–7.39 (m, 2H), 7.36–7.30 (m, 1H), 3.31–3.27 (m, 2H), 3.26 (s, 3H), 2.49

(s, 3H), 1.94–1.85 (m, 2H), 1.53–1.44 (m, 2H), 0.96 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.6, 145.3, 133.0, 128.7, 126.9, 125.0, 50.2, 37.8, 24.7, 21.7, 14.3, 13.6; IR (Neat)ν_{max} 3060, 2962, 2931, 2874, 2853, 1588, 1443, 1263 cm^{-1}; HRMS (ESI) for $C_{15}H_{20}N_2NaO_3S$ $(M+Na)^+$: calcd 331.1092, found 331.1092.

General Procedure for the Synthesis of Bis–Oxazole 2u and 2v (GP–3): A mixture of arene tethered bis-ynamide **1a′/1a′′** (0.3 mmol), NIS (1.32 mmol, 297 mg), $Yb(OTf)_3$ (0.12 mmol, 74 mg) and H_2O (1.2 mmol, 22 µL) in freshly distilled acetonitrile (3.0 mL) was stirred at room temperature for 18 h. The progress of the reaction was monitered by TLC. Upon complete consumption of precursor, the reaction mixture was quenched with saturated sodium thiosulfate. The organic layer was separated and the aqeous layer was extracted with ethylacetate (2 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under the reduced pressure. The crude mixture was purified by silica gel column chromatography to give bis-oxazole **2u/2v**.

N,N'-(5,5'-(1,3-Phenylene)bis(2-methyloxazole-5,4-diyl))bis(N-benzyl-4-methylbenzene sulfonamide) (2u): Following the general procedure GP–3, compound **2u** (102 mg) was obtained in 45% yield as colorless thick liquid; R_f = 0.48 (1.5:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (br s, 1H), 7.81 (d, J = 8.4 Hz, 4H), 7.72 (dd, J = 8.0, 2.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 4H), 7.30–7.24 (m, 2H), 7.21–7.16 (m, 4H), 7.09–7.04 (m, 5H), 4.58 (br s, 4H), 2.47 (s, 6H), 2.46 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 158.4, 146.9, 144.0, 135.4, 134.7, 131.3, 129.6, 129.0, 128.4, 128.3, 128.1, 127.9, 126.7, 125.3, 121.8, 53.7, 21.6, 14.2; IR (Neat) ν_{max} 2921, 1712, 1629, 1593, 1490, 1350, 1263, 1159 cm^{-1}; HRMS (ESI) for $C_{42}H_{39}N_4O_6S_2$ $(M+H)^+$: calcd 759.2311, found 759.2313.

N,N'-(5,5'-(1,4-Phenylene)bis(2-methyloxazole-5,4-diyl))bis(N-benzyl-4-methylbenzene sulfonamide) (2v): Following the general procedure GP–3, compound **2v** (114 mg) was obtained in 50% yield as light brown solid; mp = 222–224 ^{o}C; R_f = 0.30 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 8.4 Hz, 4H), 7.64 (s, 4H), 7.35 (d, J = 8.0 Hz, 4H), 7.17 (dd, J = 6.4, 2.0 Hz, 4H), 7.12–6.07 (m, 6H), 4.57 (s, 4H), 2.46 (s, 6H), 2.42 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 158.5, 147.0, 144.1, 135.5, 134.7, 131.5, 129.6, 129.1, 128.5, 128.2, 128.0, 126.6, 125.1, 53.8, 21.6, 14.3; IR (Neat) ν_{max} 2910, 2848, 1583, 1350, 1257, 1170 cm^{-1}; HRMS (ESI) for $C_{42}H_{39}N_4O_6S_2$ $(M+H)^+$: calcd 759.2311, found 759.2304.

N,N',N''-(5,5',5''-(Benzene-1,3,5-triyl)tris(2-methyloxazole-5,4-diyl))tris(N-benzyl-4-methyl benzenesulfonamide) (2w): A mixture of **1a‴** (187 mg), N-iodosuccinimide (297 mg), $Yb(OTf)_3$ (74 mg) and H_2O (22 μL) in dry acetonitrile (3.0 mL) was stirred at room temperature for 24 h. The progress of the reaction was monitered by TLC. After completion, the reaction mixture was quenched with saturated sodium thiosulfate. The organic layer was separated and the aqeous layer was extracted with ethylacetate (2 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under the reduced pressure. The crude mixture was purified by silica gel column chromatography to give **2w** (99 mg) in 30% yield as yellow gummy liquid; R_f = 0.33 (1.5:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (s, 3H), 7.81 (d, J = 8.0 Hz, 6H), 7.30 (d, J = 8.0 Hz, 6H), 7.18 (dd, J = 7.5, 1.5 Hz, 6H), 7.02–6.07 (m, 9H), 4.59 (s, 6H), 2.54 (s, 9H), 2.43 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.7, 146.4, 143.9, 135.7, 134.8, 131.7, 129.5, 129.1, 128.5, 128.1, 127.9, 126.8, 121.6, 53.9,

21.6, 14.3; IR (Neat) ν_{max} 2926, 1707, 1624, 1578, 1490, 1454, 1350, 1263, cm^{-1}; HRMS (ESI) for $C_{60}H_{58}N_7O_9S_3$ $(M+NH_4)^+$: calcd 1116.3458, found 1116.3446.

General Procedure for the Hydroamidation of Ynamides with Acetonitrile (GP–4): A mixture of ynamide **1** (0.5 mmol), $Yb(OTf)_3$ (0.1 mmol, 62 mg) and H_2O (1.0 mmol, 18 μL) in freshly distilled acetonitrile (3.0 mL) was stirred at room temperature for 18-20 h. The progress of the reaction was monitered by TLC. After completion, the reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude mixture was purified by neutral alumina column chromatography eluting with 25% EtOAc and hexane mixture to give the desired product **3**.

(*Z*)-N-(1-(N-Benzyl-4-methylphenylsulfonamido)-2-phenylvinyl)acetamide (3a): Following the general procedure GP–4, compound **3a** (147 mg) was obtained in 70% yield as colorless solid; mp = 158–159 °C; R_f = 0.40 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-D_6): δ 8.82 (s, 1H, NH), 7.72 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.22–7.08 (m, 10H), 6.63 (s, 1H), 4.53 (s, 2H), 2.46 (s, 3H), 1.89 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-D_6): δ 169.2, 144.1, 136.7, 135.1, 134.4, 130.1, 130.0, 128.6, 128.3, 128.13, 128.09, 127.5, 127.4, 122.8, 52.0, 23.8, 21.5; IR (KBr) ν_{max} 3275, 3025, 2359, 2338, 1672, 1592, 1448, 1352 cm^{-1}; HRMS (ESI) for $C_{24}H_{24}N_2NaO_3S$ $(M+Na)^+$: calcd 443.1405, found 443.1402.

(*Z*)-N-(1-(N,4-Dimethylphenylsulfonamido)-2-phenylvinyl)acetamide (3b): Following the general procedure GP–4, compound **3b** (126 mg) was obtained in 73% yield as colorless solid; mp = 165–166 °C; R_f = 0.37 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 8.0 Hz, 2H), 7.34 (s, 1H, NH), 7.19–7.11 (m, 7H), 6.59 (s, 1H), 3.10 (s, 3H), 2.35 (s, 3H), 1.95 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 169.3, 144.0, 135.5, 133.2,

129.6, 129.4, 128.3, 128.2, 127.6, 127.5, 122.0, 36.4, 23.7, 21.5; IR (KBr) ν_{max} 3266, 3052, 1688, 1594, 1523, 1342, 1255, 1162 cm^{-1}; HRMS (ESI) for $C_{18}H_{20}N_2NaO_3S$ $(M+Na)^+$: calcd 367.1092, found 367.1097.

(*Z*)-N-(1-(N,4-Dimethylphenylsulfonamido)-2-(2-methoxyphenyl)vinyl)acetamide (3c): Following the general procedure GP–4, compound **3c** (88 mg) was obtained in 47% yield as pale yellow solid; mp = 178–179 ^oC; R_f = 0.26 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, DMSO-D_6): δ 9.55 (s, 1H, NH), 7.65 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.50 (s, 1H), 3.82 (s, 3H), 2.97 (s, 3H), 2.44 (s, 3H), 1.74 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-D_6): δ 169.4, 156.8, 143.6, 136.9, 132.0, 130.1, 129.9, 129.4, 127.9, 127.5, 122.4, 120.8, 114.0, 111.3, 55.8, 37.0, 23.1, 21.5; IR (KBr) ν_{max} 3649, 2986, 2362, 1655, 1523, 1479, 1342, 1293 cm^{-1}; HRMS (ESI) for $C_{19}H_{23}N_2O_4S$ $(M+H)^+$: calcd 375.1379, found 375.1374.

(*Z*)-N-(1-(N,4-Dimethylphenylsulfonamido)-2-(3-methoxyphenyl)vinyl)acetamide (3d): Following the general procedure GP–4, compound **3d** (86 mg) was obtained in 46% yield as colorless solid; mp = 149–150 ^oC; R_f = 0.26 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, DMSO-D_6): δ 9.56 (s, 1H, NH), 7.68 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.19 (s, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.41 (s, 1H), 3.79 (s, 3H), 3.05 (s, 3H), 2.44 (s, 3H), 1.74 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-D_6): δ 169.4, 159.7, 143.7, 136.8. 135.4, 132.1, 130.1, 130.0, 129.9, 127.6, 127.2, 121.3, 119.6, 113.9, 113.2, 55.4, 37.0, 23.1, 21.5; IR (Neat) ν_{max} 3030, 2920, 1682, 1594, 1490, 1347, 1161 cm^{-1}; HRMS (ESI) for $C_{19}H_{22}N_2NaO_4S$ $(M+Na)^+$: calcd 397.1198, found 397.1202.

(*Z*)-N-(1-(N-Benzyl-4-methylphenylsulfonamido)-2-(3-cyanophenyl)vinyl)acetamide (3e):

Following the general procedure GP–4, compound **3e** (167 mg) was obtained in 75% yield as colorless gummy liquid; R_f = 0.52 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-D_6): δ 9.07 (s, 1H, NH), 7.70 (d, J = 6.8 Hz, 2H), 7.49 (d, J = 6.8 Hz, 1H), 7.41–7.32 (m, 3H), 7.26 (br t, J = 7.2 Hz, 1H), 7.22–7.14 (m, 6H), 6.75 (s, 1H), 4.65 (br s, 2H), 2.43 (s, 3H), 1.95 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-D_6): δ 169.5, 144.2, 136.7, 135.8, 134.9, 133.3, 131.1, 130.4, 130.20, 130.16, 129.2, 128.5, 128.4, 128.0, 120.3, 119.0, 111.3, 52.1, 23.9, 21.5; IR (Neat) ν_{max} 3260, 3030, 2926, 2230, 1693, 1589, 1348, 1156 cm^{-1}; HRMS (ESI) for $C_{25}H_{24}N_3O_3S$ $(M+H)^+$: calcd 446.1538, found 446.1539.

(*Z*)-N-(1-(N,4-Dimethylphenylsulfonamido)-2-(3-fluorophenyl)vinyl)acetamide (3f):

Following the general procedure GP–4, compound **3f** (138 mg) was obtained in 76% yield as colorless solid; mp = 179–180 °C; R_f = 0.38 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-D_6): δ 9.54 (s, 1H, NH), 7.67 (d, J = 8.0 Hz, 2H), 7.45–7.38 (m, 3H), 7.28 (d, J = 8.0 Hz, 2H), 7.16–7.08 (m, 1H), 6.53 (s, 1H), 3.06 (s, 3H), 2.55 (s, 3H), 1.78 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-D_6): δ 169.4, 162.7 (d, J = 242 Hz), 143.9, 136.64 (d, J = 8.1 Hz), 136.63, 133.0, 130.7 (d, J = 8.1 Hz), 130.1, 130.0, 127.6, 127.2, 124.9 (d, J = 3.0 Hz), 118.0, 114.54 (d, J = 21.2 Hz), 114.48 (d, J = 23.2 Hz), 36.9, 23.3, 21.5; 19F NMR (376.4 MHz) δ –113.24; IR (KBr) ν_{max} 3304, 2920, 1687, 1583, 1490, 1441, 1326, 1260 cm^{-1}; HRMS (ESI) for $C_{18}H_{19}FN_2NaO_3S$ $(M+Na)^+$: calcd 385.0998, found 385.0998.

(*Z*)-N-(1-(N,4-Dimethylphenylsulfonamido)-2-(4-fluorophenyl)vinyl)acetamide (3g):

Following the general procedure GP–4, compound **3g** (145 mg) was obtained in 80% yield as colorless solid; mp = 168–170 °C; R_f = 0.31 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-D_6): δ 9.51 (s, 1H), 7.66 (d, J = 8.0 Hz, 2H), 7.57–7.49 (m, 2H), 7.41 (d, J =

8.0 Hz, 2H), 7.19 (t, *J* = 8.4 Hz, 2H), 6.47 (s, 1H), 3.04 (s, 3H), 2.43 (s, 3H), 1.74 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-D_6): δ 169.4, 161.8 (d, *J* = 246.4 Hz), 143.7, 136.8, 131.7, 130.6 (d, *J* = 3.0 Hz), 130.4 (d, *J* = 8.1 Hz), 129.9, 127.6, 118.6, 115.8 (d, *J* = 21.2 Hz), 36.9, 23.2, 21.5; ^{19}F NMR (376.4 MHz) δ -114.04; IR (KBr) ν_{max} 3331, 1693, 1600, 1512, 1342, 1227, 1156, 1084 cm^{-1}; HRMS (ESI) for $C_{18}H_{19}FN_2NaO_3S$ $(M+Na)^+$: calcd 385.0998, found 385.1005.

(*Z*)-N-(1-(N-Benzyl-4-methylphenylsulfonamido)-2-(thiophen-3-yl)vinyl)acetamide (3h):

Following the general procedure GP–4, compound **3h** (171 mg) was obtained in 80% yield as colorless solid; mp = 137–138 °C; R_f = 0.46 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-D_6): δ 8.7 (s, 1H, NH), 7.76 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.31–7.21 (m, 4H), 7.20–7.13 (m, 3H), 7.08 (d, *J* = 4.8 Hz, 1H), 6.76 (s, 1H), 4.55 (br s, 2H), 2.46 (s, 3H), 1.86 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-D_6): δ 169.0, 144.1, 136.7, 135.6, 135.2, 130.1, 128.7, 128.3, 128.22, 128.17, 128.0, 127.0, 126.2, 125.2, 124.7, 118.7, 51.7, 23.8, 21.5; IR (KBr) ν_{max} 3222, 1737, 1666, 1595, 1458, 1403, 1332, 1167 cm^{-1}; HRMS (ESI) for $C_{22}H_{23}N_2O_3S_2$ $(M+H)^+$: calcd 427.1150, found 427.1157.

(*Z*)-N-(1-(N-Benzyl-4-methylphenylsulfonamido)-2-(naphthalen-1-yl)vinyl)acetamide (3i):

Following the general procedure GP–4, compound **3i** (141 mg) was obtained in 60% yield as colorless semi-solid; R_f = 0.67 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-D_6): δ 9.16 (s, 1H, NH), 7.84 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.63–7.54 (m, 3H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.23–7.15 (m, 3H), 7.03 (d, *J* = 7.2 Hz, 1H), 7.01–6.92 (m, 5H), 4.44 (s, 2H), 2.37 (s, 3H), 1.99 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-D_6): δ 169.5, 143.8, 136.7, 135.2, 133.3, 131.5, 131.4, 129.8, 129.7, 129.6, 128.5, 128.1, 127.9, 127.8, 127.7, 126.1, 126.0, 125.9, 125.4, 124.8, 119.5, 52.4,

23.9, 21.5; IR (Neat) ν_{max} 3057, 2931, 2350, 1687, 1594, 1501, 1452, 1342, 1265 cm^{-1}; HRMS (ESI) for $C_{28}H_{27}N_2O_3S$ $(M+H)^+$: calcd 471.1742, found 471.1743.

General Procedure for the Iodo-Imidation of Ynamide (GP−5): A mixture of ynamide **1** (0.5 mmol), NIS (1.1 mmol, 247 mg) and $Yb(OTf)_3$ (0.1 mmol, 62 mg) in dry dichloromethane (3.0 mL) was stirred at room temperature for 8−9 h. The progress of the reaction was monitered by TLC. After completion, the reaction mixture was quenched with saturated sodium thiosulfate. The organic layer was separated and the aqeous layer was extracted with dichloromethane (2 × 15 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography eluting with mixture of hexane/EtOAc to give the desired product **4**.

(*Z*)-N-Benzyl-N-(1-(2,5-dioxopyrrolidin-1-yl)-2-iodo-2-phenylvinyl)-4-methylbenzenesulf Onamide (4a): Following the general procedure GP−5, compound **4a** (191 mg) was obtained in 69% yield as yellow solid; mp = 215−216 ^oC; R_f = 0.55 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 8.5 Hz, 2H), 7.51 (dd, J = 8.0, 2.0 Hz, 2H), 7.36−7.29 (m, 5H), 7.24−7.19 (m, 3H), 7.18−7.15 (m, 2H), 4.94 (s, 2H), 2.46 (s, 3H), 2.41 (d, J = 13.5 Hz, 2H), 2.13 (d, J = 14 Hz, 2H); $^{13}C\{^1H\}$ NMR (125.77 MHz, $CDCl_3$): δ 144.1, 141.3, 136.5, 136.2, 129.9, 129.7, 129.3, 129.1, 128.5, 128.1, 128.0, 127.8, 127.3, 107.4, 55.7, 27.8, 21.6; IR (KBR) ν_{max} 1720, 1589, 1490, 1353, 1156, 1090 cm^{-1}; HRMS (ESI) for $C_{26}H_{23}IN_2NaO_4S$(M+Na): calcd 609.0321, found 609.0321.

(*Z*)-N-Benzyl-N-(2-(3,4-dimethylphenyl)-1-(2,5-dioxopyrrolidin-1-yl)-2-iodovinyl)-4-methylbenzenesulfonamide (4b): Following the general procedure GP−5, compound **4b** (197 mg) was obtained in 64% yield as yellow solid; mp = 168−170 ^oC; R_f = 0.68 (1:1

hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.53–7.47 (m, 2H), 7.37–7.27 (m, 5H), 6.94 (d, *J* = 10 Hz, 2H), 6.87 (d, *J* = 7.6 Hz, 1H), 4.93 (s, 2H), 2.45 (s, 3H), 2.41 (d, *J* = 14 Hz, 2H), 2.21–2.14 (m, 8 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.0, 138.8, 137.9, 136.5, 136.4, 136.2, 129.8, 129.6, 129.2, 128.6, 128.4, 127.9, 127.7, 124.4, 108.4, 55.7, 27.8, 21.6, 19.6, 19.5; IR (Neat) ν_{max} 3075, 2920, 1789, 1727, 1598, 1453, 1252 cm^{-1}; HRMS (ESI) for $C_{28}H_{28}IN_2O_4S$ $(M+H)^+$: calcd 615.0814, found 615.0815.

(*Z*)-N-(1-(2,5-Dioxopyrrolidin-1-yl)-2-iodo-2-(3-methoxyphenyl)vinyl)-N,4-dimethylbenzene sulfonamide (4c): Following the general procedure GP–5, compound **4c** (185 mg) was obtained in 60% yield as red solid; mp = 193–195 ^{o}C; R_f = 0.54 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 8.4 Hz, 1H), 6.77–6.71 (m, 3H), 3.75 (s, 3H), 3.46 (s, 3H), 2.58 (d, *J* = 14.0 Hz, 2H), 2.46 (s, 3H), 2.34 (d, *J* = 13.2 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.1, 144.1, 141.6, 136.2, 130.8, 129.8, 129.2, 127.8, 119.6, 115.1, 113.1, 103.1, 55.3, 39.7, 28.0, 21.6; IR (Neat) ν_{max} 3057, 2936, 1720, 1600, 1484, 1347, 1287 cm^{-1}; HRMS (ESI) for $C_{21}H_{21}N_2NaO_5S$ $(M+Na)^+$: calcd 563.0114, found 563.0117.

(*Z*)-N-Benzyl-N-(2-(4-chlorophenyl)-1-(2,5-dioxopyrrolidin-1-yl)-2-iodovinyl)-4-methylbenz enesulfonamide (4d): Following the general procedure GP–5, compound **4d** (124 mg) was obtained in 40% yield as yellow solid; mp = 240–242 ^{o}C; R_f = 0.74 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.51–7.45 (m, 2H), 7.37–7.28 (m, 5H), 7.19 (d, *J* =8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 4.92 (s, 2H), 2.46 (s, 3H) 2,44 (d, *J* = 14 Hz, 2H), 2.20 (d, *J* = 14 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.3,

139.8, 136.4, 135.9, 135.0, 129.9, 129.8, 129.7, 128.9, 128.5, 128.4, 128.1, 127.9, 105.4, 55.5, 27.9, 21.7; IR (Neat) ν_{max} 1726, 1342, 1161, 1084, 1013, 882 cm^{-1}; HRMS (ESI) for $C_{26}H_{23}ClIN_2O_4S$ $(M+H)^+$: calcd 621.0112, found 621.0114.

(*Z*)-N-(1-(2,5-Dioxopyrrolidin-1-yl)-2-(4-fluorophenyl)-2-iodovinyl)-N,4-dimethylbenzene sulfonamide (4e): Following the general procedure GP–5, compound **4e** (156 mg) was obtained in 59% yield as colorless solid; mp = 187–189 ^{o}C; R_f = 0.70 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.19–7.12 (m, 2H), 6.92 (t, *J* = 8.4 Hz, 2H), 3.45 (s, 3H), 2.60 (d, *J* = 14.0 Hz, 2H), 2.45 (s, 3H), 2.35 (d, *J* = 14.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.7 (d, *J* = 250.5 Hz), 144.2, 136.6 (d, *J* = 4.0 Hz), 136.1, 131.2, 129.9, 129.6 (d, *J* = 8.1 Hz), 127.7, 115.4 (d, *J* = 22.2 Hz), 101.7, 39.7, 28.0, 21.6; 19F NMR (470.6 MHz) δ -111.1; IR (Neat) ν_{max} 3064, 2501, 1902, 1732, 1597, 1422, 1344 cm^{-1}; HRMS (ESI) for $C_{20}H_{19}FIN_2O_4S$ $(M+H)^+$: calcd 529.0094, found 529.0092.

(*Z*)-N-Benzyl-N-(2-(3,4-dichlorophenyl)-1-(2,5-dioxopyrrolidin-1-yl)-2-iodovinyl)-4-methyl benzenesulfonamide (4f): Following the general procedure GP–5, compound **4f** (138 mg) was obtained in 42% yield as yellow solid; mp = 238–240 ^{o}C; R_f = 0.76 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.46 (dd, *J* = 7.6, 4.0 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.33–7.29 (m, 3H), 7.28 (d, *J* = 2.0 Hz, 1H), 6.99 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.90 (s, 2H), 2.46 (s, 3H), 2.44 (d, *J* = 14 Hz, 2H), 2.25 (d, *J* = 14 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.4, 141.1, 136.3, 135.7, 133.3, 132.3, 130.3, 130.2, 129.9, 129.8, 129.5, 128.4, 128.1, 128.0, 126.9, 103.1, 55.5, 27.9, 21.7; IR (Neat) ν_{max} 1720, 1336, 1216, 1156, 1079, 1030, cm^{-1}; HRMS (ESI) for $C_{26}H_{21}Cl_2IN_2NaO_4S$ $(M+Na)^+$: calcd 676.9541, found 676.9542.

(*Z*)-N-Benzyl-N-(2-(4-cyanophenyl)-1-(2,5-dioxopyrrolidin-1-yl)-2-iodovinyl)-4-methyl

benzenesulfonamide (4g): Following the general procedure GP–5, compound **4g** (70 mg) was obtained in 23% yield as light yellow solid; mp = 270–271 ^{o}C; R_f = 0.58 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 7.50–7.46 (m, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.36–7.33 (m, 3H), 7.30 (s, 1H), 7.28 (d, J = 2.8 Hz, 1H), 4.93 (s, 2H), 2.49 (s, 3H), 2.46 (d, J = 13.6 Hz, 2H), 2.21 (d, J = 13.6 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 173.8, 145.8, 144.5, 136.2, 135.6, 132.0, 130.6, 130.0, 129.9, 128.5, 128.14, 128.06, 118.0, 112.7, 103.2, 55.4, 27.8, 21.7; IR (Neat) ν_{max} 3065, 2228, 1727, 1598, 1458, 1427, 1402 cm^{-1}; HRMS (ESI) for $C_{27}H_{23}IN_3O_4S$ $(M+H)^+$: calcd 612.0454, found 612.0450.

(*Z*)-N-(1-(2,5-Dioxopyrrolidin-1-yl)-2-(3-fluorophenyl)-2-iodovinyl)-N,4-dimethylbenzene Sulfonamide (4h): Following the general procedure GP–5, compound **4h** (164 mg) was obtained in 62% yield as yellow solid; mp = 199–200 ^{o}C; R_f = 0.65 (1:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.24–7.17 (m, 1H), 6.96–6.88 (m, 3H), 3.45 (s, 3H), 2.62 (d, J = 13.6 Hz, 2H), 2.46 (s, 3H), 2.37 (d, J = 14 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.0 (d, J = 248.5 Hz), 144.2, 142.4 (d, J = 8.1 Hz), 136.1, 131.6, 129.9, 129.8 (d, J = 8.1 Hz), 127.7, 123.2 (d, J = 3.0 Hz), 116.1 (d, J = 21.2 Hz), 115.1 (d, J = 23.2 Hz), 100.1, 39.7, 28.0, 21.6; 19F NMR (470.6 MHz) δ −111.83; IR (Neat) ν_{max} 2931, 1731, 1610, 1583, 1430, 1342, 1271, 1079 cm^{-1}; HRMS (ESI) for $C_{20}H_{18}FIN_2NaO_4S$ $(M+Na)^+$: calcd 550.9914, found 550.9921.

N-Benzyl-N-(2-(bromomethyl)-5-phenyloxazol-4-yl)-4-methylbenzenesulfonamide (5): A mixture of **2a** (0.2 mmol, 84 mg), N-bromosuccinimide (NBS; 0.22 mmol, 39 mg), AIBN (0.01 mmol, 1.7 mg) in tetrachloromethane (2.0 mL) was stirred at 60 °C for 9 h. The reaction was

cooled to room temperature and the crude mixture was purified by silica gel column chromatography to give **5** (56 mg) in 56% yield as colorless solid; mp = 180–181 °C; R_f = 0.47 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79–7.73 (m, 4H), 7.37–7.30 (m, 5H), 7.19–7.16 (m, 2H), 7.11–7.07 (m, 3H), 4.58 (s, 2H), 4.37 (s, 2H), 2.47 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 155.6, 149.0, 144.2, 134.7, 134.3, 131.8, 129.7, 129.2, 128.5, 128.3, 128.2, 127.9, 126.1, 125.6, 53.9, 21.7, 20.4; IR (Neat) ν_{max} 2926, 1598, 1495, 1450, 1355, 1266 cm^{-1}; HRMS (ESI) for $C_{24}H_{21}BrN_2NaO_3S$ $(M+Na)^+$: calcd 519.0354, found 519.0354.

(4-(N-Benzyl-4-methylphenylsulfonamido)-5-phenyloxazol-2-yl)methyl benzoate (6): A mixture of **5** (0.1 mmol, 50 mg), benzoic acid (0.15 mmol, 18 mg), triethylamine (0.3 mmol, 42 μL) in acetonitrile (2.0 mL) was stirred at 80 °C for 1 h. After completion, the reaction mixture was cooled to room temperature and purified by silica gel column chromatography to give **6** (38 mg) in 70% yield as colorless solid; mp = 149–150 °C; R_f = 0.45 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 7.2 Hz, 2H), 7.83–7.75 (m, 4H), 7.65 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.2 Hz, 2H), 7.40–7.32 (m, 3H), 7.28 (d, J = 8.0 Hz, 2H), 7.22–7.18 (m, 2H), 7.14–7.07 (m, 3H), 5.35 (s, 2H), 4.61 (s, 2H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 165.6, 155.2, 148.8, 144.1, 134.9, 134.5, 133.5, 131.5, 130.0, 129.8, 129.5, 129.2, 129.13, 129.06, 128.6, 128.5, 128.3, 126.3, 125.7, 125.6, 58.2, 21.61, 21.59; IR (Neat) ν_{max} 2926, 1727, 1598, 1495, 1450, 1354, 1265 cm^{-1}; HRMS (ESI) for $C_{31}H_{26}N_2NaO_5S$ $(M+Na)^+$: calcd 561.1460, found 561.1460.

N-(2-(azidomethyl)-5-phenyloxazol-4-yl)-N-benzyl-4-methylbenzenesulfonamide (7): A mixture of **5** (0.1 mmol, 50 mg), sodium azide (0.5 mmol, 33 mg) in $(CH_3)_2CO$:H_2O (3:1; 2.0

mL) was stirred at rt for 1 h. After completion, the reaction mixture was purified by silica gel column chromatography to give **7** (38 mg) in 96% yield as colorless solid; mp = 139–140 ºC; R_f = 0.46 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 2H), 7.75 (dd, J = 8.0, 1.6 Hz, 2H), 7.37–7.31 (m, 5H), 7.18–7.14 (m, 2H), 7.11–7.05 (m, 3H), 4.58 (s, 2H), 4.32 (s, 2H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 155.1, 149.0, 144.2, 135.0, 134.4, 131.4, 129.7, 129.2, 129.1, 128.5, 128.4, 128.2, 127.9, 126.1, 125.7, 46.5, 21.7, 21.6; IR (Neat) ν_{max} 2956, 2101, 1597, 1449, 1352, 1165, 1090, 692 cm^{-1}; HRMS (ESI) for $C_{24}H_{21}N_5NaO_3S$ $(M+Na)^+$: calcd 482.1263, found 482.1262.

Gram Scale Synthesis of 2a and 2p: A mixture of ynamide **1a/1p** (1.0 g, 1.0 equiv.), N-iodosuccinimide (NIS; 2.2 equiv.), $Yb(OTf)_3$ (20 mol%) and H_2O (2.0 equiv.) in freshly distilled acetonitrile (10 mL) was stirred independently at room temperature for 8–9 h. The progress of the reaction was monitered by TLC. After completion, the reaction mixture was quenched with saturated aqueous sodium thiosulfate. The organic layer was separated and the aqeous layer was extracted with ethylacetate (2 × 40 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under the reduced pressure. The crude mixture was purified by silica gel column chromatography to give the products **2a** and **2p** in 75% (0.87 g) and 78% (0.94 g), respectively.

Gram Scale Synthesis of 3a: A mixture of ynamide **1a** (2.77 mmol, 1.0 g), $Yb(OTf)_3$ (0.55 mmol, 344 mg), and H_2O (5.54 mmol, 100 μL) in freshly distilled acetonitrile (10 mL) was stirred at room temperature for 18 h. After completion, the reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude mixture was

purified by neutral alumina column chromatography eluting with 25% EtOAc and hexane mixture to give the desired product **3a** in 70% (0.81 g) yield as colorless solid.

Gram scale synthesis of 4a: A mixture of ynamide **1a** (2.77 mmol, 1.0 g), NIS (6.09 mmol, 1.37 g), and $Yb(OTf)_3$ (0.55 mmol, 344 mg) in dry dichloromethane (10 mL) was stirred at room temperature for 9 h. After completion, the reaction mixture was quenched with saturated sodium thiosulfate. The organic layer was separated and the aqeous layer was extracted with dichloromethane (2 × 40 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography eluting with mixture of hexane/EtOAc to give the desired product **4a** in 68% (1.1 g) yield as yellow solid.

Procedure for ^{18}O-Incorporation: A mixture of ynamide **1a** (0.5 mmol, 181 mg), $Yb(OTf)_3$ (0.1 mmol, 62 mg) and H_2O^{18} (1.0 mmol, 18 μL) in freshly distilled acetonitrile (3.0 mL) was stirred at room temperature for 18 h. After completion, the reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude mixture was purified by neutral alumina column chromatography to give the ^{18}O-incorporated product as colorless solid.

Procedure for D-Incorporation: A mixture of ynamide **1a** (0.5 mmol, 181 mg), $Yb(OTf)_3$ (0.1 mmol, 62 mg), and D_2O (1.0 mmol, 18 μL) in freshly distilled acetonitrile (3.0 mL) was stirred at room temperature for 18 h. After completion, the reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude mixture was purified by neutral alumina column chromatography to give the D-incorporated products **3a''** as colorless semi solid.

ASSOCIATED CONTENT

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Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

We thank UoH, CEFIPRA (Grant no: 5505-2), UPE-II, and PURSE for financial supports. R. K. M. and P. B. thank UGC and CSIR India for fellowship. We also thank Dr. Nagarjuna and Mr. Anil for X-ray crystal analysis (DST-PURSE). Dedicated to Professor Vishwakarma Singh, IIT-Bombay, Mumbai, India, for his outstanding contribution in the area of Synthetic Organic Chemistry and also on the occasion of his 65th Birthday".

SUPPORTING INFORMATION

Detailed spectra (^{1}H and ^{13}C NMR), X-ray crystallographic data and starting material chart. This material is available free of charge via the Internet at http://pubs.acs.org.

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14. Alternatively, the possibility of *anti*-addition of nitrile to Yb-keteneiminium species followed by a sequence of hydration, demetalation, and complete isomerization of the olefin to obtain the Z-hydroamidation product although difficult but could not completely be rule out.

15. At present, we have no clear evidence to authenticate the mode of attack of nitrile to the β-iodo-keteneiminium ion (Int-**VIII**; Scheme 10). Looking in to the formation of thermodynamically stable *trans*-iodo-imidation product **4**, we believe the nitrile can undergo *trans*-attack to β-iodo-keteniminium species and hydration to provide int-**IX**.

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