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Title: Divergent Halogenation Pathways of 2,2-Dichlorobut-3-yn-1-ols to 3-Chloro-4-iodofurans and α-Chloro-γ-Iodoallenes: Electrophilic versus Pd(II)-Catalyzed Halogenation Strategies

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Divergent Halogenation Pathways of 2,2-Dichlorobut-3-yn-1-ols to 3-Chloro-4-iodofurans and α-Chloro-γ-Iodoallenes: Electrophilic versus Pd(II)-Catalyzed Halogenation Strategies

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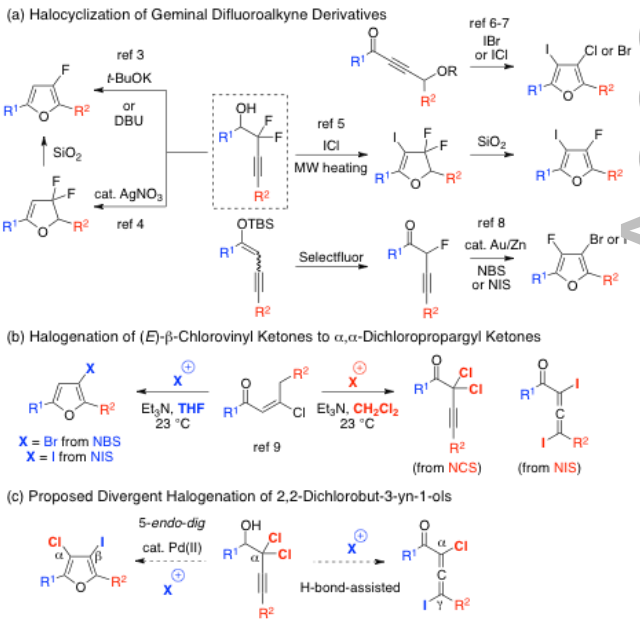
Abstract. Divergent halogenation pathways of 2,2-dichlorobut-3-yn-1-ols have been developed to give 3,4-dihalofurans and 1,3-dihaloallenyl ketones in good to excellent yields. Thus, the readily accessible 2,2-dichlorobut-3-yn-1-ols were treated with the electrophilic halogen source to provide the 1,3-dihalogen-substituted allenyl ketones, whereas the use of Pd(II) catalyst promoted the oxypalladation followed by the electrophilic halogenation to give 3,4-dihalogen-substituted furan derivatives. The synthetic utility of 3,4-dihalofurans and 1,3-dihaloallenyl ketones is demonstrated in the sequential Suzuki cross coupling strategies.

Keywords: Haloallenes; Dehydrochlorination; Divergent Halogenation; Halofurans; Palladium Catalysis

The halogenated compounds play indispensable roles in drug discovery with improved metabolic stability and lipophilicity.[1] The α,α-dihalo carbonyl compounds are useful synthetic intermediates, particularly serving as the precursors for halogen-containing chemical entities.[2] The reduction of α,α-difluoro carbonyl ketones, for example, provides 2,2-difluoro alcohols, and the presence of a suitable alkyne moiety has provided a facile access to 3-fluorofuran derivatives under the basic[3] and the $AgNO_3$ catalysis conditions[4] (Scheme 1a). In this context, the Hammond group in 2008 achieved the microwave-mediated iodocylization of 2,2-difluorobut-3-yn-1-ols with ICl to give 3-fluoro-4-iodofuran derivatives after the aromatization using silica gel.[5] The electrophilic halogenation of propargyl ketones to 3,4-dihalofurans has been developed by the Müller group[6] and Yamamoto group,[7] respectively, and the Dembinski group in 2012 reported the sequential halogenation of alkenyl silyl ethers with Selectfluor followed by the NBS or NIS treatment to give 3,4-dihalogenated furans under the catalysis of $AuCl/ZnBr_2$.[8] While the 2,2-difluorobut-3-yn-1-ol derivatives provide a ready access to 3-fluorofuran derivatives, the corresponding 2,2-dichlorobut-3-yn-1-ols are not known and their chemical reactivity is yet to be explored. The devoid of synthetic methods to 2,2-dichlorobut-3-yn-1-ol derivatives prompted us to utilize α,α-dichloropropargyl ketones, readily accessed from the selective chlorination of (*E*)-β-chlorovinyl ketones[9] (Scheme 1b). Given that the bond dissociation energies of Cα-F bonds are higher than those of Cα-Cl bonds,[10] different bond cleavage events are anticipated for the halogenation of 2,2-dichlorobut-3-yn-1-ols. Herein, we describe the divergent halogenation pathways of 2,2-dichlorobut-3-yn-1-ols to 1,3-dihaloallenyl ketones and 3,4-dihalofurans (Scheme 1c). The strikingly different reactivity behavior of 2,2-dichlorobut-3-yn-1-ols highlights the unique stereoelectronic effect of chlorine atoms[11] and the superior π interactions of the Pd(II) catalysts.



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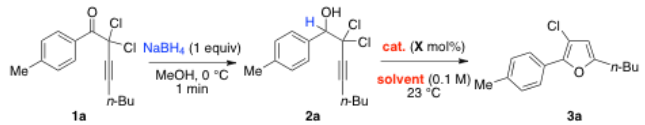
Scheme 1. Divergent electrophilic cyclization of α,α-dihalobut-3-yn-1-ols.

To establish a ready access to 2,2-dichlorobut-3-yn-1-ols, the α,α-dichloropropargyl ketone **1a** was reduced by $NaBH_4$ at ambient temperature (Table 1). After work-up and removal of solvent, an analytically pure 2,2-dichlorobut-3-yn-1-ol **2a** was obtained. Thus, without further purification the THF solution of **2a** was subjected to a variety of metal catalysts. The use of copper (CuCl, $CuCl_2$), zinc ($Zn(OTf)_2$), indium ($In(OTf)_3$), and nickel ($Ni(OAc)_2$) catalysts did not promote the cyclization of **2a**, however the utilization of $AgNO_3$ under refluxing THF provided the desired 3-chlorofuran **3a** in 21% yield (entry 1). While the $AgNO_3$-catalyzed cyclization of 2,2-difluorobut-3-yn-1-ols was demonstrated with 10 mol% catalyst loading by Hammond,[3] a stoichiometric amount of $AgNO_3$ was required for the cyclization of 2,2-dichlorobut-3-yn-1-ol **2a**. To our delight, the high catalytic activity was observed with Au(I) catalyst (entry 2) and Pd(II) catalysts (entries 3-6). Among them, the use of $Pd(TFA)_2$ provided the desired product **3a** in 81% yield (entry 6). The $Pd(TFA)_2$-catalyzed reaction also proceeded in other solvents, although somewhat diminished yields of **3a** was observed in 47-61% (entries 7-9). The control experiment confirmed the optimal $Pd(TFA)_2$ catalyst loading to be 5 mol%, where the use of 1 mol% loading significantly slowed down the reaction (entry 10).

Table 1. Optimization of metal-catalyzed 5-*endo-dig* cyclization.[a]

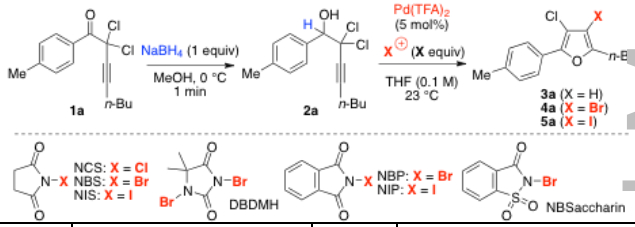


entry	cat. (mol%)	solvent	*T* (h)	yield (%)[b]
1[c]	$AgNO_3$ (20)	THF	6	21
2	Me_2SAuCl (5)	THF	6	64
3	$PdCl_2$ (5)	THF	6	68
4	$Pd(CH_3CN)_2Cl_2$	THF	3	72
5	$Pd(OAc)_2$ (5)	THF	3	64
6	$Pd(TFA)_2$ (5)	THF	3	81(83)[d]
7	$Pd(TFA)_2$ (5)	CH_2Cl_2	3	61
8	$Pd(TFA)_2$ (5)	$PhCH_3$	5	55
9	$Pd(TFA)_2$ (5)	CH_3OH	3	47
10	$Pd(TFA)_2$ (1)	THF	72	19

[a] Thee crude **2a** (0.3 mmol) from the $NaBH_4$ reduction was dissolved in 1 mL solvent (0.1 M) with metal catalyst (**x** mol%) at ambient temperature under argon atmosphere. [b]Isolated yields after column chromatography. [c]Reaction at 66 °C. [d] Reaction in 1 mmol scale.

Motivated by the possibility of Pd-catalyzed halogenation without the use of directing groups,[12] further synthetic exploration of the $Pd(TFA)_2$-catalyzed 5-*endo-dig* cyclization of 2,2-dichlorobut-3-yn-1-ols was examined in the presence of electrophilic halogen sources (Table 2). Thus, under the optimized $Pd(TFA)_2$-catalyzed conditions the electrophilic chlorine source was added (entry 1). Unfortunately, the chlorocyclization of 2,2-dichlorobut-3-yn-1-ol **2a** was not observed, only leading to 3-chlorofuran **3a** in 20% yield. The use of electrophilic brominating reagents provided the desired 3-bromo-4-chlorofuran **4a** in 13-23% yields, however the formation of **3a** was also accompanied (entries 2-5). The employment of iodinating reagent, I_2, provided the desired 3-chloro-4-iodofuran **5a** in 10% yield (entry 6). Switching the iodinating reagent to N-iodosuccinimde (NIS) improved the yield of **5a** to 66% yield (entry 7). A 1:5.3 mixture of 3-chlorofuran **3a** and 3-chloro-4-iodofuran **5a** was observed upon using N-iodophthalimide (NIP) (entry 8). The varied amounts of NIS revealed that 1.1 equiv of NIS was optimal for the iodocyclization of 2,2-dichlorobut-3-yn-1-ol (entry 9), where the desired product 3-chloro-4-iodofuran **5a** was obtained in 79% yield.

Table 2. Optimization of $Pd(TFA)_2$-Catalyzed 5-*endo-dig* Halocyclization.[a]



entry	halogen (equiv)	*T* (h)	yield (%)[b]
1	NCS (1.5)	24	20% (**3a**)
2[c]	NBS (1.5)	9	28%+13% (**3a**+**4a**)
3[c]	NBP (1.5)	4	14%+23% (**3a**+**4a**)
4[c]	NBSaccharin (1.5)	1	28%+21% (**3a**+**4a**)
5[c]	DBDMH (2.0)	1	10%+18% (**3a**+**4a**)
6[c]	I_2 (1.5)	1	10%, **5a**
7	NIS (1.5)	1	66%, **5a**
8[c]	NIP (1.5)	1	5%+27% (**3a**+**5a**)
9	NIS (1.1)	3	79 (81)[d], **5a**

[a] The crude **2a** (0.3 mmol) from the $NaBH_4$ reduction was dissolved in 1 mL solvent (0.1 M) with $Pd(TFA)_2$ (5 mol%) at ambient temperature under argon atmosphere. [b]Isolated yields after column chromatography. [c] Halofurans obtained as an inseparable mixture. [d] Reaction in 1 mmol scale.

Under the optimized $Pd(TFA)_2$-catalyzed 5-*endo-dig* (iodo)cyclization conditions, the substrate scope of 2,2-dichlorobut-3-yn-1-ols was examined (Scheme 2). The reactions, in general, worked well

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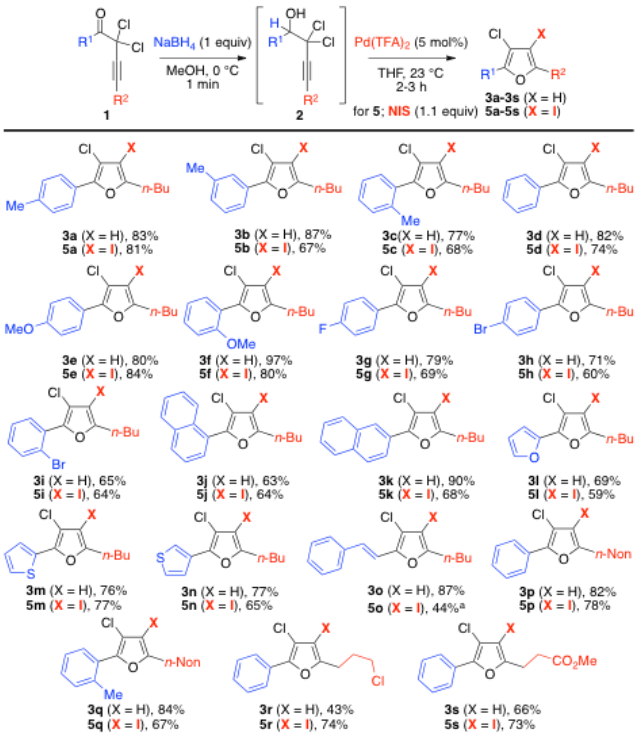
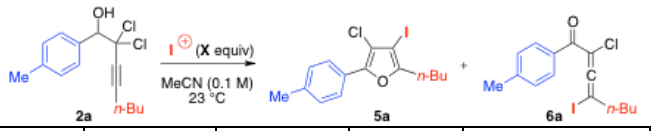
for various 2,2-dichlorobut-3-yn-1-ols, where the aryl bromide **3h/5h-3i/5i**, heterocycle **3l/5l-3n/5n**, alkene **3o/5o**, alkyl chloride **3r/5r**, and ester **3s/5s** moieties were tolerated to give the desired 3-chlorofurans **3** and 3-chloro-4-iodofurans **5** in 43-97% yields.



Scheme 2. Substrate scope of $Pd(TFA)_2$-catalyzed 5-*endo-dig* (iodo)cyclization.

The 5-*endo-dig* iodocyclization pathway of 2,2-dichlorobut-3-yn-1-ol **2a** was suppressed in the absence of $Pd(TFA)_2$ catalyst (Table 3). Thus, the use of 3 equiv of NIS in combination of $NaHCO_3$ provided a mixture of 3-chloro-4-iodofuran **5a** and α-chloro-γ-iodoallenyl ketone **6a** in 37% and 13% yield, respectively (entry 1). Since the reaction outcome was precarious due to the small amount of water/MeOH impurities from the reduction of allenyl ketone **1a**, the purified 2,2-dichlorobut-3-yn-1-ol **2a** was used in the presence of dehydrating agents (entries 2-3). The use of Na_2SO_4 improved the formation of **6a** to 47% yield, however the allenyl product **6a** could not be separated from the furanyl product **5a** (entry 3). The nature of base was critical since Na_2CO_3 instead of $NaHCO_3$ provided the 3-chloro-4-iodofuran **5a** as a major product in 51% yield (entry 4). The use of LiOH provided a similar outcome as $NaHCO_3$, leading to a 1:3 mixture of **5a** and **6a** (entry 5). The final fine-tuning of the reaction conditions focused on to the use of 3.0 equiv of NIS and degassed MeCN (entry 7). Gratifyingly, such modification provided the *exclusive* formation of **6a** in 76% yield without the formation of **5a**. The control experiment demonstrated the importance of NIS and $NaHCO_3$ amounts for the selective formation of α-chloro-γ-iodoallenyl ketone **6a** (entries 8-9). The current dehydrochlorinative iodination of **2a** did not work with other iodinating reagents (entries 10-11), and the use of $NaHCO_3$ was needed for the faster reaction (entry 12), possibly mopping the HCl by-product.

Table 3. Optimization of dehydrochlorinative iodination.[a]



entry	halogen (equiv)	base (equiv)	additive	yield (%)[b] **5a**	**6a**
1	NIS (3.3)	$NaHCO_3$ (3.3)	-	37%	13%
2	NIS (3.3)	$NaHCO_3$ (3.3)	4 Å MS	15%	8%
3	NIS (3.3)	$NaHCO_3$ (3.3)	Na_2SO_4	15%	47%
4	NIS (3.3)	Na_2CO_3 (3.3)	Na_2SO_4	51%	20%
5	NIS (3.3)	LiOH (3)	Na_2SO_4	15%	45%
6	NIS (3.0)	$NaHCO_3$ (3.0)	Na_2SO_4	13%	56%
7[c]	NIS (3.0)	$NaHCO_3$ (3.0)	Na_2SO_4	0%	76%
8[c]	NIS (2.5)	$NaHCO_3$ (2.5)	Na_2SO_4	15%	46%
9[c]	NIS (3.5)	$NaHCO_3$ (3.5)	Na_2SO_4	7%	42%
10[c]	NIP (3.0)	$NaHCO_3$ (3.0)	Na_2SO_4	0%	0%
11[c]	I_2 (3.0)	$NaHCO_3$ (3.0)	-	64%	0%
12[c]	NIS (3.0)	-	-	0%	27%

[a] Reaction using **2a** (0.3 mmol) in MeCN (3 mL, 0.10 M) with halogen source (**x** equiv), base (**x** equiv), and additive (300 mg) at ambient temperature under argon atmosphere. [b]Isolated yields after column chromatography. [c] Degassed for 20 min.

The scope and limitation of dehydrochlorinative iodination of 2,2-dichlorobut-3-yn-1-ols are illustrated in Scheme 3. Of note, the α-chloro-γ-iodoallenyl ketones were not stable upon prolonged exposure to the reaction conditions, thus speeding-up the reaction was required in more concentrated conditions. Thus, the reactions of 2,2-dichlorobut-3-yn-1-ols **2b** and **2c** were performed in 0.6 M concentration, where the formation of the corresponding products **6b** and **6c** was accomplished within 5 min. Also, the 2,2-dichlorobut-3-yn-1-ols **2g** and **2h** were subjected to the 0.3 M concentration to give the products **6g** and **6h** in 66% and 69% yields, respectively. While the presence of furan and ester moieties in **2l** and **2s** presented the functional group compatibility issue, the corresponding α-chloro-γ-iodoallenyl ketones with thiophene **6m-6n**, alkene **6o**, and alkyl chloride **6r** were obtained in 30-69% yields.

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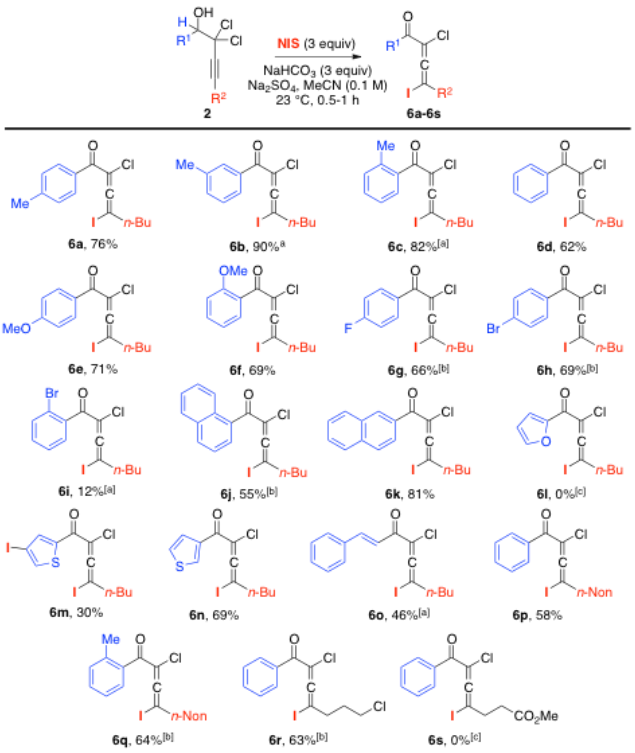
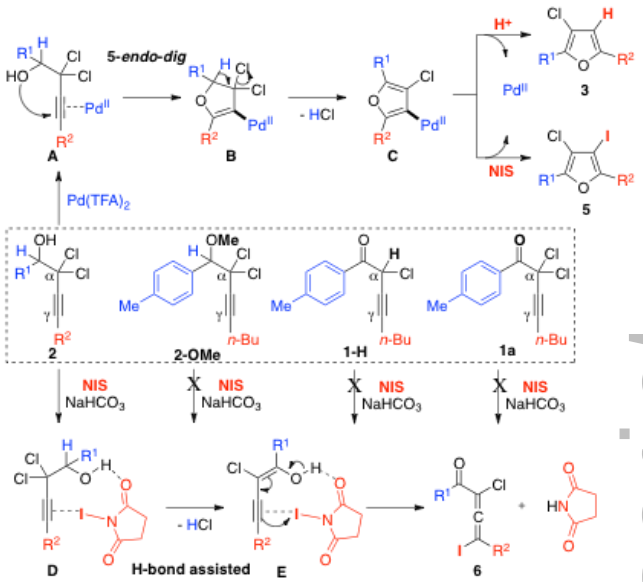


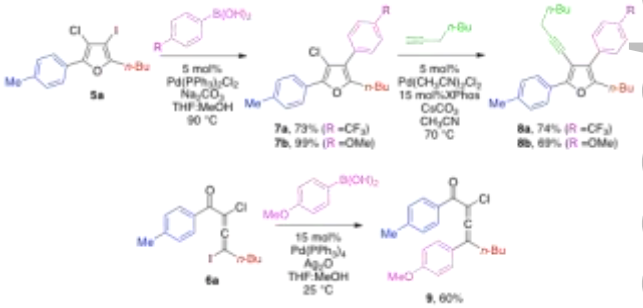
Scheme 3. Substrate scope of dehydrochlorinative iodination to α-chloro-γ-iodoallenyl ketones ([a]Reaction for 5 min in 0.6 M. [b]Reaction for 10 min in 0.3 M. [c]Decomposition).

The divergent halogenation of 2,2-dichlorobut-3-yn-1ols **2** to 3-chloro-4-iodofuran **5** and α-chloro-γ-iodoallenyl ketones **6** could be rationalized based on the π-acidity of Pd(II) species (Scheme 4). Thus, the presence of highly electrophilic $Pd(TFA)_2$ promotes the π-coordination of Pd(II) catalyst **A**. The subsequent 5-*endo-dig* cyclization of **A** leads to the formation of the cyclic palladate **B**, which undergoes the dehydrochlorination to **C**. The fate of furanyl palladate **C** is guided by the electrophilic species in the reaction mixture, diverging to 3-chlorofurans **3** and 3-chloro-4-iodofurans **5**. The fact that the highly electrophilic iodinating reagent, NIS, readily provided the 3-chloro-4-iodofurans **5** clearly demonstrates the preferential π-coordination of $Pd(TFA)_2$ over the electrophilic halogen source, NIS. Our control experiment confirmed that the 3-chlorofurans **3** were not converted to the 3-chloro-4-iodofurans **5** under the halogenation conditions. The treatment of 2,2-dichlorobut-3-yn-1ols **2** with NIS in the absence of Pd(II) catalyst allows the π-coordination of NIS. Since $NaHCO_3$ alone did not promote the dehydrochlorination of 2,2-dichlorobut-3-yn-1ols **2**, the electrophilic activation of **2** by NIS parameterizes the C–H bond of the alcohol moiety, promoting the dehydrochlorination to the enol species **E**. The iodination occurs at the γ-position due to the steric reasons.[13] The use of **2-OMe** substrate without an alcohol moiety did not lead to the formation of α-chloro-γ-iodoallenyl ketone **6a** and the non-basic reaction condition was also confirmed with α-chloroallenyl ketone **1-H**. These results collectively suggest the possible role of the alcohol moiety for the H-bonding assistance. A complex mixture of unknown products was observed from the reaction of α,α-dichloroallenyl ketone **1a** under the optimized conditions, illustrating the unique reactivity pattern of 2,2-dichlorobut-3-yn-1ols **2**.



Scheme 4. Mechanistic rationale for divergent halogenation pathways of 2,2-dichlorobut-3-yn-1ols.

The synthetic utilization of 3-chloro-4-iodofuran **5** and α-chloro-γ-iodoallenyl ketone **6** was demonstrated in the cross-coupling strategies (Scheme 5). Thus, the Suzuki coupling of furan **5a** with electronically different boronic acids smoothly provided the corresponding 3-chlorofurans **7a-7b** in 73-99% yields. The subsequent Sonogashira coupling with hept-1-yne also led to the formation of fully substituted furans **8a-8b** in 69-74% yields. Likewise, the selective Suzuki coupling of allenyl ketone **6a** could be achieved in 60% to give the allenyl ketone **9**.



Scheme 5. Synthesis of fully substituted furans and allenyl ketone.

In summary, we have developed the divergent halogenation pathways of 2,2-dichlorobut-3-yn-1ols to give dihalofurans and dihaloallenyl ketones. The preferential π-acidity of Pd(II) catalyst allowed the 5-*endo-dig* (halo)cyclization pathway of 2,2-dichlorobut-3-yn-1ols, whereas the H-bonding assisted direct halogenation pathway was observed in the absence of Pd(II) catalyst. Given that the C_{sp2}-Cl and C_{sp2}-I bonds are selectively functionalized using the metal-catalyzed cross coupling strategies, the divergent halogenation reactions of 2,2-dichlorobut-

3-yn-1ols should contribute to the synthetic toolbox in the arsenal of synthetic methods. Our current research efforts are directed to the synthetic utility of α,α-dichloroallenyl ketones, and these results will be reported in near future.

Experimental Section

General Procedure for the Pd(TFA)$_2$-Catalyzed 5-*endo-dig* Cyclization

Sodium borohydride (1 equiv., 1 mmol, 37.8 mg) was added portion-wise to a solution of *α*,*α*-dichloropropargyl ketone **1a** (1 mmol, 283.2 mg) in anhydrous methanol (0.1 M, 10 mL) at 0 °C, and the reaction mixture was stirred for 1 minute at the same temperature. After concentrating under vacuum, the remaining residue was dissolved in ethyl acetate (30 mL), washed with water and extracted with ethyl acetate (30 mL x 2). The combined organic layers were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting crude compound **2a** was used in the next step without purification. After dissolving the compound **2a** in anhydrous THF (0.1 M, 10 mL), Pd(TFA)$_2$ (5 mol%, 0.05 mmol, 16.6 mg) was added, and the reaction was stirred under nitrogen at room temperature until the reaction was complete by TLC (3 h). The reaction mixture was concentrated *in vacuo* and purified by silica gel column chromatography to provide **3a** (eluent: Hexanes) in 83% yield.

5-Butyl-3-chloro-2-(*p*-tolyl)furan (3a): Colorless oil (206.2 mg, 83%); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.77 (d, 2H, Ar-H, *J* = 8.40 Hz), 7.21 (d, 2H, Ar-H, *J* = 8.40 Hz), 6.07 (s, 1H, Furan-CH), 2.64 (t, 2H, $\underline{CH_2}(CH_2)_2CH_3$, *J* = 7.80 Hz), 2.37 (s, 3H, Ar-CH_3), 1.68-1.63 (m, 2H, $CH_2\underline{CH_2}CH_2CH_3$), 1.44-1.38 (m, 2H, $CH_2CH_2\underline{CH_2}CH_3$), 0.95 (t, 3H, $(CH_2)_3\underline{CH_3}$, *J* = 7.20 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 154.9, 145.7, 137.1, 129.1, 127.2, 124.6, 110.9, 109.2, 29.9, 27.8, 22.2, 21.3, 13.8; HRMS (ESI): m/z calcd for $C_{15}H_{18}ClO$ [(M+H)$^+$] 249.1041, found 249.1030; IR (Neat, Thermo Nicolet): 2958, 2930, 2872, 2862, 1602, 1558, 1502 cm^{-1}.

General Procedure for the Pd(TFA)$_2$-Catalyzed 5-*endo-dig* Iodocyclization

α,*α*-Dichloropropargyl ketone **1a** (1 mmol, 283.2 mg) was dissolved in anhydrous methanol (0.1 M, 10 mL) under nitrogen followed by the portion-wise addition of sodium borohydride (1 equiv., 1 mmol, 37.8 mg) at 0 °C. After 1 min stirring at the same temperature, methanol was completely removed under vacuum and then the remaining residues were dissolved in ethyl acetate (30 mL), washed with water and further extracted with ethyl acetate (30 mL x 2). After drying the combined organic layers using anhydrous magnesium sulfate, the ethyl acetate was completely evaporated under reduced pressure followed by azeotropic drying using anhydrous toluene to provide a fully dried crude alcohol **2a**. The resulting crude alcohol **2a** was dissolved in anhydrous THF (0.1 M, 10 mL) with the addition of *N*-iodosuccinimide (1.1 equiv, 1.1 mmol, 247.5 mg) under nitrogen. The reaction mixture was stirred until *N*-iodosuccinimide was completely dissolved (about 1 min), and then Pd(TFA)$_2$ (5 mol%, 0.05 mmol, 16.6 mg) was added to this solution. The reaction was stirred for 3 h at room temperature and terminated by the dropwise addition of aqueous saturated sodium thiosulfate until the solution became pale-yellow. The crude product **5a** was extracted with ethyl acetate (30 mL x 3), washed with brine and dried over magnesium sulfate. Purification by silica gel column chromatography gave pure **5a** (eluent: Hexanes) in 81% yield.

2-Butyl-4-chloro-3-iodo-5-(*p*-tolyl)furan (5a): Colorless oil (301.7 mg, 81%); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.76 (d, 2H, Ar-H, *J* = 8.40 Hz), 7.23 (d, 2H, Ar-H, *J* = 8.40 Hz), 2.74 (t, 2H, $\underline{CH_2}(CH_2)_2CH_3$, *J* = 7.20 Hz), 2.37 (s, 3H, Ar-CH_3), 1.70-1.65 (m, 2H, $CH_2\underline{CH_2}CH_2CH_3$), 1.43-1.37 (m, 2H, $CH_2CH_2\underline{CH_2}CH_3$), 0.96 (t, 3H, $(CH_2)_3\underline{CH_3}$, *J* = 7.80 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 155.6, 146.6, 137.8, 129.2, 126.5, 124.8, 115.2, 70.8, 30.0, 28.0, 22.1, 21.3, 13.8; HRMS (ESI): m/z calcd for $C_{15}H_{17}ClIO$ [(M+H)$^+$] 375.0007, found 374.9995; IR (Neat, Thermo Nicolet): 2956, 2928, 2871, 2860, 1588, 1558, 1501, 1464, 1457, 1107, 1088, 1020, 1014 cm^{-1}.

General Procedure for the Dehydrochlorinative Iodination

To a degassed 50 mL round bottom flask charged with 2,2-dichlorobut-3-yn-1-ols **2a** (1 mmol, 285.2 mg) and anhydrous sodium sulfate (999.5 mg), anhydrous and degassed acetonitrile (0.1 M, 10 mL) was added under nitrogen followed by stirring at room temperature until the complete dissolving of **2a**. Sodium bicarbonate (3 equiv., 3mmol, 251.9 mg) and *N*-iodosuccinimide (3 equiv., 3mmol, 674.7 mg) were subsequently added and the reaction was stirred at room temperature for 1 h under nitrogen atmosphere. The reaction mixture color changed gradually from colorless to yellow and then to deep brown. After the compete conversion of **2a** (monitored by TLC), the reaction was quenched by adding saturated aqueous sodium thiosulfate solution until the appearance of pale yellow color. The reaction mixture was extracted using ethyl acetate (30 mL x 3), washed with brine, dried over anhydrous magnesium sulfate and then the solvent was removed *in vacuo* to give the crude **6a** as a yellowish residue. Pure product **6a** was obtained by silica gel column chromatography using a mixture of hexanes and ethyl acetate (v:v = 98:2) as yellow oil in 76% yield.

2-Chloro-4-iodo-1-(*p*-tolyl)octa-2,3-dien-1-one (6a): Yellow oil (85.8 mg, 76%); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.74 (d, 2H, Ar-H, *J* = 7.80 Hz), 7.28 (d, 2H, Ar-H, *J* = 7.80 Hz), 2.89 (t, 2H, $\underline{CH_2}(CH_2)_2CH_3$, *J* = 7.20 Hz), 2.42 (s, 3H, Ar-CH_3), 1.51-1.46 (m, 2H, $CH_2\underline{CH_2}CH_2CH_3$), 1.29-1.23 (m, 2H, $CH_2CH_2\underline{CH_2}CH_3$), 0.86 (t, 3H, $(CH_2)_3\underline{CH_3}$, *J* = 7.20 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 197.2, 187.8, 146.1, 145.3, 130.9, 129.6, 129.5, 104.4, 41.4, 26.1, 21.9, 21.8, 13.7; HRMS (ESI): m/z calcd for $C_{15}H_{17}ClIO$ [(M+H)$^+$] 375.0007, found 375.0014; IR (Neat, Thermo Nicolet): 2958, 2930, 2871, 1678, 1605, 1543 cm^{-1}.

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