

Gold(I)-Catalyzed Reactivity of Furan-ynes with *N*-Oxides: Synthesis of Substituted Dihydropyridinones and Pyranones

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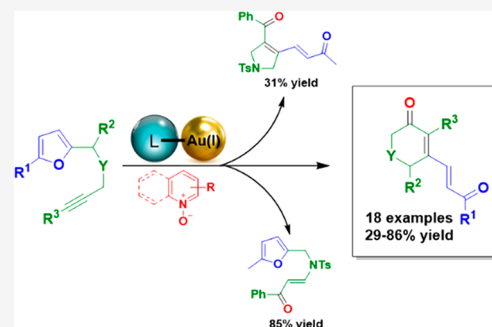


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ABSTRACT: The reactivity of “furan-ynes” in combination with pyridine and quinoline *N*-oxides in the presence of a Au(I) catalyst, has been studied, enabling the synthesis of three different heterocyclic scaffolds. Selective access to two out of the three possible products, a dihydropyridinone and a furan enone, has been achieved through the fine-tuning of the reaction conditions. The reactions proceed smoothly at room temperature and open-air, and were further extended to a broad substrate scope, thus affording functionalized dihydropyridinones and pyranones.



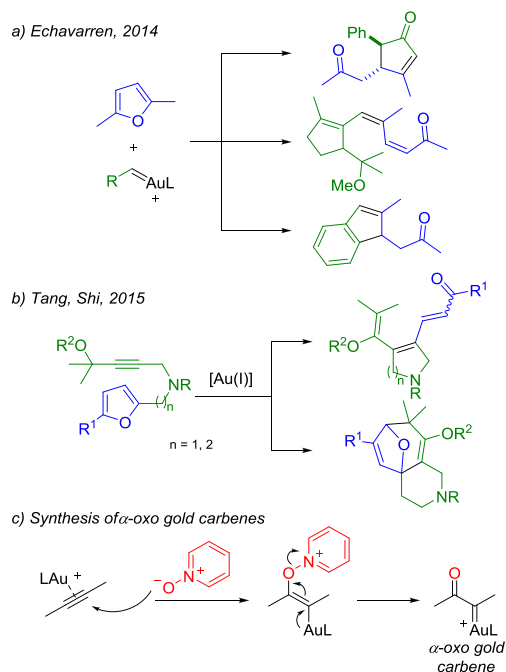
INTRODUCTION

The activation of alkynes toward the attack of a nucleophile by means of gold catalysis is a well-established tool in modern organic synthesis.¹ Since the beginning of this century, the furan ring has emerged as a versatile candidate for both Au(I)- and Au(III)-catalyzed transformations, by virtue of its nucleophilicity.² A successful example in this regard is represented by the synthesis of phenols from furan-tethered alkynes (“furan-ynes”), which has been widely explored throughout the years, mainly by Hashmi and his group, enabling the synthesis of a variety of molecular scaffolds.³ More recently, the combination of furans with Au(I) carbene chemistry has disclosed intriguing synthetic possibilities. In 2014, Echavarren reported that three different types of Au(I) carbenes, generated respectively by rearrangement of propargyl esters, cycloisomerization of 1,6-enynes, and *retro*-Buchner reaction, underwent intermolecular reaction with furans through related mechanistic pathways, thus giving access to an array of diverse molecular frames (Scheme 1a).⁴ Gold(I) carbenes obtained from propargyl esters were later employed by Tang and Shi in intramolecular reactions with furans, achieving the synthesis of functionalized *N*-heterocycles and *O*-bridged tricyclic scaffolds (Scheme 1b).⁵ Another relevant class of Au(I) carbenes is represented by α -oxo gold(I) carbenes. These reactive intermediates can be accessed by treatment of an alkyne with either a pyridine or quinoline *N*-oxide in the presence of a Au(I) complex, through nucleophilic attack of the O atom of the *N*-oxide onto the gold-activated triple bond and subsequent cleavage of the pyridine or quinoline (Scheme 1c).⁶

α -Oxo gold(I) carbenes can undergo several reaction pathways, including cyclopropanations, migrations, ring expansions, insertions, and reactions with nucleophiles.⁷

On these premises, following our interest for the synthetic manipulation of heterocycles through gold catalysis,⁸ we

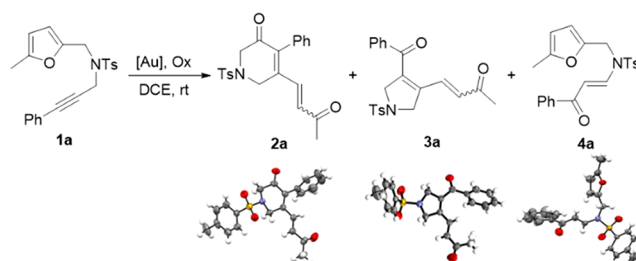
Scheme 1. Background of the Work



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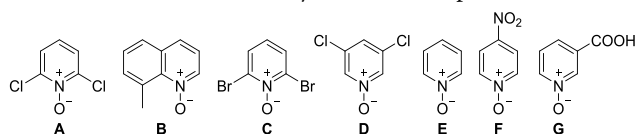


Table 1. Optimization of the Reaction Conditions^a

entry	[Au]	Ox	time	yield % ^b		
				2a (E/Z)	3a (E/Z)	4a
1	[(IPr)Au(NTf ₂)]	A	6 h	81 (12/88)	–	–
2	[((2,4- ^t Bu ₂ C ₆ H ₃ O) ₃ P)AuCl]/AgNTf ₂	A	6 h	15 (0/100)	6 (0/100)	11
3	[((<i>p</i> -CF ₃ Ph) ₃ P)AuCl]/AgNTf ₂	A	6 h	23 (0/100)	6 (0/100)	8
4	[(JohnPhos)AuCl]/AgNTf ₂	A	6 h	77 (6/94)	–	–
5	[(JohnPhos)Au(NCMe)]SbF ₆	A	6 h	40 (25/75)	–	–
6	[(^t BuXPhos)AuCl]/AgNTf ₂	A	6 h	67 (10/90)	–	–
7	[(IPr)Au(NTf ₂)]	B	6 h	–	31 (0/100)	60
8	[(IPr)Au(NTf ₂)]	C	6 h	48 (10/90)	–	–
9	[(IPr)Au(NTf ₂)]	D	6 h	56 (14/86)	17 (0/100)	27
10	[(IPr)Au(NTf ₂)]	E	6 h	–	–	22
11	[(IPr)Au(NTf ₂)]	F	6 h	68 (1/99)	–	–
12	[(IPr)Au(NTf ₂)]	G	6 h	–	–	–
13	[(IPr)Au(NTf ₂)]	F	20 h	96 (2/98)	–	–
14	[(MorDalPhos)Au(NCMe)]SbF ₆	B	20 h	–	4 (0/100)	85 ^c
15	[((2,4- ^t Bu ₂ C ₆ H ₃ O) ₃ P)AuCl]/AgNTf ₂	B	20 h	–	13 (0/100)	29
16	[(JohnPhos)AuCl]/AgNTf ₂	B	20 h	–	15 (0/100)	60
17	[((C ₆ F ₅) ₃ P)AuCl]/AgNTf ₂	B	20 h	–	4 (0/100)	11

^aConditions: 0.1 mmol of **1a**, 0.12 mmol of Ox, 0.005 mmol of Au(I) complex, and, when specified, 0.005 mmol of Ag salt, in 1.0 mL of DCE.

^bDetermined by ¹H NMR with *n*-heptane as internal standard. ^c74% yield of isolated product.



decided to investigate the reactivity of furan-yne **1a**, in the presence of a gold catalyst.

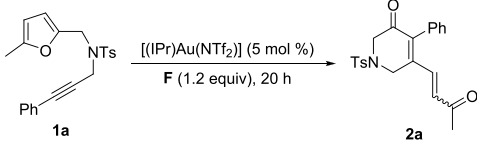
RESULTS AND DISCUSSION

To start the investigation, furan-yne **1a**, provided with a phenyl terminus at the alkyne moiety,⁹ was reacted with the Au(I) complex [(IPr)Au(NTf₂)] and 2,6-dichloropyridine *N*-oxide **A**, at room temperature in 1,2-dichloroethane (Table 1, entry 1). Under these conditions, the complete consumption of the starting material and the formation of the 6-membered dihydropyridinone **2a** in 81% yield were observed after 6 h. The structure of **2a** was unequivocally identified through X-ray diffraction.¹⁰ On the other hand, when [((2,4-^tBu₂C₆H₃O)₃P)AuCl] was used as the Au(I) complex, in combination with AgNTf₂, the formation of two other products was observed: the 5-membered dihydropyrrole **3a** and the furan enone **4a**, whose structures were again confirmed by XRD.¹⁰ However, in this case the yields of all three products were quite low (entry 2).

With the aim of optimizing and driving the selectivity of the reaction, several conditions and gold complexes were tested (entries 3–6; see Table S1 in the Supporting Information (SI) for the complete list of experiments), but none of them outdid [(IPr)Au(NTf₂)] in terms of the yield of **2a**. It should also be noted that the reaction proceeded with good stereoselectivity for the configuration of the exocyclic C–C double bond in **2a** and

3a, observing a general preference for the *Z* isomer. With the best performing Au(I) complex, [(IPr)Au(NTf₂)], we shifted our attention to a screening of *N*-oxides (entries 7–12), and we found that the selectivity of the reaction was sensitively affected by the choice of this reagent. With 8-methylquinoline *N*-oxide **B**, the formation of **2a** was completely suppressed in favor of a 1/2 ratio of **3a** and **4a** (entry 7). Other *N*-oxides were either less selective (**D**, entry 9) or less active (entries 8, 10–12). However, 4-nitropyridine *N*-oxide **F** afforded **2a** with a remarkably high *Z* selectivity (entry 11). Eventually, we identified the most suitable conditions for the synthesis of **2a** with oxidant **F**, by extending the reaction time up to 20 h (entry 13).

We then considered the outcome of the reaction with **B** and [(IPr)Au(NTf₂)] (entry 7), and we deemed it worthwhile to further explore the reactivity of this oxidant with different Au(I) complexes. With [(MorDalPhos)Au(NCMe)]SbF₆ the selective synthesis of the furan enone **4a** was achieved (entry 14). Unfortunately, we were not able to increase the yield of **3a** beyond 31%, which remained as the best result for this product (entry 7). With the conditions in entry 13 (Table 1), product **2a** was isolated in good yields, however we found that the *Z* isomer slowly isomerized into (*E*)-**2a** over time. On this basis, we decided to direct the reaction toward complete *E* selectivity, by a further optimization of the conditions described in entry 13. As shown in Table 2, the first parameter we investigated was the

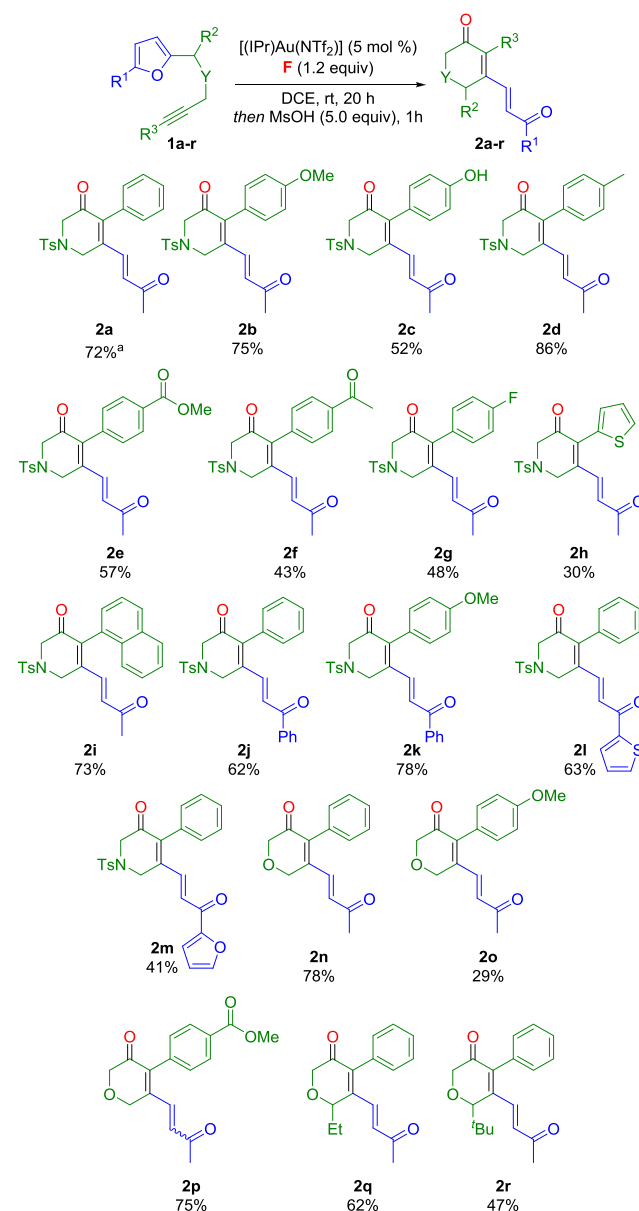
Table 2. Optimization of the *E/Z* Ratio in the Synthesis of **2a**^a


entry	T (°C)	solvent	additive	yield % ^b (<i>E/Z</i>)
1	80 °C	DCE	–	66 (23/77)
2	rt	DCE	TFA (2.0 equiv)	73 (16/84)
3	rt	DCE	<i>p</i> -TsOH (2.0 equiv)	43 (100/0)
4	rt	DCE	MsOH (2.0 equiv)	58 (100/0)
5	rt	CHCl ₃	–	63 (3/97)
6	rt	HFIP	–	–
7	rt	DCE	<i>p</i> -TsOH (2.0 equiv) ^c	89 (11/89)
8	rt	DCE	MsOH (2.0 equiv) ^c	94 (17/83)
9	rt	DCE	MsOH (5.0 equiv) ^c	80 ^d (100/0)

^aTFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol.
^bDetermined by ¹H NMR with *n*-heptane as internal standard.
^cAdded after 20 h, then stirred for one additional hour. ^d72% yield of isolated product.

temperature, which was raised to 80 °C (Table 2, entry 1). This resulted indeed in an improvement of the *E/Z* ratio, but with a decrease in the overall yield. A different approach, based on the addition of a Brønsted acid as promoter of the isomerization, afforded (*E*)-**2a** with complete selectivity, but the yields were again not satisfactory (*p*-toluenesulfonic acid, *p*-TsOH, and methanesulfonic acid, MsOH, entries 3 and 4). Also attempts to perform the reaction in more acidic solvents, such as chloroform and hexafluoroisopropanol (entries 5 and 6), were met with failure. The decrease in the yield may be attributed to the possible degradation of the starting material **1a** in the presence of a Brønsted acid. On this basis, we decided to add the acid only at the end of the Au(I)-catalyzed step, *i.e.* after 20 h (entries 7–9): under these conditions, with MsOH a remarkable 80% NMR yield of (*E*)-**2a** (72% after isolation) was obtained by adjusting the amount of MsOH to 5.0 equiv (entry 9; see Table S2 in the SI for the complete list of experiments).

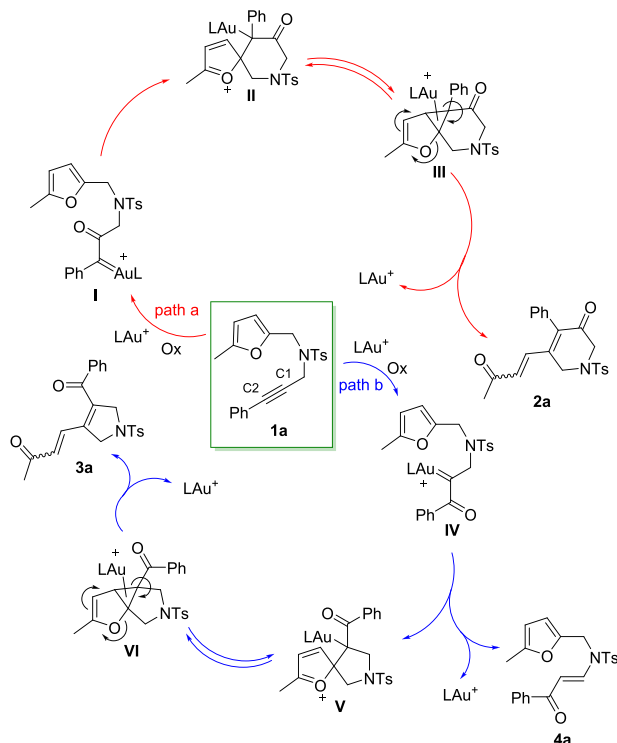
Having identified the most suitable conditions to orient the divergent reactivity of **1a** toward the exclusive formation of dihydropyridinone **2a** as the *E* isomer, we investigated the possible extension of the reaction substrate scope. Furan-ynes **1b–r** were synthesized and reacted with 4-nitropyridine *N*-oxide **F** and [(IPr)Au(NTf₂)] for 20 h, after which 5.0 equiv of MsOH were added, and the mixture was stirred for one additional hour (Scheme 2). Variations on the terminal aromatic ring were introduced, proving that a variety of electron-donating (**2b–d**) and electron-withdrawing (**2e–g**) functional groups are well tolerated. Apart from substituted phenyl rings, thiophene and naphthalene were also suitable (**2h–i**). Conversely, in the presence of an alkyl chain (R³ = *n*-Bu) the reaction did not occur, and degradation of the starting material was observed. The methyl group on the furan ring in the starting material was replaced with phenyl, thienyl, and furyl groups, obtaining aryl ketones **2j–m** as product. Unfortunately, with R¹ = H (**1s**; see the SI), the reaction was troublesome and hardly reproducible. On the other hand, replacing the *N*-Ts linker with an *O* linker resulted in the synthesis of pyranones **2n–p**. Substituents on the heterocyclic ring were also successfully introduced, affording pyranones **2q–r**. In all cases, apart from product **2p**, complete *E* selectivity was observed, and the yields ranged from moderate to high.

Scheme 2. Substrate Scope for the Synthesis of Dihydropyridinones and Pyranones^a

^aYield unchanged at 1.3 mmol scale. ^aReactions performed at a 0.2 mmol scale. Yields of isolated products. *E/Z* ratio 100/0 in all cases, except for **2p** (*E/Z* 40/60).

A plausible mechanistic picture for the formation of products **2a**, **3a**, and **4a** from furan-yn **1a** is depicted in Scheme 3.^{5,6,11} Upon activation of the alkyne moiety in substrate **1a** by the Au(I) complex, the attack of the *N*-oxide onto the C1 atom of the triple bond leads to α -oxo gold(I) carbene **I** (see Scheme 1c), which then undergoes cyclization through nucleophilic attack by the furan ring, affording the spirocyclic intermediate **II** (path a). A cyclopropanation/cyclopropane opening sequence eventually determines the opening of the furan ring, leading to the formation of **2a**. Intermediate **II** might also convert directly to **2a** through an elimination step. Based on the results presented in Tables 1 and 2, the *Z* isomer is likely first formed and then converted into (*E*)-**2a**.¹² If the regioselectivity of the *N*-oxide attack is switched, the spirocyclic intermediate **V** is formed upon attack of the furan onto Au(I) carbene **IV** (path b). Then, the

Scheme 3. Mechanistic Pathways for 2a, 3a, and 4a



final product **3a** is obtained through a mechanism analogous to the one described for **2a**. Alternatively, the α -oxo gold(I) carbene intermediate **IV** may also undergo a 1,2-H shift with the neighboring CH_2 group, leading to the formation of furanone **4a**.^{8c,13}

It should be pointed out that the best selectivity for **4a** was obtained with the gold(I) complex [(MorDalPhos)Au(NCMe)]SbF₆ (Table 1, entry 14). The MorDalPhos ligand has been reported to temper the electrophilicity of the Au(I) carbene through bidentate coordination from both the P and the N atom.¹⁴ This would be consistent what was observed in our case, as the less electrophilic carbene is likely less prone to get attacked by the nucleophilic furan ring, and thus more available to selectively undergo a 1,2-H shift. However, when more electrophilic Au(I) complexes were employed, the expected enhancement in the selectivity toward **3a** was not observed (Table 1, entries 15 and 17).

As highlighted by the study on the reaction conditions (Table 1), the C1 vs C2 regioselectivity of the nucleophilic attack is highly dependent on the nature of the *N*-oxide reagent, while the electronic effects of the alkyne substituent R^3 are not relevant in modifying this selectivity (Scheme 2). To better elucidate the influence of the electronic and steric factors, we studied the attack of *N*-oxides **F** and **B** onto the [LAu]⁺-**1a** π -complex through DFT calculation (Table 3). The Natural Bond Analysis of this intermediate revealed that the charge density values on C1 and C2 are very small, being slightly negative on C1 (−0.10) and slightly positive on C2 (+0.04). On the other hand, the partial negative charge on the O atom in the *N*-oxide is larger in **B** (−0.55) than in **F** (−0.49). By considering the charge density only, **B** would be expected to be more reactive than **F** and C2 would be the preferential site of reaction. Thus, a more detailed study on the transition states for the attack of **B** and **F** onto C1 and C2 was carried out, and the results are reported in Table 3. The addition of **B** to C1 is preferred to the addition to C2: the

Table 3. Free Energy Barriers and Energy Decomposition Analysis,^a in kcal mol^{−1}, for the Addition of B and F to C1 and C2

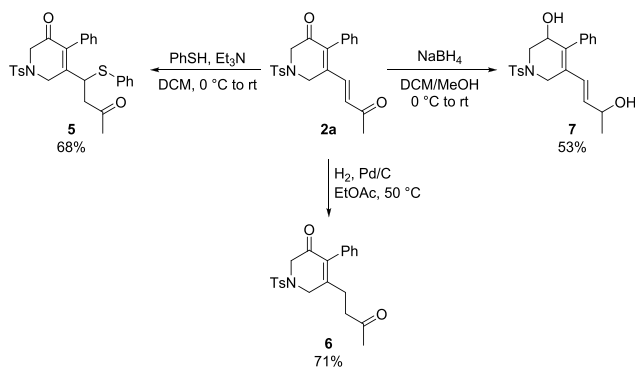
Ox	carbon	ΔG^\ddagger	ΔE_s^\ddagger	ΔE_e^\ddagger	ΔE_q^\ddagger	$\Delta E_{\text{tot}}^\ddagger$
B	C1	25.5	−552.4	104.2	444.0	−4.2
B	C2	20.2	−487.8	99.0	382.7	−6.8
F	C1	26.3	−448.6	104.8	346.2	2.3
F	C2	26.9	−373.2	84.2	292.5	3.8

^aCalculated at M06/def2-SVP level. L = IPr.

free energy barriers (ΔG^\ddagger) are 20.2 and 25.5 kcal mol^{−1}, respectively. On the other hand, **F** displays opposite behavior, with a smaller barrier for the addition to C1 (26.3 kcal mol^{−1}). **B** appears to be more reactive than **F**. To explain the regioselectivity, Shubin Liu's energy decomposition analysis (EDA-SBL) was carried out. The EDA-SBL method splits the total energy (E_{tot}) in three components: E_e (sum of nuclear–nuclear, electron–electron, and nuclear–electron electrostatic interactions), E_q (quantum interaction: sum of exchange–correlation and Pauli energies, associated to the repulsion between filled orbitals), and E_s (steric energy repulsion). The larger values of the three components indicate the main effects responsible for the barriers. In all the four reactions, the barriers are dominated by change of steric (ΔE_s^\ddagger) and quantum (ΔE_q^\ddagger) effects. The quantum effect contributes positively to the height of the barrier, and the steric effect, negatively. Electrostatic effects (ΔE_e^\ddagger) are relevant but less important. By comparing the ΔE_s^\ddagger for C1 and C2, the addition to the former displays less negative values. The difference $\Delta E_s^\ddagger(\text{C2}) - \Delta E_s^\ddagger(\text{C1})$ is 64.4 and 75.4 for **B** and **F** respectively, which could indicate a larger steric effect when addition occurs to C2. The regioselectivity is supposed to depend on a delicate balance between density of charge on the oxidant, responsible for the positive contribution to the barrier, and steric effect. By comparison, *N*-oxide **D** shows a charge density on the O atom of −0.52, intermediate between **B** and **F**, and its attack on both C1 and C2 (Table 1, entry 9). Noncovalent interaction plots (Figure S5 in the SI) visualize noncovalent interactions from the topological analysis of the electron density. These highlight the presence of van der Waals attractive interactions between the phenyl group and the pyridine or quinoline rings, while strong steric repulsion between the *N*-oxide and the reactant are lacking in the transition structures.

To provide a glimpse of the synthetic value of the products of our Au(I)-catalyzed methodology, we subjected **2a** to the synthetic manipulations reported in Scheme 4. Remarkably, the Michael addition of thiophenol, catalyzed by Et₃N,¹⁵ proceeded smoothly at room temperature with complete selectivity for the exocyclic double bond over the endocyclic one, thus obtaining sulfide **5**. Similarly to the Michael addition, also the hydrogenation over Pd/C was selective for the exocyclic double bond, affording the partially saturated compound **6**. On the other hand, reduction with NaBH₄ did not discriminate between the two carbonyl groups, and diol **7** was obtained as the product.

Scheme 4. Synthetic Manipulations of 2a



CONCLUSION

In conclusion, the study of the reactivity of furan-ynes with *N*-oxides, in the presence of a Au(I) catalyst, has disclosed an intriguing divergent mechanistic picture, with the formation of three possible densely functionalized heterocyclic scaffolds. This work contributes to extend the wide landscape of synthetic opportunities offered by the powerful combination of gold catalysis and furans, enabling the straightforward synthesis of dihydropyridinones and pyranones through control over the product selectivity and the diastereoselectivity of the reaction. Moreover, the good tolerance of structural variations in the substrate, as well as of the presence of either nucleophilic or electrophilic functional groups, allows for a tailored application of the methodology, in view of its exploitation in synthesis. The theoretical investigation on the regioselectivity contributes to the understanding of the role of electronic and steric effects in the mechanism of this class of reactions, and could potentially prompt a systematic more-in-detail analysis of previously reported similar methodologies.

EXPERIMENTAL SECTION

Computational Method. The stationary points were optimized in the gas phase with the DFT M06 functional,¹⁶ with the ONIOM procedure.¹⁷ In this procedure, the molecule is divided into two layers treated with different levels of calculations. This approach has been found to be useful for modeling large molecular systems. In this work, the higher layer was treated at the M06/def2-SVP¹⁸ level, whereas for the lower layer the chosen level was M06/STO-3G¹⁹ (for Au only, effective core potential LanL2DZ was used). This procedure was labeled as ONIOM(M06/def2-SVP:M06/STO-3G). The figures showing the layers assignment of the atoms are reported in the Supporting Information (Figure S4). The energies were refined by single-point energy calculations at level ONIOM(M06/def2-TZVP:M06/STO-3G) including the solvent effect (dichloroethane) by the Solvation Model based on Density (SMD).²⁰ The relative Gibbs free energies in solution (ΔG) were estimated at $T = 298$ K. Multiwfn software²¹ was used for the noncovalent interaction analysis (NCI)²² and for Shubin Liu's energy decomposition analysis (EDA-SBL).²³ Geometry optimizations and thermochemistry calculations were carried out by using the Gaussian 16 programs.

General Information. Flasks and all equipment used for the generation and reaction of moisture-sensitive compounds were dried by electric heat gun under nitrogen. Reaction heating was provided through an oil bath. Reagents and solvents were purchased from Merck, Acros Organics, TCI or Alfa Aesar. Anhydrous THF was obtained by distillation over LiAlH₄, followed by distillation over Na-benzophenone; Et₃N was distilled over CaH₂. All other reagents were used as received, without further purification. Flash column chromatography was performed over silica gel (40–63 μ m, 230–400 mesh); R_f values refer to TLC carried out on silica gel plates. ¹H NMR and ¹³C NMR

spectra were recorded on a Jeol ECZR600, in CDCl₃ or in CD₃OD, using the residual solvent peak as an internal reference (CHCl₃, ¹H: 7.26 ppm; CDCl₃, ¹³C: 77.16 ppm; CH₃OH, ¹H: 3.34 ppm; CD₃OD, ¹³C: 49.86 ppm). Multiplicity is reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). GC-MS spectra were recorded at an ionizing voltage of 70 eV. HRMS analysis were run on a high resolving power hybrid mass spectrometer (HRMS) Orbitrap Fusion (Thermo Scientific, Rodano, Italy), equipped with an ESI ion source. The samples were analyzed in acetonitrile solution using a syringe pump at a flow rate of 5 μ L/min. The tuning parameters adopted for the ESI source were as follows: source voltage 5.0 kV, source current 0.5 μ A, capillary voltage 32 V, tube lens voltage 75 V. The heated capillary temperature was maintained at 275 °C. Crystals of 2a, 3a, and 4a were obtained by slow evaporation from a MeCN solution at 4–6 °C. Reaction schemes for the synthesis of the substrates, as well as details about XRD analysis, are available in the Supporting Information.

Synthesis of Furan-2-ylboronic Acid, int-1. This is a modified literature procedure.²⁴ A solution of furan (1.0 equiv, 20 mmol) in anhydrous THF (1.0 M), under a N₂ atmosphere, was cooled down to –10 °C. *n*-BuLi (1.0 equiv, 2.5 M solution in hexane) was added, and the mixture was allowed to warm to 0 °C and stirred for 1 h. Then, triisopropylborate (2.0 equiv) was added, and the mixture was allowed to warm to room temperature and stirred for 30 min, before addition of 50 mL of a 3 M HCl solution. The mixture was extracted three times with Et₂O, and the combined organic layers were extracted three times with a 1 M NaOH solution. The combined NaOH aqueous layers were brought to acidic pH with a 6 M HCl solution and extracted three times with Et₂O; the combined organic layers were dried over anhydrous Na₂SO₄ and filtered, and the volatiles were evaporated under reduced pressure to afford furan-2-ylboronic acid as a yellow solid, which was used for the next step without further purification (1.320 g, 59% yield). ¹H NMR (600 MHz, dmsd-d₆) δ (ppm): 8.21 (br s, 2H), 7.84 (d, 1H, $J = 1.7$ Hz), 7.09 (d, 1H, $J = 3.3$ Hz), 6.50 (dd, 1H, $J = 3.3, 1.7$ Hz).

General Procedure for the Suzuki Coupling of 5-Bromo-2-furaldehyde (GP1).²⁵ Into a flask, 2-bromofuraldehyde (1.0 equiv, 15 mmol), arylboronic acid (1.1 equiv), palladium(II) acetate (0.02 equiv), potassium carbonate (2.5 equiv), and tetrabutylammonium bromide (1.0 equiv) were added, then deionized H₂O (0.5 M with respect to 2-bromofuraldehyde) was added, and the mixture was vigorously stirred for 2 h at room temperature. Then, the mixture was extracted three times with EtOAc; the combined organic layers were dried over anhydrous Na₂SO₄ and filtered, and the volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography to obtain the pure 5-aryl substituted furfural.

5-Phenylfuran-2-carbaldehyde, int-2. Synthesized according to the general procedure GP1. Yellow oil, 1.93 g, 75% yield. R_f 0.46 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 9.66 (s, 1H), 7.85–7.82 (m, 2H), 7.47–7.44 (m, 2H), 7.42–7.39 (m, 1H), 7.33 (d, 1H, $J = 3.7$ Hz), 6.85 (d, 1H, $J = 3.7$ Hz). GC-MS m/z (%): 172 [M]⁺ (100), 171 (45), 115 (77).

5-(Thiophen-2-yl)furan-2-carbaldehyde, int-3. Synthesized according to the general procedure GP1. Yellow oil, 2.54 g, 95% yield. R_f 0.46 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 9.62 (s, 1H), 7.53 (dd, 1H, $J = 3.7, 1.2$ Hz), 7.41 (dd, 1H, $J = 5.0, 1.2$ Hz), 7.29 (d, 1H, $J = 3.8$ Hz), 7.11 (dd, 1H, $J = 5.0, 3.7$ Hz), 6.68 (d, 1H, $J = 3.7$ Hz). GC-MS m/z (%): 178 [M]⁺ (100), 121 (72).

[2,2'-Bifuran]-5-carbaldehyde, int-4. Synthesized according to the general procedure GP1. Yellow oil, 2.06 g, 85% yield. R_f 0.36 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 9.62 (s, 1H), 7.52 (dd, 1H, $J = 1.8, 0.8$ Hz), 7.30 (d, 1H, $J = 3.7$ Hz), 6.91 (dd, 1H, $J = 3.4, 0.8$ Hz), 6.73 (d, 1H, $J = 3.7$ Hz), 6.53 (dd, 1H, $J = 3.5, 1.8$ Hz). GC-MS m/z (%): 162 [M]⁺ (100), 105 (65).

General Procedure for the Synthesis of Terminal Alkynes with *N*-Ts Linker (GP2).²⁹ To a 1.0 M solution of furaldehyde (1.0 equiv, 10–20 mmol) in DCM, MgSO₄ (1.1 equiv) and propargylamine (1.0 equiv) were added, and the mixture was stirred at room temperature for 24–48 h (GC-MS monitoring). The mixture was filtered over silica with EtOAc, and the volatiles were evaporated under

reduced pressure to obtain the crude imine, which was used for the next step without further purification.

To a 1.0 M solution of the crude furanyl imine in MeOH, NaBH₄ (1.0 equiv) was added portionwise at 0 °C. The mixture was allowed to reach room temperature and stirred for 5–10 min (GC-MS monitoring) until complete conversion. Then, MeOH was evaporated to half of the initial volume under reduced pressure. Water was added, and the mixture was extracted three times with EtOAc; the combined organic layers were dried over Na₂SO₄ and filtered, and the volatiles were evaporated under reduced pressure to obtain the crude amine, which was used for the next step without further purification.

To a 1.0 M solution of the crude amine in DCM, Et₃N (1.0 equiv) was added, then *p*-toluenesulfonyl chloride (1.0 equiv) was added portionwise, and the mixture was stirred at room temperature overnight. Then, water was added, and the mixture was extracted three times with DCM; the combined organic layers were dried over Na₂SO₄ and filtered, and the volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography to obtain the pure *N*-Ts product.

***N*-(Furan-2-ylmethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide, **int-5**.** Synthesized according to the general procedure GP2. White solid, 1.46 g, 51% yield (3 steps). *R*_f 0.47 (80/15/5 PE/DCM/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.75–7.73 (m, 2H), 7.35 (dd, 1H, *J* = 1.8, 0.9 Hz), 7.31–7.28 (m, 2H), 6.31 (dd, 1H, *J* = 3.3, 1.8 Hz) superimposed to 6.30 (dd, 1H, *J* = 6.3, 0.8 Hz), 4.43 (s, 2H), 4.02 (d, 2H, *J* = 2.5 Hz), 2.43 (s, 3H), 2.07 (t, 1H, *J* = 2.5 Hz). GC-MS *m/z* (%): 289 [M]⁺ (1), 134 (100), 106 (32), 91 (31), 81 (17).

4-Methyl-*N*-(5-methylfuran-2-yl)methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide, **int-6.** Synthesized according to the general procedure GP2. White solid, 3.82 g, 63% yield (3 steps). *R*_f 0.31 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.75–7.73 (m, 2H), 7.30–7.28 (m, 2H), 6.16 (d, 1H, *J* = 3.0 Hz), 5.86 (dq, 1H, *J* = 3.0 Hz, 1.0 Hz), 4.37 (s, 2H), 4.02 (d, 2H, *J* = 2.5 Hz), 2.43 (s, 3H), 2.20 (d, 3H, *J* = 1.0 Hz), 2.05 (t, 1H, *J* = 2.5 Hz). GC-MS *m/z* (%): 303 [M]⁺ (3), 148 (100), 147 (36), 120 (77), 95 (82), 91 (42).

4-Methyl-*N*-(5-phenylfuran-2-yl)methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide, **int-7.** Synthesized according to the general procedure GP2. White solid, 2.33 g, 64% yield (3 steps), mp 89–91 °C (Et₂O). *R*_f 0.38 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.76–7.74 (m, 2H), 7.56–7.54 (m, 2H), 7.37–7.34 (m, 2H), 7.28–7.24 (m, 3H), 6.55 (d, 1H, *J* = 3.3 Hz), 6.37 (d, 1H, *J* = 3.3 Hz), 4.52 (s, 2H), 4.09 (d, 2H, *J* = 2.5 Hz), 2.38 (s, 3H), 2.11 (t, 1H, *J* = 2.5 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 154.5 (Cq), 148.2 (Cq), 143.8 (Cq), 136.2 (Cq), 130.5 (Cq), 129.7 (CH), 128.7 (CH), 127.8 (CH), 127.7 (CH), 123.9 (CH), 112.3 (CH), 105.7 (CH), 76.7 (Cq), 74.1 (CH), 43.1 (CH₂), 36.5 (CH₂), 21.6 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₁H₁₉NO₃SNa⁺ 388.0978; found 388.0974.

4-Methyl-*N*-(prop-2-yn-1-yl)-*N*-(5-(thiophen-2-yl)furan-2-yl)methylbenzenesulfonamide, **int-8.** Synthesized according to the general procedure GP2. White solid, 2.42 g, 65% yield (3 steps), mp 127–131 °C (decomposition). *R*_f 0.46 (8/2 DCM/PE). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.74 (d, 2H, *J* = 8.2 Hz), 7.27 (d, 2H, *J* = 8.3 Hz), 7.22 (d, 1H, *J* = 5.0 Hz), 7.16 (d, 1H, *J* = 3.5 Hz), 7.03–7.00 (m, 1H), 6.38 (d, 1H, *J* = 3.3 Hz), 6.34 (d, 1H, *J* = 3.3 Hz), 4.49 (s, 2H), 4.08 (d, 2H, *J* = 2.4 Hz), 2.39 (s, 3H), 2.11 (t, 1H, *J* = 2.5 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 149.9 (Cq), 147.9 (Cq), 143.8 (Cq), 136.1 (Cq), 133.4 (Cq), 129.7 (CH), 127.8 (CH), 127.7 (CH), 124.5 (CH), 123.0 (CH), 112.2 (CH), 105.8 (CH), 76.7 (Cq), 74.1 (CH), 43.0 (CH₂), 36.5 (CH₂), 21.6 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₉H₁₇NO₃S₂Na⁺ 394.0542; found 394.0528.

***N*-(2,2'-Bifuran)-5-ylmethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide, **int-9**.** Synthesized according to the general procedure GP2. White solid, 2.22 g, 63% yield (3 steps), mp 136–138 °C (EtOAc). *R*_f 0.43 (7/3 DCM/PE). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.76–7.73 (m, 2H), 7.39 (dd, 1H, *J* = 1.7, 0.7 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 3.47 (d, 1H, *J* = 3.1 Hz), 6.45–6.43 (m, 2H), 6.35 (d, 1H, *J* = 3.4 Hz), 4.48 (s, 2H), 4.06 (d, 2H, *J* = 2.4 Hz), 2.40 (s, 3H), 2.09 (t, 1H, *J* = 2.5 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 147.9 (Cq), 147.1 (Cq), 146.3 (Cq), 143.8 (Cq), 142.0 (CH), 136.0 (Cq),

129.6 (CH), 127.8 (CH), 112.0 (CH), 111.5 (CH), 105.8 (CH), 105.6 (CH), 76.6 (Cq), 74.2 (CH), 43.0 (CH₂), 36.4 (CH₂), 21.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₉H₁₇NO₄SNa⁺ 378.0770; found 378.0781.

General Procedure A for the Synthesis of Terminal Alkynes with O Linker (GP3A).³¹ To a 1.0 M solution of furaldehyde (1.0 equiv, 10 mmol) in MeOH, NaBH₄ (1.0 equiv) was added portionwise at 0 °C. The mixture was allowed to reach room temperature and stirred overnight. Then, MeOH was evaporated to half of the initial volume under reduced pressure. Water was added, and the mixture was extracted three times with DCM; the combined organic layers were dried over Na₂SO₄ and filtered, and the volatiles were evaporated under reduced pressure to obtain the crude furyl alcohol, which was used for the next step without further purification.

To a 1.0 M solution of the crude furanyl alcohol in anhydrous DMF, at 0 °C under a N₂ atmosphere, NaH (1.5 equiv) was added portionwise. The mixture was stirred at 0 °C for 15 min, then propargyl bromide (1.5 equiv) was added, and the mixture was allowed to reach room temperature and stirred overnight. Then, the mixture was cooled down to 0 °C, water was added, and the mixture was extracted three times with DCM; the combined organic layers were washed three times with water, dried over anhydrous Na₂SO₄, and filtered, and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography to obtain the pure *O*-propargyl product.

General Procedure B for the Synthesis of Terminal Alkynes with O Linker (GP3B).³² To a 0.5 M solution of furaldehyde (1.0 equiv, 10 mmol) in anhydrous THF, at 0 °C under a N₂ atmosphere, a solution of Grignard reagent (1.2 equiv) was added. The mixture was allowed to reach room temperature and stirred for 1–2 h (GC-MS monitoring). Then, a saturated NH₄Cl solution was added, and the mixture was extracted three times with DCM; the combined organic layers were dried over Na₂SO₄, filtered and the volatiles were evaporated under reduced pressure to obtain the crude furyl alcohol, which was used for the next step without further purification.

To a 1.0 M solution of the crude furanyl alcohol in anhydrous DMF, at 0 °C under a N₂ atmosphere, NaH (1.5 equiv) was added portionwise. The mixture was stirred at 0 °C for 15 min, then propargyl bromide (1.5 equiv) was added, and the mixture was allowed to reach room temperature and stirred overnight. Then, the mixture was cooled down to 0 °C, water was added, and the mixture was extracted three times with DCM; the combined organic layers were washed three times with water, dried over anhydrous Na₂SO₄, and filtered, and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography to obtain the pure *O*-propargyl product.

2-Methyl-5-((prop-2-yn-1-yloxy)methyl)furan, **int-10.** Synthesized according to the general procedure GP3A. Pale yellow oil, 1.01 g, 67% yield (2 steps). *R*_f 0.18 (99/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.25 (dd, 1H, *J* = 3.0, 0.6 Hz), 5.92 (dq, 1H, *J* = 3.1 Hz, 1.1 Hz), 4.50 (s, 2H), 4.16 (d, 2H, *J* = 2.4 Hz), 2.43 (s, 3H), 2.29 (d, 3H, *J* = 1.0 Hz). GC-MS *m/z* (%): 150 [M]⁺ (30), 110 (21), 95 (100).

2-Methyl-5-(1-(prop-2-yn-1-yloxy)propyl)furan, **int-11.** Synthesized according to the general procedure GP3B with EtMgBr (3.0 M in Et₂O). Yellow oil, 820 mg, 46% yield (2 steps). *R*_f 0.29 (98/2 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.17 (d, 1H, *J* = 3.0 Hz), 5.89 (dq, 1H, *J* = 3.1, 1.0 Hz), 4.34 (t, 1H, *J* = 7.1 Hz), 4.13 (dd, 1H, *J* = 15.8, 2.4 Hz), 3.95 (dd, 1H, *J* = 15.8, 2.4 Hz), 2.38 (t, 1H, *J* = 2.4 Hz), 2.27 (d, 3H, *J* = 1.0 Hz), 1.95–1.81 (m, 2H), 0.90 (t, 3H, *J* = 7.5 Hz). GC-MS *m/z* (%): 178 [M]⁺ (5), 149 (100), 123 (38), 120 (24), 109 (36), 91 (22), 77 (33), 43 (41).

2-(2,2-Dimethyl-1-(prop-2-yn-1-yloxy)propyl)-5-methylfuran, **int-12.** Synthesized according to the general procedure GP3B with *t*-BuMgCl (1.0 M in THF). Yellow oil, 720 mg, 35% yield (2 steps). *R*_f 0.45 (99/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.13 (d, 1H, *J* = 3.0 Hz), 5.91 (dd, 1H, *J* = 3.0, 1.0 Hz), 4.16 (dd, 1H, *J* = 15.6, 2.4 Hz), 4.12 (s, 1H), 3.87 (dd, 1H, *J* = 16.0, 2.3 Hz), 2.37 (t, 1H, *J* = 2.4 Hz), 2.28 (d, 3H, *J* = 0.8 Hz), 0.96 (s, 9H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 151.8 (Cq), 151.0 (Cq), 110.4 (CH), 105.9 (CH), 82.1 (CH), 80.3 (Cq), 74.0 (CH), 56.0 (CH₂),

35.3 (Cq), 26.4 (CH₃), 13.8 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₃H₁₈O₂Na⁺ 229.1199; found 229.1193.

General Procedure for the Sonogashira Coupling (GP4).³³ In a vial under a N₂ atmosphere, a 2.0 M solution of the terminal alkyne (1.0 equiv, 1.0–2.0 mmol) in anhydrous THF was prepared. The aryl iodide or aryl bromide (1.5 equiv) and Et₃N (2.0 equiv) were added, and the mixture was degassed for 10–15 min. Then, [(Ph₃P)₂PdCl₂] (0.02 equiv) and CuI (0.04 equiv) were added, and the mixture was stirred at room temperature (for ArI) or at 60 °C (for ArBr) overnight. After that time, a saturated NH₄Cl solution was added, and the mixture was extracted three times with EtOAc; the combined organic layers were dried over Na₂SO₄ and filtered, and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography to obtain pure aryl alkynes **1** as the product.

4-Methyl-N-((5-methylfuran-2-yl)methyl)-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide, 1a. Synthesized according to the general procedure GP4 at rt with PhI. White solid, 252 mg, 68% yield, mp 81–83 °C (Et₂O). *R*_f 0.17 (95/5 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.78 (d, 2H, *J* = 8.2 Hz), 7.31–7.23 (m, 5H), 7.09 (d, 2H, *J* = 8.1 Hz), 6.20 (d, 1H, *J* = 2.8 Hz), 5.88 (d, 1H, *J* = 2.0 Hz), 4.42 (s, 2H), 4.24 (s, 2H), 2.34 (s, 3H), 2.22 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 153.0 (Cq), 146.7 (Cq), 143.6 (Cq), 136.2 (Cq), 131.7 (CH), 129.6 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 122.4 (Cq), 111.2 (CH), 106.4 (CH), 85.9 (Cq), 81.9 (Cq), 43.4 (CH₂), 37.1 (CH₂), 21.6 (CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₂H₂₁NO₃SNa⁺ 402.1134; found 402.1127.

N-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-((5-methylfuran-2-yl)methyl)benzenesulfonamide, 1b. Synthesized according to the general procedure GP4 at rt with *p*-iodoanisole. White solid, 568 mg, 69% yield, mp 92–94 °C (Et₂O). *R*_f 0.28 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.79–7.77 (m, 2H), 7.27–7.25 (m, 2H), 7.06–7.03 (m, 2H), 6.79–6.76 (m, 2H), 6.19 (d, 1H, *J* = 3.0 Hz), 5.87 (dq, 1H, *J* = 3.0, 1.0 Hz), 4.41 (s, 2H), 4.22 (s, 2H), 3.80 (s, 3H), 2.36 (s, 3H), 2.22 (d, 3H, *J* = 0.9 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 159.8 (Cq), 153.0 (Cq), 146.8 (Cq), 143.5 (Cq), 136.3 (Cq), 133.2 (CH), 129.6 (CH), 128.0 (CH), 114.5 (Cq), 113.9 (CH), 111.1 (CH), 106.4 (CH), 85.8 (Cq), 80.4 (Cq), 55.4 (CH₃), 43.3 (CH₂), 37.2 (CH₂), 21.6 (CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₃H₂₃NO₄SNa⁺ 432.1240; found 432.1230.

N-(3-(4-Hydroxyphenyl)prop-2-yn-1-yl)-4-methyl-N-((5-methylfuran-2-yl)methyl)benzenesulfonamide, 1c. Synthesized according to the general procedure GP4 at rt with *p*-iodophenol. White solid, 236 mg, 60% yield, mp 100–103 °C (DCM/pentane). *R*_f 0.27 (8/2 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.79 (m, 2H), 7.27–7.24 (m, 2H), 7.01–6.98 (m, 2H), 6.73–6.70 (m, 2H), 6.19 (d, 1H, *J* = 3.1 Hz), 5.87 (dd, 1H, *J* = 3.0, 1.0 Hz), 5.03 (br s, 1H), 4.41 (s, 2H), 4.21 (s, 3H), 2.36 (s, 3H), 2.22 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 156.1 (Cq), 153.0 (Cq), 146.7 (Cq), 143.7 (Cq), 136.1 (Cq), 133.3 (CH), 129.6 (CH), 128.0 (CH), 115.4 (CH), 114.5 (Cq), 111.2 (CH), 106.4 (CH), 85.9 (Cq), 80.2 (Cq), 43.2 (CH₂), 37.2 (CH₂), 21.6 (CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₂₂H₂₂NO₄S⁺ 396.1264; found 396.1265.

4-Methyl-N-((5-methylfuran-2-yl)methyl)-N-(3-(*p*-tolyl)prop-2-yn-1-yl)benzenesulfonamide, 1d. Synthesized according to the general procedure GP5 at rt with *p*-iodotoluene. White solid, 272 mg, 69% yield, mp 58–60 °C (Et₂O). *R*_f 0.18 (93/7 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.79–7.77 (m, 2H), 7.26 (d, 2H, *J* = 7.9 Hz), 7.05 (d, 2H, *J* = 7.8 Hz), 6.99–6.97 (m, 2H), 6.19 (d, 1H, *J* = 3.0 Hz), 5.88–5.87 (m, 1H), 4.41 (s, 2H), 4.22 (s, 2H), 2.36 (s, 3H), 2.33 (s, 3H), 2.22 (d, 3H, *J* = 1.0 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 153.0 (Cq), 146.7 (Cq), 143.6 (Cq), 138.7 (Cq), 136.2 (Cq), 131.6 (CH), 129.6 (CH), 129.0 (CH), 128.0 (CH), 119.3 (Cq), 111.1 (CH), 106.4 (CH), 86.0 (Cq), 81.1 (Cq), 43.3 (CH₂), 37.1 (CH₂), 21.6 (2 x CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₃H₂₃NO₃SNa⁺ 416.1291; found 416.1281.

Methyl 4-(3-((4-Methyl-N-((5-methylfuran-2-yl)methyl)phenyl)sulfonamido)prop-1-yn-1-yl)benzoate, 1e. Synthesized according to the general procedure GP4 at rt with methyl *p*-iodobenzoate. White solid, 373 mg, 85% yield, mp 133–135 °C

(Et₂O). *R*_f 0.26 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.93–7.90 (m, 2H), 7.79–7.76 (m, 2H), 7.26–7.24 (m, 2H), 7.15–7.13 (m, 2H), 6.19 (d, 1H, *J* = 3.1 Hz), 5.89–5.87 (dq, 1H, *J* = 3.1, 1.2 Hz), 4.42 (s, 2H), 4.25 (s, 2H), 3.92 (d, 3H, *J* = 0.7 Hz), 2.34 (s, 3H), 2.21 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 166.5 (Cq), 153.1 (Cq), 146.6 (Cq), 143.7 (Cq), 136.1 (Cq), 131.6 (CH), 129.8 (Cq), 129.7 (CH), 129.4 (CH), 128.0 (CH), 127.0 (Cq), 111.2 (CH), 106.5 (CH), 85.1 (Cq), 85.1 (Cq), 52.4 (CH₃), 43.6 (CH₂), 37.1 (CH₂), 21.6 (CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₄H₂₃NO₅SNa⁺ 460.1189; found 460.1180.

N-(3-(4-Acetylphenyl)prop-2-yn-1-yl)-4-methyl-N-((5-methylfuran-2-yl)methyl)benzenesulfonamide, 1f. Synthesized according to the general procedure GP4 at rt with 4'-iodoacetophenone. White solid, 307 mg, 73% yield, mp 91–93 °C (Et₂O). *R*_f 0.32 (8/2 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.85–7.83 (m, 2H), 7.79–7.77 (m, 2H), 7.28–7.25 (m, 2H), 7.19–7.16 (m, 2H), 6.18 (d, 1H, *J* = 3.0 Hz), 5.88 (dq, 1H, *J* = 3.0, 1.0 Hz), 4.42 (s, 2H), 4.26 (s, 2H), 2.59 (s, 3H), 2.35 (s, 3H), 2.21 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.3 (Cq), 153.1 (Cq), 146.6 (Cq), 143.7 (Cq), 136.5 (Cq), 136.2 (Cq), 131.8 (CH), 129.7 (CH), 128.2 (CH), 128.0 (CH), 127.2 (Cq), 111.2 (CH), 106.5 (CH), 85.6 (Cq), 85.0 (Cq), 43.6 (CH₂), 37.1 (CH₂), 26.7 (CH₃), 21.6 (CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₂₄H₂₄NO₄S⁺ 422.1421; found 422.1416.

N-(3-(4-fluorophenyl)prop-2-yn-1-yl)-4-methyl-N-((5-methylfuran-2-yl)methyl)benzenesulfonamide, 1g. Synthesized according to the general procedure GP4 at rt with *p*-fluoriodobenzene. White solid, 339 mg, 86% yield, mp 86–88 °C (Et₂O). *R*_f 0.36 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.78 (d, 2H, *J* = 8.3 Hz), 7.27–7.25 (m, 2H), 7.10–7.06 (m, 2H), 6.97–6.92 (m, 2H), 6.18 (d, 1H, *J* = 3.0 Hz), 5.88 (d, 1H, *J* = 2.9 Hz), 4.41 (s, 2H), 4.22 (s, 2H), 2.36 (s, 3H), 2.21 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 162.6 (Cq, *d*, *J* = 250.0 Hz), 153.0 (Cq), 146.7 (Cq), 143.6 (Cq), 136.2 (Cq), 133.6 (CH, *d*, *J* = 8.6 Hz), 129.6 (CH), 128.0 (CH), 118.5 (Cq, *d*, *J* = 3.3 Hz), 115.6 (CH, *d*, *J* = 21.6 Hz), 111.1 (CH), 106.4 (CH), 84.8 (Cq), 81.7 (Cq), 43.4 (CH₂), 37.1 (CH₂), 21.6 (CH₃), 13.7 (CH₃). ¹⁹F NMR (564 MHz, CDCl₃) δ (ppm): –110.4 (tt, *J* = 8.6, 5.4 Hz). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₂H₂₀FNO₃SNa⁺ 420.1040; found 420.1027.

4-methyl-N-((5-methylfuran-2-yl)methyl)-N-(3-(thiophen-2-yl)prop-2-yn-1-yl)benzenesulfonamide, 1h. Synthesized according to the general procedure GP4 at 60 °C with 2-bromothiophene. White solid, 166 mg, 43% yield, mp 87–89 °C (Et₂O). *R*_f 0.34 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.79–7.76 (m, 2H), 7.30–7.27 (m, 2H), 7.21 (dd, 1H, *J* = 5.1, 1.2 Hz), 6.25 (dd, 1H, *J* = 3.6, 1.2 Hz), 6.92 (dd, 1H, *J* = 5.2, 3.6 Hz), 6.19 (d, 1H, *J* = 3.0 Hz), 5.88 (dq, 1H, *J* = 3.0, 1.0 Hz), 4.39 (s, 2H), 4.25 (s, 2H), 2.38 (s, 3H), 2.22 (d, 3H, *J* = 1.1 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 153.1 (Cq), 146.6 (Cq), 143.7 (Cq), 136.0 (Cq), 132.4 (CH), 129.7 (CH), 127.9 (CH), 127.4 (CH), 126.9 (CH), 122.3 (Cq), 111.2 (CH), 106.5 (CH), 85.9 (Cq), 79.1 (Cq), 43.5 (CH₂), 37.3 (CH₂), 21.7 (CH₃), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₂₀H₂₀NO₃S₂⁺ 386.0879; found 386.0879.

4-Methyl-N-((5-methylfuran-2-yl)methyl)-N-(3-(naphthalen-1-yl)prop-2-yn-1-yl)benzenesulfonamide, 1i. Synthesized according to the general procedure GP4 at rt with 1-iodonaphthalene. White solid, 324 mg, 75% yield, mp 107–109 °C (Et₂O). *R*_f 0.41 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.90 (d, 1H, *J* = 7.7 Hz), 7.84–7.79 (m, 4H), 7.53–7.47 (m, 2H), 7.17 (d, 2H, *J* = 8.0 Hz), 6.25 (d, 1H, *J* = 3.0 Hz), 5.91–5.89 (m, 1H), 4.52 (s, 2H), 4.41 (s, 2H), 2.24 (s, 3H), 2.17 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 153.1 (Cq), 146.7 (Cq), 143.7 (Cq), 136.1 (Cq), 133.2 (Cq), 130.7 (CH), 129.7 (CH), 129.0 (CH), 128.4 (CH), 128.1 (Cq), 127.9 (CH), 126.9 (CH), 126.5 (CH), 126.1 (CH), 125.1 (CH), 120.1 (Cq), 11.2 (CH), 106.5 (CH), 86.8 (Cq), 84.2 (Cq), 43.5 (CH₂), 37.3 (CH₂), 21.4 (CH₃), 13.8 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₆H₂₃NO₃SNa⁺ 452.1291; found 452.1278.

4-Methyl-N-((5-phenylfuran-2-yl)methyl)-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide, 1j. Synthesized according to the general procedure GP4 at rt with PhI. White solid, 357 mg, 81% yield,

110–111 °C (CHCl₃). *R*_f 0.41 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.80 (d, 2H, *J* = 8.3 Hz), 7.60–7.58 (m, 2H), 7.35 (t, 2H, *J* = 7.7 Hz), 7.31–7.29 (m, 1H), 7.26–7.22 (m, 5H), 7.12 (dd, 2H, *J* = 8.3, 1.2 Hz), 6.56 (d, 1H, *J* = 3.3 Hz), 6.41 (d, 1H, *J* = 3.3 Hz), 4.56 (s, 2H), 4.31 (s, 2H), 2.32 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 154.5 (Cq), 148.3 (Cq), 143.7 (Cq), 136.1 (Cq), 131.7 (CH), 130.6 (Cq), 129.7 (CH), 128.7 (Cq), 128.6 (CH), 128.3 (CH), 127.9 (CH), 127.7 (CH), 123.9 (CH), 122.3 (Cq), 112.3 (CH), 105.8 (CH), 86.0 (Cq), 81.9 (Cq), 43.5 (CH₂), 37.5 (CH₂), 21.5 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₂₇H₂₄NO₃S⁺ 442.1471; found 442.1463.

N-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-((5-phenylfuran-2-yl)methyl)benzenesulfonamide, 1k. Synthesized according to the general procedure GP4 at rt with *p*-iodoanisole. White solid, 435 mg, 93% yield, 130–132 °C (EtOAc). *R*_f 0.24 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.81–7.79 (m, 2H), 7.59–7.57 (m, 2H), 7.37–7.34 (m, 2H), 7.27–7.24 (m, 3H), 7.08–7.05 (m, 2H), 6.78–6.75 (m, 2H), 6.56 (d, 1H, *J* = 3.3 Hz), 6.41 (d, 1H, *J* = 3.3 Hz), 4.55 (s, 2H), 4.29 (s, 2H), 3.80 (s, 3H), 2.33 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 159.8 (Cq), 154.5 (Cq), 148.4 (Cq), 143.6 (Cq), 136.2 (Cq), 133.2 (CH), 130.6 (Cq), 129.7 (CH), 128.7 (CH), 127.9 (CH), 127.6 (CH), 123.9 (CH), 114.4 (Cq), 113.9 (CH), 112.2 (CH), 105.8 (CH), 85.9 (Cq), 80.4 (Cq), 55.4 (CH₃), 43.4 (CH₂), 37.5 (CH₂), 21.6 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₈H₂₅NO₄Na⁺ 494.1397; found 494.1385.

4-Methyl-N-(3-phenylprop-2-yn-1-yl)-N-((5-(thiophen-2-yl)furan-2-yl)methyl)benzenesulfonamide, 1l. Synthesized according to the general procedure GP4 at rt with PhI. Yellow solid, 318 mg, 71%, mp 90–92 °C (Et₂O). *R*_f 0.23 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.80 (d, 2H, *J* = 8.3 Hz), 7.31–7.28 (m, 1H), 7.27–7.23 (m, 4H), 7.21 (dd, 1H, *J* = 5.0, 1.0 Hz), 7.19 (dd, 1H, *J* = 3.6, 1.0 Hz), 7.14–7.11 (m, 2H), 7.01 (dd, 1H, *J* = 5.0, 3.6 Hz), 6.41 (d, 1H, *J* = 3.3 Hz), 6.38 (d, 1H, *J* = 3.4 Hz), 4.53 (s, 2H), 4.30 (s, 2H), 2.32 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 150.0 (Cq), 148.0 (Cq), 143.8 (Cq), 136.0 (Cq), 133.4 (Cq), 131.7 (CH), 129.7 (CH), 128.6 (CH), 128.3 (CH), 127.9 (CH), 127.2 (CH), 124.5 (CH), 123.0 (CH), 122.3 (Cq), 112.2 (CH), 105.8 (CH), 86.1 (Cq), 81.8 (Cq), 43.4 (CH₂), 37.4 (CH₂), 21.6 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₅H₂₁NO₃S₂Na⁺ 470.0855; found 470.0840.

N-((2,2'-Bifuran)-5-ylmethyl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide, 1m. Synthesized according to the general procedure GP4 at rt with PhI. Yellow solid, 303 mg, 70% yield, mp 84–86 °C (CHCl₃). *R*_f 0.54 (7/3 DCM/PE). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.29 (d, 2H, *J* = 8.3 Hz), 7.40–7.39 (m, 1H), 7.31–7.28 (m, 1H), 7.27–7.23 (m, 4H), 7.11–7.09 (m, 2H), 6.49 (d, 1H, *J* = 3.4 Hz), 6.46 (d, 1H, *J* = 3.3 Hz), 6.44 (dd, 1H, *J* = 3.4, 1.8 Hz), 6.39 (d, 1H, *J* = 3.3 Hz), 4.53 (s, 2H), 4.38 (s, 2H), 2.33 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 148.1 (Cq), 147.1 (Cq), 146.3 (Cq), 143.8 (Cq), 142.0 (CH), 136.0 (Cq), 131.7 (CH), 129.7 (CH), 128.6 (CH), 128.3 (CH), 128.0 (CH), 122.3 (Cq), 112.0 (CH), 111.5 (CH), 105.9 (CH), 105.8 (CH), 86.1 (Cq), 81.7 (Cq), 43.4 (CH₂), 37.4 (CH₂), 21.6 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₅H₂₁NO₄Na⁺ 454.1083; found 454.1078.

2-Methyl-5-(((3-phenylprop-2-yn-1-yl)oxy)methyl)furan, 1n. Synthesized according to the general procedure GP4 at rt with PhI. Colorless oil, 166 mg, 74% yield. *R*_f 0.21 (99/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.48–7.44 (m, 2H), 7.34–7.30 (m, 3H), 6.28 (d, 1H, *J* = 3.0 Hz), 5.94 (dq, 1H, *J* = 3.0, 1.0 Hz), 4.56 (s, 2H), 4.39 (s, 2H), 2.30 (d, 3H, *J* = 0.8 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 153.1 (Cq), 149.2 (Cq), 131.9 (CH), 128.6 (CH), 128.4 (CH), 122.8 (Cq), 111.2 (CH), 106.4 (CH), 86.6 (Cq), 85.0 (Cq), 63.5 (CH₂), 57.6 (CH₂), 13.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₅H₁₅O₂⁺ 227.1067; found 227.1067.

2-(((3-(4-Methoxyphenyl)prop-2-yn-1-yl)oxy)methyl)-5-methylfuran, 1o. Synthesized according to the general procedure GP4 at rt with *p*-iodoanisole. Colorless oil, 170 mg, 66% yield. *R*_f 0.28 (96/4 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.41–7.38 (m, 2H), 6.86–6.83 (m, 2H), 6.27 (d, 1H, *J* = 3.0 Hz), 5.93 (dd, 1H, *J* = 3.1, 1.0 Hz), 4.55 (s, 2H), 4.38 (s, 2H), 3.81 (s, 3H), 2.29 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 159.8 (Cq), 153.1 (Cq),

149.3 (Cq), 133.4 (CH), 114.9 (Cq), 114.0 (CH), 111.2 (CH), 106.4 (CH), 86.6 (Cq), 83.5 (Cq), 63.4 (CH₂), 57.7 (CH₂), 55.4 (CH₃), 13.8 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₆H₁₇O₃⁺ 257.1172; found 257.1175.

Methyl 4-(3-((5-Methylfuran-2-yl)methoxy)prop-1-yn-1-yl)benzoate, 1p. Synthesized according to the general procedure GP4 at rt with methyl *p*-iodobenzoate. White solid, 211 mg, 75% yield, mp 45–47 °C (Et₂O). *R*_f 0.15 (96/4 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 8.00–7.98 (m, 2H), 7.52–7.50 (m, 2H), 6.28 (d, 1H, *J* = 3.1 Hz), 5.94 (dq, 1H, *J* = 3.0, 1.1 Hz), 4.56 (s, 2H), 4.40 (s, 2H), 3.92 (s, 3H), 2.30 (d, 3H, *J* = 1.0 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 166.6 (Cq), 153.2 (Cq), 149.1 (Cq), 131.8 (CH), 129.9 (Cq), 129.6 (CH), 127.5 (Cq), 111.4 (CH), 106.5 (CH), 88.1 (Cq), 85.9 (Cq), 63.7 (CH₂), 57.5 (CH₂), 52.4 (CH₃), 13.8 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₇H₁₆O₄Na⁺ 307.0941; found 307.0940.

2-Methyl-5-((1-((3-phenylprop-2-yn-1-yl)oxy)propyl)furan, 1q. Synthesized according to the general procedure GP4 at rt with PhI. Colorless oil, 193 mg, 76% yield. *R*_f 0.34 (99/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.45–7.42 (m, 2H), 7.32–7.29 (m, 3H), 6.22 (d, 1H, *J* = 3.0 Hz), 5.93–5.91 (m, 1H), 4.42 (t, 1H, *J* = 7.1 Hz), 4.36 (d, 1H, *J* = 15.8 Hz), 4.21 (d, 1H, *J* = 15.8 Hz), 2.28 (d, 3H, *J* = 0.9 Hz), 2.00–1.85 (m, 2H), 0.93 (t, 3H, *J* = 7.5 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 152.3 (Cq), 151.6 (Cq), 131.8 (CH), 128.4 (CH), 128.3 (CH), 122.9 (Cq), 109.9 (CH), 106.0 (CH), 85.9 (Cq), 85.6 (Cq), 75.3 (CH), 56.3 (CH₂), 27.1 (CH₂), 13.7 (CH₃), 10.3 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₇H₁₈O₂Na⁺ 277.1199; found 277.1197.

2-(2,2-Dimethyl-1-((3-phenylprop-2-yn-1-yl)oxy)propyl)-5-methylfuran, 1r. Synthesized according to the general procedure GP4 at rt with PhI. Colorless oil, 165 mg, 58% yield. *R*_f 0.20 (99/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.44–7.42 (m, 2H), 7.32–7.29 (m, 3H), 6.16 (d, 1H, *J* = 3.0 Hz), 5.92 (dq, 1H, *J* = 3.0, 1.0 Hz), 4.38 (d, 1H, *J* = 16.1 Hz), 4.19 (s, 1H), 4.11 (d, 1H, *J* = 16.1 Hz), 2.28 (s, 3H), 0.98 (s, 9H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 151.9 (Cq), 151.2 (Cq), 131.8 (CH), 128.4 (CH), 128.4 (CH), 123.1 (Cq), 110.3 (CH), 105.9 (CH), 85.9 (Cq), 82.2 (Cq), 56.9 (CH₂), 35.4 (Cq), 26.4 (CH₃), 13.8 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₉H₂₂O₂Na⁺ 305.1512; found 305.1500.

N-(Furan-2-ylmethyl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide, 1s. Synthesized according to the general procedure GP4 at rt with PhI. White solid, 280 mg, 77% yield, mp 68–70 °C (Et₂O). *R*_f 0.18 (95/5 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.79 (d, 2H, *J* = 8.3 Hz), 7.38 (q, 1H, *J* = 0.9 Hz), 7.31–7.23 (m, 5H), 7.11–7.08 (m, 2H), 6.35–6.32 (m, 2H), 4.48 (s, 2H), 4.24 (s, 2H), 2.35 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 148.9 (Cq), 143.7 (Cq), 143.2 (CH), 136.1 (Cq), 131.7 (CH), 129.7 (CH), 128.6 (CH), 128.3 (CH), 128.0 (CH), 122.3 (Cq), 110.6 (CH), 110.1 (CH), 86.0 (Cq), 81.7 (Cq), 43.2 (CH₂), 37.3 (CH₂), 21.6 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₁H₁₉NO₃Na⁺ 388.0978; found 388.0974.

General Procedure for Gold(I)-Catalyzed Synthesis of Dihydropyridinones and Pyranones (GP5). A solution of the furan-yne substrate (1.0 equiv, 0.2 mmol) and 4-nitropyridine *N*-oxide (1.2 equiv) in DCE (0.1 M with respect to the furan-yne) was prepared, then [(IPr)Au(NTf₂)] (0.05 equiv) was added, and the mixture was stirred at room temperature for 20 h. Then, MsOH (5.0 equiv) was added, and the mixture was stirred at room temperature for 1 h. A few drops of Et₃N were added, and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography to afford pure dihydropyridinones or pyranones **2** as the product.

(E)-5-(3-Oxobut-1-en-1-yl)-4-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2a. Synthesized according to the general procedure GP5. Yellow solid, 57 mg, 72% yield, mp 176–177 °C (MeCN, decomposition). The reaction was also repeated at 1.3 mmol scale, obtaining 367 mg (71% yield) of product. *R*_f 0.21 (75/25 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.73–7.69 (m, 2H), 7.39–7.34 (m, 5H), 7.03 (d, 1H, *J* = 16.6 Hz), 6.87–6.84 (m, 2H), 6.46 (d, 1H, *J* = 16.6 Hz), 4.31 (s, 2H), 4.04 (s, 2H), 2.44 (s, 3H), 2.19 (s,

3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.3 (Cq), 190.4 (Cq), 144.9 (Cq), 144.1 (Cq), 141.4 (Cq), 137.9 (CH), 133.4 (Cq), 132.2 (CH), 131.3 (Cq), 130.5 (CH), 130.4 (CH), 129.2 (CH), 128.3 (CH), 127.8 (CH), 53.3 (CH_2), 45.1 (CH_2), 28.0 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{22}\text{NO}_4\text{S}^+$ 396.1264; found 396.1262.

(E)-4-(4-Methoxyphenyl)-5-(3-oxobut-1-en-1-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2b. Synthesized according to the general procedure GP5. Yellow solid, 64 mg, 75% yield, mp 150–153 °C (decomposition). R_f 0.24 (7/3 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.69 (d, 2H, $J = 8.3$ Hz), 7.35 (d, 2H, $J = 8.1$ Hz), 7.09 (d, 1H, $J = 16.6$ Hz), 6.90–6.87 (m, 2H), 6.82–6.79 (m, 2H), 6.45 (d, 1H, $J = 16.6$ Hz), 4.29 (s, 2H), 4.03 (s, 2H), 3.83 (s, 3H), 2.44 (s, 3H), 2.22 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.4 (Cq), 190.7 (Cq), 160.3 (Cq), 144.8 (Cq), 143.5 (Cq), 140.9 (Cq), 138.2 (CH), 133.3 (Cq), 132.0 (CH), 131.8 (CH), 130.4 (CH), 127.8 (CH), 123.3 (Cq), 113.8 (CH), 55.4 (CH_3), 53.3 (CH_2), 45.2 (CH_2), 28.1 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ $\text{C}_{23}\text{H}_{23}\text{NO}_5\text{SNa}^+$ 448.1189; found 448.1094.

(E)-4-(4-Hydroxyphenyl)-5-(3-oxobut-1-en-1-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2c. Synthesized according to the general procedure GP5. Yellow solid, 42 mg, 52% yield, mp 170–174 °C (decomposition). R_f 0.25 (9/1 DCM/EtOAc). ^1H NMR (600 MHz, CD_3OD) δ (ppm): 7.74–7.72 (m, 2H), 7.42 (d, 2H, $J = 7.9$ Hz), 7.07 (d, 1H, $J = 16.4$ Hz), 6.78–6.75 (m, 2H), 6.69 (d, 1H, $J = 16.4$ Hz), 6.64–6.62 (m, 2H), 4.51 (s, 2H), 4.17 (s, 2H), 2.45 (s, 3H), 2.24 (s, 3H), 2.19 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CD_3OD) δ (ppm): 200.5 (Cq), 193.7 (Cq), 160.2 (Cq), 146.9 (Cq), 145.9 (Cq), 143.0 (Cq), 140.2 (CH), 136.9 (Cq), 134.1 (CH), 133.4 (CH), 132.3 (CH), 129.6 (CH), 124.6 (Cq), 116.5 (CH), 55.2 (CH_2), 47.1 (CH_2), 29.1 (CH_3), 22.3 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_5\text{SNa}^+$ 434.1033; found 434.1024.

(E)-5-(3-Oxobut-1-en-1-yl)-4-(p-tolyl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2d. Synthesized according to the general procedure GP5. Yellow solid, 71 mg, 86% yield, mp 166–167 °C (Et_2O). R_f 0.25 (75/25 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.71–7.69 (m, 2H), 7.35 (d, 2H, $J = 8.0$ Hz), 7.16 (d, 2H, $J = 7.8$ Hz), 7.07 (d, 1H, $J = 16.6$ Hz), 6.75–6.72 (m, 2H), 6.45 (d, 1H, $J = 16.5$ Hz), 4.30 (s, 2H), 4.04 (s, 2H), 2.44 (s, 3H), 2.36 (s, 3H), 2.21 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.4 (Cq), 190.6 (Cq), 144.8 (Cq), 143.7 (Cq), 141.4 (Cq), 139.3 (Cq), 138.1 (CH), 133.4 (Cq), 131.9 (CH), 130.4 (CH), 129.1 (CH), 128.2 (Cq), 127.8 (CH), 53.3 (CH_2), 45.1 (CH_2), 28.1 (CH_3), 21.7 (CH_3), 21.5 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{24}\text{NO}_4\text{S}^+$ 410.1421; found 410.1415.

Methyl (E)-4-(3-Oxo-5-(3-oxobut-1-en-1-yl)-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)benzoate, 2e. Synthesized according to the general procedure GP5. Light orange solid, 52 mg, 57% yield, mp 186–191 °C (decomposition). R_f 0.21 (65/35 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 8.04–8.02 (m, 2H), 7.71–7.69 (m, 2H), 7.36 (d, 2H, $J = 8.0$ Hz), 6.95 (d, 1H, $J = 16.6$ Hz) superimposed to 6.94–6.92 (m, 2H), 6.50 (d, 1H, $J = 16.5$ Hz), 4.34 (s, 2H), 4.06 (s, 2H), 3.93 (s, 3H), 2.45 (s, 3H), 2.20 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.0 (Cq), 190.0 (Cq), 166.6 (Cq), 145.0 (Cq), 144.8 (Cq), 140.4 (Cq), 137.0 (CH), 136.0 (Cq), 133.4 (Cq), 132.7 (CH), 130.7 (Cq), 130.6 (CH), 130.5 (CH), 129.5 (CH), 127.8 (CH), 53.2 (CH_2), 52.5 (CH_3), 45.1 (CH_2), 28.2 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{24}\text{NO}_6\text{S}^+$ 454.1319; found 454.1307.

(E)-4-(4-Acetylphenyl)-5-(3-oxobut-1-en-1-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2f. Synthesized according to the general procedure GP5. White solid, 37 mg, 43% yield, mp 161–164 °C (decomposition). R_f 0.24 (6/4 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.96–7.93 (m, 2H), 7.71 (d, 2H, $J = 8.3$ Hz), 7.37 (d, 2H, $J = 8.0$ Hz), 6.96 (d, 1H, $J = 16.4$ Hz) superimposed to 6.98–6.95 (m, 2H), 6.51 (d, 1H, $J = 16.4$ Hz), 4.34 (s, 2H), 4.06 (s, 2H), 2.62 (s, 3H), 2.45 (s, 3H), 2.22 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.6 (Cq), 196.9 (Cq), 190.0 (Cq), 145.0 (Cq), 144.8 (Cq), 140.4 (Cq), 137.4 (Cq), 136.9 (CH), 136.2 (Cq), 133.4 (Cq), 132.7 (CH), 130.8 (CH), 130.5 (CH), 128.2 (CH), 127.8 (CH), 53.2 (CH_2),

45.1 (CH_2), 28.4 (CH_3), 26.8 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{23}\text{NO}_5\text{SNa}^+$ 460.1189; found 460.1182.

(E)-4-(4-Fluorophenyl)-5-(3-oxobut-1-en-1-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2g. Synthesized according to the general procedure GP5. Yellow solid, 40 mg, 48% yield, mp 149–153 °C (decomposition). R_f 0.16 (7/3 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.70 (d, 2H, $J = 8.3$ Hz), 7.36 (d, 2H, $J = 7.9$ Hz), 7.08–7.05 (m, 2H), 7.01 (d, 1H, $J = 16.4$ Hz), 6.87–6.83 (m, 2H), 6.49 (d, 1H, $J = 16.5$ Hz), 4.31 (s, 2H), 4.04 (s, 2H), 2.44 (s, 3H), 2.22 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.1 (Cq), 190.4 (Cq), 163.2 (Cq, $d, J = 250.1$ Hz), 144.9 (Cq), 144.4 (Cq), 140.3 (Cq), 137.4 (CH), 133.3 (Cq), 132.4 (CH, $d, J = 8.7$ Hz), 132.3 (CH), 130.4 (CH), 127.8 (CH), 127.1 (Cq), 115.5 (CH, $d, J = 21.5$ Hz), 53.3 (CH_2), 45.1 (CH_2), 28.3 (CH_3), 21.7 (CH_3). ^{19}F NMR (564 MHz, CDCl_3) δ (ppm): (–111.4)–(–112.0) (m). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{20}\text{FNO}_4\text{SNa}^+$ 436.0989; found 436.0969.

(E)-5-(3-Oxobut-1-en-1-yl)-4-(thiophen-2-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2h. Synthesized according to the general procedure GP5. Yellow solid, 24 mg, 30% yield, mp 146–148 °C (Et_2O , decomposition). R_f 0.23 (7/3 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.70–7.67 (m, 2H), 7.52 (dd, 1H, $J = 5.2, 1.2$ Hz), 7.36 (d, 1H, $J = 16.5$ Hz), 7.32 (d, 2H, $J = 8.0$ Hz), 7.06 (dd, 1H, $J = 5.1, 3.6$ Hz), 6.81 (dd, 1H, $J = 3.6, 1.2$ Hz), 6.55 (d, 1H, $J = 16.5$ Hz), 4.31 (s, 2H), 4.1 (s, 2H), 2.39 (s, 3H), 2.29 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.3 (Cq), 189.9 (Cq), 144.9 (Cq), 143.9 (Cq), 138.0 (CH), 134.4 (Cq), 133.2 (Cq), 132.4 (CH), 131.8 (CH), 131.1 (Cq), 130.5 (CH), 130.4 (CH), 127.7 (CH), 126.7 (CH), 53.3 (CH_2), 45.7 (CH_2), 28.3 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_4\text{S}_2^+$ 402.0828; found 402.0827.

(E)-4-(Naphthalen-1-yl)-5-(3-oxobut-1-en-1-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2i. Synthesized according to the general procedure GP5. Yellow solid, 65 mg, 73% yield, mp 131–141 °C (decomposition). R_f 0.16 (7/3 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.89 (d, 1H, $J = 8.3$ Hz), 7.87 (d, 1H, $J = 8.2$ Hz), 7.77 (d, 2H, $J = 8.4$ Hz), 7.49–7.44 (m, 2H), 7.42 (d, 2H, $J = 7.9$ Hz), 7.38–7.35 (m, 1H), 7.20 (d, 1H, $J = 8.4$ Hz), 6.91 (dd, 1H, $J = 7.0, 1.0$ Hz), 6.79 (d, 1H, $J = 16.6$ Hz), 6.45 (d, 1H, $J = 16.6$ Hz), 4.42 (d, 1H, $J = 17.2$ Hz), 4.34 (d, 1H, $J = 17.4$ Hz), 4.14 (dd, 1H, $J = 16.7, 1.3$ Hz), 4.04 (dd, 1H, $J = 16.7, 1.4$ Hz), 2.49 (s, 3H), 2.01 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 197.3 (Cq), 190.3 (Cq), 152.2 (CH), 146.4 (Cq), 145.0 (Cq), 140.8 (Cq), 137.5 (CH), 133.6 (Cq), 133.0 (Cq), 132.5 (CH), 132.0 (Cq), 130.5 (CH), 129.8 (CH), 129.4 (Cq), 128.8 (CH), 128.4 (CH), 127.9 (CH), 126.8 (CH), 126.4 (CH), 125.1 (CH), 125.0 (CH), 53.3 (CH_2), 44.9 (CH_2), 27.7 (CH_3), 21.8 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_4\text{S}^+$ 446.1421; found 446.1410.

(E)-5-(3-Oxo-3-phenylprop-1-en-1-yl)-4-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2j. Synthesized according to the general procedure GP5. Yellow solid, 57 mg, 62% yield, mp 175–178 °C (decomposition). R_f 0.23 (8/2 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.92 (d, 2H, $J = 7.2$ Hz), 7.72 (d, 2H, $J = 8.3$ Hz), 7.64–7.60 (m, 1H), 7.51 (t, 2H, $J = 7.8$ Hz), 7.37–7.34 (m, 5H), 7.29 (d, 2H, $J = 1.3$ Hz), 6.82 (dd, 2H, $J = 7.7, 1.6$ Hz), 4.49 (s, 2H), 4.11 (s, 2H), 2.44 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 190.6 (Cq), 189.3 (Cq), 144.9 (Cq), 144.1 (Cq), 141.5 (Cq), 139.2 (CH), 137.2 (Cq), 133.7 (CH), 133.7 (Cq), 131.3 (Cq), 130.5 (CH), 130.5 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.3 (CH), 127.8 (CH), 127.7 (CH), 53.3 (CH_2), 45.2 (CH_2), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{23}\text{NO}_4\text{SNa}^+$ 480.1240; found 480.1220.

(E)-4-(4-Methoxyphenyl)-5-(3-oxo-3-phenylprop-1-en-1-yl)-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2k. Synthesized according to the general procedure GP5. Yellow solid, 77 mg, 78% yield, mp 159–163 °C (decomposition). R_f 0.40 (99/1 DCM/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.96–7.94 (m, 2H), 7.73–7.70 (m, 2H), 7.63 (tt, 1H, $J = 7.1, 1.2$ Hz), 7.54–7.51 (m, 2H), 7.36 (d, 1H, $J = 16.0$ Hz) superimposed to 7.34 (d, 2H, $J = 7.9$ Hz), 7.28 (d, 1H, $J = 16.0$ Hz), 6.88–6.86 (m, 2H), 6.79–6.77 (m, 2H), 4.47 (s, 2H), 4.09 (s, 2H), 3.82 (s, 3H), 2.43 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 190.9 (Cq), 189.3 (Cq), 160.3 (Cq), 144.9 (Cq), 143.4 (Cq), 141.1 (Cq), 139.7 (CH), 137.7 (Cq), 133.7 (CH), 133.7 (Cq), 132.1 (CH),

130.5 (CH), 129.1 (CH), 128.8 (CH), 127.7 (CH), 127.3 (CH), 123.4 (Cq), 113.8 (CH), 55.4 (CH₃), 53.4 (CH₂), 45.4 (CH₂), 21.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₈H₂₅NO₅Na⁺ 510.1346; found 510.1324.

(E)-5-(3-Oxo-3-(thiophen-2-yl)prop-1-en-1-yl)-4-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2l. Synthesized according to the general procedure GP5. Yellow solid, 58 mg, 63% yield, mp 145–149 °C (decomposition). *R_f* 0.24 (7/3 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.82 (dd, 1H, *J* = 3.8, 1.0 Hz), 7.74 (dd, 1H, *J* = 4.9, 1.0 Hz), 7.72–7.70 (m, 2H), 7.37–7.32 (m, 5H) superimposed to 7.32 (d, 1H, *J* = 15.6 Hz), 7.21 (dd, 1H, *J* = 4.9, 3.9 Hz), 7.14 (d, 1H, *J* = 15.8 Hz), 6.80–8.78 (m, 2H), 4.49 (s, 2H), 4.12 (s, 2H), 2.44 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 190.6 (Cq), 180.9 (Cq), 144.9 (Cq), 144.8 (Cq), 143.8 (Cq), 141.6 (Cq), 138.6 (CH), 135.4 (CH), 133.8 (Cq), 132.8 (CH), 131.2 (Cq), 130.5 (CH), 130.5 (CH), 129.2 (CH), 128.7 (CH), 128.3 (CH), 127.7 (CH), 127.5 (CH), 53.4 (CH₂), 45.3 (CH₂), 21.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₅H₂₁NO₄S₂Na⁺ 486.0804; found 486.0784.

(E)-5-(3-(Furan-2-yl)-3-oxoprop-1-en-1-yl)-4-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one, 2m. Synthesized according to the general procedure GP5. Yellow solid, 37 mg, 41% yield, mp 159–162 °C (decomposition). *R_f* 0.20 (99/1 DCM/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.73–7.71 (m, 2H), 7.68 (dd, 1H, *J* = 1.7, 0.8 Hz), 7.37–7.31 (m, 7H), 7.22 (d, 1H, *J* = 16.1 Hz), 6.80–6.78 (m, 2H), 6.63 (dd, 1H, *J* = 3.6, 1.7 Hz), 4.50 (s, 2H), 4.12 (s, 2H), 2.44 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 190.6 (Cq), 176.7 (Cq), 153.3 (Cq), 147.3 (CH), 144.9 (Cq), 143.9 (Cq), 141.6 (Cq), 138.5 (CH), 133.9 (Cq), 131.2 (Cq), 130.6 (CH), 130.5 (CH), 129.2 (CH), 128.3 (CH), 127.7 (CH), 127.2 (CH), 118.7 (CH), 113.2 (CH), 53.4 (CH₂), 45.2 (CH₂), 21.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₂₅H₂₂NO₅S⁺ 448.1213; found 448.1202.

(E)-5-(3-Oxobut-1-en-1-yl)-4-phenyl-2H-pyran-3(6H)-one, 2n. Synthesized according to the general procedure GP5. Yellow solid, 38 mg, 78% yield, mp 104–106 °C (Et₂O). *R_f* 0.44 (6/4 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.46–7.41 (m, 3H), 7.20–7.17 (m, 2H) superimposed to 7.15 (d, 1H, *J* = 16.7 Hz), 6.32 (d, 1H, *J* = 16.7 Hz), 4.72 (s, 2H), 4.34 (s, 2H), 2.19 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.6 (Cq), 193.2 (Cq), 146.6 (Cq), 140.1 (Cq), 137.5 (CH), 132.0 (CH), 131.3 (Cq), 130.7 (CH), 129.1 (CH), 128.4 (CH), 72.5 (CH₂), 65.6 (CH₂), 27.6 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₅H₁₅O₃⁺ 243.1016; found 243.1017.

(E)-4-(4-Methoxyphenyl)-5-(3-oxobut-1-en-1-yl)-2H-pyran-3(6H)-one, 2o. Synthesized according to the general procedure GP5. Yellow solid, 16 mg, 29% yield. *R_f* 0.35 (75/25 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.21 (d, 1H, *J* = 16.8 Hz), 7.15–7.12 (m, 2H), 6.98–6.95 (m, 2H), 6.32 (d, 1H, *J* = 16.7 Hz), 4.70 (s, 2H), 4.33 (s, 2H), 3.86 (s, 3H), 2.21 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.7 (Cq), 193.6 (Cq), 160.3 (Cq), 145.0 (Cq), 139.7 (Cq), 137.9 (CH), 132.3 (CH), 131.6 (CH), 123.4 (Cq), 113.9 (CH), 72.6 (CH₂), 65.7 (CH₂), 55.5 (CH₃), 27.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₆H₁₇O₄⁺ 273.1121; found 273.1124.

Methyl 4-(3-Oxo-5-(3-oxobut-1-en-1-yl)-3,6-dihydro-2H-pyran-4-yl)benzoate, 2p. Synthesized according to the general procedure GP5. Yellow solid, 45 mg, 75% yield, *E/Z* ratio 40/60. *R_f* 0.13 (7/3 PE/EtOAc). **(E)-2p** ¹H NMR (600 MHz, CDCl₃) δ (ppm): 8.11 (d, 2H, *J* = 8.1 Hz), 7.27 (d, 2H, *J* = 8.3 Hz), 7.07 (d, 1H, *J* = 16.6 Hz), 6.35 (d, 1H, *J* = 16.7 Hz), 4.73 (s, 2H), 4.35 (s, 2H), 3.95 (s, 3H), 2.19 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.2 (Cq), 192.7 (Cq), 166.7 (Cq), 147.3 (Cq), 139.2 (Cq), 136.6 (CH), 136.0 (Cq), 132.5 (CH), 130.8 (CH), 130.7 (Cq), 129.6 (CH), 72.4 (CH₂), 65.5 (CH₂), 52.4 (CH₃), 27.8 (CH₃). **(Z)-2p** ¹H NMR (600 MHz, CDCl₃) δ (ppm): 8.02 (d, 2H, *J* = 8.2 Hz), 7.20 (d, 2H, *J* = 8.3 Hz), 6.25 (d, 1H, *J* = 12.3 Hz), 6.21 (d, 1H, *J* = 12.3 Hz), 4.56 (s, 2H), 4.35 (s, 2H), 3.92 (s, 3H), 2.23 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 198.3 (Cq), 193.0 (Cq), 166.8 (Cq), 153.2 (Cq), 137.3 (Cq), 135.9 (Cq), 135.3 (CH), 131.2 (CH), 130.5 (CH), 130.2 (Cq), 129.3 (CH), 72.8 (CH₂), 67.6 (CH₂), 52.4 (CH₃), 31.1 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₇H₁₆O₅Na⁺ 323.0890; found 323.0873.

(E)-6-Ethyl-5-(3-oxobut-1-en-1-yl)-4-phenyl-2H-pyran-3(6H)-one, 2q. Synthesized according to the general procedure GP5.

Yellow oil, 33 mg, 62% yield. *R_f* 0.12 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.34–7.27 (m, 3H), 7.07–7.04 (m, 2H), 6.29 (dd, 1H, *J* = 12.2, 1.6 Hz), 6.10 (d, 1H, *J* = 12.2 Hz), 4.75–4.72 (m, 1H), 4.42 (d, 1H, *J* = 16.4 Hz), 4.32 (dd, 1H, *J* = 16.4, 1.3 Hz), 2.08 (s, 3H), 1.79–1.73 (m, 2H), 1.03 (t, 3H, *J* = 7.4 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.7 (Cq), 193.3 (Cq), 156.9 (Cq), 136.8 (CH), 134.9 (Cq), 133.2 (Cq), 130.1 (CH), 129.6 (CH), 128.1 (CH), 128.1 (CH), 77.2 (CH), 70.5 (CH₂), 30.9 (CH₃), 25.9 (CH₂), 10.1 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₇H₁₉O₃⁺ 271.1329; found 271.1338.

(E)-6-(tert-Butyl)-5-(3-oxobut-1-en-1-yl)-4-phenyl-2H-pyran-3(6H)-one, 2r. Synthesized according to the general procedure GP5. Brown oil, 28 mg, 47% yield. *R_f* 0.17 (95/5 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.34–7.27 (m, 3H), 7.05–7.02 (m, 2H), 6.41 (d, 1H, *J* = 12.1 Hz), 6.00 (d, 1H, *J* = 12.1 Hz), 4.48 (d, 1H, *J* = 16.5 Hz), 4.41 (s, 1H) superimposed to 4.39 (d, 1H, *J* = 16.7 Hz), 1.08 (s, 9H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.6 (Cq), 193.2 (Cq), 139.3 (Cq), 135.6 (Cq), 133.9 (Cq), 129.7 (CH), 129.7 (CH), 128.3 (CH), 128.3 (CH), 128.0 (CH), 84.2 (CH), 70.4 (CH₂), 37.6 (Cq), 31.0 (CH₃), 28.2 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₁₉H₂₂O₃Na⁺ 321.1461; found 321.1443.

Gold(I)-Catalyzed Synthesis of (E)-4-(4-Benzoyl-1-tosyl-2,5-dihydro-1H-pyrrol-3-yl)but-3-en-2-one, 3a. A solution of **1a** (1.0 equiv, 0.2 mmol) and 8-methylquinoline *N*-oxide (1.2 equiv) in DCE (0.1 M with respect to the furan-yne) was prepared, then [(IPr)Au(NTf₂)] (0.05 equiv) was added, and the mixture was stirred at 80 °C for 6 h. Then, a few drops of Et₃N were added, and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography to afford pure dihydropyrrole **3a** as the product. Yellow solid, 21 mg, 27% yield, mp 139–140 °C (Et₂O). *R_f* 0.24 (75/25 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.77–7.75 (m, 2H), 7.67–7.65 (m, 2H), 7.64–7.61 (m, 1H), 7.49–7.46 (m, 2H), 7.37 (d, 2H, *J* = 8.1 Hz), 6.93 (d, 1H, *J* = 16.4 Hz), 6.01 (d, 1H, *J* = 16.4 Hz), 4.56 (t, 2H, *J* = 4.1 Hz), 4.46 (t, 2H, *J* = 4.1 Hz), 2.46 (s, 3H), 2.06 (s, 3H). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 197.7 (Cq), 191.8 (Cq), 144.4 (Cq), 140.3 (Cq), 138.5 (Cq), 137.2 (Cq), 134.3 (CH), 133.3 (Cq), 132.3 (CH), 132.2 (CH), 130.3 (CH), 129.3 (CH), 129.1 (CH), 127.7 (CH), 57.5 (CH₂), 55.2 (CH₂), 27.3 (CH₃), 21.7 (CH₃). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₂H₂₁NO₄Na⁺ 418.1083; found 418.1057.

Gold(I)-Catalyzed Synthesis of (E)-4-Methyl-*N*-(5-methylfuran-2-yl)methyl-*N*-(3-oxo-3-phenylprop-1-en-1-yl)-benzenesulfonamide, 4a. A solution of **1a** (1.0 equiv, 0.2 mmol) and 8-methylquinoline *N*-oxide (1.2 equiv) in DCE (0.1 M with respect to the furan-yne) was prepared, then [(MorDalPhos)Au(NCMe)]SbF₆ (0.05 equiv) was added, and the mixture was stirred at room temperature for 20 h. Then, a few drops of Et₃N were added, and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography to afford pure vinyl ketone **4a** as the product. White solid, 59 mg, 74% yield, mp 127–128 °C (EtOAc). *R_f* 0.20 (9/1 PE/EtOAc). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 8.26 (d, 1H, *J* = 13.6 Hz), 7.88–7.85 (m, 2H), 7.71 (d, 2H, *J* = 8.4 Hz), 7.54–7.51 (m, 1H), 7.46–7.42 (m, 2H), 7.29 (d, 2H, *J* = 8.0 Hz), 6.50 (d, 1H, *J* = 13.6 Hz), 6.07 (d, 1H, *J* = 3.1 Hz), 5.85–5.84 (m, 1H), 4.74 (s, 2H), 2.42 (s, 3H), 2.07 (d, 3H, *J* = 1.1 Hz). ¹³C{¹H} NMR (150 MHz, CDCl₃) δ (ppm): 189.4 (Cq), 152.4 (Cq), 146.0 (Cq), 144.9 (Cq), 142.6 (CH), 138.7 (Cq), 135.7 (Cq), 132.5 (CH), 130.1 (CH), 128.6 (CH), 128.2 (CH), 127.6 (CH), 110.7 (CH), 106.7 (CH), 104.0 (CH), 43.3 (CH₂), 21.7 (CH₃), 13.5 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₂₂H₂₂NO₄S⁺ 396.1264; found 396.1263.

Synthesis of 5-(3-Oxo-1-(phenylthio)butyl)-4-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one, 5. A reported procedure was followed.¹⁵ To a 0.1 M solution of **2a** (1.0 equiv, 0.1 mmol) in DCM, at 0 °C under air, thiophenol (1.2 equiv) and Et₃N (0.1 equiv) were added. The mixture was allowed to warm to room temperature and was stirred for 2 h. Then, the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography to obtain pure sulfide **5** as the product. Two diastereoisomers, arising from the chiral carbon and atropisomerism, could be separated. Colorless oil, 34 mg, 68% overall yield. **5-DI** *R_f* 0.15

(8/2 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.70–7.68 (m, 2H), 7.34 (d, 2H, $J = 7.9$ Hz), 7.32–7.30 (m, 3H), 7.29–7.26 (m, 1H), 7.25–7.22 (m, 2H), 7.12–7.10 (m, 2H), 6.81–6.78 (m, 2H), 4.17 (dd, 1H, $J = 18.4, 1.6$ Hz), 4.06 (dd, 1H, $J = 18.4, 1.6$ Hz), 3.98 (dd, 1H, $J = 16.7, 1.6$ Hz), 3.79 (dd, 1H, $J = 16.7, 1.7$ Hz), 3.38 (t, 1H, $J = 7.7$ Hz), 2.65 (dd, 1H, $J = 14.8, 7.4$ Hz), 2.59 (dd, 1H, $J = 14.9, 8.1$ Hz), 2.45 (s, 3H), 2.07 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 203.3 (Cq), 190.1 (Cq), 152.6 (Cq), 144.6 (Cq), 138.0 (Cq), 133.4 (Cq), 132.9 (CH), 132.7 (Cq), 131.8 (Cq), 130.3 (CH), 129.5 (CH), 129.5 (CH), 128.8 (CH), 128.7 (CH), 128.4 (CH), 127.8 (CH), 54.5 (CH), 52.8 (CH_2), 49.2 (CH_2), 34.1 (CH_2), 27.6 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{NO}_4\text{S}_2\text{Na}^+$ 528.1274, found 528.1265. **5-D2** R_f 0.08 (8/2 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.75 (d, 2H, $J = 8.2$ Hz), 7.40–7.35 (m, 3H), 7.33–7.30 (m, 1H), 7.26–7.21 (m, 6H), 7.20–7.14 (m, 2H), 4.56 (dd, 1H, $J = 17.1, 1.6$ Hz), 4.32 (t, 1H, $J = 7.6$ Hz), 3.93 (dd, 1H, $J = 17.0, 1.7$ Hz) superimposed to 3.92 (dd, 1H, $J = 16.8, 1.6$ Hz), 3.79 (dd, 1H, $J = 16.7, 1.7$ Hz), 2.86 (dd, 1H, $J = 17.1, 7.5$ Hz), 2.65 (dd, 1H, $J = 17.1, 7.5$ Hz), 2.46 (s, 3H), 2.10 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 203.8 (Cq), 190.7 (Cq), 152.2 (Cq), 144.7 (Cq), 137.3 (Cq), 134.6 (CH), 133.0 (Cq), 131.9 (Cq), 131.8 (Cq), 130.3 (CH), 129.6 (CH), 129.5 (CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 128.1 (CH), 53.4 (CH_2), 46.7 (CH), 45.7 (CH_2), 44.9 (CH_2), 30.4 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{NO}_4\text{S}_2\text{Na}^+$ 528.1274; found 528.1265.

Synthesis of 5-(3-Oxobutyl)-4-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one, 6. To 0.1 M solution of **2a** (1.0 equiv, 0.1 mmol) in EtOAc, Pd/C (10% w/w) was added. The flask was evacuated and backfilled with H_2 three times, and then the mixture was stirred at 50°C under a H_2 atmosphere for 2 h. After that time, the mixture was cooled down to room temperature and filtered over a Celite pad, and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography to afford the partially hydrogenated product **6**. Colorless oil, 28 mg, 71% yield. R_f 0.22 (65/35 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.72–7.69 (m, 2H), 7.41–7.36 (m, 2H), 7.34–7.29 (m, 3H), 6.84–6.82 (m, 2H), 4.05 (s, 2H), 3.91 (s, 2H), 2.46 (s, 3H), 2.43 (t, 2H, $J = 7.7$ Hz), 2.33 (t, 2H, $J = 7.6$ Hz), 2.05 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 206.2 (Cq), 190.2 (Cq), 154.7 (Cq), 144.7 (Cq), 137.3 (Cq), 133.1 (Cq), 132.9 (Cq), 130.3 (CH), 129.4 (CH), 128.6 (CH), 128.2 (CH), 127.9 (CH), 52.9 (CH_2), 48.1 (CH_2), 40.9 (CH_2), 29.8 (CH_2), 26.9 (CH_2), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{24}\text{NO}_4\text{S}^+$ 398.1421; found 398.1418.

Synthesis of (E)-5-(3-Hydroxybut-1-en-1-yl)-4-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-ol, 7. To 0.1 M solution of **2a** (1.0 equiv, 0.1 mmol) in DCM/MeOH 1/1 at 0°C , NaBH_4 (1.0 equiv) was added, and the mixture was allowed to warm to room temperature and stirred for 1.5 h. Then, the solvent was evaporated under reduced pressure to a quarter of the initial volume. Water was added, and the mixture was extracted three times with DCM; the combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography to afford the diol product **7** as a 1/1 mixture of diastereoisomers. Colorless oil, 21 mg, 53% yield. R_f 0.24 (6/4 PE/EtOAc). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.76 (d, 2H, $J = 8.2$ Hz) superimposed to 7.76 (d, 2H, $J = 8.3$ Hz), 7.40–7.37 (m, 4H), 7.26–7.34 (m, 4H), 7.33–7.30 (m, 2H), 7.17–7.14 (m, 4H), 6.12 (d, 2H, $J = 16.2$ Hz), 5.71 (dd, 1H, $J = 16.2, 6.4$ Hz) superimposed to 5.71 (dd, 1H, $J = 16.2, 6.7$ Hz), 4.42–4.38 (m, 2H), 4.25–4.17 (m, 4H), 3.74 (dd, 1H, $J = 11.8, 3.4$ Hz), 3.68 (dd, 1H, $J = 11.8, 3.6$ Hz), 3.44 (d, 1H, $J = 15.6$ Hz), 3.40 (d, 1H, $J = 15.6$ Hz), 3.02 (dd, 1H, $J = 11.9, 3.3$ Hz), 2.95 (dd, 1H, $J = 11.8, 3.2$ Hz), 2.46 (s, 6H), 1.23 (d, 3H, $J = 6.4$ Hz), 1.20 (d, 3H, $J = 6.3$ Hz). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ (ppm): 144.3 (Cq), 144.2 (Cq), 138.4 (Cq), 138.4 (Cq), 138.2 (Cq), 138.1 (Cq), 134.7 (CH), 134.6 (CH), 132.9 (Cq), 132.8 (Cq), 130.1 (CH), 129.3 (CH), 129.3 (CH), 128.8 (Cq), 128.8 (Cq), 128.6 (CH), 128.0 (CH), 128.0 (CH), 126.2 (CH), 125.9 (CH), 69.1 (CH), 69.0 (CH), 67.8 (CH), 67.8 (CH), 50.7 (CH_2), 50.6 (CH_2), 45.5 (CH_2), 45.5 (CH_2), 23.5 (CH_3), 23.5 (CH_3), 21.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_4\text{SNa}^+$ 422.4942; found 422.4946.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.1c00746>.

Complete list of optimization experiments, reaction schemes for the synthesis of substrates, crystallographic details, computational details, NMR spectra of new compounds (PDF)

FAIR data, including the primary NMR FID files, for compounds **1a–s**, **2a–r**, **int-7**, **int-8**, **int-9**, **int-12**, **5**, **6**, **7** (ZIP)

Accession Codes

CCDC 2067578–2067580 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Cristina Prandi: conceptualization, writing, funding acquisition, supervision. Stefano Nejrotti: conceptualization, investigation, data analysis, writing. Francesco Marra, Emanuele Priola: investigation, data analysis. Andrea Maranzana: investigation, data analysis, writing. All authors have given approval to the final version of the manuscript.

Notes

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■ REFERENCES

- (1) (a) Hashmi, A. S. K. Homogeneous Gold Catalysts and Alkynes: A Successful Liaison. *Gold Bull.* **2003**, *36*, 3–9. (b) Hashmi, A. S. K. Gold-Catalyzed Organic Reactions. *Chem. Rev.* **2007**, *107*, 3180–3211. (c) Li, Z.; Brouwer, C.; He, C. Gold-Catalyzed Organic Transformations. *Chem. Rev.* **2008**, *108*, 3239–3265. (d) Dorel, R.; Echavarren, A. M. Gold(I)-Catalyzed Activation of Alkynes for the

Construction of Molecular Complexity. *Chem. Rev.* **2015**, *115*, 9028–9072.

(2) (a) First report: Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. A New Gold-Catalyzed C–C Bond Formation. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285–2288. (b) Kirillova, M. S.; Miloserdov, F. M.; Echavarren, A. M. Hydroarylation of Alkynes using Cu, Ag, and Au Catalysts. *Catalytic Hydroarylation of Carbon-Carbon Multiple Bonds* **2017**, 217–303. (c) Muratore, M. E.; Echavarren, A. M. Gold-catalyzed hydroarylation of alkynes. *PATAI'S Chemistry of Functional Groups* **2015**, 1–96. (d) Nejrrotti, S.; Prandi, C. Gold Catalysis and Furans: A Powerful Match for Synthetic Connections. *Synthesis* **2021**, *53*, 1046–1060.

(3) (a) Hashmi, A. S. K.; Frost, T. M.; Bats, J. Highly Selective Gold-Catalyzed Arene Synthesis. *J. Am. Chem. Soc.* **2000**, *122*, 11553–11554. (b) Hashmi, A. S. K.; Grundl, L. Gold Catalysis: Five New Bonds by a Domino Hydroarylation/Cycloisomerization. *Tetrahedron* **2005**, *61*, 6231–6236. (c) Hashmi, A. S. K.; Weyrauch, J. P.; Kurpejović, E.; Frost, T. M.; Miehlisch, B.; Frey, W.; Bats, J. W. Gold Catalysis: Phenol Synthesis in the Presence of Functional Groups. *Chem. - Eur. J.* **2006**, *12*, 5806–5814. (d) Hashmi, A. S. K.; Salathé, R.; Frey, W. Gold Catalysis: No Steric Limitations in the Phenol Synthesis. *Chem. - Eur. J.* **2006**, *12*, 6991–6996. (e) Hashmi, A. S. K.; Kurpejović, E.; Wölfle, M.; Frey, W.; Bats, J. W. Gold Catalysis: Oxepines from γ -Alkynylfurans. *Adv. Synth. Catal.* **2007**, *349*, 1743–1750. (f) Hashmi, A. S. K.; Rudolph, M.; Siehl, H.-U.; Tanaka, M.; Bats, J. W.; Frey, W. Gold Catalysis: Deuterated Substrates as the Key for an Experimental Insight into the Mechanism and Selectivity of the Phenol Synthesis. *Chem. - Eur. J.* **2008**, *14*, 3703–3708. (g) Hashmi, A. S. K.; Rudolph, M.; Huck, J.; Frey, W.; Bats, J. W.; Hamzić, M. Gold Catalysis: Switching the Pathway of the Furan-Yne Cyclization. *Angew. Chem., Int. Ed.* **2009**, *48*, 5848–5852. (h) Rudolph, M.; McCreery, M. Q.; Frey, W.; Hashmi, A. S. K. High Chemoselectivity in the Phenol Synthesis. *Beilstein J. Org. Chem.* **2011**, *7*, 794–801. (i) Hashmi, A. S. K.; Häffner, T.; Rudolph, M.; Rominger, F. Gold Catalysis: Domino Reaction of Endiynes to Highly Substituted Phenols. *Chem. - Eur. J.* **2011**, *17*, 8195–8201. (j) Zeiler, A.; Ziegler, M. J.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Scope and Limitations of the Intermolecular Furan-Yne Cyclization. *Adv. Synth. Catal.* **2015**, *357*, 1507–1514.

(4) Leboeuf, D.; Gaydou, M.; Wang, Y.; Echavarren, A. M. Intermolecular reactions of gold(I)-carbenes with furans by related mechanisms. *Org. Chem. Front.* **2014**, *1*, 759–764.

(5) Yang, J. M.; Tang, X. Y.; Shi, M. Gold(I)-Catalyzed Intramolecular Cycloisomerization of Propargylic Esters with Furan Rings. *Chem. - Eur. J.* **2015**, *21*, 4534–4540.

(6) α -Oxo gold carbenes are in equilibrium with the corresponding carbenoid species, generated by attack of the pyridine onto the carbene center. (a) Schulz, J.; Jasikova, L.; Skriba, A.; Roithova, J. Role of Gold(I) α -Oxo Carbenes in the Oxidation Reactions of Alkynes Catalyzed by Gold(I) Complexes. *J. Am. Chem. Soc.* **2014**, *136*, 11513–11523. (b) Schulz, J.; Jašík, J.; Gray, A.; Roithová, J. Formation of Oxazoles from Elusive Gold(I) α -Oxocarbenes: A Mechanistic Study. *Chem. - Eur. J.* **2016**, *22*, 9827–9834.

(7) Seminal reports: (a) Li, G.; Zhang, L. Gold-Catalyzed Intramolecular Redox Reaction of Sulfinyl Alkynes: Efficient Generation of α -Oxo Gold Carbenoids and Application in Insertion into R-CO Bonds. *Angew. Chem., Int. Ed.* **2007**, *46*, 5156–5159. (b) Shapiro, N. D.; Toste, F. D. Rearrangement of Alkynyl Sulfoxides Catalyzed by Gold(I) Complexes. *J. Am. Chem. Soc.* **2007**, *129*, 4160–4161. Reviews on the topic: (c) Yeom, H.-S.; Shin, S. Catalytic Access to α -Oxo Gold Carbenes by N–O Bond Oxidants. *Acc. Chem. Res.* **2014**, *47*, 966–977. (d) Zhang, L. A Non-Diazo Approach to α -Oxo Gold Carbenes via Gold-Catalyzed Alkyne Oxidation. *Acc. Chem. Res.* **2014**, *47*, 877–888. (e) Bhunia, S.; Ghosh, P.; Patra, S. R. Gold-Catalyzed Oxidative Alkyne Functionalization by N–O/S–O/C–O Bond Oxidants. *Adv. Synth. Catal.* **2020**, *362*, 3664–3708. For a recent systematic study on this chemistry, see: (f) Schießl, J.; Stein, P. M.; Stirn, J.; Emler, K.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Strategic Approach on N-Oxides in Gold Catalysis – A Case Study. *Adv. Synth. Catal.* **2019**, *361*, 725–738.

(8) (a) Oppedisano, A.; Prandi, C.; Venturello, P.; Deagostino, A.; Goti, G.; Scarpi, D.; Occhiato, E. G. Synthesis of Vinylogous Amides by Gold(I)-Catalyzed Cyclization of *N*-Boc-Protected 6-Alkynyl-3,4-dihydro-2*H*-pyridines. *J. Org. Chem.* **2013**, *78*, 11007–11016. (b) Scarpi, D.; Begliomini, S.; Prandi, C.; Oppedisano, A.; Deagostino, A.; Gómez-Bengo, E.; Fiser, B.; Occhiato, E. G. Gold-Catalyzed Synthesis of Exocyclic Vinylogous Amides and β -Amino Ketones: A Detailed Study on the 5-*exo*/6-*endo*-*dig* Selectivity, Methodology and Scope. *Eur. J. Org. Chem.* **2015**, *2015*, 3251–3265. (c) Nejrrotti, S.; Prina Cerai, G.; Oppedisano, A.; Maranzana, A.; Occhiato, E. G.; Scarpi, D.; Deagostino, A.; Prandi, C. A Gold(I)-Catalyzed Oxidative Rearrangement of Heterocycle-Derived 1,3-Enynes Provides an Efficient and Selective Route to Divinyl Ketones. *Eur. J. Org. Chem.* **2017**, *2017*, 6228–6238. (d) Nejrrotti, S.; Ghinato, S.; Gini, E. C.; Scarpi, D.; Occhiato, E. G.; Maranzana, A.; Prandi, C. Gold(I)-Catalyzed Hydroarylation of Lactam-Derived Enynes as an Entry to Tetrahydrobenzo[*g*]quinolines. *Eur. J. Org. Chem.* **2020**, *2020*, 646–653.

(9) The “classical” furan-yne with a terminal alkyne (**int-6** in the **SI**) only underwent the Hashmi’s phenol synthesis, and oxidative reaction was not observed under the tested reaction conditions.

(10) CCDC codes 2067578–2067580 contain the supplementary crystallographic data for **2a**, **3a**, and **4a**.

(11) (a) Ito, M.; Kawasaki, R.; Kanyiva, K. S.; Shibata, T. Catalytic Dearomative Spirocyclization via Gold Carbene Species Derived from Ynamides: Efficient Synthesis of 2-Azaspiro[4.5]decan-3-ones. *Chem. - Eur. J.* **2018**, *24*, 3721–3724 see also: (b) Hashmi, A. S. K. Homogeneous Gold Catalysis Beyond Assumptions and Proposals—Characterized Intermediates. *Angew. Chem., Int. Ed.* **2010**, *49*, 5232–5241. (c) Lauterbach, T.; Asiri, A. M.; Hashmi, A. S. K. Organometallic Intermediates of Gold Catalysis. *Adv. Organomet. Chem.* **2014**, *62*, 261–297.

(12) Hashmi, A. S. K.; Wölfle, M.; Ata, F.; Hamzić, M.; Salathé, R.; Frey, W. Gold Catalysis: Dihydroisobenzofurans and Isochromanes by the Intramolecular Furan/Alkyne Reaction. *Adv. Synth. Catal.* **2006**, *348*, 2501–2508.

(13) (a) Lu, B.; Li, C.; Zhang, L. Gold-Catalyzed Highly Regioselective Oxidation of C–C Triple Bonds without Acid Additives: Propargyl Moieties as Masked α,β -Unsaturated Carbonyls. *J. Am. Chem. Soc.* **2010**, *132*, 14070–14072. (b) Davies, P. W.; Cremonesi, A.; Martin, N. Site-Specific Introduction of Gold-Carbenoids by Intermolecular Oxidation of Ynamides or Ynol Ethers. *Chem. Commun.* **2011**, *47*, 379–381. (c) Ji, K.; D’souza, B.; Nelson, J.; Zhang, L. Gold-Catalyzed Oxidation of Propargylic Ethers with Internal C–C Triple Bonds: Impressive Regioselectivity Enabled by Inductive Effect. *J. Organomet. Chem.* **2014**, *770*, 142–145.

(14) Ji, K.; Zheng, Z.; Wang, Z.; Zhang, L. Enantioselective Oxidative Gold Catalysis Enabled by a Designed Chiral P,N-Bidentate Ligand. *Angew. Chem., Int. Ed.* **2015**, *54*, 1245–1249.

(15) Jouha, J.; Buttard, F.; Lorion, M.; Berthonneau, C.; Khouili, M.; Hiebel, M.-A.; Guillaumet, G.; Brière, J.-F. o.; Suzenet, F. Domino Aza-Michael-*ih*-Diels–Alder Reaction to Various 3-Vinyl-1,2,4-triazines: Access to Polysubstituted Tetrahydro-1,6-naphthyridines. *Org. Lett.* **2017**, *19*, 4770–4773.

(16) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Non-covalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Functionals. *Theor. Chem. Acc.* **2008**, *120*, 215–241.

(17) Dapprich, S.; Komáromi, I.; Byun, K. S.; Morokuma, K.; Frisch, M. J. A New ONIOM Implementation in Gaussian 98. 1. The Calculation of Energies, Gradients and Vibrational Frequencies and Electric Field Derivatives. *J. Mol. Struct.: THEOCHEM* **1999**, *462*, 1–21.

(18) Weigend, F. Accurate Coulomb-Fitting Basis Sets for H to Rn. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057–1065.

(19) Collins, J. B.; von R. Schleyer, P.; Binkley, J. S.; Pople, J. A. Self-Consistent Molecular Orbital Methods. XVII. Geometries and Binding

Energies of Second-Row Molecules. A Comparison of Three Basis Sets. *J. Chem. Phys.* **1976**, *64*, 5142–5151.

(20) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

(21) Lu, T.; Chen, F. Multiwfn: a Multifunctional Wavefunction Analyzer. *J. Comput. Chem.* **2012**, *33*, 580–592.

(22) Johnson, E. R.; Keinan, S.; Mori-Sánchez, P.; Contreras-García, J.; Cohen, A. J.; Yang, W. Revealing Noncovalent Interactions. *J. Am. Chem. Soc.* **2010**, *132*, 6498–6506.

(23) Liu, S. Steric Effects: a Quantitative Description from Density Functional Theory. *J. Chem. Phys.* **2007**, *126*, 244103.

(24) Deng, K.; Bensari-Bouguerra, A.; Whetstone, J.; Cohen, T. Cyclization by Intramolecular Carbolithiation of Alkyl- and Vinyl-lithiums Prepared by the Action of Aromatic Radical Anions on Phenyl Thioethers. High Stereoselectivity in the Cyclization Accelerated by an Allylic Lithium Oxyanion. *J. Org. Chem.* **2006**, *71*, 2360–2372.

(25) Geyer, A. G.; McClellan, W. J.; Rockway, T. W.; Stewart, K. D.; Weitzberg, M.; Wendt, M. D. Urokinase inhibitors. US6,258,822B1, 2001.

(26) Bussolari, J. C.; Rehborn, D. C. Preparation of 5-Aryl Furfurals and Aryl Thiophene-2-carboxaldehydes via Palladium-Catalyzed C–C Bond Formation in Aqueous Media. *Org. Lett.* **1999**, *1*, 965–967.

(27) Martín-Matute, B.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. Intramolecular Reactions of Alkynes with Furans and Electron Rich Arenes Catalyzed by PtCl₂: The Role of Platinum Carbenes as Intermediates. *J. Am. Chem. Soc.* **2003**, *125*, 5757–5766.

(28) Lin, J.; Jin, X.; Bu, Y.; Cao, D.; Zhang, N.; Li, S.; Sun, Q.; Tan, C.; Gao, C.; Jiang, Y. Efficient Synthesis of RITA and its Analogues: Derivation of Analogues with Improved Antiproliferative Activity via Modulation of p53/miR-34a Pathway. *Org. Biomol. Chem.* **2012**, *10*, 9734–9746.

(29) Terai, T.; Kohno, M.; Boncompain, G.; Sugiyama, S.; Saito, N.; Fujikake, R.; Ueno, T.; Komatsu, T.; Hanaoka, K.; Okabe, T. *J. Am. Chem. Soc.* **2015**, *137*, 10464–10467.

(30) Carrettin, S.; Blanco, M. C.; Corma, A.; Hashmi, A. S. K. Artificial Ligands of Streptavidin (ALiS): Discovery, Characterization, and Application for Reversible Control of Intracellular Protein Transport. *Adv. Synth. Catal.* **2006**, *348*, 1283–1288.

(31) Feng, W.; Jiang, D.; Kee, C. W.; Liu, H.; Tan, C. H. Bicyclic Guanidine Catalyzed Asymmetric Tandem Isomerization Intramolecular-Diels–Alder Reaction: The First Catalytic Enantioselective Total Synthesis of (+)-alpha-Yohimbine. *Chem. - Asian J.* **2016**, *11*, 390–394.

(32) Hashmi, A. S. K.; Hengst, T.; Lothschütz, C.; Rominger, F. New and Easily Accessible Nitrogen Acyclic Gold(I) Carbenes: Structure and Application in the Gold-Catalyzed Phenol Synthesis as well as the Hydration of Alkynes. *Adv. Synth. Catal.* **2010**, *352*, 1315–1337.

(33) Hashmi, A. S. K.; Häffner, T.; Yang, W.; Pankajakshan, S.; Schäfer, S.; Schultes, L.; Rominger, F.; Frey, W. Gold Catalysis: Non-Spirocyclic Intermediates in the Conversion of Furanyne by the Formal Insertion of an Alkyne into an Aryl–Alkyl C–C Single Bond. *Chem. - Eur. J.* **2012**, *18*, 10480–10486.