JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Brønsted Acid Catalyzed and NIS-Promoted Cyclization of Diynones: Selective Synthesis of 4-Pyrone, 4-Pyridone, and 3-Pyrrolone Derivatives

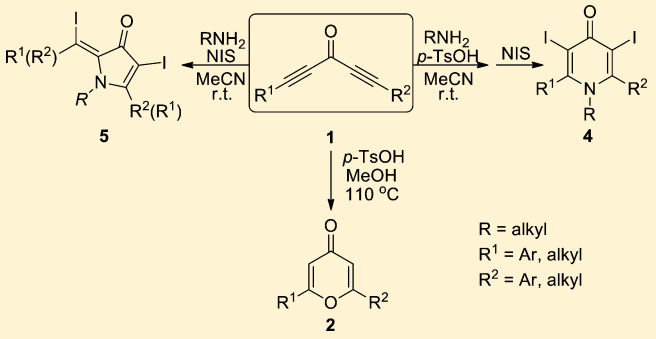
Yi-Feng Qiu,[†] Fang Yang,[†] Zi-Hang Qiu,[†] Mei-Jin Zhong,[†] Li-Jing Wang,[†] Yu-Ying Ye,[†] Bo Song,[†] and Yong-Min Liang*[,†,‡]

[†]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, People's Republic of China

[‡]State Key Laboratory of Solid Lubrication, Lanzhou Institute of Chemical Physics, Chinese Academy of Science, Lanzhou 730000, People's Republic of China

Supporting Information

ABSTRACT: Brønsted acid catalyzed tandem cyclization was found to be highly effective for the preparation of a series of polysubstituted 4-pyrones from diynones (yield up to 99%). 4-Pyridone and 3-pyrrolone derivatives were also selectively synthesized by employing NIS and/or Brønsted acid. NIS as an electrophilic reagent could promote these reactions efficiently and rapidly under very mild reaction conditions.



INTRODUCTION

Five- and six-membered oxygen- or nitrogenated heterocycles, such as 4-pyrone, 4-pyridone, and 3-pyrrolone, are greatly valuable intermediates[1] for the synthesis of pharmacologically relevant therapeutic agents and biologically active natural products.[2] As the key structural subunit, 4-pyrone occurred widely in lots of drug molecules, such as phenoxan,[3a,b] maltol,[3c] and kojic acid.[3d,e] Meanwhile 4-pyridone and 3-pyrrolone subunits are also found in many representative bioactive molecules, such as aspernigrin A,[4a] iodopyridone,[4b] clopidol,[4c] and vermelhotin.[5] So far, various conventional methods have been reported for the development of these skeletons. The well-known synthetic routes to 4-pyrones are via the condensation cyclization reaction of the carbonyl compounds,[3b,6] while the traditional methods for preparing 4-pyridones are involved in the reaction of primary amines with 4-pyrones[2l,m,3d,7] or 1,3,5-triketones[6a] and the three-component hetero-Diels–Alder reaction.[8] Recently, the synthetic strategy via a *N* to *C* 1,3-acyl migration of *N*-aryl acetoacetamides has been reported.[9] The oxidation of substituted pyrrolols,[10] cyclization of carbonyl compounds,[1m,2n,11] and flash vacuum pyrolysis of *N*,*N*-disubstituted aminomethylene Meldrum's acid derivatives[12] are considered to be efficient methods for the synthesis of polysubstituted 3-pyrrolones as well.[13] However, there are still some limitations for the development of these synthetic methods due to the expensive transition-metal catalysts[6d,8,11c,13] and not readily available substrates.[7,8b,10−12] Therefore, a new environmentally friendly (metal free) synthetic strategy for the synthesis of these heterocyclic compounds with high efficiency warrants further investigation.

It is known that diynones are symmetric molecules with multiple reaction sites, which lead to diverse types of interesting cyclization products. Previously, our group has reported Brønsted acid catalyzed highly regioselective cycloisomerization of 5,2-enyn-1-ones to prepare various 4-pyranones,[14a] as well as Brønsted acid catalyzed and iodine-promoted tandem cyclization of the similar substrates to selectively synthesize highly substituted benzene derivatives.[14b] (Scheme 1) Thus, we designed Brønsted acid catalyzed and NIS-promoted C–O and C–N bond formations for the synthesis of 4-pyrone and 4-pyridone derivatives by using diynones with an alcohol and an amine as a nucleophile, respectively. In the process of exploring the synthesis of 4-pyridone derivatives, an NIS-promoted cyclization reaction for the synthesis of 3-pyrrolone derivatives was discovered occasionally. Herein, different reaction systems with diverse nucleophiles afforded various 4-pyrone, 4-pyridone, and 3-pyrrolone derivatives are reported.

RESULTS AND DISCUSSION

Initially, we attempted to explore the designed reaction for the synthesis of 4-pyrones by employing 1,5-diphenylpenta-1,4-diyn-3-one **1a** with *p*-TsOH (20 mol %) in methanol at 65 °C (Table 1, entry 1).[14] After 24 h, we got 35% of the corresponding product **2a** and 32% of the substrate **1a** was recovered.

Received: September 16, 2013
Published: November 1, 2013

 © 2013 American Chemical Society dx.doi.org/10.1021/jo402055a | *J. Org. Chem.* 2013, 78, 12018−12028

Scheme 1. Design of Proposed Cyclization of Ynones

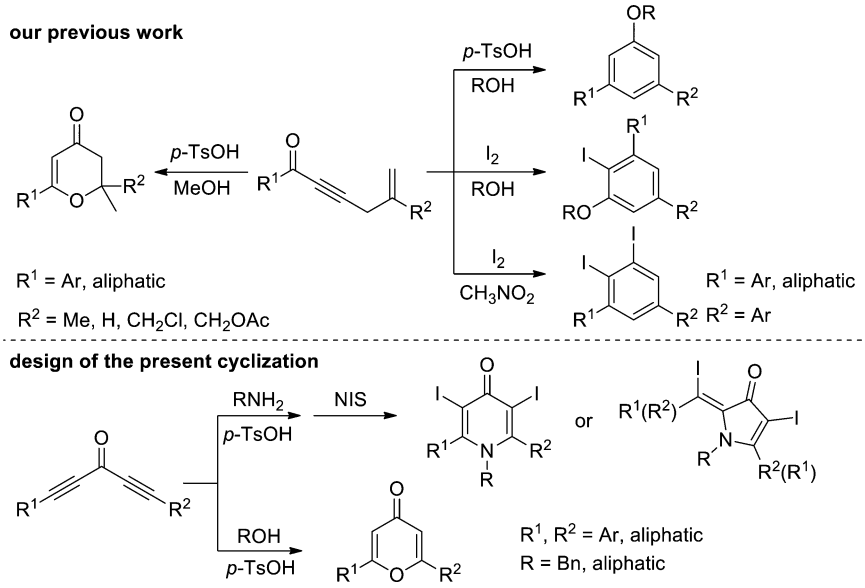
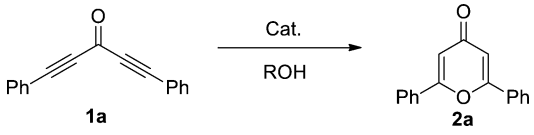


Table 1. Optimization of Cascade Cyclization for the Synthesis of 2a[a]



entry	cat. (mol %)	temp. (°C)	time (h)	yield (%)
1	*p*-TsOH (20)	65	24	35[b]
2	*p*-TsOH (20)	90	10	86
3	TfOH (20)	90	9	70
4	TFA (20)	90	10.5	24
5	HCl (20)	90	12	56
6	4-chlorobenzoic acid (20)	90	18	trace[c]
7	MSA[d] (20)	90	9	72
8	$FeCl_3$	90	7	67
9	$HAuCl_4{\cdot}4H_2O$	90	5	78
10	$AuCl_3$	90	9	84
11	$(PPh_3)AuNTf_2$	90	8	80
12[e]	I_2	90	2	
13[e]	NIS	90	3	
14	*p*-TsOH (15)	90	14	93
15	*p*-TsOH (10)	90	19	74
16	*p*-TsOH (15)	100	12	94
17	***p*-TsOH (15)**	**110**	**8.5**	**99**
18[f]	*p*-TsOH (15)	110	9	95
19[g]	*p*-TsOH (15)	110	9	91
20[h]	*p*-TsOH (15)	110	9	62

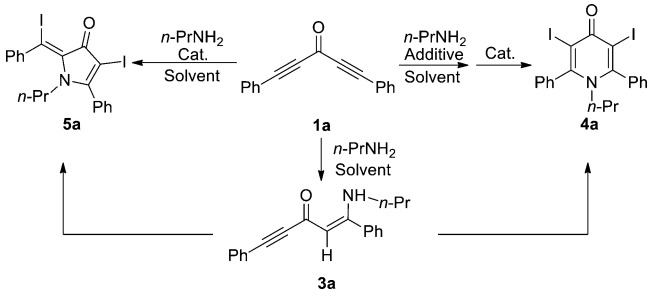
[a]Reaction conditions: **1a** (0.1 mmol) and MeOH (1.0 mL) in the presence of Brønsted or Lewis acids. [b]32% of **1a** was recovered, and 20% of intermediate **A** was isolated. [c]44% of **1a** was recovered, and 40% of intermediate **A** was isolated. [d]MSA = methylsulfonic acid. [e]Products cannot be detected. [f]In ethanol. [g]In MeOH (1.0 mL) with H_2O (1.0 equiv). [h]In MeOH (1.0 mL) with H_2O (10.0 equiv).

Therefore, we raised the temperature to 90 °C. Encouragingly, 86% of **2a** was isolated, and no residual **1a** was detected by TLC analysis (Table 1, entry 2). Followed by this approach, after attempting a series of different Brønsted acids, we found that *p*-TsOH was proved to be the most efficient catalyst (Table 1, entries 3−7). A variety of Lewis acids, such as $FeCl_3$, $HAuCl_4{\cdot}4H_2O$, $AuCl_3$, and $(PPh_3)AuNTf_2$, were also screened; however, no superior yields were obtained (Table 1, entries 8−13). To further optimize the conditions, we adjusted *p*-TsOH to 15 mol %, and the yield increased to 93% after 14 h (Table 1, entry 14). When the temperature was increased to 110 °C, **2a** was isolated in a yield of 99% after 8.5 h (Table 1, entry 17). Finally, with the series of detailed attempts mentioned above, the use of *p*-TsOH (15 mol %) in methanol (1.0 mL) at 110 °C was considered to be the optimal reaction conditions for producing **2a** (conditions **A**).

At the beginning, we used propylamine (1.1 equiv) as a nucleophile in acetonitrile to try to perform our envisaged reaction for the synthesis of 4-pyridones, with $FeCl_3$ (20 mol %) and $HAuCl_4{\cdot}4H_2O$ (20 mol %) as catalysts at room temperature, respectively (Table 2, entries 1 and 2). However, only an intermediate (*Z*)-1,5-diphenyl-1-(propylamino)pent-1-en-4-yn-3-one **3a** was obtained through Michael addition of **1a** with propylamine without further cyclization after 24 h. It even could be isolated in a high yield of 96% without adding any catalysts (Table 2, entry 3). After attempting a series of iodine-containing reagents, we found that a new product (*E*)-4-iodo-2-(iodo(phenyl)methylene)-5-phenyl-1-propyl-1*H*-pyrrol-3(2*H*)-one **5a** was formed with NIS (2.0 equiv) (Table 2, entries 4−7). From the above, we believed that ferric chloride as a strong Lewis acid may activate the carbonyl of the intermediate **3a**, which subsequently went through further cyclization in the presence of iodine-containing reagents.[14b,15] Therefore, ferric chloride (20 mol %) was added first, and then, NIS (2.0 equiv) was added after **1a** completely converted to **3a** (determined by TLC analysis). Finally, we got 28% of the expected product **4a**; meanwhile, 21% of **5a** and 15% of **1a** were isolated (Table 2, entry 9). We increased the amount of NIS to 3.0 equiv, and ferric chloride to 1 equiv. In this way, the reaction progressed to completion and the selectivity was improved at the same time (Table 2, entry 11). Then a series of Lewis acids and Brønsted acids as additives were screened to improve the selectivity (Table 2, entries 12−17). As a result, reaction with *p*-TsOH (1.0 equiv) gave the highest yield of 78% for **4a**, and no **5a** was detected by TLC analysis (Table 2, entry 16). The optimal ratio of NIS and *p*-TsOH was finalized after a series of adjustments (Table 2, entries 18−20).

dx.doi.org/10.1021/jo402055a | *J. Org. Chem.* 2013, 78, 12018−12028

Table 2. Optimization of Cyclization for the Synthesis of 4a[a] and 5a[b]



			yield (%)	
entry	cat. (equiv)	additive (equiv)	4a	5a
1	$FeCl_3$ (0.2)			
2	$HAuCl_4{\cdot}4H_2O$ (0.2)			
3[c]				
4[d]	I_2 (2)			
5[d]	IBr (2)			
6[d]	ICl (2)			
7[e]	NIS (2)		trace	49
8[e]	I_2 (2)	$FeCl_3$ (0.2)		
9[f]	NIS (2)	$FeCl_3$ (0.2)	28	21
10	NIS (3)	$FeCl_3$ (0.2)	33	45
11	NIS (3)	$FeCl_3$ (1.0)	56	22
12	NIS (3)	$Sc(OTf)_3$ (1.0)	trace	53
13	NIS (3)	$AlCl_3$ (1.0)	45	33
14	NIS (3)	$BF_3{\cdot}Et_2O$ (1.0)	22	49
15	NIS (3)	TfOH (1.0)	26	51
16	NIS (3)	*p*-TsOH (1.0)	78	0
17	NIS (3)	TFA (1.0)	74	trace
18	NIS (3)	*p*-TsOH (1.2)	80	0
19	**NIS (2.8)**	***p*-TsOH (1.2)**	**81**	**0**
20	NIS (2.5)	*p*-TsOH (1.2)	63	0
21	NIS (2.5)		0	69
22	**NIS (2.8)**		**0**	**82**
23	NIS (3.0)		0	80

[a]Reaction conditions: **1a** (0.1 mmol) and propylamine (1.1 mmol) in the presence of Brønsted or Lewis acids in MeCN (1.0 mL) at room temperature; NIS was added after **1a** completely converted to **3a**. [b]Reaction conditions: **1a** (0.1 mmol) and propylamine (1.1 mmol) in the presence of NIS in MeCN (1.0 mL) at room temperature. [c]96% of intermediate **3a** was isolated. [d]Products cannot be detected. [e]20% of intermediate **3a** was recovered. [f]15% of intermediate **3a** was recovered.

Meanwhile, the best conditions to generate **5a** were also settled by modifying the dose of NIS (Table 2, entries 21−23). Ultimately, the optimal conditions for generating **4a** were identified as propylamine (1.1 equiv) and *p*-TsOH (1.2 equiv) in MeCN (1.0 mL); NIS (2.8 equiv) was added after the full conversion of **1a** at room temperature (conditions **B**). The best conditions for generating **5a** were propylamine (1.1 equiv) in MeCN with NIS (2.8 equiv) at room temperature (conditions **C**).

A series of symmetrical and asymmetrical diynones (**1b**−**1m**, **1t**, and **1n**−**1s**) were prepared to investigate the scope of the *p*-TsOH-catalyzed electrophilic cyclization reaction. The corresponding substituted 4-pyrone derivatives **2a**−**2s** were obtained in moderate to good yields under conditions **A** (Table 3). The structure of **2a** was confirmed by X-ray crystal structure analysis (see the Supporting Information). The influences of substituent electronic effects on the reaction were shown as the following: unsubstituted phenyl and aryl with weak electron-donating groups (EDG) gave the satisfying yields (**2a**−**2d**, except **2e**), whereas aryl with electron-withdrawing groups (EWG) slightly decreased the yields (**2g**−**2j**). Furthermore, substrates bearing larger and more branched alkyl groups worked better for this transformation (**2f**, **2k**−**2m**). However, when R^1 and R^2 were both a *p*-methoxyphenyl group, only a trace amount of **2t** was detected, whereas 66% of **2o** was still obtained when one substituent was replaced by phenyl. We believed that the strong EDG increased the electron density and decreased the electrophilicity of the carbon−carbon triple bond of the substrate, which made it difficult for oxygen atom to attack. When R^1 was an aryl group, and R^2 was a sterically hindered group (1-naphthyl group; **1r**) or a heterocyclic group (2-thienyl; **1s**), the reaction still occurred smoothly and the yields of 64% and 65% for their corresponding products were obtained.

Subsequently, we explored the scope of the NIS-promoted selective synthesis of 4-pyridone derivatives under standard conditions **B**, with the above substrates (shown in Table 3). Notably, most of the substrates converted into the corresponding 4-pyridone derivatives in moderate yields. The reaction was more sensitive to substituent electronic effects than the *p*-TsOH-catalyzed reaction mentioned above, but with the similar rules. Substrates with alkyl groups gave lower yields (**4f**), even trace yields of the products (**4k**−**4m**). For aryl and cyclopropyl groups, the enamine tautomer with a more nucleophile nitrogen is more stable due to conjugation of these groups with the alkene. For alkyl groups, formation of a less nucleophilic imine tautomer is consistent with the observed results. However, the substrate contained a sterically hindered group, the 1-naphthyl group, **1r**, which gave the much lower yield than phenyl, indicating that the steric effect played a major role in this transformation. When R^2 was a *tert*-butyl group, 29% yield of **4p** was obtained and a trace of **4q** was detected by MS.

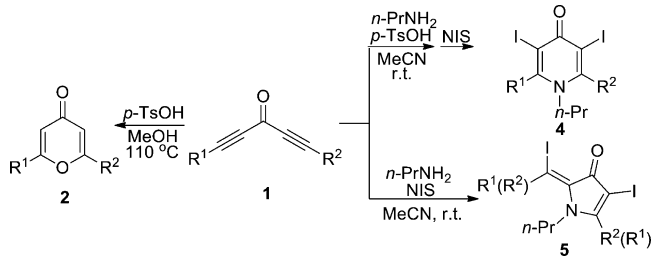
Next, we tested the substrate tolerance of NIS-promoted selective synthesis of 3-pyrrolone derivatives under conditions **C**. Various symmetrical diynones proceeded smoothly to afford the corresponding products in moderate yields. The electronic effect and steric effect of the substituents were similar to the NIS-promoted synthesis of 4-pyridone derivatives. The selective addition of propylamine with asymmetrical diynones would lead to different 3-pyrrolones. Then we chose substrates **1n** and **1p** to study the regioselectivity of the reaction of amines and the alkyne moiety. We found that nucleophiles tended to attack the carbon−carbon triple with EWG; the yields of **5na** and **5pb** were better than **5nb** and **5pa**, respectively.

To explore the scope of NIS promoting the synthesis of 4-pyridone and 3-pyrrolone derivatives for the amines and electrophilic reagents, we also investigated different amines and electrophilic reagents under conditions **B** and **C**, respectively (Scheme 2). Aliphatic amines could react with good yields, whereas the aromatic amine only gave a trace yield. We believe, due to that the lone pair electrons of nitrogen atoms in arylamines made conjugation with aryl groups, the nucleophilicity of arylamines was weaker than aliphatic amines. Therefore, a 37% yield of intermediate **3ad** from aniline was obtained. The structure of **4ab** was confirmed by X-ray crystal structure analysis (see the Supporting Information).

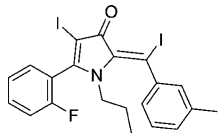
An obvious feature of our method is that the iodosubstituted 4-pyridones and 3-pyrrolones generated by NIS-promoted cyclization can be the advantageous intermediates for the synthesis of some natural products by using various palladium-catalyzed reactions.[16] For example, the Suzuki coupling[17] of **4a**,

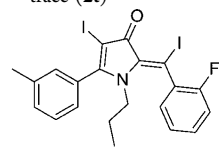
dx.doi.org/10.1021/jo402055a | J. Org. Chem. 2013, 78, 12018−12028

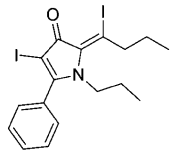
Table 3. Synthesis of 4-Pyrone Derivatives 2, 4-Pyridone Derivatives 4, and 3-Pyrrolone Derivatives 5 from Diynones 1[a]

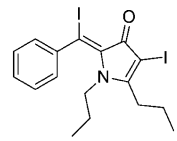


			yield (%)		
entry	substrate (R^1)	substrate (R^2)	2	4	5
1	Ph	Ph	99 (**2a**)	81 (**4a**)	82 (**5a**)
2	*m*-MeC_6H_4	*m*-MeC_6H_4	99 (**2b**)	90 (**4b**)	93 (**5b**)
3	*p*-MeC_6H_4	*p*-MeC_6H_4	84 (**2c**)	85 (**4c**)	82 (**5c**)
4	*p*-EtC_6H_4	*p*-EtC_6H_4	81 (**2d**)	76 (**4d**)	79 (**5d**)
5	*p*-(*n*-PrC_6H_4)	*p*-(*n*-PrC_6H_4)	55 (**2e**)	55 (**4e**)	58 (**5e**)
6	cyclopropyl	cyclopropyl	83 (**2f**)	45 (**4f**)	46 (**5f**)
7	*o*-FC_6H_4	*o*-FC_6H_4	84 (**2g**)	81 (**4g**)	79 (**5g**)
8	*m*-FC_6H_4	*m*-FC_6H_4	60 (**2h**)	63 (**4h**)	51 (**5h**)
9	*p*-FC_6H_4	*p*-FC_6H_4	88 (**2i**)	90 (**4i**)	86 (**5i**)
10	*p*-ClC_6H_4	*p*-ClC_6H_4	61 (**2j**)	35 (**4j**)	42 (**5j**)
11	*tert*-butyl	*tert*-butyl	99 (**2k**)	trace (**4k**)[c]	trace (**5k**)[c]
12	*n*-Pr	*n*-Pr	76 (**2l**)	trace (**4l**)[c]	trace (**5l**)[c]
13	*n*-pentyl	*n*-pentyl	64 (**2m**)	trace (**4m**)[c]	trace (**5m**)[c]
14	*m*-MeC_6H_4	*o*-FC_6H_4	93 (**2n**)	67 (**4n**)	
15	Ph	*p*-$OMeC_6H_4$	66 (**2o**)	40 (**4o**)	
16	Ph	*n*-Pr	70 (**2p**)	29 (**4p**)	
17	*p*-MeC_6H_4	*tert*-butyl	78 (**2q**)	trace (**4q**)[d]	
18	*p*-MeC_6H_4	1-naphthyl	64 (**2r**)	39 (**4r**)	
19	Ph	2-thienyl	65 (**2s**)	46 (**4s**)	
20	*p*-$OMeC_6H_4$	*p*-$OMeC_6H_4$	trace (**2t**)[b]	trace (**4t**)[b]	trace (**5t**)[b]


5na (62%)


5nb (19%)


5pa (22%)


5pb (49%)

[a]Conditions **A** for **2**: the reaction was carried out by using **1** (0.1 mmol) and *p*-TsOH (15 mol %) in methanol (1.0 mL) at 110 °C. Conditions **B** for **4**: the reaction was carried out by using **1** (0.1 mmol) and propylamine (1.1 equiv) with *p*-TsOH (1.2 equiv) in acetonitrile (1.0 mL) at room temperature. NIS (2.8 equiv) was added after **1** converted into **3** completely (detected by TLC analysis). Conditions **C** for **5**: the reaction was carried out by using **1** (0.1 mmol) and propylamine (1.1 equiv) with NIS (2.8 equiv) in acetonitrile (1.0 mL) at room temperature. [b]Decomposed. [c]Over 50% of intermediate **3** could be obtained without adding NIS. [d]52% of (*Z*)-6,6-dimethyl-1-(propylamino)-1-(*p*-tolyl)hept-1-en-4-yn-3-one and 43% of (*Z*)-6,6-dimethyl-5-(propylamino)-1-(*p*-tolyl)hept-4-en-1-yn-3-one were obtained without adding NIS (distinguished by ^{1}H NMR and H−H COSY).

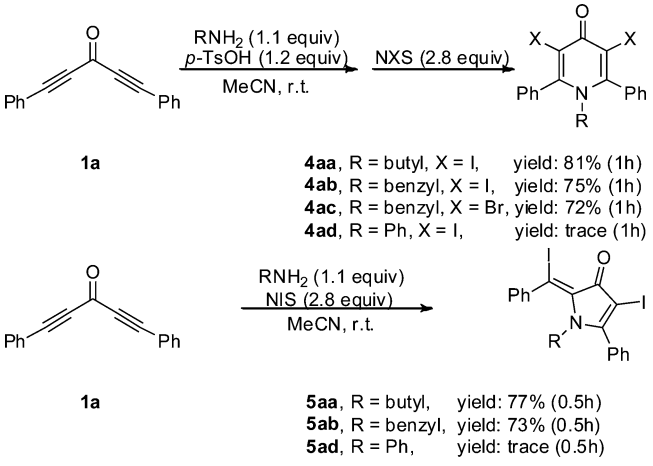
4b, and **5ab** afforded the corresponding products **6a**, **6b**, and **6ab** in good yields, respectively (Scheme 3).

On the basis of the above observations and the isolation of intermediate **A**,[18a,19] a possible reaction mechanism for the synthesis of **2** is proposed, as depicted in Scheme 4. Brønsted acid activates the carbonyl, followed by methanol attacks the carbon−carbon triple bond and via keto−enol tautomerization[14] generates intermediate **A**. Upon heating, **A** undergoes subsequent conversion to **B** by the configuration turning. Once again, attack of the intramolecular methoxyl group onto the carbon−carbon triple bond of **B** affords **C**, which undergoes demethylation to produce 4-pyrones **2**.

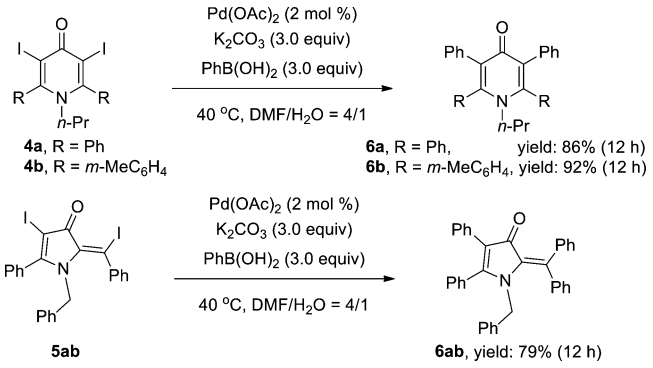
On the basis of the study about the intermediate **3**,[18b,c] we propose the following plausible mechanisms for the formation of **4** and **5**. Amines as nucleophiles react via Michael addition with **1** to form intermediate **3**. The electrophile (iodine cation) attacks the carbon−carbon triple bond (or double bond) of **3** to afford iodonium ion **D** (or **H**). After an intramolecular nucleophilic attack and the attack of the second iodine cation on the double bond (or triple bond), **G** (or **I**) formed rapidly. Again, the

dx.doi.org/10.1021/jo402055a | J. Org. Chem. 2013, 78, 12018−12028

Scheme 2. Influence of Different Amines and Electrophilic Reagents for the Synthesis of 4 and 5



Scheme 3. Palladium-Catalyzed Suzuki Coupling Reaction



nitrogen atom attacks the iodonium ion, which generates **J**, which subsequently afforded 3-pyrrolone **5** via proton capture.[20]

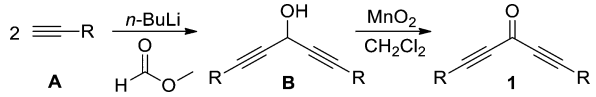
The proton from the Brønsted acid activates the carbonyl oxygen atom of **D**, which gives complex **E**. An endo attack of the intramolecular nitrogen atom onto the carbon−carbon triple bond of the other side affords **F**, which undergoes the second attack by the iodine cation released by NIS to generate 4-pyridone **4**.[20]

CONCLUSION

In summary, we have reported a Brønsted acid catalyzed direct and efficient protocol for preparing polysubstituted 4-pyrone derivatives and NIS-promoted selective synthesis of 4-pyridone and 3-pyrrolone derivatives from diynones. For different nucleophiles, different catalysts were employed to facilitate cyclization. Some of the 4-pyrones can be obtained in very high yields up to 99%. As an electrophilic reagent, NIS promotes the cyclization of diynones rapidly with high capacity and selectivity under considerably gentle reaction conditions (at room temperature). In addition, these reactions provide a metal-free and straightforward route for C−O and C−N bond formation, and the position of cyclization can be selected by adding Brønsted acid, which is more environmentally friendly and efficient compared to traditional synthesis methods.

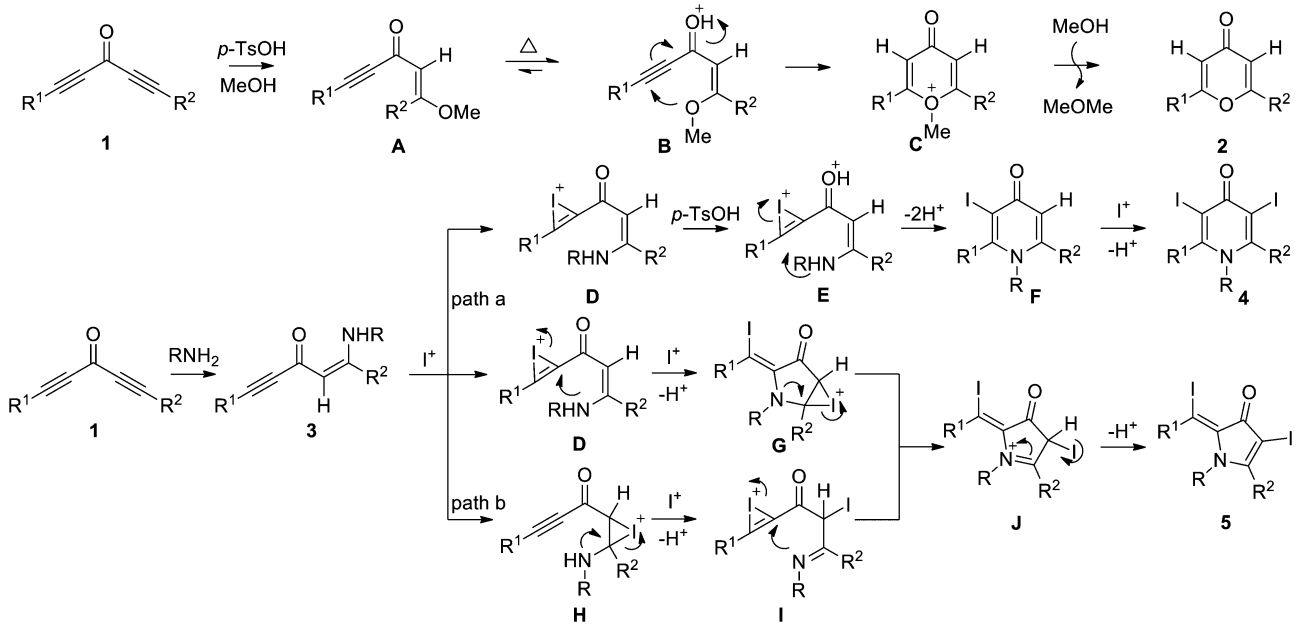
EXPERIMENTAL SECTION

General Procedure A: Synthesis of 1a−1m, 1t.



For the synthesis of **1a**: To a stirred solution of phenylacetylene (**A**; 1.76 mL, 16.0 mmol) in dry THF (30 mL) under argon was added *n*-BuLi (6.72 mL, 16.8 mmol, 2.5 M solution in hexane) via a syringe at 0 °C. The mixture was allowed to stir for 15 min at 0 °C. Then methyl formate (0.49 mL, 8 mmol) was added. The mixture was allowed to stir for an additional 5 min at 0 °C, and then for 2 h at room temperature. The mixture was poured into an aqueous saturated solution of NH_4Cl, and the product was extracted with ether. The combined organic layers were washed with a saturated aqueous sodium chloride solution, dried over Na_2SO_4, and filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, PE/EA = 10/1) to give 1,5-diphenylpenta-1,4-diyn-3-ol **B** (85%).

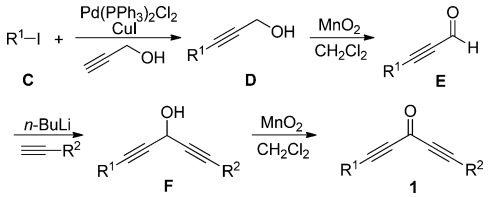
Scheme 4. Proposed Mechanisms



dx.doi.org/10.1021/jo402055a | J. Org. Chem. 2013, 78, 12018−12028

MnO_2 (75 mmol, 15 equiv) was added to a solution of 1,5-diphenylpenta-1,4-diyn-3-ol (**B**; 5 mmol) in CH_2Cl_2 (15 mL) at room temperature. The resulting mixture was stirred overnight. Then the solid was filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, PE/EA = 50/1) to give 1,5-diphenylpenta-1,4-diyn-3-one **1a** (82%).

General Procedure B: Synthesis of 1n−1s.



For the synthesis of **1o**: To a stirred solution of iodobenzene (**C**; 2.04 g, 10 mmol) in triethylamine (20 mL) under argon were sequentially added $Pd(PPh_3)_2Cl_2$ (105.3 mg, 0.15 mmol) and CuI (57.1 mg, 0.3 mmol) at room temperature. The mixture was allowed to stir for 10 min. Then prop-2-yn-1-ol (0.62 g, 11 mmol) was added. The mixture was allowed to stir overnight. The mixture was poured into an aqueous saturated solution of NH_4Cl, and the product was extracted with ether. The combined organic layers were washed with a saturated aqueous sodium chloride solution, dried over Na_2SO_4, and filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, PE/EA = 4/1) to give the 3-phenylprop-2-yn-1-ol **D** (99%).

D used the same procedure as general procedure **A** to give 3-phenylpropiolaldehyde **E** (90%) (silica gel, PE/EA = 10/1).

To a stirred solution of 1-ethynyl-4-methoxybenzene (1.06 g, 8 mmol) in dry THF (30 mL) under argon was added *n*-BuLi (3.36 mL, 8.4 mmol, 2.5 M solution in hexane) via a syringe at 0 °C. The mixture was allowed to stir for 15 min at 0 °C. Then 3-phenylpropiolaldehyde (**E**; 1.04 g, 8 mmol) was added. The mixture was allowed to stir for an additional 5 min at 0 °C, and then for 2 h at room temperature. It was then poured into aqueous saturated NH_4Cl solution and extracted with ether. The combined organic layers were washed with a saturated aqueous sodium chloride solution, dried over Na_2SO_4, and filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, PE/EA = 5/1) to give 1-(4-methoxyphenyl)-5-phenylpenta-1,4-diyn-3-ol **F** (85%).

F used the same procedure as general procedure **A** to give 1-(4-methoxyphenyl)-5-phenylpenta-1,4-diyn-3-one **1o** (80%) (silica gel, PE/EA = 50/1).

General Procedure C: Synthesis of 2. For the synthesis of **2a**: To a solution of 1,5-diphenylpenta-1,4-diyn-3-one **1a** (0.10 mmol) in MeOH (1.0 mL) was added 15 mol % of *p*-TsOH. The resulting mixture was stirred at 110 °C in a sealed tube. When the reaction was considered complete, as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (30 mL), washed with water and saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford the product 2,6-diphenyl-4*H*-pyran-4-one **2a**.

General Procedure D: Synthesis of 4. For the synthesis of **4a**: To a solution of 1,5-diphenylpenta-1,4-diyn-3-one **1a** (0.10 mmol) in acetonitrile (1.0 mL) was sequentially added 1.1 equiv of propylamine and 1.2 equiv of *p*-TsOH. The resulting mixture was stirred at room temperature. NIS (2.8 equiv) was added after **1a** converted into **3a** completely, detected by TLC analysis. When the reaction was considered complete, as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (30 mL), washed with 5% of an aqueous solution of potassium hydroxide and saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford the product 3,5-diiodo-2,6-diphenyl-1-propylpyridin-4(1*H*)-one **4a**.

General Procedure E: Synthesis of 5. For the synthesis of **5a**: To a solution of 1,5-diphenylpenta-1,4-diyn-3-one **1a** (0.10 mmol) in acetonitrile (1.0 mL) were sequentially added 1.1 equiv of propylamine and 2.8 equiv of NIS. The resulting mixture was stirred at room temperature. When the reaction was considered complete, as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (30 mL), washed with 5% of an aqueous solution of potassium hydroxide and saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford the product (*E*)-4-iodo-2-(iodo(phenyl)methylene)-5-phenyl-1-propyl-1*H*-pyrrol-3(2*H*)-one **5a**. The reaction and after-treatment procedures should be away from light.

General Procedure F: Synthesis of 6. For the synthesis of **6a**: To a solution of 3,5-diiodo-2,6-diphenyl-1-propylpyridin-4(1*H*)-one **4a** (0.20 mmol) in DMF (1.0 mL) with H_2O (0.25 mL) under argon were sequentially added 2 mol % of $Pd(OAc)_2$, 3.0 equiv of K_2CO_3, and $PhB(OH)_2$. Then the reaction mixture was allowed to stir at 40 °C for 12 h. The reaction mixture was diluted with ethyl ether (30 mL), washed with saturated brine twice, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford the product 2,3,5,6-tetraphenyl-1-propylpyridin-4(1*H*)-one **6a**.

Characterization Data of 2a−2s. *2,6-Diphenyl-4H-pyran-4-one (**2a**).* Yield 99%; 24.6 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.87−7.85 (m, 4H), 7.54−7.53 (m, 6H), 6.82 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.2, 163.3, 131.5, 131.4, 129.1, 125.9, 111.4; IR (neat, cm^{-1}) 3059, 2924, 1647, 1614, 1604, 1493, 1449, 1390, 945, 772, 685; HRMS (ESI) calcd for $C_{17}H_{12}O_2$ ([M + H]$^+$) = 249.0910; found, 249.0913.

*2,6-Di-m-tolyl-4H-pyran-4-one (**2b**).* Yield 99%; 27.3 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.67−7.63 (m, 4H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 2H), 6.78 (s, 2H), 2.46 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.2, 163.5, 138.9, 132.1, 131.5, 129.0, 126.5, 123.1, 111.3, 21.5; IR (neat, cm^{-1}) 3062, 2922, 1644, 1611, 1484, 1427, 1384, 1262, 924, 784, 693, 423; HRMS (ESI) calcd for $C_{19}H_{16}O_2$ ([M + H]$^+$) = 277.1223; found, 277.1228.

*2,6-Di-p-tolyl-4H-pyran-4-one (**2c**).* Yield 84%; 23.3 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.74 (d, *J* = 8.0 Hz, 4H), 7.32 (d, *J* = 7.6 Hz, 4H), 6.76 (s, 2H), 2.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.3, 163.4, 141.9, 129.8, 128.7, 125.8, 110.6, 21.5; IR (neat, cm^{-1}) 3065, 2920, 1646, 1607, 1569, 1508, 1414, 1384, 942, 818, 716, 637, 528, 482; HRMS (ESI) calcd for $C_{19}H_{16}O_2$ ([M + H]$^+$) = 277.1223; found, 277.1229.

*2,6-Bis(4-ethylphenyl)-4H-pyran-4-one (**2d**).* Yield 81%; 24.6 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (d, *J* = 8.0 Hz, 4H), 7.35 (d, *J* = 8.4 Hz, 4H), 6.77 (s, 2H), 2.73 (q, *J* = 7.6 Hz, 4H), 1.29 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.4, 163.5, 148.2, 129.0, 128.6, 126.0, 110.7, 28.8, 15.2; IR (neat, cm^{-1}) 3070, 2963, 2929, 1649, 1610, 1510, 1457, 1420, 1385, 1187, 1014, 945, 837, 643; HRMS (ESI) calcd for $C_{21}H_{20}O_2$ ([M + H]$^+$) = 305.1536; found, 305.1536.

*2,6-Bis(4-propylphenyl)-4H-pyran-4-one (**2e**).* Yield 55%; 18.3 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (d, *J* = 8.4 Hz, 4H), 7.33 (d, *J* = 8.4 Hz, 4H), 6.78 (s, 2H), 2.67 (t, *J* = 7.6 Hz, 4H), 1.74−1.65 (m, 4H), 0.97 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.4, 163.5, 146.6, 129.2, 129.0, 125.9, 110.7, 37.9, 24.3, 13.7; IR (neat, cm^{-1}) 3212, 2957, 2927, 2864, 1651, 1609, 1508, 1460, 1419, 1381, 945, 839, 810, 646, 474; HRMS (ESI) calcd for $C_{23}H_{24}O_2$ ([M + H]$^+$) = 333.1849; found, 333.1835.

*2,6-Dicyclopropyl-4H-pyran-4-one (**2f**).* Yield 83%; 14.6 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.06 (s, 2H), 1.78−1.71 (m, 2H), 1.02−0.96 (m, 4H), 0.96−0.90 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 179.4, 168.4, 111.1, 13.7, 7.7; IR (neat, cm^{-1}) 3051, 2925, 2855, 1655, 1601, 1453, 1401, 1096, 1055, 862; HRMS (ESI) calcd for $C_{11}H_{12}O_2$ ([M + H]$^+$) = 177.0910; found, 177.0904.

*2,6-Bis(2-fluorophenyl)-4H-pyran-4-one (**2g**).* Yield 84%; 23.9 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.84−7.80 (m, 2H), 7.54−7.49 (m, 2H), 7.34−7.30 (m, 2H), 7.23 (dd, *J* = 11.6 Hz 7.6 Hz, 2H), 6.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 179.9, 160.4 (d, *J* = 234 Hz, 1C), 159.1 (d, *J* = 16 Hz, 1C), 132.8 (d, *J* = 9 Hz, 1C), 128.7, 124.7 (d, *J* = 4 Hz, 1C), 119.8 (d, *J* = 10 Hz, 1C), 117.0 (d, *J* = 22 Hz, 1C), 115.9 (d, *J* = 11 Hz, 1C); IR (neat, cm^{-1}) 3071, 2924, 1663, 1613, 1577, 1487, 1453, 1389, 1215, 945, 863, 756, 644; HRMS (ESI) calcd for $C_{17}H_{10}F_2O_2$ ([M + H]$^+$) = 285.0722; found, 285.0728.

dx.doi.org/10.1021/jo402055a | *J. Org. Chem.* 2013, 78, 12018−12028

*2,6-Bis(3-fluorophenyl)-4H-pyran-4-one (**2h**).* Yield 60%; 17.0 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.64 (d, J = 7.6 Hz, 2H), 7.56−7.50 (m, 4H), 7.28−7.24 (m, 2H), 6.81 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 179.7, 163.1 (d, J = 227 Hz, 1C), 161.9 (d, J = 17 Hz, 1C), 133.4 (d, J = 8 Hz, 1C), 130.5 (d, J = 8 Hz, 1C), 121.7 (d, J = 3 Hz, 1C), 118.5 (d, J = 21 Hz, 1C), 113.0 (d, J = 24 Hz, 1C), 112.2; IR (neat, cm^{-1}) 3084, 1658, 1586, 1490, 1438, 1395, 1276, 929, 870, 782, 689; HRMS (ESI) calcd for $C_{17}H_{10}F_2O_2$ ([M + H]$^+$) = 285.0722; found, 285.0718.

*2,6-Bis(4-fluorophenyl)-4H-pyran-4-one (**2i**).* Yield 88%; 25.0 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.86−7.83 (m, 4H), 7.26−7.21 (m, 4H), 6.75 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 179.8, 164.6 (d, J = 252 Hz, 1C), 162.3, 128.1 (d, J = 9 Hz, 1C), 127.6 (d, J = 3 Hz, 1C), 116.4 (d, J = 22 Hz, 1C), 111.2; IR (neat, cm^{-1}) 3068, 2922, 1667, 1601, 1505, 1415, 1379, 1238, 836, 778, 583; HRMS (ESI) calcd for $C_{17}H_{10}F_2O_2$ ([M + H]$^+$) = 285.0722; found, 285.0729.

*2,6-Bis(4-chlorophenyl)-4H-pyran-4-one (**2j**).* Yield 61%; 19.3 mg; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.77 (d, J = 8.8 Hz, 4H), 7.51 (d, J = 8.8 Hz, 4H), 6.79 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 179.7, 162.3, 137.8, 129.7, 129.5, 127.2, 111.6; IR (neat, cm^{-1}) 3204, 3057, 1656, 1596, 1557, 1488, 1410, 1379, 1090, 830, 724, 666; HRMS (ESI) calcd for $C_{17}H_{10}Cl_2O_2$ ([M + H]$^+$) = 317.0131; found, 317.0125.

*2,6-Di-tert-butyl-4H-pyran-4-one (**2k**).* Yield 99%; 20.3 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.14 (s, 2H), 1.29 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 181.4, 175.2, 109.4, 36.2, 27.7; IR (neat, cm^{-1}) 2969, 2873, 1659, 1614, 1491, 1464, 1399, 1371, 1259, 1101, 943, 867; HRMS (ESI) calcd for $C_{13}H_{20}O_2$ ([M + H]$^+$) = 209.1536; found, 209.1539.

*2,6-Dipropyl-4H-pyran-4-one (**2l**).* Yield 76%; 13.7 mg; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.07 (s, 2H), 2.47 (t, J = 7.6 Hz, 4H), 1.73−1.63 (m, 4H), 0.99 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.5, 168.9, 113.1, 35.4, 20.1, 13.4; IR (neat, cm^{-1}) 3461, 2964, 2875, 1665, 1619, 1461, 1398, 1148, 933, 864; HRMS (ESI) calcd for $C_{11}H_{16}O_2$ ([M + H]$^+$) = 181.1223; found, 181.1222.

*2,6-Dipentyl-4H-pyran-4-one (**2m**).* Yield 64%; 15.1 mg; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.06 (s, 2H), 2.48 (t, J = 7.6 Hz, 4H), 1.68−1.61 (m, 4H), 1.37−1.31 (m, 8H), 0.92−0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.4, 169.1, 113.0, 33.4, 30.9, 26.3, 22.2, 13.8; IR (neat, cm^{-1}) 2957, 2930, 2864, 1666, 1625, 1462, 1395, 1146, 928, 866; HRMS (ESI) calcd for $C_{15}H_{24}O_2$ ([M + H]$^+$) = 237.1849; found, 237.1853.

*2-(2-Fluorophenyl)-6-(m-tolyl)-4H-pyran-4-one (**2n**).* Yield 93%; 26.0 mg; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.84−7.81 (m, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.51 (t, J = 6.4 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 2H), 7.24−7.21 (m, 1H), 6.89 (d, J = 1.6 Hz, 1H), 6.80 (d, J = 1.2 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.1, 162.7 (d, J = 236 Hz, 1C), 159.0, 159.0, 138.9, 132.7 (d, J = 9 Hz, 1C), 132.3, 131.3, 129.0, 128.8 (d, J = 1 Hz, 1C), 126.5, 124.7 (d, J = 4 Hz, 1C), 123.2, 120.0 (d, J = 11 Hz, 1C), 117.0 (d, J = 22 Hz, 1C), 116.0 (d, J = 9 Hz, 1C), 111.3, 21.5; IR (neat, cm^{-1}) 3066, 2923, 1648, 1614, 1489, 1453, 1384, 1215, 868, 764, 696; HRMS (ESI) calcd for $C_{18}H_{13}FO_2$ ([M + H]$^+$) = 281.0972; found, 281.0983.

*2-(4-Methoxyphenyl)-6-phenyl-4H-pyran-4-one (**2o**).* Yield 66%; 18.4 mg; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.86−7.80 (m, 4H), 7.54−7.52 (m, 3H), 7.03 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 2.0 Hz, 1H), 6.73 (d, J = 2.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.3, 163.4, 163.1, 162.2, 131.5, 131.3, 129.1, 127.6, 125.9, 123.7, 114.5, 111.2, 109.9, 55.5; IR (neat, cm^{-1}) 3435, 3067, 2929, 2843, 1642, 1605, 1511, 1450, 1424, 1392, 1025, 836, 773, 690; HRMS (ESI) calcd for $C_{18}H_{14}O_3$ ([M + H]$^+$) = 279.1016; found, 279.1012.

*2-Phenyl-6-propyl-4H-pyran-4-one (**2p**).* Yield 70%; 15.0 mg; orange solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.77−7.75 (m, 2H), 7.50−7.48 (m, 3H), 6.71 (d, J = 2.0 Hz, 1H), 6.19 (d, J = 2.4 Hz, 1H), 2.61 (t, J = 7.6 Hz, 2H), 1.83−1.74 (m, 2H), 1.04 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.3, 168.7, 163.4, 131.4, 131.2, 129.0, 125.7, 113.7, 110.8, 35.5, 20.2, 13.5; IR (neat, cm^{-1}) 3065, 2963, 1659, 1617, 1493, 1451, 1395, 1160, 937, 866, 772, 691; HRMS (ESI) calcd for $C_{14}H_{14}O_2$ ([M + H]$^+$) = 215.1067; found, 215.1072.

*2-(tert-Butyl)-6-(p-tolyl)-4H-pyran-4-one (**2q**).* Yield 78%; 18.9 mg; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 6.67 (d, J = 1.6 Hz, 1H), 6.26 (d, J = 2.0 Hz, 1H), 2.42 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.9, 175.2, 163.5, 141.8, 129.7, 128.8, 125.6, 110.3, 109.8, 36.3, 28.0, 21.4; IR (neat, cm^{-1}) 2969, 2927, 1653, 1611, 1510, 1459, 1417, 1384, 1101, 945, 866, 822; HRMS (ESI) calcd for $C_{16}H_{18}O_2$ ([M + H]$^+$) = 243.1380; found, 243.1388.

*2-(Naphthalen-1-yl)-6-(p-tolyl)-4H-pyran-4-one (**2r**).* Yield 64%; 20.0 mg; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.14−8.12 (m, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.97−7.95 (m, 1H), 7.76−7.69 (m, 4H), 7.60−7.57 (m, 3H), 7.32 (d, J = 8.0 Hz, 1H), 6.90 (s, 1H), 6.69 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.2, 164.9, 164.1, 142.1, 133.8, 131.4, 130.4, 130.1, 129.8, 128.7, 128.4, 127.9, 127.5, 126.6, 125.8, 125.1, 124.7, 116.7, 110.5, 21.5; IR (neat, cm^{-1}) 3059, 2923, 1650, 1610, 1509, 1452, 1413, 1383, 1245, 1187, 945, 866, 820, 776, 733, 645; HRMS (ESI) calcd for $C_{22}H_{16}O_2$ ([M + H]$^+$) = 313.1223; found, 313.1236.

*2-Phenyl-6-(thiophen-2-yl)-4H-pyran-4-one (**2s**).* Yield 65%; 16.5 mg; deep yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.83 (dd, J = 5.6 Hz 2.0 Hz, 2H), 7.65 (dd, J = 2.4 Hz 1.6 Hz, 1H), 7.56−7.52 (m, 4H), 7.19−7.17 (m, 1H), 6.76 (d, J = 1.6 Hz, 1H), 6.68 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 179.7, 162.7, 158.9, 134.6, 131.4, 131.0, 129.7, 129.1, 128.4, 127.7, 125.8, 111.2, 109.7; IR (neat, cm^{-1}) 3059, 2928, 1643, 1616, 1496, 1450, 1424, 1397, 1258, 1078, 1048, 1000, 942, 899, 839, 768, 736, 685, 638; HRMS (ESI) calcd for $C_{15}H_{10}O_2S$ ([M + H]$^+$) = 255.0474; found, 255.0470.

Characterization Data of A. *(E)-1-Methoxy-1,5-diphenylpent-1-en-4-yn-3-one (**A**).* Yield 20%; 5.2 mg; light yellow liquid; 20^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.58−7.56 (m, 2H), 7.44−7.40 (m, 3H), 7.32 (t, J = 7.6 Hz, 1H), 7.24−7.20 (m, 2H), 7.09−7.07 (m, 2H), 5.82 (s, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 176.5, 173.7, 134.6, 132.8, 130.7, 129.9, 128.1, 128.0, 127.9, 120.4, 105.6, 91.0, 88.7, 56.8; IR (neat, cm^{-1}) 3057, 2930, 2193, 1591, 1561, 1490, 1441, 1364, 1225, 1126, 1089, 760, 692; HRMS (ESI) calcd for $C_{18}H_{14}O_2$ ([M + H]$^+$) = 263.1067; found, 263.1065.

Characterization Data of 3a, 3ab, 3qa, and 3qb. *(Z)-1,5-Diphenyl-1-(propylamino)pent-1-en-4-yn-3-one (**3a**).* Yield 96%; 27.8 mg; light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.52−7.51 (m, 2H), 7.44−7.42 (m, 3H), 7.37−7.29 (m, 5H), 5.39 (s, 1H), 3.16 (q, J = 6.8 Hz, 2H), 1.60−1.51 (m, 2H), 0.90 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 172.6, 166.9, 134.5, 132.3, 129.6, 129.2, 128.4, 128.2, 127.5, 121.5, 100.1, 89.9, 86.2, 46.5, 23.8, 11.0; IR (neat, cm^{-1}) 3059, 2965, 2931, 2874, 2204, 1591, 1485, 1328, 1262, 1165, 1123, 1024, 1002, 919, 760, 696, 609, 525; HRMS (ESI) calcd for $C_{20}H_{19}NO$ ([M + H]$^+$) = 290.1539; found, 290.1543.

*(Z)-1-(Benzylamino)-1,5-diphenylpent-1-en-4-yn-3-one (**3ab**).* Yield 91%; 30.7 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 11.36 (s, 1H), 7.54−7.52 (m, 2H), 7.44−7.25 (m, 11H), 7.19 (d, J = 7.2 Hz, 2H), 5.48 (m, 1H), 4.42 (d, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 173.3, 166.8, 137.9, 134.3, 132.4, 129.9, 129.4, 128.7, 128.5, 128.3, 127.6, 127.5, 126.7, 121.5, 100.8, 89.9, 86.7, 48.5; IR (neat, cm^{-1}) 2925, 2858, 2197, 1565, 1537, 1480, 1447, 1368, 1324, 1116, 1070, 919, 763, 693, 671, 476; HRMS (ESI) calcd for $C_{24}H_{19}NO$ ([M + H]$^+$) = 338.1539; found, 338.1551.

*(Z)-6,6-Dimethyl-1-phenyl-1-(propylamino)hept-1-en-4-yn-3-one (**3qa**).* Yield 52%; 14.0 mg; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.99 (s, 1H), 7.23 (s, 4H), 5.22 (s, 1H), 3.15 (q, J = 6.8 Hz, 2H), 2.39 (s, 3H), 1.57−1.48 (m, 2H), 1.25 (s, 9H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 173.4, 166.5, 139.5, 131.8, 128.9, 127.4, 99.7, 96.1, 80.7, 46.3, 30.3, 27.4, 23.8, 21.2, 11.0; IR (neat, cm^{-1}) 2967, 2928, 2862, 2206, 1593, 1563, 1496, 1452, 1324, 1254, 1137, 826, 772, 610, 489; HRMS (ESI) calcd for $C_{18}H_{23}NO$ ([M + H]$^+$) = 270.1852; found, 270.1855.

*(Z)-6,6-Dimethyl-1-phenyl-5-(propylamino)hept-4-en-1-yn-3-one (**3qb**).* Yield 43%; 11.6 mg; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 11.93 (s, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 5.42 (s, 1H), 3.52−3.47 (m, 2H), 2.34 (s, 3H), 1.73−1.64 (m, 2H), 1.30 (s, 9H), 1.04 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 175.4, 172.1, 139.3, 132.2, 129.0, 118.6, 95.2, 89.8, 85.9, 47.4, 35.8, 28.8,

23.6, 21.4, 11.2; IR (neat, cm^{-1}) 2975, 2926, 2870, 2193, 1611, 1561, 1513, 1456, 1324, 1258, 1134, 908, 820, 725; HRMS (ESI) calcd for $C_{18}H_{23}NO$ ($[M + H]^+$) = 270.1852; found, 270.1859.

Characterization Data of 4a−4j, 4n−4p, 4r, and 4s. *3,5-Diiodo-2,6-diphenyl-1-propylpyridin-4(1H)-one (**4a**).* Yield 81%; 43.8 mg; light yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.57−7.49 (m, 6H), 7.34−7.29 (m, 4H), 3.50−3.46 (m, 2H), 1.42−1.32 (m, 2H), 0.25 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.1, 152.9, 138.0, 129.7, 128.9, 128.6, 93.8, 56.2, 24.2, 10.4; IR (neat, cm^{-1}) 3055, 2968, 2926, 2866, 1599, 1560, 1515, 1445, 1408, 1199, 1083, 1026, 752, 701, 667; HRMS (ESI) calcd for $C_{20}H_{17}I_2NO$ ($[M + H]^+$) = 541.9472; found, 541.9467.

*3,5-Diiodo-1-propyl-2,6-di-m-tolylpyridin-4(1H)-one (**4b**).* Yield 90%; 51.2 mg; light yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.42 (t, J = 8.0 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 7.11 (s, 4H), 3.50−3.46(m, 2H), 2.43(s, 6H), 1.42−1.30 (m, 2H), 0.28 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.2, 153.1, 138.8, 138.0, 130.4, 129.1, 128.8, 125.8, 93.7, 56.2, 24.4, 21.5, 10.5; IR (neat, cm^{-1}) 2967, 2926, 2873, 2234, 1599, 1561, 1515, 1469, 1410, 1217, 1181, 1082, 914, 782, 732; HRMS (ESI) calcd for $C_{22}H_{21}I_2NO$ ($[M + H]^+$) = 569.9785; found, 569.9789.

*3,5-Diiodo-1-propyl-2,6-di-p-tolylpyridin-4(1H)-one (**4c**).* Yield 85%; 48.4 mg; white solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.34 (d, J = 7.6 Hz, 4H), 7.19 (d, J = 7.6 Hz, 4H), 3.49 (t, J = 8.0 Hz, 2H), 2.45 (s, 6H), 1.40−1.29 (m, 2H), 0.28 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.3, 153.1, 139.8, 135.3, 129.6, 128.5, 94.1, 56.2, 24.3, 21.5, 10.5; IR (neat, cm^{-1}) 2975, 2922, 1600, 1563, 1490, 1463, 1404, 1198, 1082, 807, 754, 697; HRMS (ESI) calcd for $C_{22}H_{21}I_2NO$ ($[M + H]^+$) = 569.9785; found, 569.9778.

*2,6-Bis(4-ethylphenyl)-3,5-diiodo-1-propylpyridin-4(1H)-one (**4d**).* Yield 76%; 45.4 mg; light yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.35 (d, J = 7.6 Hz, 4H), 7.21 (d, J = 8.0 Hz, 4H), 3.48 (t, J = 8.4 Hz, 2H), 2.50 (q, J = 8.0 Hz, 4H), 1.29 (d, J = 7.6 Hz, 6H), 0.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.4, 153.2, 146.1, 135.6, 128.6, 128.4, 94.1, 56.3, 28.7, 24.3, 15.2, 10.5; IR (neat, cm^{-1}) 2966, 2928, 1597, 1561, 1506, 1458, 1408, 1082, 838, 757, 730, 693, 526; HRMS (ESI) calcd for $C_{24}H_{25}I_2NO$ ($[M + H]^+$) = 598.0098; found, 598.0094.

*3,5-Diiodo-1-propyl-2,6-bis(4-propylphenyl)pyridin-4(1H)-one (**4e**).* Yield 55%; 34.4 mg; yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.33 (d, J = 8.0 Hz, 4H), 7.20 (d, J = 8.0 Hz, 4H), 3.50−3.46 (m, 2H), 2.70−2.67 (m, 4H), 1.75−1.65 (m, 4H), 1.39−1.30 (m, 2H), 0.95 (t, J = 7.2 Hz, 6H), 0.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.4, 153.2, 144.5, 135.6, 129.0, 128.5, 94.1, 56.3, 37.7, 24.3, 24.2, 13.6, 10.5; IR (neat, cm^{-1}) 2959, 2868, 1602, 1564, 1508, 1489, 1461, 1408, 1200, 1084, 1021, 846, 798, 756, 732, 641, 559; HRMS (ESI) calcd for $C_{26}H_{29}I_2NO$ ($[M + H]^+$) = 626.0411; found, 626.0417.

*2,6-Dicyclopropyl-3,5-diiodo-1-propylpyridin-4(1H)-one (**4f**).* Yield 45%; 21.1 mg; yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 4.72 (t, J = 7.2 Hz, 2H), 1.88−1.81 (m, 2H), 1.63−1.53 (m, 2H), 1.44−1.39 (m, 4H), 0.86 (t, J = 7.6 Hz, 3H), 0.81−0.77 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.3, 154.2, 96.8, 50.8, 24.9, 19.1, 14.0, 11.2; IR (neat, cm^{-1}) 3082, 3001, 2963, 2232, 1594, 1558, 1504, 1459, 1405, 1163, 1076, 910, 730; HRMS (ESI) calcd for $C_{14}H_{17}I_2NO$ ($[M + H]^+$) = 469.9472; found, 469.9462.

*2,6-Bis(4-ethylphenyl)-3,5-diiodo (**4g**).* Yield 81%; 46.7 mg; light yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.59−7.53 (m, 2H), 7.37−7.29 (m, 5H), 7.24 (s, 1H), 3.51 (t, J = 8.4 Hz, 2H), 1.42−1.32 (m, 2H), 0.33 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.2, 158.5 (d, J = 248 Hz, 1C), 148.2, 132.5, 130.9 (d, J = 29 Hz, 1C), 125.9 (d, J = 16 Hz, 1C), 124.9 (d, J = 27 Hz, 1C), 116.9, 116.6 (d, J = 12 Hz, 1C), 116.4, 95.0, 56.6, 23.6, 10.7; IR (neat, cm^{-1}) 2926, 1598, 1564, 1487, 1450, 1415, 1197, 1078, 814, 760, 732; HRMS (ESI) calcd for $C_{20}H_{15}F_2I_2NO$ ($[M + H]^+$) = 577.9284; found, 577.9279.

*2,6-Bis(3-fluorophenyl)-3,5-diiodo-1-propylpyridin-4(1H)-one (**4h**).* Yield 63%; 36.3 mg; orange solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.58−7.51 (m, 2H), 7.26−7.22 (m, 2H), 7.13 (d, J = 7.6 Hz, 2H), 7.07−7.05 (m, 2H), 3.52−3.47 (m, 2H), 1.44−1.35 (m, 2H), 0.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.1, 162.6 (d, J = 249 Hz, 1C), 151.6, 139.5 (d, J = 8 Hz, 1C), 131.1 (d, J = 5 Hz, 1C), 124.7, 117.2 (d, J = 20 Hz, 1C), 116.2 (d, J = 23 Hz, 1C), 93.9, 56.3, 24.5, 10.5; IR (neat, cm^{-1}) 2967, 2930, 1586, 1562, 1518, 1474, 1435, 1259, 1219, 788, 731, 692, 667; HRMS (ESI) calcd for $C_{20}H_{15}F_2I_2NO$ ($[M + H]^+$) = 577.9284; found, 577.9284.

*2,6-Bis(4-fluorophenyl)-3,5-diiodo-1-propylpyridin-4(1H)-one (**4i**).* Yield 90%; 51.9 mg; white solid; ^1H NMR (400 MHz, acetone) δ ppm 7.59−7.55 (m, 4H), 7.41−7.36 (m, 4H), 3.60−3.56 (m, 2H), 1.53−1.43 (m, 2H), 0.30 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, acetone) δ ppm 171.0, 163.8 (d, J = 247 Hz, 1C), 153.1, 135.6 (d, J = 4 Hz, 1C), 132.2 (d, J = 9 Hz, 1C), 116.6 (d, J = 22 Hz, 1C), 94.4, 57.0, 24.3, 10.5; IR (neat, cm^{-1}) 2968, 2932, 1601, 1579, 1506, 1486, 1409, 1225, 1081, 843, 819, 786; HRMS (ESI) calcd for $C_{20}H_{15}F_2I_2NO$ ($[M + H]^+$) = 577.9284; found, 577.9283.

*2,6-Bis(4-chlorophenyl)-3,5-diiodo-1-propylpyridin-4(1H)-one (**4j**).* Yield 35%; 21.3 mg; light yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.54 (dd, J = 6.8 Hz 2.0 Hz, 4H), 7.27−7.26 (m, 4H), 3.49−3.45 (m, 2H), 1.40−1.30 (m, 2H), 0.34 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.2, 151.9, 136.3, 136.2, 130.2, 129.6, 94.3, 56.3, 24.4, 10.6; IR (neat, cm^{-1}) 2925, 2855, 1639, 1593, 1465, 1403, 1090, 1015, 815, 756, 713; HRMS (ESI) calcd for $C_{20}H_{15}Cl_2I_2NO$ ($[M + H]^+$) = 609.8693; found, 609.8688.

*2-(2-Fluorophenyl)-3,5-diiodo-1-propyl-6-(m-tolyl)pyridin-4(1H)-one (**4n**).* Yield 67%; 38.4 mg; yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.58−7.59 (m, 1H), 7.45−7.41 (m, 1H), 7.37−7.31 (m, 3H), 7.24 (d, J = 8.8 Hz, 1H), 7.12 (s, 2H), 3.60−3.51 (m, 1H), 3.48−3.93 (m, 1H), 2.43 (s, 3H), 1.40−1.35 (m, 2H), 0.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.2, 158.4 (d, J = 239 Hz, 1C), 153.5, 147.7, 138.9 (d, J = 14 Hz, 1C), 137.9, 132.4 (d, J = 8 Hz, 1C), 130.9 (d, J = 19 Hz, 1C), 130.6, 129.0, 128.9 (d, J = 10 Hz, 1C), 125.9 (d, J = 13 Hz, 1C), 125.7 (d, J = 7 Hz, 1C), 124.8, 116.4 (d, J = 15 Hz, 1C), 94.8, 93.8, 56.4, 23.9, 21.5, 10.5; IR (neat, cm^{-1}) 2967, 2928, 2236, 1605, 1557, 1519, 1483, 1413, 1195, 1080, 911, 761, 732, 672; HRMS (ESI) calcd for $C_{21}H_{18}FI_2NO$ ($[M + H]^+$) = 573.9535; found, 573.9537.

*3,5-Diiodo-2-(4-methoxyphenyl)-6-phenyl-1-propylpyridin-4(1H)-one (**4o**).* Yield 40%; 22.8 mg; light yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.56−7.49 (m, 3H), 7.32−7.30 (m, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.50 (t, J = 8.4 Hz, 2H), 1.40−1.29 (m, 2H), 0.28 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.4, 160.4, 152.9, 138.3, 130.5, 130.1, 129.8, 129.0, 128.7, 114.3, 94.8, 93.9, 56.3, 55.4, 24.3, 10.5; IR (neat, cm^{-1}) 2964, 2930, 1598, 1557, 1502, 1462, 1251, 1085, 911, 732, 703; HRMS (ESI) calcd for $C_{21}H_{19}I_2NO_2$ ($[M + H]^+$) = 571.9578; found, 571.9590.

*3,5-Diiodo-2-phenyl-1,6-dipropylpyridin-4(1H)-one (**4p**).* Yield 29%; 14.7 mg; yellow liquid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.53 (d, J = 6.4 Hz, 3H), 7.25−7.23 (m, 2H), 3.72 (t, J = 8.0 Hz, 2H), 3.06 (t, J = 8.0 Hz, 2H), 1.78−1.68 (m, 2H), 1.63−1.53 (m, 2H), 1.11 (t, J = 7.2 Hz, 3H), 0.66 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.2, 152.9, 152.4, 138.5, 129.8, 129.1, 128.6, 94.3, 92.9, 54.8, 40.1, 24.6, 21.9, 14.2, 10.7; IR (neat, cm^{-1}) 2962, 2928, 1595, 1565, 1514, 1462, 1415, 1198, 1082, 763, 702; HRMS (ESI) calcd for $C_{17}H_{19}I_2NO$ ($[M + H]^+$) = 507.9629; found, 507.9634.

*3,5-Diiodo-2-(naphthalen-1-yl)-1-propyl-6-(p-tolyl)pyridin-4(1H)-one (**4r**).* Yield 39%; 23.6 mg; deep yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.01 (d, J = 8.4 Hz, 1H), 7.97−7.95 (m, 1H), 7.61−7.55 (m, 2H), 7.50 (d, J = 7.6 Hz, 2H), 7.34 (d, J = 6.0 Hz, 3H), 7.20−7.17 (m, 2H), 3.50−3.45 (m, 2H), 2.45 (s, 3H), 1.39−1.30 (m, 2H), 0.11 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.5, 153.6, 151.5, 140.0, 135.3, 135.2, 133.5, 130.4, 129.8, 129.7, 129.0, 128.6, 128.2, 127.8, 126.9, 125.2, 123.9, 94.8, 94.5, 56.4, 24.8, 21.5, 10.5; IR (neat, cm^{-1}) 2958, 2923, 1597, 1557, 1498, 1462, 1404, 1084, 802, 780, 729, 649; HRMS (ESI) calcd for $C_{25}H_{21}I_2NO$ ($[M + H]^+$) = 605.9785; found, 605.9804.

*3,5-Diiodo-1-propyl-2-(thiophen-2-yl)-6-(p-tolyl)pyridin-4(1H)-one (**4s**).* Yield 46%; 25.3 mg; deep yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.58−7.50 (m, 4H), 7.32 (d, J = 7.2 Hz, 2H), 7.18 (t, J = 3.6 Hz, 2H), 3.59 (t, J = 8.4 Hz, 2H), 1.51−1.43 (m, 2H), 0.36 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.1, 153.4, 146.3, 138.0, 129.9, 129.9, 129.0, 128.7, 128.3, 127.3, 97.5, 94.3, 56.7, 25.0, 10.5; IR (neat, cm^{-1}) 2966, 2930, 1596, 1563, 1463, 1410, 1197, 1083,

dx.doi.org/10.1021/jo402055a | J. Org. Chem. 2013, 78, 12018−12028

910, 766, 732, 706; HRMS (ESI) calcd for $C_{18}H_{15}I_2NOS$ ([M + H]$^+$) = 547.9036; found, 547.9030.

Characterization Data of 4aa, 4ab, and 4ac. *1-Butyl-3,5-diiodo-2,6-diphenylpyridin-4(1H)-one (**4aa**).* Yield 81%; 45.0 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.57−7.49 (m, 6H), 7.34−7.32 (m, 4H), 3.54 (t, J = 8.4 Hz, 2H), 1.37−1.29 (m, 2H), 0.67−0.58 (m, 2H), 0.38 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.2, 152.9, 138.0, 129.8, 128.9, 128.7, 93.8, 54.5, 32.4, 19.0, 12.5; IR (neat, cm^{-1}) 3059, 2960, 2868, 2237, 1587, 1520, 1461, 1444, 1411, 1200, 1087, 918, 731, 701, 647; HRMS (ESI) calcd for $C_{21}H_{19}I_2NO$ ([M + H]$^+$) = 555.9629; found, 555.9621.

*1-Benzyl-3,5-diiodo-2,6-diphenylpyridin-4(1H)-one (**4ab**).* Yield 75%; 44.2 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.41−7.35 (m, 6H), 7.22−7.17 (m, 3H), 7.09 (s, 4H), 6.57−6.55 (m, 2H), 4.81 (d, J = 18.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.6, 153.7, 137.8, 136.6, 129.8, 128.8, 128.6, 128.5, 127.7, 125.2, 94.2, 58.1; IR (neat, cm^{-1}) 3059, 3029, 2236, 1713, 1598, 1562, 1486, 1448, 1409, 1215, 1083, 911, 757, 732, 700; HRMS (ESI) calcd for $C_{24}H_{17}I_2NO$ ([M + H]$^+$) = 589.9472; found, 589.9461.

*1-Benzyl-3,5-dibromo-2,6-diphenylpyridin-4(1H)-one (**4ac**).* Yield 72%; 35.5 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.42−7.31 (m, 7H), 7.22−7.16 (m, 3H), 7.12 (d, J = 6.0 Hz, 4H), 6.55 (d, J = 6.4 Hz, 2H), 4.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 168.7, 150.6, 136.3, 134.4, 129.8, 128.8, 128.6, 128.4, 127.7, 125.2, 116.1, 56.8; IR (neat, cm^{-1}) 3060, 3032, 2235, 1705, 1606, 1572, 1530, 1488, 1217, 1103, 912, 846, 757, 732, 698; HRMS (ESI) calcd for $C_{24}H_{17}Br_2NO$ ([M + H]$^+$) = 493.9750; found, 493.9747.

Characterization Data of 5a−5j, 5ab, 5na, 5nb, 5pa, and 5pb. *(E)-4-Iodo-2-(iodo(phenyl)methylene)-5-phenyl-1-propyl-1H-pyrrol-3(2H)-one (**5a**).* Yield 82%; 44.4 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.51−7.41 (m, 9H), 7.34 (t, J = 7.2 Hz, 1H), 2.76 (t, J = 7.6 Hz, 1H), 1.09−0.99 (m, 2H), 0.31 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.1, 168.5, 143.3, 135.6, 130.9, 130.1, 129.6, 129.2, 129.2, 128.7, 128.5, 92.1, 68.7, 49.2, 21.1, 10.6; IR (neat, cm^{-1}) 2962, 2926, 1670, 1576, 1538, 1483, 1444, 1063, 753, 694; HRMS (ESI) calcd for $C_{20}H_{17}I_2NO$ ([M + H]$^+$) = 541.9472; found, 541.9480.

*(E)-4-Iodo-2-(iodo(m-tolyl)methylene)-1-propyl-5-(m-tolyl)-1H-pyrrol-3(2H)-one (**5b**).* Yield 93%; 52.9 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.44−7.37 (m, 1H), 7.34−7.21 (m, 7H), 7.16 (d, J = 7.6 Hz, 1H), 2.79 (t, J = 7.6 Hz, 2H), 2.44 (s, 3H), 2.40 (s, 3H), 1.11−1.02 (m, 2H), 0.33 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.0, 168.6, 143.3, 138.5, 138.3, 135.3, 131.6, 130.3, 129.9, 129.6, 129.4, 128.6, 128.3, 126.2, 126.1, 92.1, 68.3, 49.0, 21.4, 21.3, 21.1, 10.5; IR (neat, cm^{-1}) 2961, 2925, 2867, 1670, 1582, 1535, 1477, 1066, 764, 734, 706; HRMS (ESI) calcd for $C_{22}H_{21}I_2NO$ ([M + H]$^+$) = 569.9785; found, 569.9780.

*(E)-4-Iodo-2-(iodo(p-tolyl)methylene)-1-propyl-5-(p-tolyl)-1H-pyrrol-3(2H)-one (**5c**).* Yield 82%; 46.7 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.37 (t, J = 8.4 Hz, 4H), 7.30−7.27 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 2.81 (t, J = 7.2 Hz, 2H), 2.50−2.38 (m, 6H), 1.07−0.98 (m, 2H), 0.32 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.0, 168.5, 141.3, 140.3, 139.9, 135.5, 129.7, 129.3, 129.3, 129.1, 129.1, 128.9, 126.9, 92.6, 68.5, 49.2, 21.6, 21.3, 10.7; IR (neat, cm^{-1}) 2962, 2924, 1669, 1609, 1542, 1497, 1458, 1363, 1063, 815, 761, 732, 686; HRMS (ESI) calcd for $C_{22}H_{21}I_2NO$ ([M + H]$^+$) = 569.9785; found, 569.9774.

*(E)-5-(4-Ethylphenyl)-2-((4-ethylphenyl)iodomethylene)-4-iodo-1-propyl-1H-pyrrol-3(2H)-one (**5d**).* Yield 79%; 47.2 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.42−7.35 (m, 5H), 7.31 (d, J = 8.0 Hz, 2H), 7.27−7.7.24 (m, 3H), 2.80 (t, J = 7.6 Hz, 2H), 2.73−2.68 (m, 4H), 1.26 (q, J = 8.0 Hz, 6H), 1.07−0.98 (m, 2H), 0.31 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.0, 168.5, 147.4, 146.1, 140.5, 135.5, 129.4, 129.2, 128.1, 127.9, 127.1, 92.5, 68.5, 49.2, 28.7, 28.6, 21.0, 15.2, 15.0, 10.6; IR (neat, cm^{-1}) 2965, 2930, 2872, 2244, 1668, 1609, 1540, 1496, 1459, 1364, 1064, 839, 761, 733; HRMS (ESI) calcd for $C_{24}H_{25}I_2NO$ ([M + H]$^+$) = 598.0098; found, 598.0089.

*(E)-4-Iodo-2-(iodo(4-propylphenyl)methylene)-1-propyl-5-(4-propylphenyl)-1H-pyrrol-3(2H)-one (**5e**).* Yield 58%; 36.3 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.40−7.37 (m, 4H), 7.30−7.27 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 2.79 (t, J = 7.6 Hz, 2H), 2.64 (q, J = 7.6 Hz, 4H), 1.73−1.61 (m, 4H), 1.06−0.99 (m, 2H), 0.95 (q, J = 7.2 Hz, 6H), 0.30 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.0, 168.5, 145.9, 144.6, 140.6, 135.5, 129.3, 129.1, 128.7, 128.5, 127.2, 92.4, 68.5, 49.2, 37.9, 37.7, 24.2, 24.1, 21.0, 13.8, 13.6, 10.6; IR (neat, cm^{-1}) 2964, 2930, 2876, 1671, 1602, 1540, 1493, 1462, 1364, 1067, 840, 765, 730; HRMS (ESI) calcd for $C_{26}H_{29}I_2NO$ ([M + H]$^+$) = 626.0411; found, 626.0418.

*(E)-5-Cyclopropyl-2-(cyclopropyliodomethylene)-4-iodo-1-propyl-1H-pyrrol-3(2H)-one (**5f**).* Yield 46%; 21.6 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.15 (t, J = 7.6 Hz, 2H), 1.50−1.43 (m, 2H), 1.09−1.05 (m, 5H), 0.87−0.83 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.3, 171.6, 140.3, 122.9, 68.9, 48.2, 21.6, 12.3, 11.5, 11.2, 8.6, 8.5; IR (neat, cm^{-1}) 2963, 2928, 1601, 1481, 1293, 1100, 908, 732; HRMS (ESI) calcd for $C_{14}H_{17}I_2NO$ ([M + H]$^+$) = 469.9472; found, 469.9483.

*(E)-5-(2-Fluorophenyl)-2-((2-fluorophenyl)iodomethylene)-4-iodo-1-propyl-1H-pyrrol-3(2H)-one (**5g**).* Yield 79%; 45.6 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.55−7.50 (m, 1H), 7.42−7.31 (m, 4H), 7.30−7.18 (m, 2H), 7.14−7.10 (m, 1H), 2.79 (q, J = 7.6 Hz, 2H), 1.19−1.05 (m, 2H), 0.34−0.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.3 (d, J = 7 Hz, 1C), 163.6, 161.8 (d, J = 344 Hz, 1C), 158.5 (d, J = 195 Hz, 1C), 156.9 (d, J = 23 Hz, 1C), 134.9 (d, J = 7 Hz, 1C), 133.0, 131.7, 131.1, 130.8, 130.6 (d, J = 12 Hz, 1C), 124.6 (d, J = 22 Hz, 1C), 124.1, 118.1 (d, J = 14 Hz, 1C), 116.4 (d, J = 39 Hz, 1C), 81.6, 67.4 (d, J = 13 Hz, 1C), 48.8 (d, J = 15 Hz, 1C), 21.4, 10.5 (d, J = 12 Hz, 1C); IR (neat, cm^{-1}) 2963, 2927, 1642, 1614, 1508, 1462, 1229, 1105, 816, 759; HRMS (ESI) calcd for $C_{20}H_{15}F_2I_2NO$ ([M + H]$^+$) = 577.9284; found, 577.9289.

*(E)-5-(3-Fluorophenyl)-2-((3-fluorophenyl)iodomethylene)-4-iodo-1-propyl-1H-pyrrol-3(2H)-one (**5h**).* Yield 51%; 29.4 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.54−7.39 (m, 2H), 7.29−7.18 (m, 5H), 7.09−7.04 (m, 1H), 2.80 (t, J = 7.6 Hz, 2H), 1.12−1.03 (m, 2H), 0.37 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.0, 167.1 (d, J = 2 Hz, 1C), 163.5 (d, J = 39 Hz, 1C), 161.0 (d, J = 40 Hz, 1C), 145.1 (d, J = 7 Hz, 1C), 135.7, 131.9 (d, J = 7 Hz, 1C), 130.7 (d, J = 8 Hz, 1C), 130.2 (d, J = 8 Hz, 1C), 125.0, 124.9 (d, J = 2 Hz, 1C), 118.0 (d, J = 21 Hz, 1C), 116.7 (d, J = 21 Hz, 1C), 116.4 (d, J = 8 Hz, 1C), 116.1 (d, J = 9 Hz, 1C), 89.8 (d, J = 2 Hz, 1C), 69.3, 49.3, 21.1, 10.6; IR (neat, cm^{-1}) 2965, 2928, 2246, 1672, 1582, 1541, 1478, 1436, 1260, 1062, 955, 783, 734, 707; HRMS (ESI) calcd for $C_{20}H_{15}F_2I_2NO$ ([M + H]$^+$) = 577.9284; found, 577.9280.

*(E)-5-(4-Fluorophenyl)-2-((4-fluorophenyl)iodomethylene)-4-iodo-1-propyl-1H-pyrrol-3(2H)-one (**5i**).* Yield 86%; 49.6 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.52−7.47 (m, 4H), 7.21 (t, J = 8.4 Hz, 2H), 7.14 (t, J = 8.8 Hz, 2H), 2.78 (t, J = 7.6 Hz, 2H), 1.90−1.00 (m, 2H), 0.36 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.9, 166.4 (d, J = 224 Hz, 1C), 163.5 (d, J = 151 Hz, 1C), 161.7, 139.2 (d, J = 3 Hz, 1C), 135.8, 131.4 (d, J = 7 Hz, 1C), 131.4 (d, J = 6 Hz, 1C), 125.8 (d, J = 4 Hz, 1C), 116.2 (d, J = 22 Hz, 1C), 115.7 (d, J = 22 Hz, 1C), 90.7, 69.5, 49.3, 20.9, 10.7; IR (neat, cm^{-1}) 2965, 2929, 2246, 1667, 1601, 1543, 1496, 1462, 1407, 1232, 1156, 1064, 844, 763, 733; HRMS (ESI) calcd for $C_{20}H_{15}F_2I_2NO$ ([M + H]$^+$) = 577.9284; found, 577.9284.

*(E)-5-(4-Chlorophenyl)-2-((4-chlorophenyl)iodomethylene)-4-iodo-1-propyl-1H-pyrrol-3(2H)-one (**5j**).* Yield 42%; 25.6 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.55 (t, J = 6.0 Hz, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 2.0 Hz, 1H), 7.42 (s, 4H), 7.34 (d, J = 3.2 Hz, 1H), 2.79 (t, J = 7.6 Hz, 2H), 1.90−1.00 (m, 2H), 0.37 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.0, 167.3, 141.6, 137.3, 135.8, 130.7, 130.6, 129.3, 128.9, 128.6, 128.3, 90.5, 69.6, 49.4, 21.0, 10.7; IR (neat, cm^{-1}) 2963, 2927, 1670, 1596, 1537, 1481, 1398, 1365, 1179, 1092, 1063, 1012, 817, 733; HRMS (ESI) calcd for $C_{20}H_{15}Cl_2I_2NO$ ([M + H]$^+$) = 609.8693; found, 609.8695.

*(E)-1-Butyl-4-iodo-2-(iodo(phenyl)methylene)-5-phenyl-1H-pyrrol-3(2H)-one (**5aa**).* Yield 77%; 42.7 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.48−7.40 (m, 9H), 7.33 (q, J = 2.4 Hz, 1H), 2.82−2.79 (m, 2H), 0.97 (d, J = 4.8 Hz, 2H), 0.65−0.62 (m, 2H), 0.51−0.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.9, 168.3, 143.1, 135.5, 130.8, 129.8, 129.5, 129.2, 129.0, 128.6, 128.4, 92.1, 68.7, 47.4, 29.6, 19.2, 13.3; IR (neat, cm^{-1}) 2964, 2932, 1670, 1578, 1548, 1483,

1444, 1063, 757, 699; HRMS (ESI) calcd for $C_{21}H_{19}I_2NO$ ([M + H]$^+$) = 555.9629; found, 555.9629.

*(E)-1-Benzyl-4-iodo-2-(iodo(phenyl)methylene)-5-phenyl-1H-pyrrol-3(2H)-one (**5ab**).* Yield 73%; 43.0 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46 (t, J = 7.6 Hz, 5H), 7.41−7.32 (m, 5H), 7.15−7.06 (m, 3H), 6.43 (d, J = 6.8 Hz, 2H), 4.11 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.9, 168.1, 143.0, 136.2, 135.8, 131.0, 129.8, 129.7, 129.2, 128.7, 128.3, 128.3, 127.5, 126.4, 93.5, 69.4, 51.2; IR (neat, cm^{-1}) 2966, 2942, 1670, 1579, 1543, 1481, 1440, 1062, 757, 698; HRMS (ESI) calcd for $C_{24}H_{17}I_2NO$ ([M + H]$^+$) = 589.9472; found, 589.9477.

*(E)-5-(2-Fluorophenyl)-4-iodo-2-(iodo(m-tolyl)methylene)-1-propyl-1H-pyrrol-3(2H)-one (**5na**).* Yield 62%; 35.5 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.59−7.41 (m, 2H), 7.38−7.09 (m, 6H), 2.73 (t, J = 7.6 Hz, 2H), 2.38 (m, 2H), 2.38 (m, 3H), 1.11−1.02 (m, 2H), 0.31 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.6, 163.3, 160.1, 157.6, 143.1, 138.2, 134.6, 132.9, 132.8, 131.2, 130.4, 129.8, 128.3, 126.5, 124.5, 124.5, 118.4, 118.3, 116.6, 116.4, 92.9, 68.2, 49.0, 21.5, 21.3, 10.5; IR (neat, cm^{-1}) 2964, 2878, 1728, 1669, 1615, 1548, 1450, 1458, 1378, 1066, 762; HRMS (ESI) calcd for $C_{21}H_{18}FI_2NO$ ([M + H]$^+$) = 573.9535; found, 573.9531.

*(E)-2-((2-Fluorophenyl)iodomethylene)-4-iodo-1-propyl-5-(m-tolyl)-1H-pyrrol-3(2H)-one (**5nb**).* Yield 19%; 10.9 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.40−7.34 (m, 3H), 7.30 (d, J = 7.6 Hz, 1H), 7.26−7.22 (m, 4H), 2.85−2.79 (m, 2H), 2.42 (s, 3H), 1.44−1.06 (m, 2H), 0.23 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.7, 168.8, 159.4, 156.9, 138.6, 135.8, 131.7, 131.5, 131.4, 130.9, 129.8, 129.4, 128.6, 126.2, 124.4, 124.3, 117.9, 116.3, 116.1, 81.0, 67.4, 48.9, 21.4, 21.0, 10.6; IR (neat, cm^{-1}) 2966, 2927, 1727, 1672, 1536, 1481, 1455, 1361, 1064, 897, 798, 710; HRMS (ESI) calcd for $C_{21}H_{18}FI_2NO$ ([M + H]$^+$) = 573.9535; found, 573.9542.

*(E)-4-Iodo-2-(1-iodobutylidene)-5-phenyl-1-propyl-1H-pyrrol-3(2H)-one (**5pa**).* Yield 22%; 11.2 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.42−7.31 (m, 5H), 2.88 (t, J = 8.0 Hz, 2H), 2.62 (t, J = 8.0 Hz, 2H), 1.65−1.69 (m, 2H), 1.22−1.42 (m, 2H), 1.05 (t, J = 7.6 Hz, 3H), 0.45 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 182.2, 169.8, 143.3, 134.7, 129.3, 128.8, 128.3, 89.5, 66.2, 47.2, 30.5, 21.9, 21.1, 13.9, 10.5; IR (neat, cm^{-1}) 2964, 2928, 2872, 1670, 1539, 1390, 1052, 703, 612; HRMS (ESI) calcd for $C_{17}H_{19}I_2NO$ ([M + H]$^+$) = 507.9629; found, 507.9633.

*(E)-4-Iodo-2-(iodo(phenyl)methylene)-1,5-dipropyl-1H-pyrrol-3(2H)-one (**5pb**).* Yield 49%; 24.8 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66−7.60 (m, 2H), 7.50−7.44 (m, 3H), 2.86 (t, J = 7.2 Hz, 2H), 2.44 (t, J = 7.6 Hz, 2H), 1.66−1.61 (m, 2H), 1.19−1.14 (m, 2H), 0.97 (t, J = 7.6 Hz, 3H), 0.53 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 184.0, 168.8, 143.2, 135.2, 129.3, 128.7, 128.4, 90.1, 61.4, 47.5, 34.6, 25.8, 25.6, 13.9, 11.5; IR (neat, cm^{-1}) 2964, 2881, 1658, 1483, 1436, 1331, 899, 806, 728; HRMS (ESI) calcd for $C_{17}H_{19}I_2NO$ ([M + H]$^+$) = 507.9629; found, 507.9628.

Characterization Data of 6a, 6b, and 6ab. *2,3,5,6-Tetraphenyl-1-propylpyridin-4(1H)-one (**6a**).* Yield 86%; 37.9 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.26 (s, 10H), 7.10−7.08 (m, 7H), 7.06 (d, J = 4.8 Hz, 1H), 7.04−7.00 (m, 2H), 3.51−3.47 (m, 2H), 1.40−1.31 (m, 2H), 0.29 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 175.3, 149.3, 135.3, 134.4, 131.1, 130.0, 128.5, 128.1, 127.1, 126.1, 52.7, 36.4, 24.0, 10.6; IR (neat, cm^{-1}) 2962, 1675, 1583, 1480, 1443, 1077, 748; HRMS (ESI) calcd for $C_{32}H_{27}NO$ ([M + H]$^+$) = 442.2165; found, 442.2180.

*3,5-Diphenyl-1-propyl-2,6-di-m-tolylpyridin-4(1H)-one (**6b**).* Yield 92%; 43.2 mg; light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.14−7.05 (m, 14H), 7.03−6.97 (m, 4H), 3.49 (t, J = 8.0 Hz, 2H), 2.28 (s, 3H), 2.26 (s, 3H), 1.40−1.31 (m, 2H), 0.32 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 175.3, 149.4, 137.7, 137.6, 135.5, 134.3, 131.2, 131.1, 130.6, 130.5, 129.1, 128.4, 128.1, 127.9, 127.9, 127.2, 127.1, 127.0, 126.0, 52.6, 24.1, 21.2, 21.2, 10.6; IR (neat, cm^{-1}) 2964, 2862, 1612, 1522, 1425, 1370, 1296, 1082, 792, 759; HRMS (ESI) calcd for $C_{34}H_{31}NO$ ([M + H]$^+$) = 470.2478; found, 470.2487.

*1-Benzyl-2-(diphenylmethylene)-4,5-diphenyl-1H-pyrrol-3(2H)-one (**6ab**).* Yield 79%; 38.6 mg; red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.63 (d, J = 4.4 Hz, 2H), 7.52 (d, J = 5.2 Hz, 4H), 7.46−7.45 (m, 4H), 7.37−7.34 (m, 3H), 7.30−7.24 (m, 3H), 7.18−7.12 (m, 4H), 7.02 (d, J = 7.2 Hz, 3H), 6.61 (d, J = 7.2 Hz, 2H), 4.18 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 183.4, 169.7, 140.6, 139.9, 138.5, 136.5, 136.3, 134.3, 131.7, 131.3, 130.9, 130.9, 130.1, 129.6, 129.3, 128.9, 128.8, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 127.1, 126.8, 51.5; IR (neat, cm^{-1}) 2967, 2930, 1586, 1561, 1514, 1478, 1434, 798, 721; HRMS (ESI) calcd for $C_{36}H_{27}NO$ ([M + H]$^+$) = 490.2165; found, 490.2168.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: liangym@lzu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support was received from the National Science Foundation (NSF 21072080), the National Basic Research Program of China (973 Program, 2010CB833203), the Program for Changjiang Scholars and Innovative Research Team in University (IRT1138), and the Fundamental Research Funds for the Central Universities (lzujbky-2013-ct02).

■ REFERENCES

(1) For 4-pyrone, see: (a) Jones, R. G.; Mann, M. J. *J. Am. Chem. Soc.* **1953**, *75*, 4048. (b) Stossel, D.; Chan, T. *J. Org. Chem.* **1988**, *53*, 4901. (c) Molenda, J. J.; Jones, M. M.; Johnston, D. S.; Walker, E. M., Jr.; Cannon, D. J. *J. Med. Chem.* **1994**, *37*, 4363. (d) Luo, S.; Mi, X.; Xu, H.; Wang, P. G.; Cheng, J.-P. *J. Org. Chem.* **2004**, *69*, 8413. (e) Reddy, D. S.; Vander Velde, D.; Aubé, J. *J. Org. Chem.* **2004**, *69*, 1716. For 4-pyridone, see: (f) Katritzky, A. R.; Khan, G. R.; Leahy, D. E.; De Rosa, M. *J. Org. Chem.* **1984**, *49*, 4784. (g) Abe, H.; Machiguchi, H.; Matsumoto, S.; Inouye, M. *J. Org. Chem.* **2008**, *73*, 4650. (h) Kempson, J.; Spergel, S. H.; Guo, J.; Quesnelle, C.; Gill, P.; Belanger, D.; Dyckman, A. J.; Li, T.; Watterson, S. H.; Langevine, C. M. *J. Med. Chem.* **2009**, *52*, 1994. (i) Gao, X.; Singh, R. P.; Corey, E. *Org. Lett.* **2010**, *12*, 1812. (j) Rycke, N. D.; Berionni, G.; Couty, F.; Mayr, H.; Goumont, R.; David, O. R. *Org. Lett.* **2010**, *13*, 530. (k) Larionov, E.; Mahesh, M.; Spivey, A. C.; Wei, Y.; Zipse, H. *J. Am. Chem. Soc.* **2012**, *134*, 9390. For 3-pyrrolone, see: (l) Freeman, J. P.; Haddadin, M. J. *J. Org. Chem.* **1980**, *45*, 4898. (m) Gaywood, A. P.; McNab, H. *J. Org. Chem.* **2009**, *74*, 4278. (n) Hemming, K.; Khan, M. N.; Kondakal, V. V.; Pitard, A.; Qamar, M. I.; Rice, C. R. *Org. Lett.* **2012**, *14*, 126.

(2) For 4-pyrone see: (a) Ellis, B. L.; Duhme, A. K.; Hider, R. C.; Hossain, M. B.; Rizvi, S.; van der Helm, D. *J. Med. Chem.* **1996**, *39*, 3659. (b) Caturla, F.; Jiménez, J.-M.; Godessart, N.; Amat, M.; Cárdenas, A.; Soca, L.; Beleta, J.; Ryder, H.; Crespo, M. I. *J. Med. Chem.* **2004**, *47*, 3874. (c) Abe, I.; Utsumi, Y.; Oguro, S.; Morita, H.; Sano, Y.; Noguchi, H. *J. Am. Chem. Soc.* **2005**, *127*, 1362. (d) Puerta, D. T.; Mongan, J.; Tran, B. L.; McCammon, J. A.; Cohen, S. M. *J. Am. Chem. Soc.* **2005**, *127*, 14148. (e) Sibi, M. P.; Zimmerman, J. *J. Am. Chem. Soc.* **2006**, *128*, 13346. (f) Hollick, J. J.; Rigoreau, L. J.; Cano-Soumillac, C.; Cockcroft, X.; Curtin, N. J.; Frigerio, M.; Golding, B. T.; Guiard, S.; Hardcastle, I. R.; Hickson, I. *J. Med. Chem.* **2007**, *50*, 1958. For 4-pyridone see: (g) Mitscher, L. A. *Chem. Rev.* **2005**, *105*, 559. (h) Kitagawa, H.; Ozawa, T.; Takahata, S.; Iida, M.; Saito, J.; Yamada, M. *J. Med. Chem.* **2007**, *50*, 4710. (i) Kim, K. S.; Zhang, L.; Schmidt, R.; Cai, Z.-W.; Wei, D.; Williams, D. K.; Lombardo, L. J.; Trainor, G. L.; Xie, D.; Zhang, Y.; An, Y.; Sack, J. S.; Tokarski, J. S.; Darienzo, C.; Kamath, A.; Marathe, P.; Zhang, Y.; Lippy, J.; Jeyaseelan, R.; Wautlet, B.; Henley, B.; Gullo-Brown, J.; Manne, V.; Hunt, J. T.; Fargnoli, J.; Borzilleri, R. M. *J. Med. Chem.* **2008**, *51*, 5330. (j) Yeates, C. L.; Batchelor, J. F.; Capon, E. C.;

Cheesman, N. J.; Fry, M.; Hudson, A. T.; Pudney, M.; Trimming, H.; Woolven, J.; Bueno, J. M. *J. Med. Chem.* **2008**, *51*, 2845. (k) Jessen, H. J.; Schumacher, A.; Schmid, F.; Pfaltz, A.; Gademann, K. *Org. Lett.* **2011**, *13*, 4368. (l) Brown, M. F.; Mitton-Fry, M. J.; Arcari, J. T.; Barham, R.; Casavant, J.; Gerstenberger, B. S.; Han, S.; Hardink, J. R.; Harris, T. M.; Hoang, T. *J. Med. Chem.* **2013**, *56*, 5541. (m) Kawasuji, T.; Johns, B. A.; Yoshida, H.; Weatherhead, J. G.; Akiyama, T.; Taishi, T.; Taoda, Y.; Mikamiyama-Iwata, M.; Murai, H.; Kiyama, R. *J. Med. Chem.* **2013**, *56*, 1124. For 3-pyrrolone see: (n) Murugesan, D.; Mital, A.; Kaiser, M.; Shackleford, D. M.; Morizzi, J.; Katneni, K.; Campbell, M.; Hudson, A.; Charman, S. A.; Yeates, C.; Gilbert, I. H. *J. Med. Chem.* **2013**, *56*, 2975.

(3) (a) Garey, D.; Ramirez, M.-l.; Gonzales, S.; Wertsching, A.; Tith, S.; Keefe, K.; Pena, M. R. *J. Org. Chem.* **1996**, *61*, 4853. (b) Ishibashi, Y.; Ohba, S.; Nishiyama, S.; Yamamura, S. *Tetrahedron lett.* **1996**, *37*, 2997. (c) Jo, Y. J.; Cho, I. H.; Song, C. K.; Shin, H. W.; Kim, Y. S. *J. Food Sci.* **2011**, *76*, C368. (d) Li, D.-F.; Hu, P.-P.; Liu, M.-S.; Kong, X.-L.; Zhang, J.-C.; Hider, R. C.; Zhou, T. *J. Agric. Food. Chem.* **2013**, *61*, 6597. (e) Shahrisa, A.; Esmati, S.; Miri, R.; Firuzi, O.; Edraki, N.; Nejati, M. *Eur. J. Med. Chem.* **2013**, *66*, 388.

(4) (a) Ye, Y. -H.; Zhu, H. -L.; Song, Y. -C.; Liu, J. -Y.; Tan, R. -X. *J. Nat. Prod.* **2005**, *68*, 1106. (b) Maloney, K. N.; MacMillan, J. B.; Kauffman, C. A.; Jensen, P. R.; DiPasquale, A. G.; Rheingold, A. L.; Fenical, W. *Org. Lett.* **2009**, *11*, 5422. (c) Rodrigues, T.; da Cruz, F. P.; Lafuente-Monasterio, M. J.; Gonçalves, D.; Ressurreição, A. S.; Sitoe, A. R.; Bronze, M. R.; Gut, J.; Schneider, G.; Mota, M. M. *J. Med. Chem.* **2013**, *56*, 4811.

(5) Pansanit, A.; Park, E. J.; Kondratyuk, T. P.; Pezzuto, J. M.; Lirdprapamongkol, K.; Kittakoop, P. *J. Nat. Prod.* **2013**, *76*, 1824.

(6) (a) Light, R. J.; Hauser, C. R. *J. Org. Chem.* **1960**, *25*, 538. (b) Work, S. D.; Hauser, C. R. *J. Org. Chem.* **1963**, *28*, 725. (b) Morris, J.; Luke, G. P.; Wishka, D. G. *J. Org. Chem.* **1996**, *61*, 3218. (c) Li, C.-S.; Lacasse, E. *Tetrahedron Lett.* **2002**, *43*, 3565. (d) Boukouvalas, J.; Wang, J.-X. *Org. Lett.* **2008**, *10*, 3397.

(7) (a) Freeman, S. K.; Ringk, W. F.; Spoerri, P. E. *J. Am. Chem. Soc.* **1947**, *69*, 858. (b) Dimroth, K. *Angew. Chem.* **1960**, *72*, 331. (c) Elkaschef, M. A.-F.; Nosseir, M. H. *J. Am. Chem. Soc.* **1960**, *82*, 4344. (d) Rumbo, A.; Mouriño, A.; Castedo, L.; Mascareñas, J. L. *J. Org. Chem.* **1996**, *61*, 6114.

(8) (a) Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3558. (b) Zulfiqar, F.; Kitazume, T. *Green Chem.* **2000**, *2*, 137. (c) Dziedzic, M.; Malecka, M.; Furman, B. *Org. Lett.* **2005**, *7*, 1725.

(9) Zhang, Z.; Fang, S.; Liu, Q.; Zhang, G. *J. Org. Chem.* **2012**, *77*, 7665.

(10) (a) Momose, T.; Tanaka, T.; Yokota, T.; Nagamoto, N.; Yamada, K. *Chem. Pharm. Bull.* **1979**, *27*, 1448. (b) Capon, B.; Kwok, F.-C. *Tetrahedron lett.* **1986**, *27*, 3275.

(11) (a) Haddadin, M. J.; Amalu, S.; Freeman, J. P. *J. Org. Chem.* **1984**, *49*, 2824. (b) Flitsch, W.; Hampel, K.; Hohenhorst, M. *Tetrahedron lett.* **1987**, *28*, 4395. (c) Binder, J. T.; Crone, B.; Kirsch, S. F.; Liebert, C.; Menz, H. *Eur. J. Org. Chem.* **2007**, 1636.

(12) McNab, H.; Monahan, L. C. *J. Chem. Soc., Perkin Trans. 1* **1988**, *4*, 863.

(13) (a) Smith, C. R.; Bunnelle, E. M.; Rhodes, A. J.; Sarpong, R. *Org. Lett.* **2007**, *9*, 1169. (b) Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838.

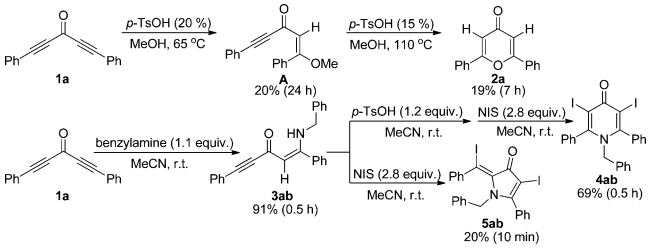
(14) (a) Yang, F.; Ji, K.-G.; Zhao, S.-C.; Ali, S.; Ye, Y.-Y.; Liu, X.-Y.; Liang, Y.-M. *Chem.—Eur. J.* **2012**, *18*, 6470. (b) Yang, F.; Qiu, Y.-F.; Ji, K.-G.; Niu, Y.-N.; Ali, S.; Liang, Y.-M. *J. Org. Chem.* **2012**, *77*, 9029.

(15) (a) Mothe, S. R.; Kothandaraman, P.; Rao, W.; Chan, P. W. *J. Org. Chem.* **2011**, *76*, 2521. (b) Zhu, H.-T.; Ji, K.-G.; Yang, F.; Wang, L.-J.; Zhao, S.-C.; Shaukat, A.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 684. (c) Shaukat, A.; Zhu, H.-T.; Xia, X.-F.; Ji, K.-G.; Yang, Y.-F.; Song, X.-R.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 2598. (d) Fang, C.; Paull, D. H.; Hethcox, J. C.; Shugrue, C. R.; Martin, S. F. *Org. lett.* **2012**, *14*, 6290. (e) Okamoto, N.; Yanada, R. *J. Org. Chem.* **2012**, *77*, 3944. (f) Shaukat, A.; Li, Y.-X.; Saeed, A.; Yang, F.; Chen, Z.-S.; Liang, Y.-M. *J. Org. Chem.* **2012**, *77*, 424. (g) Wang, L.-J.; Zhu, H.-T.; Lu, L.; Yang, F.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2012**, *14*, 1990. (h) Reddy, M. S.; Thirupathi, N.; Babu, M. H.; Puri, S. *J. Org. Chem.* **2013**, *78*, 5878.

(16) (a) Sakamoto, T.; Kondo, Y.; Watanabe, R.; Yamanaka, H. *Chem. Pharm. Bull.* **1986**, *34*, 2719. (b) Bradbury, R. H.; Allott, C. P.; Dennis, M.; Girdwood, J. A.; Kenny, P. W.; Major, J. S.; Oldham, A. A.; Ratcliffe, A. H.; Rivett, J. E. *J. Med. Chem.* **1993**, *36*, 1245. (c) Almeida, A. I.; Silva, A. M.; Cavaleiro, J. A. *Synlett* **2010**, *2010*, 462. (d) Almeida, A. I.; Silva, A. M.; Cavaleiro, J. A. *Synlett* **2011**, *2011*, 2955. (e) Audisio, D.; Messaoudi, S.; Peyrat, J.-F. o.; Brion, J.-D.; Alami, M. *J. Org. Chem.* **2011**, *76*, 4995. (f) Mugnaini, C.; Falciani, C.; De Rosa, M.; Brizzi, A.; Pasquini, S.; Corelli, F. *Tetrahedron* **2011**, *67*, 5776.

(17) For reviews see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *Organomet. Chem.* **1999**, *576*, 147.

(18) (a) Intermediate **A** was isolated in 20% yield after 24 h. When **A** was subjected to the same reaction conditions (at high temperature), **2a** was obtained in 19% after 7 h. (b) Intermediate **3ab** was isolated in 91% yield after 0.5 h. When **3ab** was subjected to the same reaction conditions (at room temperature), **4ab** was obtained in 69% after 0.5 h (c) Meanwhile, no intermediates were observed by TLC due to the high activity of synthesis of **5** with a fast conversion rate. However, when intermediate **3ab** was added to 2.8 equiv of NIS (with the same reaction conditions at room temperature), **5ab** was isolated in 67% in 10 min.



(19) (a) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 10204. (b) Rauhala, V.; Nättinen, K.; Rissanen, K.; Koskinen, A. M. P. *Eur. J. Org. Chem.* **2005**, 4119. (c) Schultz, T. W.; Yarbrough, J. W.; Hunter, R. S.; Aptula, A. O. *Chem. Res. Toxicol.* **2007**, *20*, 1359. (d) Mendoza, A.; Pardo, P.; Rodríguez, F.; Fañanás, F. *Chem.—Eur. J.* **2010**, *16*, 9758.

(20) (a) Bradbury, R. H.; Allott, C. P.; Dennis, M.; Girdwood, J. A.; Kenny, P. W.; Major, J. S.; Oldham, A. A.; Ratcliffe, A. H.; Rivett, J. E. *J. Med. Chem.* **1993**, *36*, 1245. (b) Hessian, K. O.; Flynn, B. L. *Org. Lett.* **2006**, *8*, 243. (c) Cross, R. M.; Manetsch, R. *J. Org. Chem.* **2010**, *75*, 8654. (d) Mugnaini, C.; Falciani, C.; De Rosa, M.; Brizzi, A.; Pasquini, S.; Corelli, F. *Tetrahedron* **2011**, *67*, 5776. (e) Klier, L.; Bresser, T.; Nigst, T. A.; Karaghiosoff, K.; Knochel, P. *J. Am. Chem. Soc.* **2012**, *134*, 13584. (f) Halim, R.; Aurelio, L.; Scammells, P. J.; Flynn, B. L. *J. Org. Chem.* **2013**, *78*, 4708.