Direct Synthesis of α-Iodoenones by IPy_2BF_4-Promoted Rearrangement of Propargylic Esters.

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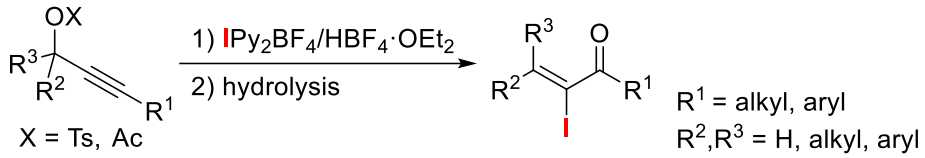


ABSTRACT: A direct access to α-iodoeones from iodonium ion and propargylic tosylates or acetates is described. Bis(pyridine) iodonium tetrafluoroborate (IPy_2BF_4, Barluenga's reagent) promotes the rearrangement of these propargylic alcohol derivatives in mild conditions. The transformation gives β-unsubstituted, β-monosubstituted and β,β-disubstituted α-iodoenones in high yields. β-Substituted-α-iodoenones are obtained with excellent (*Z*)-selectivity.

■ INTRODUCTION

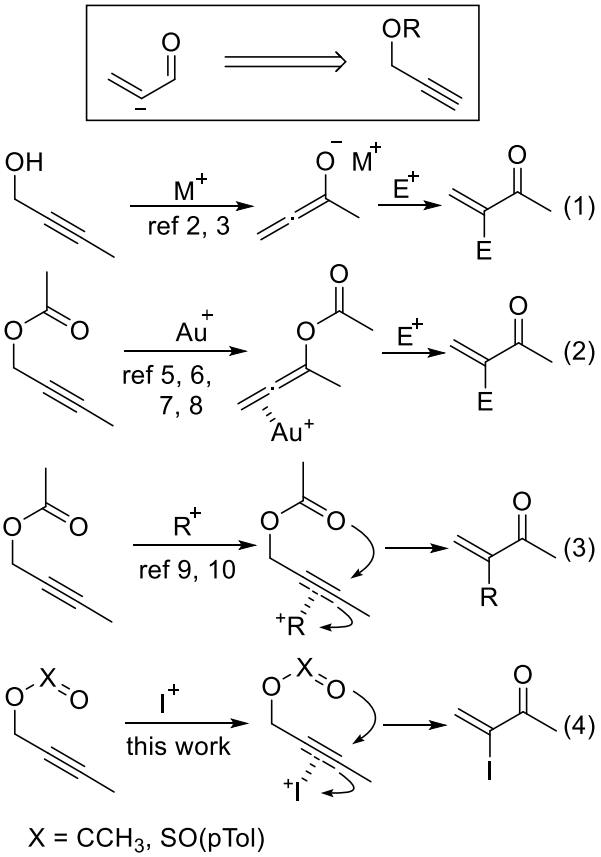
The availability of propargylic alcohol derivatives and their ability to undergo rearrangement transformations to allenol derivatives, have recently inspired many researchers to use them as α-acylvinyl anion equivalents, and thereby as an alternative to the classical Morita-Baylis-Hillman reaction for the synthesis of α-substituted-α,β-unsaturated carbonyl compounds.[1]

In this regard, it has been described recently the generation of metal allenolate species, ready to couple with different electrophiles, by rearrangement of α-hydroxypropargylsilanes,[2] or by bimetallic dual-catalyzed rearrangement/coupling reactions of propargylic alcohols[3] (Scheme 1, eq 1). Additionally, Au and Ag-catalyzed rearrangements of propargylic esters to allenyl carboxylates, followed by intramolecular cyclization

have been intensively studied.[4] However, there are few examples of the intermolecular version of this reaction such as the Au-catalyzed coupling of propargylic esters with isochromane acetal analogs,[5] in situ generated carbocations,[6] arylboronic acids,[7] or NIS (*N*-iodosuccinimide)[8] (Scheme 1, eq 2).

Very recently, it was demonstrated that rearrangements of propargylic esters can be induced directly by a carbocation[9] or an oxocarbenium ion[10] to the direct formation of the coupling products without the use of a metal catalyst (Scheme 1, eq 3). In the other hand, we previously proposed that reactive iodonium ion, generated from bis(pyridine) iodonium tetrafluroborate (IPy_2BF_4, Barluenga's reagent),[11] promotes the activation of the C-C triple bond moiety in the presence of nucleophiles.[12] This led us to consider that this iodinating agent could mediate the rearrangement reaction of propargylic ester derivatives to provide directly α-iodoenones without the use of a metal catalyst (Scheme 1 eq 4).

Scheme 1. Examples of propargylic alcohol derivatives as α-acylvinyl equivalents.



α-Iodoenones are useful intermediates in synthesis[13] because of their ability to undergo transition metal-catalyzed cross-coupling reactions that makes them good precursors of enones bearing different class of α-carbon substituents.[14] In the past decade, some authors have described more efficient and versatile methods for the synthesis of α-iodoenones based in the rearrangement of propargylic alcohol derivatives, that improve the limitations from the use of enone derivatives as precursors.[15] Interestingly, apart from some studies limited to tertiary propargylic alcohols using iodine and an oxidant,[16] and a recent example through oxidation of internal alkynes in the presence of NIS,[17] most general methods require the employment of at least one metal catalytic species to promote the reaction.[3c, 8, 18]

Considering this, we describe herein the rearrangement reaction of propargylic alcohol derivatives promoted by reactive iodonium ion, and its use as a new, versatile and general metal-free synthetic method of α-iodoenones.

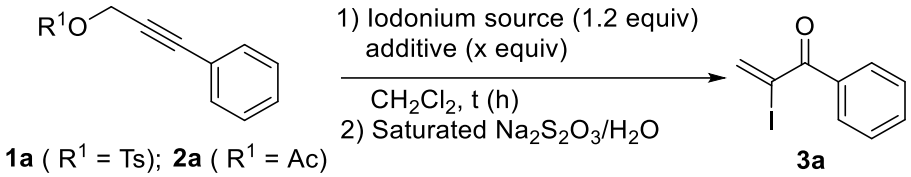
■ RESULTS AND DISCUSSION

We include in our study, apart from the propargylic acetate derivatives, the corresponding tosylates since these compounds had been reported to participate in rearrangement reactions.[19] Moreover, we first focused in the use of primary propargylic alcohols esters, taking into account the few examples described in the literature.[3c]

Thus, our preliminary study included the corresponding tosylate **1a** (R^1 = Ts), and acetate **2a** (R^1 = Ac) of 3-phenyl-2-propynol (Table 1). First, tosylate **1a** was treated with different iodonium sources (I_2, ICl, NIS, IPy_2BF_4) in a 0.05M CH_2Cl_2 solution at rt, none conversion was observed after 14 h of reaction when NIS, I_2 and IPy_2BF_4 were used (entries 1-3).[20] On the other hand, the reaction in the same conditions with ICl allowed to obtain iodoenone **3a** in a low yield (17%, entry 4). Then, the use of $HBF_4{\cdot}OEt_2$ (1.2 equiv) as acid additive at 0ºC[21] allowed to give iodoenone **3a** after aqueous extraction and purification, with yields that go from 35% to 75% depending on the iodonium source (entries 5-7); as shown, IPy_2BF_4 resulted to be more efficient than NIS. This result could be improved using double amount of acid (2.4 eq, 93%, entry 8).[22] Similar reaction conditions were employed as well for acetate derivative **2a**, although the yield in this case was slightly lower

(86%, entry 9). Other protic (HOTf, entry 10) or Lewis acids ($BF_3 \cdot OEt_2$, entry 11) did not show to improve the preliminary results.

Table 1. Optimization studies



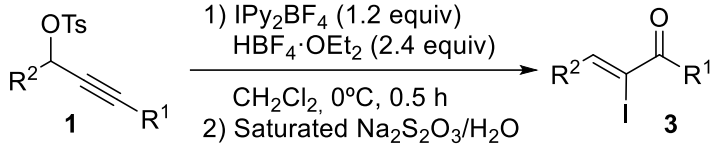
1a (R^1 = Ts); **2a** (R^1 = Ac) **3a**

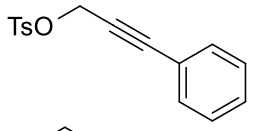
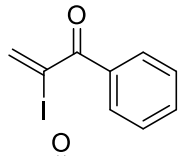
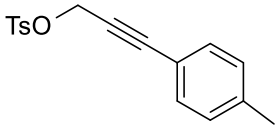
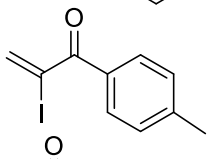
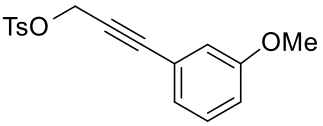
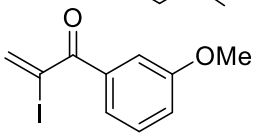
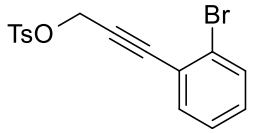
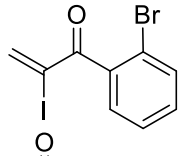
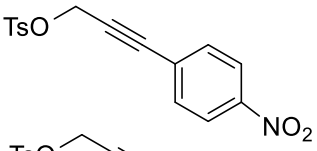
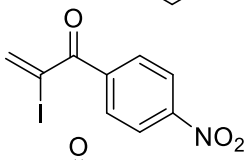
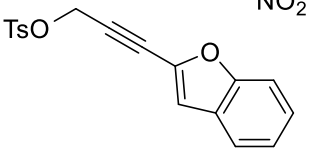
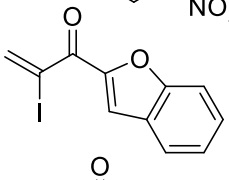
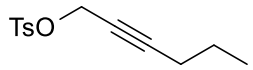
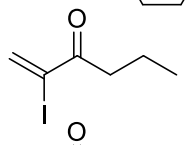
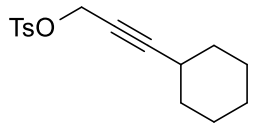
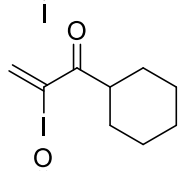
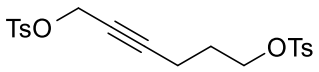
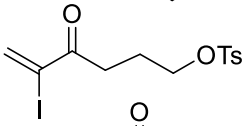
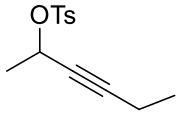
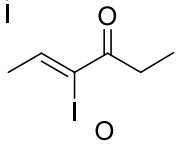
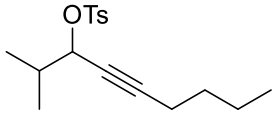
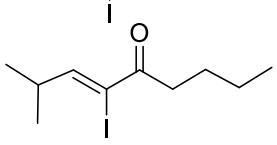
Entry	**1**/**2**	Iodonium source	Additive (equiv)	t(h)	Yield(%)[a]
1	**1a**	NIS	none	14[b]	--
2	**1a**	I_2	none	14[b]	--
3	**1a**	IPy_2BF_4	none	14[b]	--
4	**1a**	ICl	none	14[b]	17[c]
5	**1a**	NIS	$HBF_4 \cdot OEt_2$ (1.2)	0.5[d]	35[c]
6	**1a**	NIS	$HBF_4 \cdot OEt_2$ (1.2)	3[d]	39[c]
7	**1a**	IPy_2BF_4	$HBF_4 \cdot OEt_2$ (1.2)	0.5[d]	75
8	**1a**	IPy_2BF_4	$HBF_4 \cdot OEt_2$ (2.4)	0.5[d]	93
9	**2a**	IPy_2BF_4	$HBF_4 \cdot OEt_2$ (2.4)	0.5[d]	86
10	**1a**	IPy_2BF_4	HOTf (2.4)	0.5[d]	80
11	**1a**	IPy_2BF_4	$BF_3 \cdot OEt_2$ (2.4)	0.5[d]	72

[a] Isolated yields. [b]Reaction performed at room temperature. [c] Yields determined by ^{1}H-NMR with 4-bromobenzaldehyde as internal standard. [d] Reaction performed at 0ºC.

Next, we investigated the scope of the reaction using first primary tosylate derivatives **1**. As shown in Table 2, the reaction takes place with good yields (80-94%) with aryl substituted primary propargylic alcohol tosylates **1a-e** bearing either neutral (**1a,b**), electron-donating (**1c**) or electron-withdrawing substituents (**1d,e**). The reaction also tolerates the presence of heterocyclic groups (**1f**), alkyl (**1g,h)** and other functions (**1i)**. Thus, a variety of β-unsubstituted α-iodoenones **3a-i** was obtained in good yields that could be reproducible in gram scale for **3a**.

Table 2. IPy_2BF_4-promoted rearrangement reaction of propargylic tosylates **1** to α-iodoenones **3**.



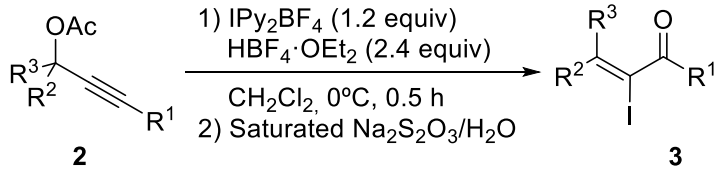
1a		**3a** (94%)[a]	
1b		**3b** (79%)	
1c		**3c** (81%)	
1d		**3d** (84%)	
1e		**3e** (80%)	
1f		**3f** (36%)	
1g		**3g** (85%)	
1h		**3h** (77%)	
1i		**3i** (82%)	
1j		**3j** (82%)[b,c]	
1k		**3k** (77%)[b,d]	

[a]Yield in gram scale. [b]Reaction time 15 min. [c]*Z*/*E* ratio > 20:1. [d] *Z*/*E* ratio = 14:1.

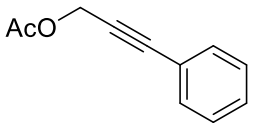
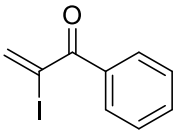
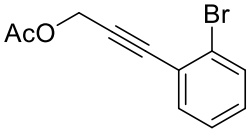
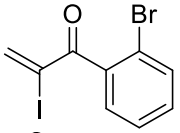
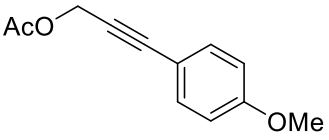
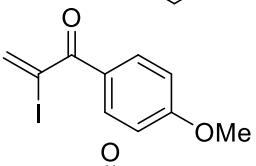
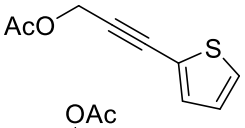
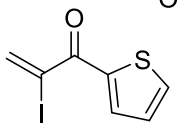
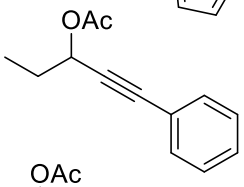
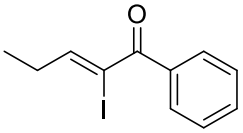
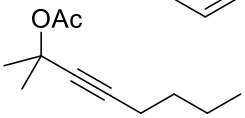
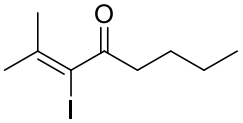
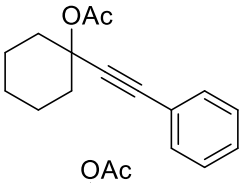
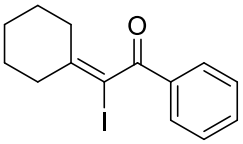
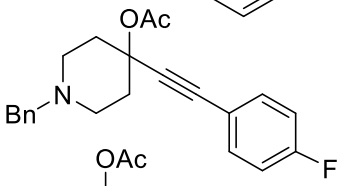
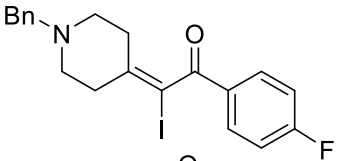
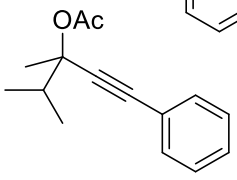
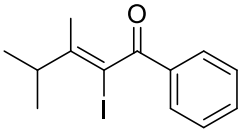
Then, we studied the behavior of secondary tosylates such as 3-alkyl substituted tosylates **1j,k** (Table 2), these compounds required shorter reaction times (15 min) to give the corresponding β-substituted iodoenones **3j-k**

in good yields (77-82%) and excellent (*Z*)-selectivity. The (Z)-configuration of products **3j** and **3k** was determined by NOESY or NOE experiments respectively.[23] Unfortunately, secondary 3-aryl substituted propargylic tosylates (R^2 = Ar) were unstable to reaction conditions, this limitation can also be extended to tertiary tosylates.

Table 3. IPy_2BF_4-promoted rearrangement reaction of propargylic acetates **2** to α-iodoenones **3**.



2 **3**

2a		**3a** (86%)	
2d		**3d** (76%)	
2l		**3l** (75%)	
2m		**3m** (86%)	
2n		**3n** (71%)[a,b]	
2o		**3o** (54%)[c]	
2p		**3p** (80%)[d]	
2q		**3q** (60%)[e]	
2r		**3r** (66%)[d,f]	

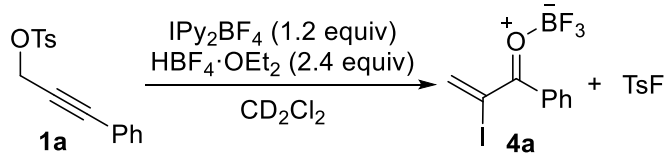
[a]Z/E ratio > 20:1.[b]Reaction time 5 min. [c]Reaction performed with 2.0 equiv of acid at - 20ºC. [d]1.2 equivalents of acid were used. [e]2.2 equivalents of acid were used. [f]Z/E ratio = 5:1.

As said above, propargylic acetates **2** can also undergo this reaction and thereby can be used as an alternative to the corresponding unstable tosylate derivatives. Table 3 shows the results employing acetates **2** derived from primary, secondary and tertiary propargylic alcohols. In this sense; apart from compounds **3a,d** obtained previously from propargylic tosylates in better yields (see Table 2), new β-unsubstituted α-iodoenones **3l,m** were synthesized (75-86% yield respectively), in those cases the reaction from the corresponding tosylate **1** failed.

We studied next the reaction in secondary and tertiary propargylic alcohol acetates **2n-r**. In general, these compounds are also more sensitive to reaction conditions and some changes in the general experimental procedure were required (see Table 3). Contrary to its tosylate counterpart, 3-aryl substituted propargylic acetate **2n** could undergo the iodonium-promoted rearrangement reaction to lead selectively to the (*Z*)-isomer (the configuration was determined by a NOE experiment)[23] of β-substituted-α-iodoenone **3n** in good yield (71%). Additionally, a variety of β,β-disubstituted α-iodoenones **3o-r**, bearing alkyl and aryl groups or other functions, could be obtained from tertiary propargylic acetates **2o-r** in moderate to good yields (54-80%). Acid equivalents and temperature should be controlled in some cases in order to prevent acetic acid elimination side reaction (see Table 3). For compound **3r** the (Z/*E*) ratio fell to 5:1. The stereochemistry of the isomers was elucidated by a NOESY experiment.[23]

In order to get some insight into the reaction course we analyzed the reaction crude by ^{1}H NMR after running the reaction of **1a** in CD_2Cl_2. Thus, the presence of the corresponding iodoenone-BF_3 complex **4a** (R^1 = Ph) and tosylfluoride were detected (Scheme 2).[24,25]

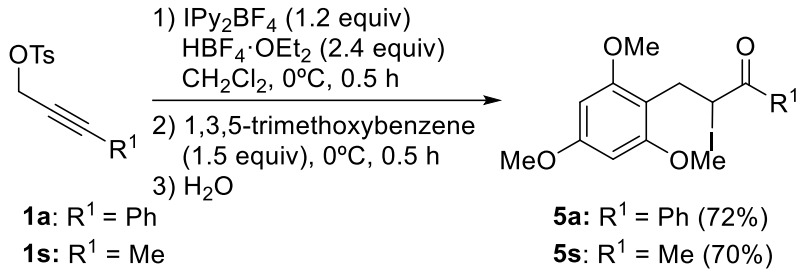
Scheme 2. NMR experiment for **1a**.



Moreover, activated enones **4a,s** could be trapped when the reactions of propargylic tosylates **1a,s** (Scheme 3) were quenched, before aqueous work up, with 1,3,5-trimethoxybenzene to furnish 1,4-nucleophylic adducts

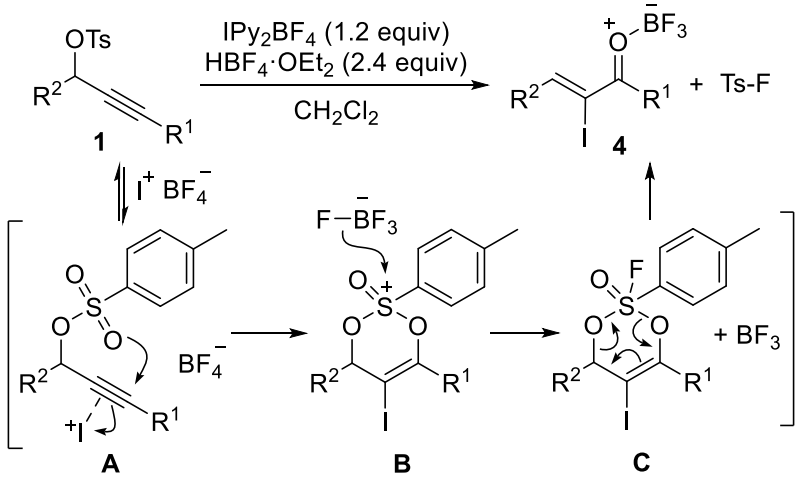
5a,s in 72 and 70% yields respectively. On the other hand, adduct **5a** was also obtained directly from enone **3a** by treatment with $BF_3{\cdot}OEt_2$ followed by the reaction with 1,3,5-trimethoxybenzene in 94% yield.

Scheme 3. In situ addition of 1,3,5-trimethoxybenzene to activated enones **4a,s**.



According to previous mechanistic proposals for electrophile-induced rearrangement reactions of propargyl acetates,[9,10] a likely mechanism for tosylates **1** could be proposed as follows; the reaction would start from the activation of the alkynyl moiety by the iodonium cation to give complex **A**, followed by the intramolecular nucleophilic attact of the tosyl group oxigen to the activated alkyne, to furnish cation **B**. The addition of a fluoride anion to **B** provides intermediate **C** which, after C–O bond cleavage, eliminates tosylfluoride to yield BF_3-coordinated-enones **4** (Scheme 4). The hydrolysis of complexes **4** finally gives the corresponding enones **3**. Furthermore, a similar pathway for acetates **2** could also be expected. In addition, Figure 1 shows a minimized 3D-model of the pseudochair conformation of intermediate **B** that would explain the *(Z)*-selectivity found in this transformation for secondary tosylates.

Scheme 4. Proposed mechanism**.**



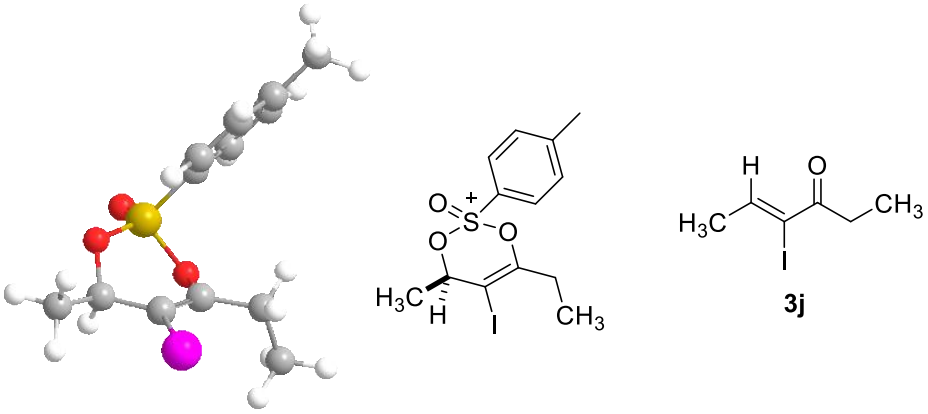


Figure 1. 3D model of cationic intermediate **B** in the formation of **3j**.

■ CONCLUSIONS

In conclusion, we have described a direct access to α-iodoenones, by treatment of propargylic tosylate or acetate derivatives with IPy_2BF_4. The reaction takes place in mild conditions and high yields with primary and secondary propargylic alcohol tosylates and alternatively with primary, secondary and tertiary propargylic alcohol acetates, to give rise to a variety of β-unsubstituted, β-substituted, and β,β–disubstituted-α-iodoenones respectively. Moreover, β-substituted iodoenones are obtained with excellent (*Z*)-selectivity. The reaction likely starts with the activation of the acetylene moiety by the iodonium cation, that promotes the rearrangement reaction to the final products.

■ EXPERIMENTAL SECTION

General Remarks. All reactions were carried out using oven-dried glassware under an atmosphere of nitrogen (99.99 %) or argon (99.999 %). Dichloromethane (DCM), was distilled from CaH_2 prior its use. The solvents used in column chromatography, hexane and ethyl acetate were obtained from commercial suppliers and used without further distillation. TLC was performed on aluminium-backed plates coated with silica gel 60 with F254 indicator (Merck), using UV light as a visualizing agent as well as phosphomolybdic acid in ethanol, potassium permanganate solution or *p*-anisaldehyde in ethanol as developing agents. Flash chromatography was performed on silica gel 60 (230-400 mesh). ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were measured in $CDCl_3$ at room temperature on a Bruker DPX-300, Bruker AV-300 MHz,

with TMS (δ = 0.0 ppm) as internal standard. Data are reported as follows: chemical shift (ppm), multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, quint; quintet, sext: sextet, septuplet: m: multiplet), coupling constants (*J* in Hz) and integration. Carbon multiplicities were assigned by DEPT techniques.

All common reagents and solvents were obtained from commercial suppliers and used without any further purification unless otherwise noted. IPy_2BF_4 was purified by precipitation from the addition of diethyl ether to a solution of IPy_2BF_4 in CH_2Cl_2.

High-resolution mass spectra (HRMS) were obtained by electron ionization techniques (EI) (70 eV) with a VG AutoSpec M mass Spectrometers and a microTOF focus (Bruker Daltonics, Bremen Germany).

Melting points (mp) of recrystallized samples were measured on a Buchi-Tottoli apparatus and were not corrected.

Preparation of Starting materials 1 and 2. Tosylates **1a**,[26] **1b**,[26] **1e**,[26] **1g**,[27] **1j**,[28] **1k**,[19b] **1s**,[29] and acetates **2**[8a,30] were prepared according to the methods described in the literature.

*Preparation of tosylates **1c,d,f,h,i**.*[31] A propargyl alcohol[32] (15 mmol) and tosyl chloride (15.75 mmol) were solved in diethyl ether (0.5-1.0 M); the solution was cooled to -50ºC and freshly powdered KOH (90 mmol) was added with vigorous sitirring. The temperature of the mixture was allowed to rise to 0 ºC and the stirring was continued for 0.5-1 hour under the same experimental conditions. When the reaction finished (confirmed by TLC), it was poured into an ice.-water mixture and extracted with diethyl ether (3 x 20 mL) and the combined extracts were washed with water and brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude purified by column chromatography or by recrystallization.

Characterization data and spectra for **1a,b,e**[26], **1g**[27], **1j**[28], **1k**[19b], **1s**[29], **2a**[33], **2d,n**[34], **2l**[10c], **2m**[9], **2o**[35], and **2p**[8a] are available in the literature.

*3-(3-Methoxyphenyl)prop-2-yn-yl 4-methylbenzenesulfonate (**1c**).* Yield 4.08 g (86%), white solid, mp = 62-64 ºC ; ^{1}H NMR δ = 2.41 (s, 3H), 3.80 (s, 3H), 4.97 (s, 2H), 6.78-6.81 (m, 1H), 6.84-6.93 (m, 2H), 7.17-7.25 (m, 1H), 7.35 (m, 2H), 7.88 (m, 2H); ^{13}C NMR δ = 21.6 (C), 55.3 (CH_2), 58.6 (CH_3), 80.3 (C),

88.9 (C), 115.5 (CH), 116.8 (CH), 122.4 (C), 124.2 (CH), 128.2 (CH), 129.3 (CH), 129.8 (CH), 133.4 (C), 145.1 (C), 159.2 (C); HRMS calcd for $C_{17}H_{16}O_4S$ $[M]^+$ 316.0769, found 316.0768.

3-(2-Bromophenyl)prop-2-yn-yl 4-methylbenzenesulfonate ***(1d)*****.** Yield 4.49 g (82%), white solid, mp = 68-70 ºC ; ^{1}H NMR δ = 2.39 (s, 3H), 5.02 (s, 2H), 7.17-7.30 (m, 3H), 7.33 (d, *J* = 8.2, 2H), 7.54-7.60 (m, 1H), 7.88 (d, *J* = 8.2, 2H); ^{13}C NMR δ = 21.6 (CH_3), 58.4 (CH_2), 85.0 (C), 87.2 (C), 123.7 (C), 125.4 (C), 126.9 (CH), 128.2 (CH), 129.8 (CH), 130.3 (CH), 132.4 (CH), 133.3 (C), 133.7 (CH), 145.1 (C); HRMS calcd for $C_{16}H_{13}BrO_3S$ $[M]^+$ 363.9769, found 363.9771.

3-(Benzofuran-2-yl)prop-2-yn-yl 4-methylbenzenesulfonate ***(1f)*****.** Yield 3.67 g (75%), white solid, mp > 59 ºC (decomposition); ^{1}H NMR δ = 2.40 (s, 3H), 5.02 (s, 2H), 6.90 (s, 1H), 7.24-7.31 (m, 1H), 7.33-7.48 (m, 4H), 7.54-7.60 (m, 1H; 7.88 (d, *J* = 8.3, 2H); ^{13}C NMR δ = 21.6 (CH_3), 57.9 (CH_2), 79.4 (C), 86.8 (C), 111.3 (CH), 113.4 (CH), 121.5 (CH), 123.5 (CH), 126.2 (CH), 127.1 (C), 128.2 (CH), 129.9 (CH), 133.0 (C), 137.0 (C), 145.3 (C), 154.9 (C); HRMS calcd for $C_{18}H_{14}O_4S$ $[M]^+$ 326.0613, found 326.0615.

3-Cyclohexylprop-2-yn-yl 4-methylbenzenesulfonate ***(1h)*****.** Yield 3.99 g (91%), colorless oil; ^{1}H NMR δ = 1.19-1.35 (m, 5H), 1.44-1.73 (m, 5H), 2.21-2.30 (m, 1H), 2.47 (s, 3H), 4.75 (d, *J* = 2.2, 2H), 7.36 (d, *J* = 8.2, 2H); ^{13}C NMR δ = 21.6 (CH_3), 24.7 (CH_2), 25.7 (CH_2), 28.9 (CH), 2.0 (CH_2), 58.9 (CH_2), 71.7 (C), 94.4 (C), 128.1 (CH), 129.7 (CH), 133.5 (C), 144.8 (C): HRMS calcd for $C_{16}H_{20}O_3S$ $[M]^+$ 292.1133, found 292.1154.

Hex-2-yne-1,6-diyl bis(4-methylbenzenesulfonate) ***(1i)*****.** Yield 4.69 g, (74%), white solid, mp = 64-66 ºC; ^{1}H NMR δ = 1.75 (quint, *J* = 6.5, 2H), 2.19 (tt, *J* = 6.5, 2.2, 2H), 2.47 (s, 3H), 2.48 (s, 3H), 4.04 (t, *J* = 6.5, 2H), 4.62 (t, *J* = 2.2, 2H), 7.33-7.41(m, 4H), 7.75-7.85 (m, 4H); ^{13}C NMR δ = 14.9 (CH_2), 21.7 (CH_3), 27.4 (CH_2), 58.3 (CH_2), 68.5 (CH_2), 73.1 (C), 87.9 (C), 127.9 (CH), 128.1 (CH), 129.8 (CH), 129.9 (CH), 132.8 (C), 133.2 (C), 144.9 (C), 145.0 (C); HRMS calcd for $C_{20}H_{22}O_6S_2$ $[M]^+$ 422.0858, found 422.0860.

1-Benzyl-4-((4-fluorophenyl)ethynyl)piperidin-4-yl acetate ***(2q)*****.** Yield 4.22 g (80%), yellowish solid, mp = 45-47 ºC; ^{1}H NMR δ = 2.09 (s, 3H), 2.12-2.38 (m, 4H), 2.47-2-76 (m, 4H), 3.56 (s, 2H), 6.97-7.06 (t, *J* = 8.7, 2H), 7.25-7.38 (m, 5H), 7.39-7.47 (m, 2H); ^{13}C NMR δ = 21.9 (CH_3), 36.7 (CH_2), 49.8 (CH_2), 62.7 (CH_2), 73.8 (C), 85.8 (C), 88.0 (C), 115.5 (d, *J* = 22.2, CH), 118.6 (d, *J* = 3.4, C), 127.1 (CH), 128.3

(CH), 129.1 (CH), 133.7 (d, *J* = 8.4, CH), 138.2 (C), 162.6 (d, J = 250 C), 169.3 (C); HRMS calcd for $C_{22}H_{22}FNO_2$ $[M]^+$ 351.1635, found 351.1636.

*3,4-Dimethyl-1-phenylpent-1-yn-3-yl acetate (**2r**).* Yield 3.01 g (87%), yellow oil; ^{1}H NMR δ = 1.07 (d, *J* = 6.6, 3H), 1.11 (d, *J* = 6.6, 3H), 1.73 (s, 3H), 2.06 (s, 3H), 2.28 (sept, *J* = 6.6, 1H), 7.27-7.32 (m, 2H), 7.42-7.47 (m, 2H); ^{13}C NMR δ = 17.3 (CH_3), 27.6 (CH_3), 22.0 (CH_3), 23.3 (CH_3), 37.5 (CH), 79.4 (C), 85.6 (C), 88.5 (C), 122.8 (C), 128.1 (CH), 128.2 (CH), 131.8 (CH), 169.3 (C). HRMS calcd for $C_{15}H_{18}O_2$ $[M]^+$ 230.1307, found 230.1305.

General Procedure for the Synthesis of α-Iodoenones 3. Tosylates **1** or acetates **2** (0,25 mmol) and IPy_2BF_4 (112 mg, 0.3 mmol, 1.2 equiv) were dissolved in anhydrous CH_2Cl_2 (5 mL) under argon atmosphere. Then, $HBF_4{\cdot}Et_2O$ (82 μL, 0.6 mmol, 2.4 equiv) (1.2 equivalents for **3p** and **3r;** 2 equiv for **3o**) was added at 0 ºC (–20 ºC for **3o**) with vigorous stirring and the reaction maintained for 30 minutes (15 minutes for **3j** and **3k**; 5 minutes for **3n**) at the same temperature. Next, H_2O (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 5 mL). The organic layer was treated with a saturated solution of $Na_2S_2O_3$ (5 mL), then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 20:1 to 5:1) to give pure α-iodoenones **3**.

Gram Scale Preparation of 3a. Tosylate **1a** (1.7 g, 6 mmol) and IPy_2BF_4 (2.7 g, 7.2 mmol, 1.2 equiv) were dissolved in 120 mL of anhydrous CH_2Cl_2 under argon atmosphere. Then, $HBF_4{\cdot}Et_2O$ (2 mL 14.4 mmol, 2.4 equiv) was added at 0 ºC with vigorous stirring and the reaction maintained for 30 minutes at the same temperature. Next, H_2O (120 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 50 mL). The organic layer was treated with a saturated solution of $Na_2S_2O_3$ (120 mL), then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 20:1) to give pure α-iodoenone **3a** (1.44 g, 94%).

*2-Iodo-1-phenylprop-2-en-1-one (**3a**).* Yield 59 mg, (from **1a**, 93%), 55 mg (from **2a**, 86%), yellow oil; ^{1}H NMR δ = 6.85 (d, *J* = 2.2, 1H), 6.89 (d, *J* = 2.2, 1H), 7.48 (m, 2H), 7.60 (m, 1H), 7.84 (d, *J* = 7.6, 2H); ^{13}C NMR δ =107.9 (C), 128.5 (CH), 129.8 (CH), 133.1 (CH), 133.8 (C), 138.2 (CH_2), 191.7 (C); HRMS calcd for C_9H_7IO $[M]^+$ 257.9543, found 257.9542.

*2-Iodo-1-(p-tolyl)prop-2-en-1-one (**3b**).* Yield 53 mg, (79%), yellow oil; ^{1}H NMR δ =2.44 (s, 3H), 6.78 (d, J = 2.2, 1H), 6.84 (d, J = 2.2, 1H), 7.28 (d, J = 8.4, 2H), 7.78 (d, J = 8.4, 2H); ^{13}C NMR δ = 21.7 (CH_3), 107.7 (C), 129.3 (CH), 130.2 (CH), 131.1 (C), 137.3 (CH_2), 144.3 (C), 191.5 (C); HRMS calcd for $C_{10}H_9IO$ $[M]^+$ 271.9696, found 271.9698.

*2-Iodo-1-(3-methoxyphenyl)prop-2-en-1-one (**3c**).* Yield 58 mg, (81%), yellow oil; ^{1}H NMR δ =3.87 (s, 3H), 6.84 (d, J = 2.3, 1H) 6.90 (d, J = 2.3, 1H), 7.11-7.18 (m, 1H), 7.33-7.36 (m, 1H), 7.37-7.41 (m, 2H); ^{13}C NMR δ = 55.9 (CH_3), 108.2 (C), 114.6 (CH), 120.0 (CH), 123.0 (CH), 129.9 (CH), 135.4 (C), 138.8 (CH_2), 160.1 (C), 192.0 (C); HRMS calcd for $C_{10}H_9IO_2$ $[M]^+$ 287.9645, found 287.9647.

*1-(2-Bromophenyl)-2-iodoprop-2-en-1-one (**3d**).* Yield 71 mg (from **1d**, 84%), 64 mg (from **2d**, 76%), yellow oil; ^{1}H NMR δ = 6.90 (d, J = 2.2, 1H), 7.05 (d, J = 2.2, 1H), 7.28-7.44 (m, 3H), 7.61-7.66 (m, 1H)); ^{13}C NMR δ = 111.9 (C), 119.9 (C), 127.6 (CH), 129.2 (CH), 132.0 (CH), 133.6 (CH), 137.9 (C), 143.4 (CH_2), 191.5 (C); HRMS calcd for C_9H_6BrIO $[M]^+$ 335.8659, found 335.8647.

*2-Iodo-1-(4-nirophenyl)prop-2-en-1-one (**3e**).* Yield 61 mg (80%), white solid, mp 87-89 °C; ^{1}H NMR δ = 6.94 (d, J = 2.5, 1H), 6.99 (d, J = 2.5, 1H), 7.96 (d, J = 8.9, 2H), 8.35 (d, J = 8.9, 2H); ^{13}C NMR δ = 107.6 (C), 124.1 (CH), 131.0 (CH), 139.6 (C), 140.6 (CH_2), 150.6 (C), 190.5 (C); HRMS calcd for $C_9H_6INO_3$ $[M]^+$ 302.9397, found 302.9392.

*1-(Benzofuran-2-yl)-2-iodoprop-2-en-1-one (**3f**).* Yield 23 mg (from **1f**, 36%), 22 mg (from **2f**, 34%), white solid, mp 82-83 °C (decomposition); ^{1}H NMR δ = 6.92 (d, J = 2.3, 1H), 7.33-7.37 (m, 1H), 7.40 (d, J = 2.3, 1H), 7.51-7.58 (m, 1H), 7.60-7.66 (m, 2H), 7.73-7.78 (m, 1H); ^{13}C NMR δ =106.0 (C), 112.6 (CH), 117.3 (CH), 123.5 (CH), 124.3 (CH), 126.7 (C), 128.9 (CH), 138.2 (CH_2), 148.4 (C), 156.3 (C), 179.8 (C); HRMS calcd for $C_{11}H_7IO_2$ $[M]^+$ 297.9492, found 297.9491.

*2-Iodohex-1-en-3-one (**3g**).* Yield 48 mg (85%), pale orange oil; ^{1}H NMR δ = 0.98 (t, J = 7.3, 3H), 1.71 (sext, J = 7.3, 2H), 2.82 (t, J = 7.3, 2H), 6.83 (d, J = 2.5, 1H), 7.26 (d, J = 2.5, 1H); ^{13}C NMR δ =14.1 (CH_3), 18.6 (CH_2), 38.9 (CH_2), 113.8 (C), 137.7 (CH_2), 195.5 (C); HRMS calcd for C_6H_9IO $[M]^+$ 223.9734, found 223.9736.

*1-Cyclohexyl-2-iodoprop-2-en-1-one (**3h**).* Yield 51 mg (77%), orange oil; ^{1}H NMR δ = 1.18-1.53 (m, 5H), 1.67-1.76 (m, 1H), 1.77-1.90 (m, 4H), 3.15 (tt, J = 11.3, 3.2, 1H), 6.81 (d, J = 2.4, 1H), 7.23 (d, J =

2.4, 1H); ^{13}C NMR δ = 26.1 (CH_2), 26.15 (CH_2), 30.1 (CH_2), 44.6 (CH), 113.3 (C), 137.1 (CH_2), 199.0 (C); HRMS calcd for $C_9H_{13}IO$ $[M]^+$ 264.0009, found 264.0011.

*5-Iodo-4-oxohex-5-en-1-yl-4-methylbenzenesulfonate (**3i**).* Yield 81 mg (82%), yellow oil; ^{1}H NMR δ = 2.03 (m, 2H), 2.48 (s, 3H), 2.94 (t, *J* = 6.9, 2H), 4.10 (t, *J* = 2.2, 2H), 6.85 (d, *J* = 2.6, 1H), 7.25 (d, *J* = 2.6, 1H), 7.37 (d, *J* = 8.5, 2H), 7.79 (d, *J* =8.5, 2H); ^{13}C NMR δ = 21,7 (CH_3), 23.7 (CH_2), 31.9 (CH_2), 69.3 (CH_2), 112.2 (C), 127.8 (CH), 129.9 (CH), 132.8 (C), 138.1 (CH_2), 144.9 (C), 193.5 (C); HRMS calcd for $C_{13}H_{15}IO_4S$ $[M]^+$ 393.9736, found 393.9737.

*(Z)-4-Iodohex-4-en-3-one (**3j**).* Yield 46 mg (82%), pale yellow oil; ^{1}H NMR δ = 1.16 (t, *J* = 7.3, 3H), 2.08 (d, *J* = 7.3, 3H), 2.86 (q, *J* = 7.6, 2H), 7.14 (q, *J* = 6.6, 1H); ^{13}C NMR δ = 9.1 (CH_3), 23.9 (CH_3), 31.2 (CH_2), 113.7 (C), 146.8 (CH), 195.3 (C); HRMS calcd for C_6H_9IO $[M]^+$ 223.9699, found 223.9698.

*(Z)-4-Iodo-2-methylnon-3-en-5-one (**3k**).* Yield 54 mg (77%), pale yellow oil; ^{1}H NMR δ = 0.94 (t, *J* = 7.3, 3H), 1.13 (d, *J* = 6.7, 6H), 1.36 (sext., *J* = 7.3, 2H), 1.6 (quint., *J* = 7.3, 2H), 2.8 (t, *J* = 7.3, 2H), 2.78-2.92 (m, 1H), 6.74 (d, *J* = 8.8, 1H); ^{13}C NMR δ = 13.9 (CH_3), 20.8 (CH_3), 22.3 (CH_2), 27.1 (CH_2), 37.4 (CH), 37.6 (CH_2), 109.7 (C), 157.2 (CH), 195.3 (C); HRMS calcd for $C_{10}H_{18}IO$ $[M + H]^+$ 281.0399, found 281.0397.

*2-Iodo-1-(4-methoxyphenyl)prop-2-en-1-one (**3l**).* Yield 54 mg (75%), pale yellow oil; ^{1}H NMR δ = 3.90 (s, 3H), 6.69 (d, *J* = 2.2, 1H), 6.77 (d, *J* = 2.2, 1H), 6.96 (d, *J* = 9.0 Hz, 2H); 7.88 (d, *J* = 9.0, 2H); ^{13}C NMR δ = 55.3 (CH_3), 106.8 (C), 113.9 (CH), 126.1 (C), 132.6 (CH), 135.8 (CH_2), 163.9 (C), 190.6 (C); HRMS calcd for $C_{10}H_9IO_2$ $[M]^+$ 287.9645, found 287.9647.

*2-Iodo-1-(thiophen-2-yl)prop-2-en-1-one (**3m**).* Yield 57 mg (86%), orange oil; ^{1}H NMR δ = 6.70 (d, *J* = 2.3, 1H), 6.99 (d, *J* = 2.3, 1H), 7.16 (t, *J* = 4.4, 1H), 7.72-7.78 (m, 2H); ^{13}C NMR δ =105.8 (C), 128.7 (CH), 135.6 (CH), 136.1 (CH), 136.4 (CH_2), 139.4 (C), 184.1 (C); HRMS calcd for C_7H_5IOS $[M]^+$ 263.9109, found 263.9106.

*(Z)-2-Iodo-1-phenylpent-2-en-1-one (**3n**).* Yield 51 mg (71%), pale orange oil; ^{1}H NMR δ = 1.13 (t, *J* = 7.0, 3H), 2.48 (quint, *J* = 7.0, 2H), 6.64 (t, *J* = 7.0, 1H), 7.43-7.50 (m, 2 H), 7.54-7.61 (m, 1H), 7.68-7.75 (m, 2H); ^{13}C NMR δ =12.0 (CH_3), 31.3 (CH_2), 107.9 (C), 128.4 (CH), 129.7 (CH), 132.4 (CH), 135.8 (C), 155.6 (CH), 192.0 (C); HRMS calcd for $C_{11}H_{11}IO$ $[M]^+$ 285.9858, found 285.9855.

*3-Iodo-2-methyloct-2-en-4-one (**3o**).* Yield 36 mg (54%), pale yellow oil; ^{1}H NMR δ = 0.94 (t, J = 7.3, 1H), 1.28-1.44 (m, 2H), 1.55-1.69 (m, 2H), 1.97 (s, 3H), 2.04 (s, 3H), 2.82 (t, J = 7.4, 2H); ^{13}C NMR δ =13.9 (CH_3), 21.9 (CH_3), 22.3 (CH_2), 26.4 (CH_2), 30.3 (CH_3), 40.5 (CH_2), 95.4 (C), 144.3 (C), 202.3 (C); HRMS calcd for $C_9H_{15}IO$ $[M]^+$ 266.0203, found 266.0201.

*2-Cyclohexylidene-2-iodo-1-phenylethan-1-one (**3p**).* Yield 65 mg (80%), pale yellow oil; ^{1}H NMR δ = 1.41-1.51 (m, 2H), 1.54-1.67 (m, 2H), 1.68-1.79 (m, 2H), 2.16-2.31 (m, 2H), 2.49-2.66 (m, 2H), 7.42-7.55 (m, 2H), 7.56-7.69 (m, 1H), 7.93-8.09 (m, 2H); ^{13}C NMR δ =26.2 (CH_2), 27.8 (CH_2), 28.0 (CH_2), 33.7 (CH_2), 39.3 (CH_2), 88.1 (C), 129.2 (CH), 130.4 (CH), 134.1 (CH), 134.4 (C), 150.0 (C), 193.6 (C); HRMS calcd for $C_{14}H_{15}IO$ $[M]^+$ 326.0165, found 326.0168.

*2-Iodo-3,4-dimethyl-1-phenylpent-en-1-one (**3r**).* Yield 47 mg (66%), *Z*/E = 5:1, pale yellow oil; ^{1}H NMR δ *major isomer* = 0.99 (d, J = 6.8, 6H), 2.04 (s, 3H), 2.53-2.85 (m, 1H). 7.43-7.55 (m, 2H), 7.56-7.67 (m, 1H) 7.93- 8.03 (m, 2H), δ *minor isomer* = 1.14 (d, J = 6.9, 6H), 1.72 (s, 3H), 3.03-3.29 (m, 1H), 7.43-7.55 (m, 2H), 7.56-7.67 (m, 1H), 7.93-8.03 (m, 2H); ^{13}C NMR δ *major isomer* δ = 19.8 (CH_3), 20.7 (CH_3), 33.9 (CH), 91.1 (C), 128.7 (CH), 130.0 (CH), 133.7 (CH), 133.8 (C), 151.0 (C), 193.2 (C); minor isomer = 14.7 (CH_3), 20.9 (CH_3), 39.2 (CH), 89.1 (C), 128.8 (CH), 129.9 (CH), 133.7 (CH), 133.8 (C), 149.7 (C), 193.0 (C); HRMS calcd for $C_9H_{15}IO$ $[M]^+$ 266.0203, found 266.0201.

Preparation of α-Iodoenone 3q. IPy_2BF_4 (112 mg, 0.3 mmol, 1.2 equiv) was dissolved under argon atmosphere of anhydrous CH_2Cl_2 (4 mL) at 0ºC. Then, $HBF_4{\cdot}Et_2O$ (41 µL, 0.3 mmol, 1.2 equiv) were added with vigorous stirring, followed by a solution of **2q** (0.25 mmol, 1 equiv) and $HBF_4{\cdot}Et_2O$ (34 µL, 0.25 mmol, 1 equiv) in anhydrous CH_2Cl_2 (1 mL). The stirring was maintained at the same temperature for 30 minutes. Next, H_2O (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 5 mL). The organic layer was treated with a saturated solution of $Na_2S_2O_3$ (5 mL), then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 3:1) to give pure **3q** (65 mg, 60%).

*2-(1-Benzylpiperidin-4-ylidene)-1-(4-fluorophenyl)-2-iodoethen-1-one (**3p**).* Pale yellow oil; ^{1}H NMR δ =2.28-2.44 (m, 2H), 2.57-2.64 (m, 2H), 2.65-2.75 (m, 2H), 3.56 (s, 3H), 7.11-7.17 (m, 2H), 7.23-

7.37 (m, 5H), 7.81-8.01 (m, 2H); ^{13}C NMR δ =33.1 (CH_2), 38.6 (CH_2), 54.0 (CH_2), 54.1 (CH_2), 62.7 (CH_2), 88.9 (CH), 116.5 (CH, d, *J* = 9.4) 127.6 (CH), 128.7 (CH), 129.4 (CH), 130.7 (C, d, *J* = 3.0), 133.1 (CH, d, *J* = 9.4) 138.4 (C), 147.4 (C), 166.6 (C, d, *J* = 257.7), 191.8 (C); HRMS calcd for $C_{20}H_{19}FINO$ $[M]^+$ 435.0486, found 435.0495.

General Procedure for the Synthesis of products 5. Tosylates **1** (0.25 mmol) and IPy_2BF_4 (112 mg, 0.3 mmol, 1.2 equiv) were dissolved in anhydrous CH_2Cl_2 (5 mL) under argon atmosphere. Then, $HBF_4{\cdot}Et_2O$ (82 μL, 0.6 mmol, 2.4 equiv) were added at 0 ºC with vigorous stirring and the reaction was maintained for 30 minutes at the same temperature. Then, 1,3,5-trimethoxybenzene (126 mg, 0.75 mmol, 1.5 equiv) was added at 0ºC and the mixture was stirred for 30 additional minutes. Then, H_2O (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 5 mL). The organic layer was treated with a saturated solution of $Na_2S_2O_3$ (5 mL), then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography previously deactivated with a 10:1 mixture of hexane/Et_3N (silica gel, hexane/ethyl acetate 10:1) to give compounds **5**.

Synthesis of 5a from α-Iodoenone 3a. α-Iodoenone **3a** (65 mg, 0.25 mmol, 1 equiv) was dissolved in CH_2Cl_2 (5 mL) under argon atmosphere and $BF_3{\cdot}Et_2O$ (31 μL, 0.25 mmol, 1 equiv) was added. The resulting solution was cooled to 0ºC; then, 1,3,5-trimethoxybenzene (63 mg, 0.38 mmol, 1.5 equiv) was added and the mixture stirred for 30 minutes at the same temperature. Next, H_2O (5 mL) was added and the reaction extracted with CH_2Cl_2 (3 x 5 mL). The organic layer was treated with a saturated solution of $Na_2S_2O_3$ (5 mL), then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 10:1) to give **5a** (100 mg, 94%).

*2-Iodo-1-phenyl-3-(2,4,6-trimethoxyphenyl)propan-1-one (**5a**).* Yield 77 mg (72%), white solid, mp 110 °C (decomposition); ^{1}H NMR δ =3.32 (dd, *J* = 14.5, 6.1, 1H), 3.63 (dd, *J* = 14.5, 8.7, 1H), 3.82 (s, 9H), 5.84 (dd, *J* = 8.7, 6.1, 1H), 6.14 (s, 2H), 7.42-7.50 (m, 2H), 7.53-7.60 (m, 1H), 7.94-8.02 (m, 2H); ^{13}C NMR δ = 26.6 (CH), 28.4 (CH_2), 55.3 (CH_3), 55.7 (CH_3), 90.6 (CH), 108.1 (C), 128.6 (CH), 128.65 (CH), 133.1 (CH), 134.5 (C), 159.1 (C), 160.2 (C), 195.2 (C); HRMS calcd for $C_{18}H_{20}IO_4$ $[M + H]^+$ 427.0402, found 427.0401.

*3-Iodo-4-(2,4,6-1-one (**5s**).* Yield 65 mg (72%), white solid, mp 70 °C (decomposition); ^{1}H NMR δ =2.44 (s, 3H), 3.29 (dd, *J* = 14.3, 7.7, 1H), 3.35 (dd, *J* = 14.3, 7.7, 1H), 3.8 (s, 9H), 4.83 (t, *J* = 7.7, 1H), 6.12 (s, 2H); ^{13}C NMR δ =25.4 (CH), 29.0 (CH_2), 33.3 (CH_3), 55.4 (CH_3), 55.7 (CH_3), 90.7 (CH), 107.7 (C), 159.0 (C), 160.5 (C), 203.7 (C); HRMS calcd for $C_{13}H_{18}IO_4$ $[M + H]^+$ 365.0249, found 365.0244.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimization studies. NMR study, and ^{1}H and ^{13}C NMR spectra (PDF).

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Ciganek, E In *Organic Reactions*; Paquette, L. A., Ed; John Wiley & Sons, Inc: Weinheim, 1997; vol 51, pp. 201-350. (b) Chinchilla, R.; Nájera, C. Acylvinyl and vinylogous synthons. *Chem. Rev.* **2000**, *100*, 1891-1928. (c) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. Recent advances in the Baylis-Hillman reaction and applications. *Chem. Rev.* **2003**, *103*, 811-891. d) Carrasco-Sánchez, V.; Simirgiotis, M. J.; Santos, L. S. The Morita-Baylis-Hillman reaction: insights into asymmetry and reaction mechanisms by electrospray ionization mass spectrometry. *Molecules*, **2009**, *14*, 3989-4021. (e) Zhu, Y.; Sun, L.; Lu, Ping, Wang, Y. Recent advances on the Lewis acid-catalyzed cascade rearrangements of propargylic alcohols and their

derivatives. *ACS Catal*. **2004**, *4*, 1911-1925. (f) Wei, Y.; Shi, M. Recent advances in organocatalytic asymmetric Morita-Baylis-Hillman/aza-Morita-Baylis-Hillman reactions. *Chem. Rev.* **2013**, *113*, 6659-6690. (g) Xie, P.; Huang, Y. Morita-Baylis-Hillman adduct derivatives (MBHADs): versatile reactivity in Lewis base-promoted annulation. *Org. Biomol. Chem*. **2015**, *13*, 2572-2595.

(2) (a) Reynolds, T. E.; Binkley, M. S.; Scheidt, K. A. Highly selective α-acylvinyl anion additions to imines. *Org. Lett*. **2008**, *10*, 5227-5230. (b) Brekan, J. A.; Reynolds, T. E.; Scheidt, K. A. Enantioselective synthesis of substituted indanones from silyloxyallenes. *J. Am. Chem. Soc.* **2010**, *132*, 1472-1473.

(3) For the propargylic alcohol rearrangement through vanadium allenolates see: (a) Trost, B. M.; Luan, X.; Miller, Y. Contemporaneous dual catalysis: chemoselective cross-coupling of catalytic vanadium-allenoate and π-allylpaladium intermediates. *J. Am. Chem. Soc.* **2011**, *133*, 12824-12833. (b) Kalek, M.; Himo, F. Mechanism and selectivity of cooperatively catalyzed Meyer-Schuster rearrangement/Tsuji-Trost allylic substitution. Evaluation of synergistic catalysis by means of combined DTF and kinetics simulations. *J. Am. Chem. Soc.* **2017**, *139*, 10250-10266. For the propargylic alcohol rearrangement through molybdenum allenolates see: (c) Yu, L.; Zhang, L. Practical synthesis of linear α-iodo/bromo-α,β-unsaturated aldehydes/ketones from propargylic alcohols via Au/Mo bimetallic catalysis. *Org. Lett.* **2009**, *11*, 3646-3649.

(4) For reviews see: (a) Shu, X.-Z.; Shu, D.; Schienebeck, C. M.; Tang, W. Rhodium-catalyzed acyloxy migration of propargylic esters in cycloadditions, inspiration from the recent "gold rush". *Chem. Soc. Rev.* **2012**, *41*, 7698-7711. (b) Shiroodi, R. K.; Gevorgyan V. Metal-catalyzed double migratory cascade reactions of propargylic esters and phosphates. *Chem. Soc. Rev.* **2013**, 42, 4991-5001. (c) Dorel, R.; Echavarren, A. M. Gold(I)-catalyzed activation of alkynes for the construction of molecular complexity. *Chem. Rev*. **2015**, *115*, 9028-9072. (d) Henrion, G.; Gagosz, F. Gold-promoted sigmatropic rearrangements. *Patai's Chemistry of Functional Groups* **2014** 1-80. (e) Echavarren, A. M.; Muratore, M. E.; López-Carrillo, V.; Escribano-Cuesta, A.; Huguet, N.; Obradors C. Gold-catalyzed cyclizations of alkynes with alkenes and arenes. *Organic Reactions*, **2017**, *92*, 1-288.

(5) Yu, Y.; Yang, W.; Rominger, F.; Hashmi, A. S. K. In situ generation of nucleophilic allenes by the gold-catalyzed rearrangement of propargylic esters for the highly diastereoselective formation of intermolecular $C(sp^3)$-$C(sp^2)$ bonds. *Angew. Chem., Int. Ed.* **2013**, *52*, 7586-7589.

(6) (a) Ji, Y.-L.; Lin, J.-H.; Xiao, J.-C.; Gu Y.-C. Stereoselective synthesis of α-trifluoromethyl enones by Au^{I}/Cu^{I}-Co-catalyzed tandem 1,3-acyloxy migration/trifluoromethylation reaction of propargyl acetates. *Eur. J. Org. Chem.* **2014**, 7948-7954. (b) Manoni, E.; Daka, M.; Mastandrea, M. M.; De Nisi, A.; Monari, M.; Bandini, M. Catalytic α-allylation of enones with alcohols *via* [gold(I)]-mediated [3,3]-sigmatropic rearrangement of propargylic carboxylates. *Adv. Synth. Catal.* **2016**, *358*, 1404-1409.

(7) Zhang, G.; Peng, Y.; Cui, L.; Zhang, L. Gold-catalyzed homogeneous oxidative cross-coupling reactions. *Angew. Chem. Int. Ed.* **2009**, *48*, 3112-3115.

(8) (a) Yu, M.; Zhang, G.; Zhang, L. Gold-catalyzed efficient preparation of linear α-iodoenones from propargylic acetates. *Org. Lett.* **2007**, *9*, 2147-2150. (b) Yu, M.; Zhang, G.; Zhang, L. Gold-catalyzed efficient preparation of linear α-haloenones from propargylic acetates. *Tetrahedron* **2009**, *65*, 1846-1855. (c) Wang, D.; Ye, X.; Shi, X. Efficient synthesis of *E*-α-haloenones through chemoselective alkyne activation over allene with triazole-Au catalysis.*Org. Lett*. **2010**, *12*, 2088-2091.

(9) Onishi, Y.; Nishimoto, Y.; Yasuda, M.; Baba, A. Indium chloride catalyzed alkylative rearrangement of propargylic acetates using alkyl chlorides, alcohols, and acetates: facile synthesis of α-alkyl-α,β-unsaturated carbonyl compounds. *Org. Lett.* **2014**, *16*, 1176-1179.

(10) (a) Karpavičienė, I.; Čikotienė, I. A unique cascade reaction between 3-arylprop-2-inylcarboxylates and benzaldehydes leading to the formation of Morita-Baylis-Hillman adducts. *Org.Lett.* **2013**, *15*, 224-227. (b) Čikotienė, I. Rearangements of propargylic esters can be induced by some electrophiles. *Org. Lett.* **2014**, *16*, 2260-2263. (c) Trujillo, C.; Sánchez-Sanz, G.; Karpavičienė, I.; Jahn, U.; Čikotienė, I.; Rulišek, L. Divergent pathways and competitive mechanisms of metathesis reactions between 3-arylprop-2-ynyl esters and aldehydes: an experimental and theoretical study. *Chem. Eur. J.* **2014**, *20*, 10360-10370.

(11) For reviews see: (a) Barluenga, J.; González J. M. Iodonium chemistry: More than a simple minicry of some transition metal based organic transformations. In *Current Trends in Organic Synthesis*. Scolastico, G.; Nicontra F.; Eds; Kluwer Academic. Plenum Publishers: New York, 1999, pp. 145-151. (b) Suárez-Pantiga, S.; González, J. M. Electrophilic activation of unsaturated systems: Applications to selective organic synthesis. *Pure Appl. Chem.* **2013**, *85*, 721-739.

(12) For intramolecular C-C bond formation see: (a) Barluenga, J.; González, J. M.; Campos, P. J.; Asensio, G. Iodine-induced stereoselective carbocyclizations: A new method for the synthesis of cyclohexane and

cyclohexene derivatives *Angew. Chem. Int. Ed* **1988**, *27*, 1546-1547. (b) Barluenga, J.; Romanelli G. D.; Álvarez-García, L. J.; Llorente, I.; González, J. M.; García-Rodríguez, E.; García-Granda S. A novel domino reaction: cyclization of alkynyl sulfides by reaction with IPy_2BF_4. *Angew. Chem. Int. Ed.* **1998**, *37*, 3136-3139. (c) Barluenga, J.; Trincado, M.; Rubio, E.; González, J. M. Direct intramolecular arylation of aldehydes promoted by reaction with IPy_2BF_4/HBF_4: Synthesis of benzocyclic ketones**.** *Angew. Chem. Int. Ed.* **2006**, *45*, 3140-3143. For intramolecular C-N bond formation see: (d) Barluenga, J.; Trincado, M.; Rubio, E. González, J. M. IPy_2BF_4-Promoted intramolecular addition of masked and unmasked anilines to alkynes: direct assembly of 3-iodoindole cores**.** *Angew. Chem. Ind. Ed.* **2003**, *42*, 2406-2409. For intramolecular C-O bond formation see: (e) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. Regioselective synthesis of substituted naphthalenes: A novel de novo approach based on a metal-free protocol for stepwise cycloaddition of *o*-alkynylbenzaldehyde derivatives with either alkynes or alkenes. *Org. Lett.* **2003**, *5*, 4121-4123. (f) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. Cyclization of carbonyl groups onto alkynes upon reaction with IPy_2BF_4 and their trapping with nucleophiles: A versatile trigger for assembling oxygen heterocycles. *J. Am. Chem. Soc.* **2003**, *125*, 9028-9029. (g) Barluenga, J.; Vázquez-Villa, H.; Merino, J.; Ballesteros, A.; González, J. M. The reaction of *o*-alkynylarene and heteroarene carboxaldehyde derivatives with iodonium ions and nucleophiles: A versatile and regioselective synthesis of 1*H*-isochromene, naphthalene, indole, benzofuran, and benzothiophene compounds**.** *Chem. Eur. J.* **2006**, *12*, 5790-5805.

(13) For selected examples see: (a). Sha, C. –K; Santhosh, K. C.; Tseng, C. -T.; Lin C. -T. Radical cyclization of α–iodo enones by photoinduced electron transfer reaction. *Chem. Commun*. **1998**, 397-398. (b) William, A. D.; Kobayashi, Y. Synthesis of tetrahydrocannabinols based on an indirect 1,4–addition strategy. *J. Org. Chem.* **2002**, *67*, 8771–8782. (c) Banwell, M. G.; Kelly, B. D.; Kokas, O. J.; Lupton, D. W. Synthesis of indoles via palladium[0]-mediated Ullmann cross-coupling of *o*-halonitroarenes with α–halo-enones or -enals. *Org. Lett.* **2003**, *5*, 2497-2500. (d) Yao, T.; Zhang, X.; Larock, R. C. $AuCl_3$-Catalyzed synthesis of highly substituted furans from 2-(1-alkynyl)-2-alken-1-ones. *J. Am. Chem. Soc.* **2004**, *126*, 11164-11165. (e) Greshock, T. J.; Funk, R. L. Synthesis of indoles via 6π-electrocyclic ring closures of trienecarbemetes. *J. Am.*

Chem. Soc. **2006**, *128*, 4946-4947. (f) Rauniyar, V.; Wang, Z. J.; Burks, H. E.; Toste, F. D. Enantioselective synthesis of highly substituted furans by a copper(II)-catalyzed cycloisomerization-indole addition reaction. *J. Am. Chem. Soc.* **2011**, *133*, 8486-8489. (g) Gärtner, M.; Qu, J.; Helmchen, G. Enantioslective syntheses of the alkaloids *cis*-195A (Pumiliotoxin C) and *trans*-195A based on multiple applications of asymmetric catalysis. *J. Org. Chem.* **2012**, *77*, 1186-1190.

(14) For a review see: (a) Negishi, E. Novel and selective α-substitution of ketones and other carbonyl compounds based on Pd-catalyzed cross coupling of α,β-unsaturated carbonyl derivatives containing α-halogen or α-metal groups. *J. Organomet. Chem.* **1999**, *576*, 179-194. For selected examples see: (b) Miller, M. W.; Johnson, C. R. Sonogashira coupling of 2-Iodo-2-cycloalkenones: synthesis of (+)- and (-)-Harveynone and (-)-Tricholomenyn A. *J. Org. Chem*. **1997**, *62*, 1582-1583. (c) Handy, S. T.; Zhang, X. Organic synthesis in ionic liquids: the Stille coupling. *Org. Lett*. **2001**, *3*, 233-236. (d) Timbart, L.; Cintrat, J.-C. Synthesis and reactivity of an α-stannyl β-silyl enamide. *Chem. Eur. J.* **2002**, *8*, 1637-1640. (e) Lee, K.; Lee, J.; Lee, P. H. Highly efficient allyl cross coupling reactions of allylindium with organic electrophiles. *J. Org. Chem.* **2002**, *67*, 8265-8268. (f) Nicolau, K. C.; Jennings, M. P.; Dagneau, P. An expedient entry into the fused polyclic skeleton of Vannusal A. *Chem. Commun.* **2002**, 2480-2481. (g) Swamy, N. K.; Tatini, L. K.; Babu, J. M.; Annamalai, P.; Pal, M. Pd-mediated synthesis of substituted benzenes fused with carbocycle/heterocycle. *Chem. Commun.* **2007**, 1035-1037. (h) Pandey, G.; Balakrishman, M. Suzuki crosss-coupling/reductive debenzyloxycarbonylation sequence for the syntheses of [c] annulated isoquinolines: application for the syntheses of Pancratistatin-like isoquinolines *J. Org. Chem.* **2008**, *73*, 8128-8131.

(15) For the use of Baylis-Hilman type synthesis of cyclic α-iodoenones see: (a) Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W.; Wovkulich, P. M.; Uskoković, M. R. Direct α-iodination of cycloalkenones. *Tetrahedron Lett.* **1992**, *33*, 917-918. (b) Sha, C.-K.; Huang, S.-J. Synthesis of β-substituted α-iodocycloalkenones. *Tetrahedron Lett*. **1995**, *36*, 6927-6928. (c) Djuardi, E.; Bovosombat, P.; Nelis, E. M Formations of α-iodoenones by iodine and catalytic amounts of amines. *Synth. Commun.* **1997**, *27*, 2497-2503. (d) Krafft, M. E.; Cran, J. W. A convenient protocol for the α-iodination of α,β-unsaturated carbonyl compounds with I_2 in an aqueous medium. *Synlett* **2005**, 1263-1266. For the use of elaborated α-sylyl and α-stannyl enones see: (e) Bellina, F.; Carpita, A.; Ciucci, D.; De Santis, M.; Rossi, R. New synthetic applications

of organotin compounds: synthesis of stereodefined 2-iodo-2-alkenones, 2-substituted (*E*)-2-alkenones and 2-methyl-2-cycloalkenones. *Tetrahedron* **1993**, *49*, 4677-4698. (f) Alimardanov, A.; Negishi, E. Synthesis of α-iodo-α,β-unsaturated ketones by the reaction of α-silyl-α,β-unsaturated ketones with ICl or ICl-$AlCl_3$. *Tetrahedron Lett.* **1999**, *40*, 3839-3842.

(16) (a) Angara, G. J.; McNelis, E. α-Haloenones from secondary alkynols. *Tetrahedron Lett.* **1991**, *32*, 2099-2100. (b) Bovonsombat, P.; McNelis; E. Ring expansions of alkynyl cyclopentanols with iodine and Koser's reagent. *Tetrahedron* **1993**, *49*, 1525-1534. (c) Morán, W. J.; Rodríguez, A. Hypoiodous acid initiated rearrangement of tertiary propargylic alcohols to α-iodoenones. *Org. Biomol. Chem.* **2012**, *10*, 8590-8592.

(17) Wang, Y.; Genoux, A.; Ghorai, S.; Chen, H.; Todd, R.; Zhang L. Direct conversion of internal alkynes into α-iodoenones: one-step collaborative iodination and oxidation. *Adv. Synth. Cat.* **2016,** *358*, 1417-1420.

(18) Yang, Y.; Hu, W.; Ye, X.; Wang, D.; Shi X. Preparation of triazole gold(III) complex as an effective catalyst for the synthesis of *E*-α-haloenones. *Adv. Synth. Cat.* **2016**, *358*, 2583-2588.

(19) (a) Suárez-Pantiga, S.; Palomas, D.; Rubio, E.; González, J. M. Consective C-H functionalization reactions of arenes: synthesis of carbo-and heteropolycyclic skeletons. *Angew. Chem. Int. Ed.* **2009**, *48*, 7857-7861. (b) Suárez-Pantiga, S.; Rubio, E.; Álvarez-Rúa, C.; González, J. M. Intermolecular reaction of internal alkynes and imines: propargyl tosylates as key partners in a gold-catalyzed [4 + 1] unusual cyclization leading to cyclopent-2-enimines.*Org. Lett.* **2009**, *11*, 13-16.

(20) (a) For an isolated NIS-promoted rearrangement example from electron-rich propargylic derivatives see: Urbanaitė, A.; Jonušis, M.; Bukšnaitienė, R.; Balkaitis, S.; Čikotienė, I. Electrophilic-mediated reactions of functionalized propargylic substrates. *Eur. J. Org. Chem.* **2015**, 7091-7113.

(21) For the use acid additives with IPy_2BF_4 see ref 12. With NIS see for instance: Prakash, G. K. S.; Mathew, T.; Hoole, D.; Esteves, P. M.; Wang, Q.; Rasul, G.; Olah, G. A. N-halosuccinimide/BF_3-H_2O, efficient electrophilic halogenating systems for aromatics. *J. Am. Chem. Soc.* **2004**, *126*, 15770-15776.

(22) At least two acid equivalents are needed to neutralize all pyridine moieties and liberate a more active iodonium ion.

(23) See Supporting Information

(24) To demonstrate the presence of **4a** in the crude reaction mixture, this complex was prepared by *in situ* reaction of enone **3a** with one equivalent of $BF_3{\cdot}OEt_2$ in CD_2Cl_2. See Suporting Information.

(25) TsF could be isolated [36.1 mg, 83%, Rf (hexame / AcOEt 20:1) = 0.3] when the reaction is run according to the general procedure described in the experimental section at 0.25 mmol scale. See Supporting Information.

(26) Omar, M. A.; Frey, W.; Conrad, J.; Beifuss, U. Transition-metal-freess synthesis of imidazo[2,1-*b*]thiazoles and thiazolo[3,2-*a*]benzimidazoles via an *S*-propargylation/5-*exo*-*dig* cyclization/isomerization sequence using propargyl tosylates as substrates**.** *J. Org. Chem.* **2014**, *79*, 10367-10377.

(27) Asano, K.; Masura, S. Amphiphilic organocatalyst for Schotten-Baumann-type tosylation of alcohols under organic solvent free condition. *Org. Let*. **2009**, *11*, 1757-1759.

(28) Loren, J. C.; Sharpless, K. B. The Banert cascade: A synthetic sequence to polyfunctional *N*H-1,2,3-triazoles. *Synthesis* **2005**, *9*, 1514-1520.

(29) Sylvester, K. T.; Chirik, P. J. Iron-catalyzed, hydrogen-mediated reductive cyclization of 1,6-enynes and diynes: evidence for bis(imino)pyridine ligand participation. *J. Am. Chem. Soc.* **2009**, *131*, 8772-8774.

30) Srihari, P.; Sridhar, Y. Total synthesis of both enantiomers of macrocyclic lactone Aspergillide C. *Eur. J. Org. Chem.* **2011, 6690-6697.**

(31) Karstens, W. F. J.; Palladium-Catalyzed Cyclization Reractions of Allene Palladium-Catalyzed Cyclization - and Acetylene-Substituted Lactams. PhD. Thesis, 2000, https://dare.uva.nl/search?identifier=51cf41c2-ca63-44d5-8ded-4df33ecc6cb3.

(32) Lian, J.-J.; Chen, P.-C.; Lin, Y.-P.; Ting, H.-C.; Liu, R.-S. Gold-catalyzed intramolecular [3 + 2]-cycloaddition of arenyne-yne functionalities. *J. Am. Chem. Soc.* **2006**, *128*, 11372-11373.

(33) Imagawa, H.; Asai, Y.; Takano, H.; Hamagaki, H.; Nishizawa, M. Mercuric triflate-catalyzed reaction of propargyl acetates with water leading vinyl ketones. *Org. Lett*. **2006**, *8*, 447-450.

(34) Tanaka, K.; Nishida, G.; Ogino, M., Hirano, M.; Noguchi, K. Enantioselective synthesis of axially chiral biaryls through rhodium-catalyzed complete intermolecular cross-cyclotrimerization of internal alkynes. *Org. Lett*. **2005**, *7*, 3119-3121.

(35) Wang, S.; Zhang, L A. Highly efficient preparative method of α-ylidene-β-diketones via Au^{III} catalyzed acyl migration of propargylic esters. *J. Am. Chem. Soc.* **2006**, *128*, 8414-8515.