JOC The Journal of Organic Chemistry

Article

Preparation of Spiro[indene-1,1'-isoindolin]-3'-ones via Sulfuric Acid-Promoted Cascade Cyclization

Lang Sun, Peng Liu, Jing Wang, Ping Lu, and Yanguang Wang

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b00958 • Publication Date (Web): 21 Jul 2017

Just Accepted

ACS Publications

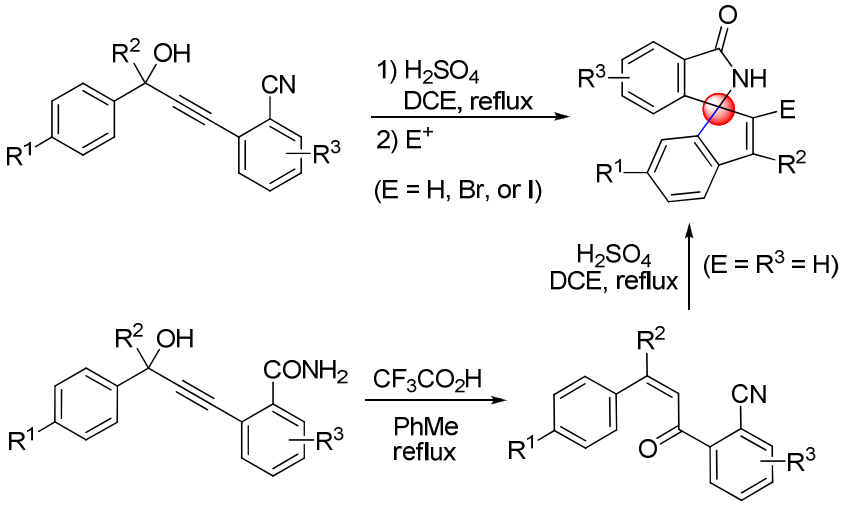
The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Preparation of Spiro[indene-1,1'-isoindolin]-3'-ones via Sulfuric Acid-Promoted Cascade Cyclization

Lang Sun, Peng Liu, Jing Wang, Ping Lu, Yanguang Wang**

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China

pinglu@zju.edu.cn; orgwyg@zju.edu.cn



ABSTRACT: The sulfuric acid-promoted cascade cyclization of 2-(3-hydroxyprop-1-ynyl)benzonitriles led to an efficient synthesis of spiro[indene-1,1'-isoindolin]-3'-ones. This class of spiro compounds could also be prepared by the sulfuric acid-catalyzed cyclization of 2-(phenylacryloyl)benzonitriles, which were readily derived from 2-(3-hydroxyprop-1-ynyl)benzamides using trifluroacetic acid as catalyst.

INTRODUCTION

Isoindolinones are an important class of nitrogen-containing heterocyclic compounds duo to their impressive bioactivities, such as antipsychotic, antiviral, anxiolytic, antifungal and anticancer activities.[1] Some of them have been clinically used as pharmaceuticals. For instance, lenalidomide is being used in the treatment of multiple myeloma (Figure 1).[1e] It has also shown efficacy in the class of hematological disorders known as myelodysplastic syndromes (MDS). Furthermore, isoindolinones are also useful building blocks for the synthesis of several drugs[2] and naturally occurring alkaloids.[3] Among a variety of isoindolinones, spiroisoindolinones have their own importance as they exhibit various properties such as anticancer activity[4] and aldose reductase inhibition[5] or can act as chemical sensors[6] (Figure 1). Consequently, the development of highly efficient methods for the preparation of this class of heterocycles has attracted much attention in recent years.[7] However, very limited methodologies for the construction of spiroisoindolinones with a spiro[indene-1,1'-isoindolin]-3'-one skeleton have been reported so far. The early examples include the dehydration of 2-(9-hydroxy-9H-fluoren-9-yl)-N-methylbenzamide (Scheme 1, Previous work A)[11] and the Pd-catalyzed cyclization of enamides of 2-iodobenzoic acid (Scheme 1, Previous work B).[12] Theses transformations suffer from low yields and limited substrate scope. More recently, Nishimura and Kim's groups independently reported more efficient syntheses of spiro[indene-1,1'-isoindolin]-3'-one skeletons by the

transition-metal-catalyzed [3+2] annulation reactions of the in situ generated ketimines with alkynes[13] or activated olefins[4] (Scheme 1, Previous work C). Therefore, the synthesis of spiro[indene-1,1'-isoindolin]-3'-one skeletons has been an attractive area for synthetic chemists.

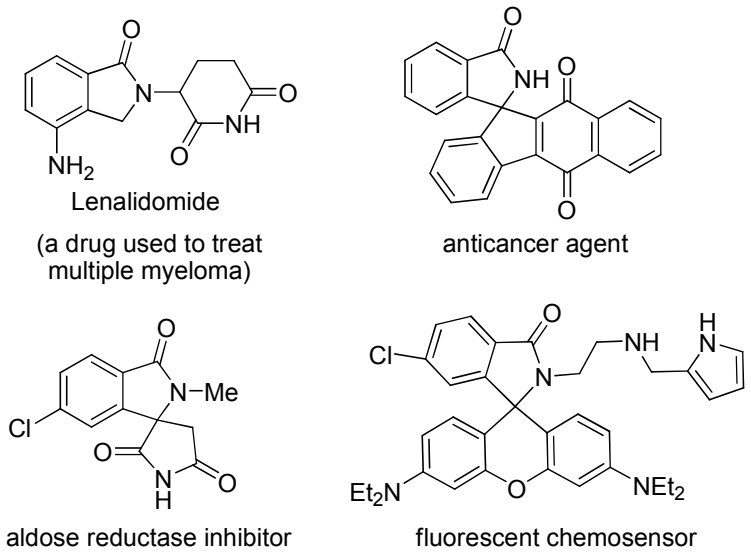
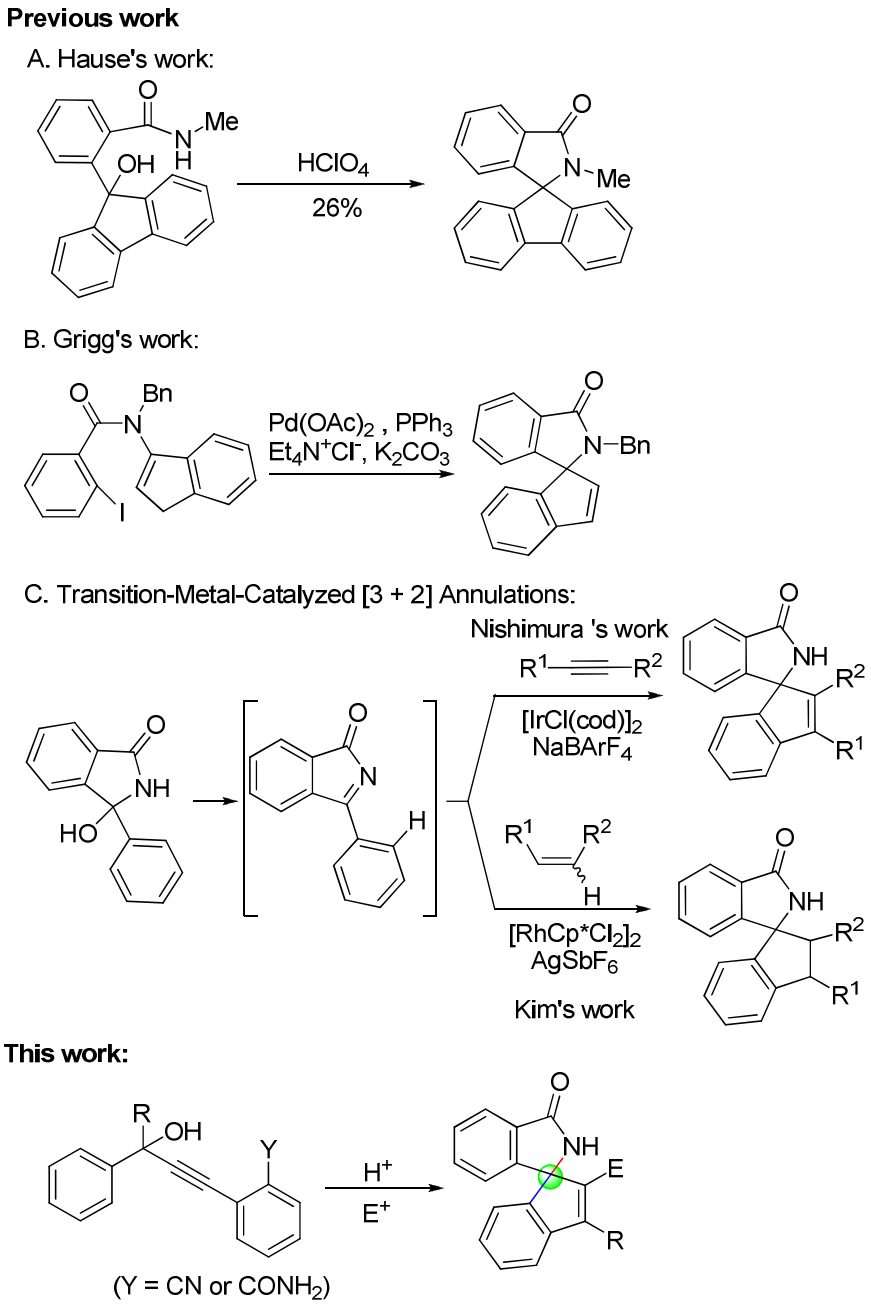


Figure 1. Typical examples of isoindolinone and spiroisoindolinone scaffolds.

In this context, propargylic alcohols are versatile building blocks in organic synthesis as they could be easily accessed from terminal alkynes and carbonyl compounds through simple nucleophilic addition and could be readily converted into a variety of important organic compounds, such as α,β-unsaturated ketones, alleneamides, allenesulfonamides, allenephosphoramides, carbocycles, and heterocycles.[8] These transformations normally proceed through a Lewis acid or Brønsted acid catalyzed Meyer-Schuster rearrangement and related cascade process.[9] As part of our ongoing program of the cascade reactions of propargylic alcohols,[10] herein we report the acid-catalyzed cyclization reactions of

3-(2-cyanophenyl)propargylic alcohols and 2-(3-hydroxyprop-1-ynyl)benzamides, furnishing a class of isoindolinone derivatives with a spiro[indene-1,1'-isoindolin]-3'-one skeleton (Scheme 1, This work). In comparison with the published methods, the features of our cascade approach to spiro[indene-1,1'-isoindolin]-3'-ones are more facile, metal-free and efficient.

Scheme 1. Previous Works and Our Design to Spiro[indene-1,1'-isoindolin]-3'-ones

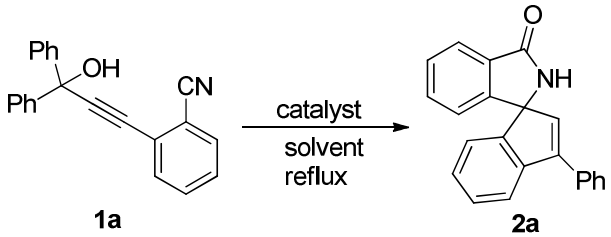


RESULTS AND DISCUSSIONS

In our primary investigations, $BF_3 \cdot Et_2O$ was used as the catalyst for the electrophilic cyclization of 3-(2-cyanophenyl)propargylic alcohol **1a**. By refluxing **1a** with $BF_3 \cdot Et_2O$ in nitromethane for 30 minutes, spiro[indene-1,1'-isoindolin]-3'-one **2a** was

isolated in 66% yield (Table 1, entry 1). Structure of **2a** was established by single crystal analysis.[11] In order to obtain a satisfied yield of **2a**, the reaction conditions were optimized and the results are summarized in Table 1. Firstly, we screened several Lewis acids and Brønsted acids, such as $BF_3 \cdot Et_2O$, TsOH, TfOH, and H_2SO_4 (Table 1, entries 1-4). Concentrated sulfuric acid was found to be the best catalyst. **2a** was not detected when CF_3COOH, AcOH, HCl, $Cu(OTf)_2$, and AgOTf were used as the catalyst, although **1a** was completely consumed afterwards (Table 1, entries 5-9). Only trace amount of **2a** was detected when $Yb(OTf)_3$ was used as the catalyst (Table 1, entry 10). By altering the solvent from nitromethane to THF, we did not observe the desired product (Table 1, entry 11). The best result (97% yield) was achieved in dichloroethane (DCE) (Table 1, entry 12). **1a** was recovered when the reaction was performed in water (Table 1, entry 13). The reaction in methanol also did not provide **2a,** although **1a** was completely consumed (Table 1, entry 14). Dichloromethane (DCM), toluene and MeCN were also screened, but they did not improve the yield (Table 1, entries 15-17). Both decreasing the catalyst amount and lowering the reaction temperature led to a decrease in the yield (Table 1, entries 18-20).

Table 1. Optimization of the Reaction Conditions[a]



1a **2a**

entry	catalyst	solvent	time (h)	temp. (^oC)	yield (%)[b]

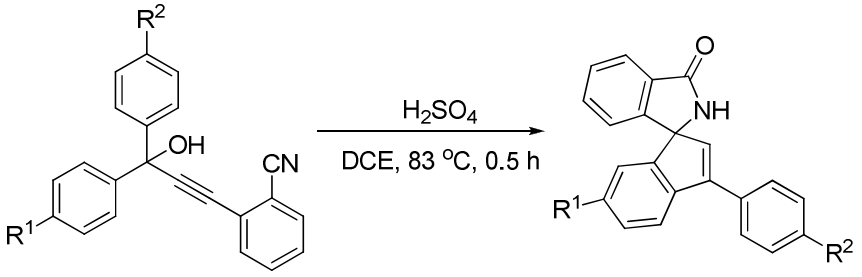
1	$BF_3 \cdot Et_2O$	CH_3NO_2	0.5	100	66
2	TsOH	CH_3NO_2	12	100	31
3	TfOH	CH_3NO_2	0.5	100	68
4	H_2SO_4	CH_3NO_2	0.5	100	90
5	CF_3CO_2H	CH_3NO_2	12	100	ND
6	AcOH	CH_3NO_2	12	100	NR
7	HCl	CH_3NO_2	12	100	ND
8	$Cu(OTf)_2$	CH_3NO_2	12	100	ND
9	AgOTf	CH_3NO_2	12	100	ND
10	$Yb(OTf)_3$	CH_3NO_2	12	100	trace
11	H_2SO_4	THF	0.5	66	ND
12	H_2SO_4	DCE	0.5	83	97
13	H_2SO_4	H_2O	0.5	100	NR
14	H_2SO_4	CH_3OH	0.5	65	ND
15	H_2SO_4	DCM	0.5	40	81
16	H_2SO_4	PhMe	0.5	110	89
17	H_2SO_4	CH_3CN	0.5	81	24
18	H_2SO_4	DCE	0.5	83	95[c]
19	H_2SO_4	DCE	2	83	ND[d]
20	H_2SO_4	DCE	2	83	82[e]

[a]Reaction conditions: **1a** (0.20 mmol), catalyst (0.24 mmol), solvent (4 mL), reflux temperature, H_2SO_4 is concentrated sulfuric acid. [b] Isolated yield referred to **1a**. [c] H_2SO_4 (0.20 mmol). [d] H_2SO_4 (0.01 mmol). [e] Room temperature.

With the optimized reaction conditions in hand, we tested the substrate diversity (Schemes 2-4). Firstly, we tested the symmetrical propargylic alcohols **1a-f** (Scheme 2). Good yields **2b** (81%) and **2d** (87%) were obtained for those substrates with a moderate electron-withdrawing (Cl, **1b**) or electron-donating group (Me, **1d**). Strong electron-donating group (OMe) or strong electron-withdrawing group (F) substituted

propargylic alcohols **1c** and **1e** provided the corresponding products **2c** (53%) and **2e** (65%) in relative lower yields. For asymmetrical propargylic alcohols, such as 2-(3-(4-Chlorophenyl)-3-hydroxy-3-phenylprop-1-yn-1-yl)benzonitrile (**1g**) and 2-(3-Hydroxy-3-(4-nitrophenyl)-3-phenylprop-1-yn-1-yl)benzonitrile (**1h**), the reaction took place to give the corresponding spiro products **2g** (94%) and **2h** (79%) in good to excellent yields. Asymmetric propargylic alcohols **1i** and **1j** were also tested (Scheme 3). In these cases, however, poor regioselectivity was observed. Thus, the cyclization of **1i** gave a mixture of **2ia** and **2ib** in 2.2 to 1 ratio, while a 1:1 mixture of **2ja** and **2jb** was obtained from **1j**.

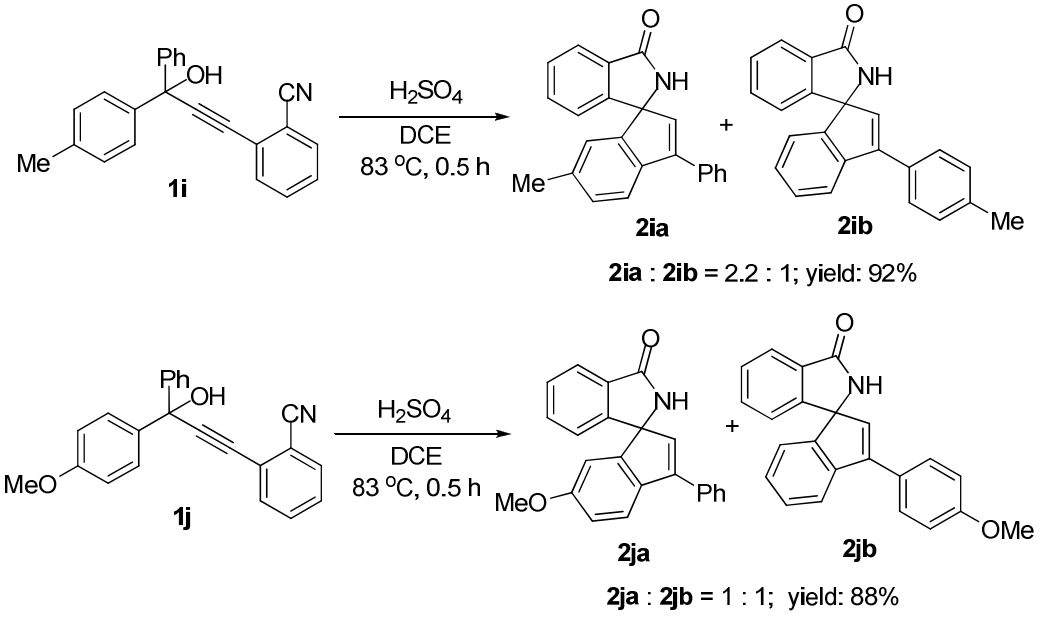
Scheme 2. Preparation of Compounds 2a-h



1a ($R^1 = R^2 = H$)
1b ($R^1 = R^2 = Cl$)
1c ($R^1 = R^2 = OMe$)
1d ($R^1 = R^2 = Me$)
1e ($R^1 = R^2 = F$)
1f ($R^1 = R^2 = Br$)
1g ($R^1 = H$, $R^2 = Cl$)
1h ($R^1 = H$, $R^2 = NO_2$)

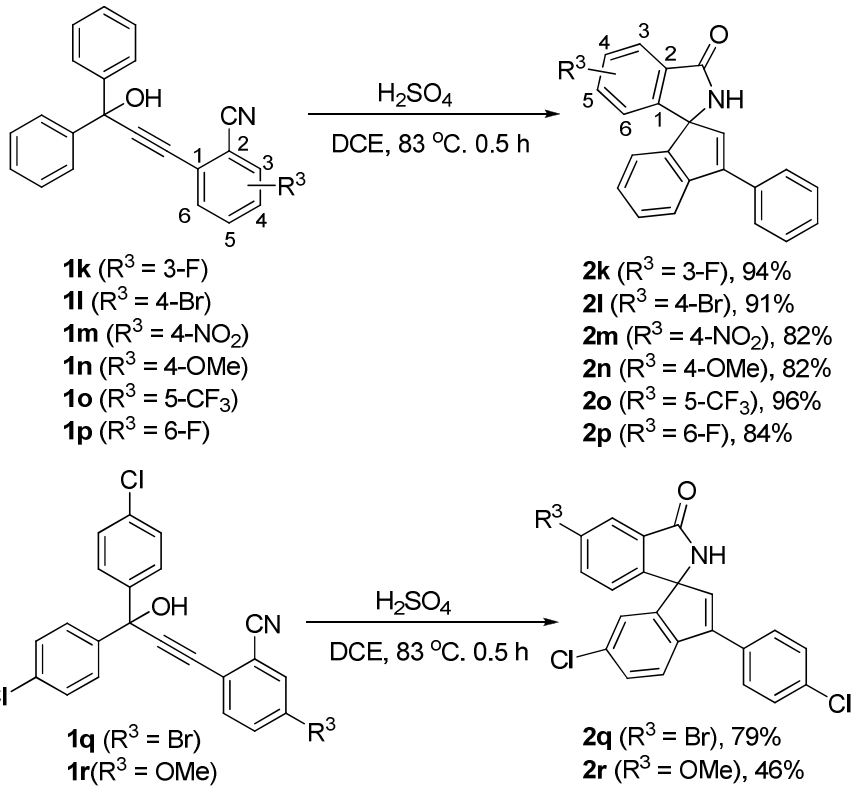
2a ($R^1 = R^2 = H$), 97%
2b ($R^1 = R^2 = Cl$), 81%
2c ($R^1 = R^2 = OMe$), 53%
2d ($R^1 = R^2 = Me$), 87%
2e ($R^1 = R^2 = F$), 65%
2f ($R^1 = R^2 = Br$), 63%
2g ($R^1 = H$, $R^2 = Cl$), 94%
2h ($R^1 = H$, $R^2 = NO_2$), 79%

Scheme 3. Preparation of Compounds (2ia + 2ib) and (2ja + 2jb)



As shown in Scheme 4, the R^3 group in propargylic alcohols **1** could be altered to 3-F (**1k**), 4-Br (**1l**), 4-NO_2 (**1m**), 4-MeO (**1n**), 5-CF_3 (**1o**), and 6-F (**1p**). In these cases, the corresponding products **2k-p** were obtained in good to excellent yields and the electronic effect of these substituted groups was not apparent. In comparison to **2l** and **2n**, **2q** and **2r** were isolated in lower yields duo to the decreased electron density of 4-chlorophenyl of propargylic alcohols **1q** and **1r**, which should be adverse to the final cyclization.

Scheme 4. Preparation of Compounds 2k-r

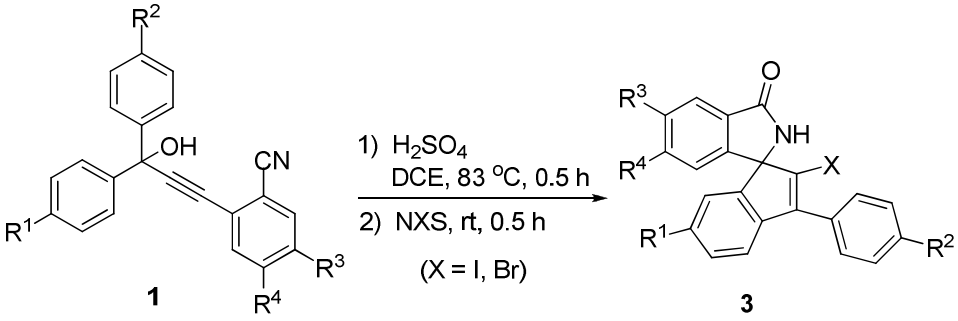


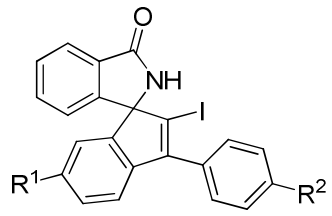
Practically, this transformation could be scaled up to gram scale. By refluxing the mixture of **1a** (4 mmol, 1.236 g) and sulfuric acid (4.8 mmol) in DCE (50 mL) for 30 minutes, 1.065 g (86% yield) of **2a** was isolated by silica gel column chromatograph.

If a strong electrophile such as NIS was added to the reaction mixture after spiro[indene-1,1'-isoindolin]-3'-ones **2** were formed, iodination occurred on the indene ring of **2** to furnish 2-iodospiro[indene-1,1'-isoindolin]-3'-ones **3a-g** in good to excellent yields (Table 2). Structure of **3a** was established by single crystal analysis.[11] The reaction was carried in a one-pot without the isolation step. Electronic effect of the substituted group on indene ring was significant. With 3-(4-nitrophenyl) substituted on indene, **3e** was obtained in the lowest yield. Electron withdrawing

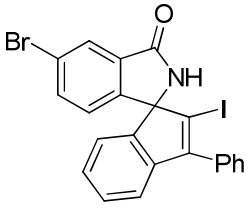
group on isoindoline ring did not affect the electrophilic substitution on the indene ring. Thus, **3f** (4-Br) and **3g** (5-CF_3) were prepared in 90% and 94% yields, respectively. With similar strategy, we also obtained 2-bromspiro[indene-1,1'-isoindolin]-3'-ones **3h-k** in yields varying from 73% to 87%. With excess amount of NIS, diiodination occurred to generate **4a** and **4b** in 77% and 64% yields, respectively (Scheme 5). However, excess amount of NBS did not give the dibrominated products.

Table 2. Preparation of Compounds 3[a]

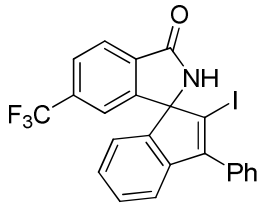




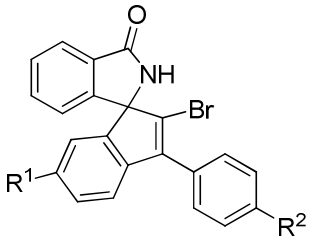
3a (R^1= R^2 = H), 86%
3b (R^1= R^2 = Cl), 65%
3c (R^1= R^2 = Me), 86%
3d (R^1, R^2 = H, Cl), 76%
3e (R^1, R^2 = H, 4-NO_2), 44%



3f, 90%



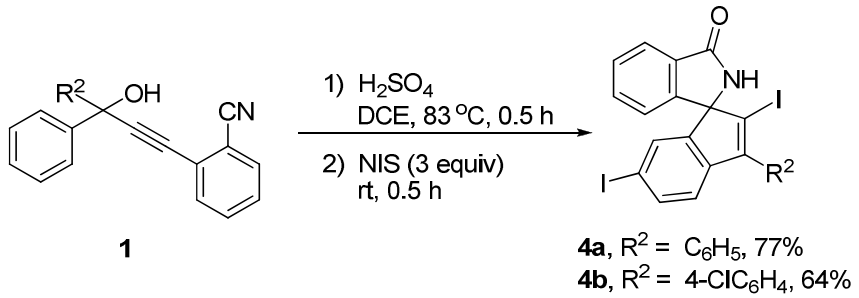
3g, 94%



3h (R^1=R^2 = H), 83%
3i (R^1=R^2 = Cl), 73%
3j (R^1=R^2 = Me), 84%
3k (R^1, R^2 = H, Cl), 87%

[a] Reaction conditions: **1** (0.2 mmol), DCE (4 mL), H_2SO_4 (0.24 mmol), 83 °C, 0.5 h; then NIS (0.2 mmol), room temperature, 0.5 h.

Scheme 5. Preparation of Compounds 4a and 4b

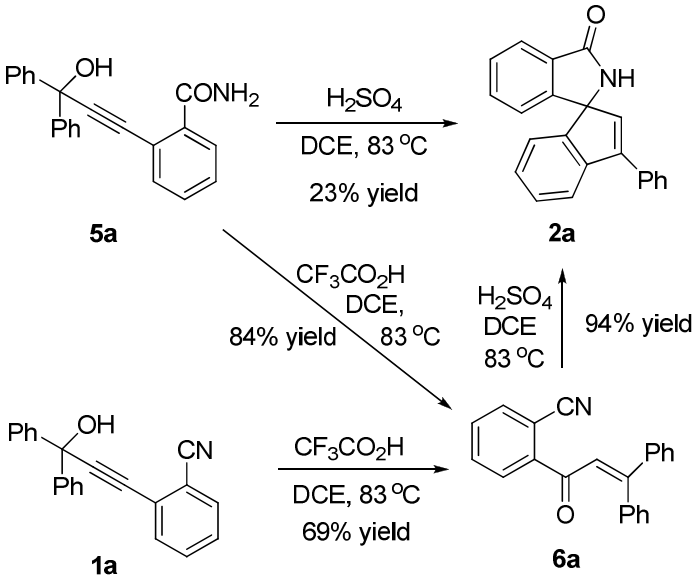


1

4a, R^2 = C_6H_5, 77%
4b, R^2 = 4-ClC_6H_4, 64%

In order to get insight into the reaction mechanism, we synthesized the substrate **5a** and subjected it to the standard conditions. Unfortunately, only 23% yield of **2a** was afforded. Surprisingly, when trifluoroacetic acid instead of sulfuric acid was used as catalyst, α,β-unsaturated ketone **6a** was prepared in 84% yield. The structure of **6a** was established by single crystal analysis.[11] **6a** also could be easily synthesized from **1a** using trifluoroacetic acid as catalyst. Moreover, further treatment of **6a** with sulfuric acid in DCE for 5 min led to the formation of **2a** in 94% yield (Scheme 6).

Scheme 6. Preparation of 6a and Its Transformation to 2a

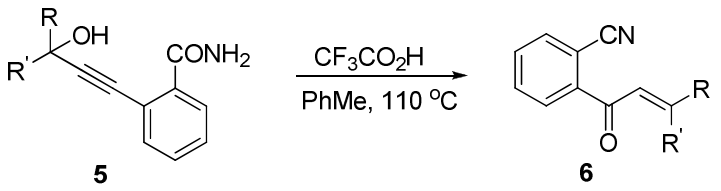


1a

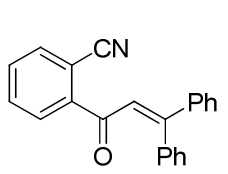
6a

As an extension, we optimized the conversion of **5a** to **6a**. Several acids and solvents (e.g. DCE, CH_3NO_2, THF, CH_3CN, toluene, and DCM) were screened and trifluoroacetic acid was found to be the most efficient catalyst while toluene was the best solvent. Lowing the reaction temperature did not improve the yield, whereas decreasing the amount of trifluoroacetic acid to 0.8 equivalent could increase the yield of **6a** up to 91% yield. Under the optimized reaction conditions, the substrate scope was investigated and nine α,β-unsaturated ketones **6a-i** were prepared (Table 3). When both R and R' were aryl groups, good to excellent yields (76%-98%) were obtained (Table 3, products **6a-f**). When R was phenyl and R' was methyl or hydrogen, the corresponding products **6g** and **6h** were prepared in relatively lower yields. However, poor yield of **6i** was isolated in the case where both R and R' were methyl group.

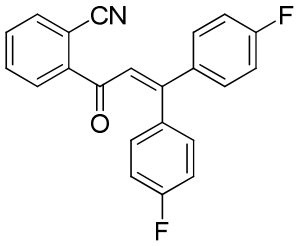
Table 3. Preparation of Compounds 6[a]



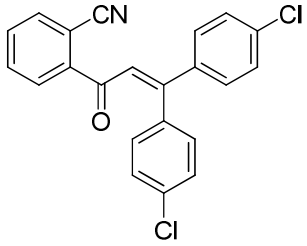
5 **6**



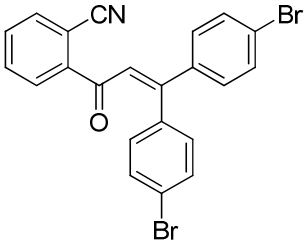
6a, 91%



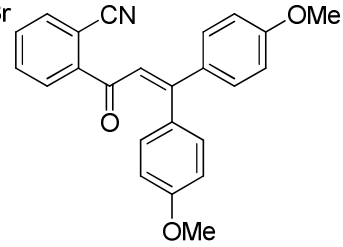
6b, 98%[b]



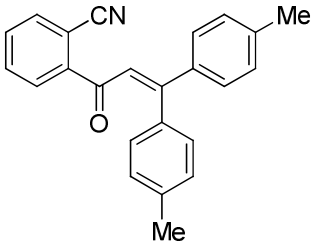
6c, 95%[b]



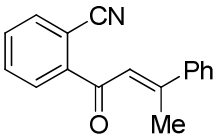
6d, 82%[c]



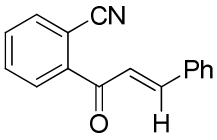
6e, 97%



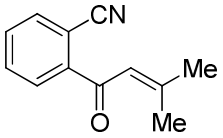
6f, 76%



6g, 69%[b]



6h, 30%[d]

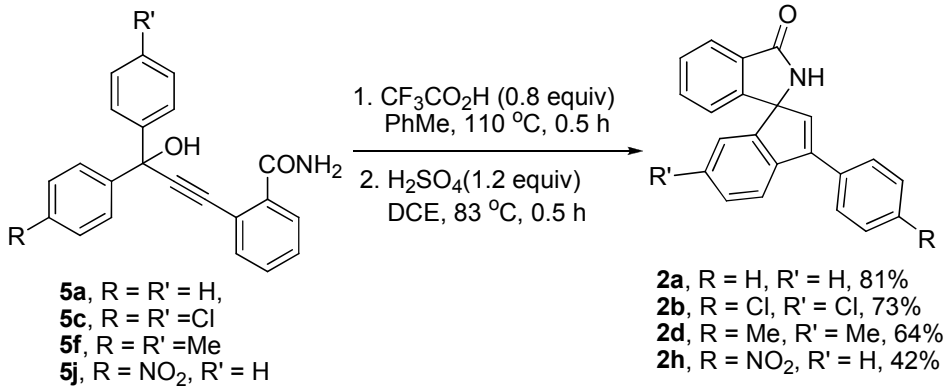


6i, 14%[d]

[a] Reaction conditions: **5** (0.2 mmol), toluene (4 mL), CF_3COOH (0.16 mmol), 110 °C, 0.5 h. [b] Reaction for 1 h. [c] Reaction for 3 h. [d] Reaction for 4 h.

As next step, we tried to convert the 2-(3-hydroxy-1-propyne)benzamides **5** into the corresponding spiro products **2** through a two-step one-pot procedure. Thus, compounds **2a**, **2b** and **2d** were successfully obtained from compounds **5a, 5c**, and **5f**, respectively (Scheme 7). The asymmetric 2-(3-hydroxy-1-propyne)benzamide **5j** could also work and furnished the desired product **2h** in a relatively lower yield.

Scheme 7. Preparation of Compounds 2 from 5

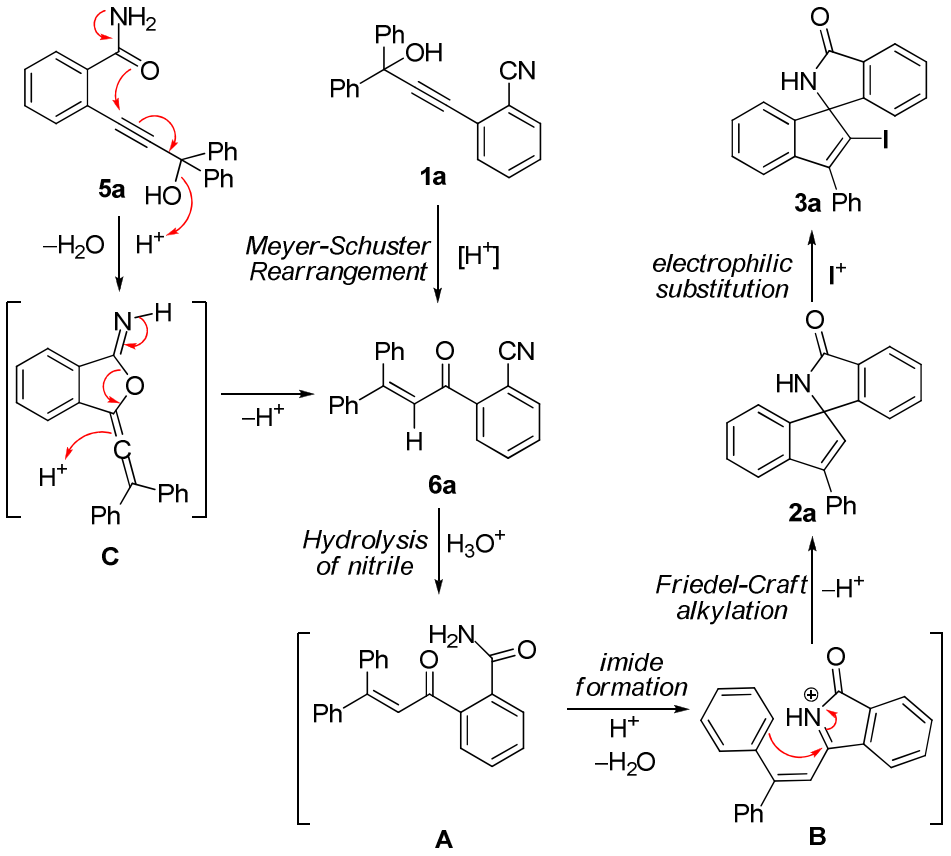


5a, R = R' = H,
5c, R = R' =Cl
5f, R = R' =Me
5j, R = NO_2, R' = H

2a, R = H, R' = H, 81%
2b, R = Cl, R' = Cl, 73%
2d, R = Me, R' = Me, 64%
2h, R = NO_2, R' = H, 42%

On the basis of these results, we propose a possible mechanism for the formation of spiro[indene-1,1'-isoindolin]-3'-ones **2** and **3** as well as α,β-unsaturated ketones **6** in Scheme 8. Firstly, the Meyer-Schuster rearrangement of propargylic alcohol **1a** in the presence of sulfuric acid forms α,β-unsaturated ketone **6a**.[5] Subsequently, the hydrolysis of cyano group of **6a** generates amide **A**, which then undergoes an intramolecular condensation to form **B**. Finally, the intramolecular Friedel-Craft alkylation occurs to generate the spiro product **2a**. In the presence of an electrophile, such as NIS, **2a** subsequently undergoes an electrophilic substitution to produce **3a**. For the transformation of **5a** to **6a**, the allene intermediate **C** might be involved in the cascade rearrangement process. In the presence of trifluoroacetic acid, **5a** undergoes an electrophilic cyclization to form **C**. Then, the ring-opening of **C** occurs to give the more stable product **6a**.

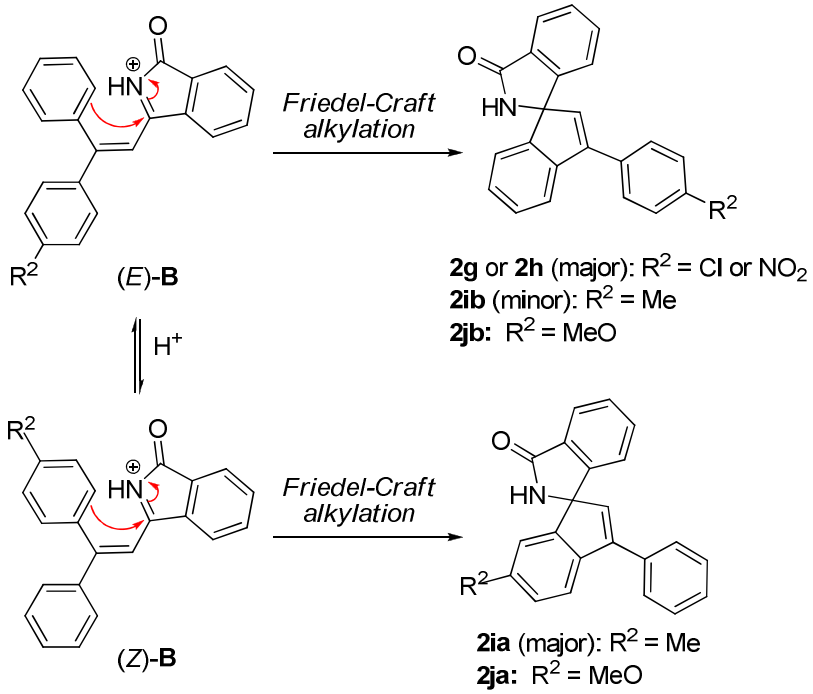
Scheme 8. Proposed Mechanism for the Formation of 2a, 3a and 6a



For asymmetric propargylic alcohols, it is possible that there is equilibrium between the intermediates (*E*)-**B** and (*Z*)-**B** under strong acid condition (Scheme 9). Since the cyclization undergoes an intramolecular Friedel-Crafts reaction, the relative electron-rich phenyl ring should react faster than the electron-deficient phenyl ring. For strong electron-withdrawing group (NO_2) substituted propargylic alcohol **1h** (Scheme 2), **2h** was obtained as a sole product because it is very difficulty that the NO_2 substituted phenyl ring undergoes the Friedel-Crafts-type cyclization. In the case where OMe substituted propargylic alcohol **1j** was used (Scheme 3), OMe substituent does not works as electron-donation group since the cyclization happens at meta-position, which led to formation of **2ja** and **2jb** with poor regiochemistry. Similar reason can be used to explain the fact that the yield of **2c** is much lower than

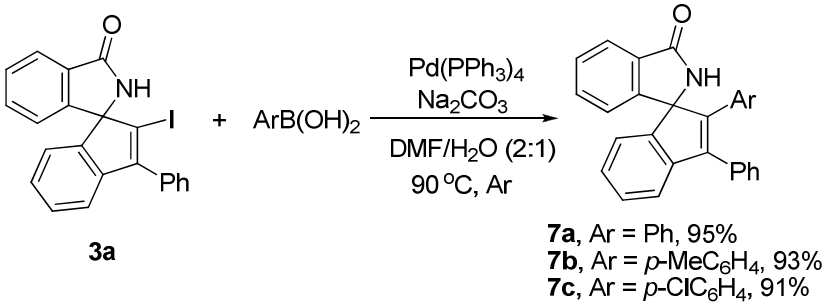
that of **2a.**

Scheme 9. Possible Explanation for the Regioselectivity of Asymmetric Propargylic Alcohols



Furthermore, the synthesized 2-iodospiro[indene-1,1'-isoindolin]-3'-one **3a** could be extended to 2-arylspiro[indene-1,1'-isoindolin]-3'-ones under the standard Suzuki coupling reaction conditions (Scheme 10). Thus, **7a**, **7b**, and **7c** were obtained from **3a** in excellent yields.

Scheme 10. Conversion from 3a to 7



CONCLUSION

In conclusion, we developed an efficient method for the synthesis of spiro[indene-1,1'-isoindolin]-3'-ones from 2-(3-hydroxyprop-1-ynyl)benzonitriles. The cascade process was triggered by sulfuric acid and occurred in a sequence of Meyer-Schuster rearrangement, hydrolysis of cyano, imide formation, and Friedel-Craft alkylation. The spiro[indene-1,1'-isoindolin]-3'-ones were obtained in moderate to excellent yields with 100% atom efficiency and high bond formation efficiency. Alternatively, 2-(3-hydroxy-1-propyne)benzamides could also be converted into the spiro[indene-1,1'-isoindolin]-3'-ones in a two-step one-pot procedure. The starting materials, 2-(3-hydroxyprop-1-ynyl)benzonitriles and 2-(3-hydroxy-1-propyne)benzamides, could be conveniently prepared by the Sonogashira coupling reaction of 1,1-diarylpropyn-1-ols with 2-iodobenzonitriles and 2-iodobenzamides, respectively. Moreover, the synthesized spiro[indene-1,1'-isoindolin]-3'-ones could be in situ extended to 2-iodospiro[indene-1,1'-isoindolin]-3'-ones, which could be further derived to 2-arylspiro[indene-1,1'-isoindolin]-3'-ones through Pd-catalyzed Suzuki coupling reaction.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. ^{1}H NMR spectra were

recorded on 400 MHz or 500 MHz spectrometer. The chemical shifts were reported relative to internal standard TMS (0 ppm) in $CDCl_3$. The following abbreviations were used to describe peak patterns where appropriate: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants were reported in Hertz (Hz). ^{13}C NMR spectra were recorded on 100 MHz or 125 MHz spectrometer and referenced to the internal solvent signals (77.27 ppm for $CDCl_3$). Infrared spectra were obtained on an FTIR spectrometer. High-resolution mass spectra (HRMS) data were obtained by using an EI-TOF or ESI mass spectrometer. Melting points were measured with a micro melting point apparatus.

Typical Procedure for the Preparation of Substrates 1. To a stirred suspension of $PdCl_2(PPh_3)_2$ (0.1 mmol), CuI (0.1 mmol), 2-iodobenzonitrile (2 mmol), and *i*-Pr_2NH (6 mL) in THF (10 mL) under N_2 atmosphere was added a solution of 1,1-diphenylpropyn-1-ol (2.2 mmol) in THF (4 mL) via syringe at 50 ^oC. The reaction mixture was stirred for 3 hours and then concentrated in vacuo. The residue was washed with saturated NH_4Cl solution (5 mL) and extracted with AcOEt (20 mL). The organic layer was washed with brine and dried over Na_2SO_4. After filtered and concentrated in vacuo, the crude was purified by column chromatography over silica gel with hexane/ AcOEt as the eluent.

*2-(3-Hydroxy-3,3-diphenylprop-1-yn-1-yl)benzonitrile (**1a**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 96% Yield (593 mg); Brown oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75-7.70 (m, 4H), 7.67 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.60-7.52 (m, 2H), 7.43 (td, *J* = 7.6, 1.6 Hz, 1H), 7.39-7.34 (m, 4H), 7.32-7.26 (m,

2H), 3.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 132.9, 132.8, 132.7, 129.0, 128.7, 128.2, 126.7, 126.4, 117.9, 115.6, 98.4, 83.4, 75.2; IR (film): 3440, 3062, 2229, 1592, 1481, 1449, 1165, 1031, 992, 762 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{15}NO$ 309.1154; found 309.1157.

*2-(3,3-Bis(4-chlorophenyl)-3-hydroxyprop-1-yn-1-yl)benzonitrile (**1b**).* Purified on silica gel with hexane/ AcOEt (4:1, v/v) as the eluent. 93% Yield (701 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.64-7.59 (m, 4H), 7.58-7.55 (m, 2H), 7.48-7.42 (m, 1H), 7.35-7.30 (m, 4H), 3.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 134.3, 132.9, 132.8, 132.7, 129.3, 128.9, 127.8, 126.2, 117.9, 115.6, 97.2, 83.9, 74.3; IR (film): 3428, 3069, 2231, 1592, 1488, 1403, 1165, 1092, 993, 762 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}Cl_2NO$ 377.0374; found 377.0370.

*2-(3-Hydroxy-3,3-bis(4-methoxyphenyl)prop-1-yn-1-yl)benzonitrile (**1c**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 90% Yield (664 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67-7.58 (m, 5H), 7.57-7.48 (m, 2H), 7.40 (td, *J* = 7.6, 1.6 Hz, 1H), 6.90-6.84 (m, 4H), 3.78 (s, 6H), 3.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 137.0, 132.8, 132.7, 132.6, 128.8, 127.7, 126.8, 118.0, 115.4, 113.9, 98.9, 83.0, 74.5, 55.5; IR (film): 3444, 2959, 2837, 2229, 1607, 1506, 1251, 1173, 1033, 831 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{19}NO_3$ 369.1365; found 369.1366.

*2-(3-Hydroxy-3,3-di-p-tolylprop-1-yn-1-yl)benzonitrile (**1d**).* Purified on silica gel with hexane/ AcOEt (4:1, v/v) as the eluent. 94% Yield (634 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.62-7.55 (m, 5H), 7.53 (td,

J = 7.6, 1.2 Hz, 1H), 7.41 (td, *J* = 7.6, 1.5 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 4H), 2.97 (s, 1H), 2.33 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 137.9, 132.9, 132.8, 132.6, 129.3, 128.9, 126.8, 126.3, 117.9, 115.6, 98.8, 83.1, 75.0, 21.3; IR (film): 3451, 2921, 2229, 1592, 1508, 1482, 1164, 1052, 995, 763 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{19}NO$ 337.1467; found 337.1464.

2-(3,3-Bis(4-fluorophenyl)-3-hydroxyprop-1-yn-1-yl)benzonitrile ***(1e)****.* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 89% Yield (614 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.62 (m, 5H), 7.59-7.52 (m, 2H), 7.46-7.41 (m, 1H), 7.07-6.99 (m, 4H), 3.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (d, $^1J_{CF}$ = 246 Hz), 140.2 (d, $^4J_{CF}$ = 3 Hz), 132.9, 132.8, 132.7, 129.2, 128.2 (d, $^3J_{CF}$ = 8 Hz), 126.3, 118.0, 115.528, 115.526 (d, $^2J_{CF}$ = 22 Hz), 97.8, 83.7, 74.3; IR (film): 3428, 3073, 2231, 1603, 1505, 1412, 1228, 1158, 1054, 995, 836 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}F_2NO$ 345.0965; found 345.0965.

2-(3,3-Bis(4-bromophenyl)-3-hydroxyprop-1-yn-1-yl)benzonitrile ***(1f)****.* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 92% Yield (856 mg); Brown solid, mp 146-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.67 (m, 1H), 7.59-7.53 (m, 6H), 7.51-7.43 (m, 5H), 3.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 132.9, 132.8, 132.7, 131.9, 129.3, 128.1, 126.2, 122.6, 117.9, 115.6, 97.0, 84.0, 74.4; IR (film): 3427, 3068, 2231, 1592, 1483, 1398, 1164, 1071, 1010, 994, 904, 807 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}Br_2NO$ 464.9364; found 464.9364.

2-(3-(4-Chlorophenyl)-3-hydroxy-3-phenylprop-1-yn-1-yl)benzonitrile ***(1g)****.* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 93% Yield (638 mg);

Brown solid, mp 102-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.62 (m, 5H), 7.57-7.49 (m, 2H), 7.44-7.38 (m, 1H), 7.38-7.33 (m, 2H), 7.32-7.26 (m, 3H), 3.34-3.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1, 143.1, 134.0, 132.8, 132.72, 132.70, 129.1, 128.75, 128.74, 128.4, 127.8, 126.4, 126.2, 117.9, 115.5, 97.8, 83.6, 74.7; IR (film): 3435, 3065, 2230, 1592, 1488, 1448, 1402, 1165, 1092, 993, 761 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}ClNO$ 343.0764; found 343.0766.

*2-(3-Hydroxy-3-(4-nitrophenyl)-3-phenylprop-1-yn-1-yl)benzonitrile (**1h**).* Purified on silica gel with hexane/ AcOEt (4:1, v/v) as the eluent. 91% Yield (644 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21-8.15 (m, 2H), 7.92-7.87 (m, 2H), 7.73-7.65 (m, 3H), 7.60-7.53 (m, 2H), 7.49-7.43 (m, 1H), 7.41-7.34 (m, 2H), 7.34-7.28 (m, 1H), 3.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 147.6, 143.4, 132.9, 132.8, 132.7, 129.4, 129.0, 128.8, 127.3, 126.2, 126.0, 123.9, 117.9, 115.6, 96.8, 84.3, 74.7; IR (film): 3432, 3068, 2230, 1593, 1519, 1448, 1346, 1165, 1052, 995, 764 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}N_2O_3$ 354.1004; found 354.1004.

*2-(3-Hydroxy-3-phenyl-3-(p-tolyl)prop-1-yn-1-yl)benzonitrile (**1i**).* Purified on silica gel with hexane/ AcOEt (4.5:1, v/v) as the eluent. 92% Yield (594 mg); Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 8.0 Hz, 2H), 7.65 (dd, J = 7.8, 0.6 Hz, 1H), 7.62-7.54 (m, 3H), 7.52 (td, J = 7.2, 1.2 Hz, 1H), 7.40 (td, J = 7.6, 1.6 Hz, 1H), 7.38-7.32 (m, 2H), 7.30-7.25 (m, 1H), 7.16 (d, J = 8.0 Hz, 2H), 3.08 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 141.6, 138.0, 132.9, 132.8, 132.6, 129.3, 128.9, 128.6, 128.1, 126.7, 126.30, 126.29, 117.9, 115.5, 98.6, 83.2, 75.1 21.3; IR (film): 3445, 3061, 2921, 2229, 1592, 1509, 1481, 1448, 1335, 1164, 1049, 994, 896,

760 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{17}NO$ 323.1310; found 323.1311.

2-(3-Hydroxy-3-(4-methoxyphenyl)-3-phenylprop-1-yn-1-yl)benzonitrile ***(1j)***. Purified on silica gel with hexane/ AcOEt (4:1, v/v) as the eluent. 83% Yield (563 mg); Brown oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.67 (m, 2H), 7.63-7.57 (m, 3H), 7.51-7.42 (m, 2H), 7.37-7.30 (m, 3H), 7.28-7.21 (m, 1H), 6.87-6.82 (m, 2H), 3.73 (s, 3H), 3.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 144.7, 136.8, 132.7, 132.64, 132.59, 128.8, 128.5, 127.9, 127.7, 126.6, 126.2, 117.9, 115.2, 113.8, 98.6, 83.0, 74.7, 55.4; IR (film): 3445, 3065, 2837, 2229, 1607, 1506, 1447, 1304, 1250, 1174, 1033, 992, 909, 761 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{17}NO_2$ 339.1259; found 339.1263.

2-Fluoro-6-(3-hydroxy-3,3-diphenylprop-1-yn-1-yl)benzonitrile ***(1k)***. Purified on silica gel with hexane/ AcOEt (4:1, v/v) as the eluent. 89% Yield (582 mg); Yellow solid, mp 134-135 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.73-7.67 (m, 4H), 7.56-7.49 (m, 1H), 7.40-7.33 (m, 5H), 7.32-7.27 (m, 2H), 7.18 (td, J = 8.6, 0.9 Hz, 1H), 3.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4 (d, $^1J_{CF}$ = 259 Hz), 144.2, 134.5 (d, $^3J_{CF}$ = 9 Hz), 128.7, 128.6 (d, $^4J_{CF}$ = 3 Hz), 128.33, 128.29 (d, $^3J_{CF}$ = 2 Hz), 126.3, 116.6 (d, $^2J_{CF}$ = 20 Hz), 113.1, 104.7 (d, $^2J_{CF}$ = 16 Hz), 99.4, 82.5 (d, $^4J_{CF}$ = 4 Hz), 75.2; IR (film): 3452, 3060, 2234, 1603, 1567, 1470, 1250, 1065, 1011, 796 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}FNO$ 327.1059; found 327.1059.

5-Bromo-2-(3-hydroxy-3,3-diphenylprop-1-yn-1-yl)benzonitrile ***(1l)***. Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 85% Yield (658 mg); Brown solid, mp 81-82 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70-7.62 (m, 5H), 7.52 (dd, J =

8.4, 2.0 Hz, 1H), 7.34-7.19 (m, 7H), 3.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 135.9, 135.1, 133.7, 128.5, 128.1, 126.2, 125.4, 122.5, 116.7, 116.5, 99.6, 82.3, 75.0; IR (film): 3451, 3062, 2232, 1598, 1482, 1450, 1274, 1183, 1031, 992, 740 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}BrNO$ 387.0259; found 387.0259.

*2-(3-Hydroxy-3,3-diphenylprop-1-yn-1-yl)-5-nitrobenzonitrile (**1m**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 81% Yield (573 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, *J* = 2.4 Hz, 1H), 8.30 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.70-7.63 (m, 5H), 7.38-7.31 (m, 4H), 7.30-7.25 (m, 2H), 3.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 143.7, 133.8, 132.6, 128.7, 128.4, 127.8, 127.3, 126.2, 116.6, 115.9, 104.0, 82.0, 75.2; IR (film): 3459, 3085, 2237, 1602, 1531, 1450, 1352, 1165, 1032, 911, 743 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}N_2O_3$ 354.1004; found 354.1008.

*2-(3-Hydroxy-3,3-diphenylprop-1-yn-1-yl)-5-methoxybenzonitrile (**1n**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 19% Yield (129 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.67 (m, 4H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.38-7.31 (m, 4H), 7.29-7.23 (m, 2H), 7.10 (d, *J* = 2.8 Hz, 1H), 7.02 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.79 (s, 3H), 3.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 144.7, 134.2, 128.6, 128.1, 126.3, 119.3, 118.7, 117.8, 117.6, 116.5, 96.6, 83.2, 75.2, 56.0; IR (film): 3454, 3060, 2230, 1601, 1501, 1450, 1315, 1162, 1043, 991, 746 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{17}NO_2$ 339.1259; found 339.1262.

*2-(3-Hydroxy-3,3-diphenylprop-1-yn-1-yl)-4-(trifluoromethyl)benzonitrile (**1o**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 93% Yield (701 mg);

Yellow solid, mp 120-121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.72-7.65 (m, 5H), 7.59 (dd, J = 8.4, 0.8 Hz, 1H), 7.37-7.30 (m, 4H), 7.28-7.22 (m, 2H), 3.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 134.6 (q, $^{2}J_{CF}$ = 34 Hz), 133.4, 129.5 (q, $^{3}J_{CF}$ = 4 Hz), 128.6, 128.2, 127.7, 126.3, 125.5 (q, $^{3}J_{CF}$ = 4 Hz), 122.8 (q, $^{1}J_{CF}$ = 272 Hz), 118.6, 116.7, 100.5, 82.0, 75.2; IR (film): 3459, 3061, 2237, 1598, 1490, 1417, 1332, 1177, 1070, 996, 906, 700 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{14}F_3NO$ 377.1027; found 377.1024.

*3-Fluoro-2-(3-hydroxy-3,3-diphenylprop-1-yn-1-yl)benzonitrile (**1p**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 16% Yield (105 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.68 (m, 4H), 7.46 (dd, J = 7.6, 1.2 Hz, 1H), 7.39-7.33 (m, 5H), 7.32-7.26 (m, 3H), 3.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7 (d, $^{1}J_{CF}$ = 254 Hz), 144.2, 130.6 (d, $^{3}J_{CF}$ = 9 Hz), 128.8 (d, $^{4}J_{CF}$ = 4 Hz), 128.7, 128.3, 126.3, 120.4 (d, $^{2}J_{CF}$ = 21 Hz), 117.1 (d, $^{4}J_{CF}$ = 3 Hz), 116.7 (d, $^{3}J_{CF}$ = 4 Hz), 115.5 (d, $^{2}J_{CF}$ = 19 Hz), 103.7 (d, $^{3}J_{CF}$ = 4 Hz), 77.2, 75.3; IR (film): 3444, 3060, 2239, 1567, 1464, 1269, 1164, 1031, 992, 766 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}FNO$ 327.1059; found 327.1058.

*2-(3,3-Bis(4-chlorophenyl)-3-hydroxyprop-1-yn-1-yl)-5-bromobenzonitrile (**1q**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 90% Yield (819 mg); Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 2.0 Hz, 1H), 7.69 (dd, J = 8.4, 2.0 Hz, 1H), 7.62-7.56 (m, 4H), 7.42 (d, J = 8.8 Hz, 1H), 7.35-7.30 (m, 4H), 3.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 136.2, 135.5, 134.5, 133.8, 129.0, 127.7, 125.1, 123.2, 117.1, 116.6, 98.4, 83.1, 74.3; IR (film): 3434, 3068, 2234, 1580, 1482,

1402, 1182, 1093, 1014, 993, 831 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{12}BrCl_2NO$ 454.9479; found 454.9483 .

2-(3,3-Bis(4-chlorophenyl)-3-hydroxyprop-1-yn-1-yl)-5-methoxybenzonitrile ***(1r)***. Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 14% Yield (114 mg); Brown oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.65-7.58 (m, 4H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.34-7.28 (m, 4H), 7.13 (d, *J* = 2.4 Hz, 1H), 7.06 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.84 (s, 3H), 3.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 142.9, 134.21, 134.18, 128.8, 127.8, 119.4, 118.2, 117.8, 117.7, 116.7, 95.5, 83.9, 74.3, 56.1; IR (film): 3436, 2941, 2840, 2231, 1602, 1489, 1403, 1316, 1234, 1092, 1014, 905, 835 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{15}Cl_2NO_2$ 407.0480; found 407.0482.

General Procedure for the Synthesis of 2. To a stirred solution of **1** (0.2 mmol) in DCE (4 mL) was added concentrated H_2SO_4 (12.8 μL, 0.24 mmol). The reaction mixture was stirred at 83 ^oC for 30 min. After the reaction completed, the mixture was concentrated under reduced pressure and the residue was purified by column chromatography over silica gel with hexane/ AcOEt as the eluent to give pure **2**.

3-Phenylspiro[indene-1,1'-isoindolin]-3'-one ***(2a)***. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 97% yield (60 mg); Yellow solid); mp 115-116 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.0 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.52-7.40 (m, 5H), 7.34 (td, *J* = 7.5, 0.5 Hz, 1H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 7.0 Hz, 1H), 6.25 (s, 1H), 6.21 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 146.9, 146.4, 145.8, 142.6, 134.4, 133.5, 132.7, 131.8, 129.07, 129.05, 129.0, 128.9, 127.8, 127.4, 124.4, 123.2,

122.1, 121.6, 72.6; IR (film): 3399, 3224, 3066, 1694, 1466, 1313, 909, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{15}NO$ 309.1154; found 309.1147.

*6-Chloro-3-(4-chlorophenyl)spiro[indene-1,1'-isoindolin]-3'-one (**2b**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 81% Yield (61 mg); White solid, mp 271-272 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.0 Hz, 1H), 7.57-7.53 (m, 2H), 7.52-7.44 (m, 4H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.32 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.99 (d, *J* = 7.0 Hz, 1H), 6.53 (s, 1H), 6.22 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 147.8, 145.4, 145.1, 140.6, 135.1, 134.2, 133.8, 133.0, 132.4, 131.7, 129.4, 129.3, 129.0, 124.6, 124.0, 122.3, 122.0, 72.2; IR (film): 3410, 3222, 3075, 2926, 1698, 1489, 1463, 1312, 1088, 731 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}Cl_2NO$ 377.0374; found 377.0370.

*6-Methoxy-3-(4-methoxyphenyl)spiro[indene-1,1'-isoindolin]-3'-one (**2c**).* Purified on silica gel with hexane/ AcOEt (2:1, v/v) as the eluent. 53% Yield (39 mg); White solid, mp 215-217 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.0 Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.48-7.38 (m, 3H), 6.99 (d, *J* = 8.5 Hz, 3H), 6.83 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.58 (d, *J* = 2.0 Hz, 1H), 6.47 (s, 1H), 6.00 (s, 1H), 3.86 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 160.1, 159.7, 147.9, 146.9, 146.0, 135.3, 132.7, 131.7, 129.9, 128.9, 128.7, 127.1, 124.3, 122.2, 122.1, 114.4, 114.1, 109.5, 72.3, 55.8, 55.6; IR (film): 3390, 3227, 3071, 2936, 1698, 1611, 1509, 1467, 1249, 1030, 910, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{19}NO_3$ 369.1365; found 369.1364.

*6-Methyl-3-(p-tolyl)spiro[indene-1,1'-isoindolin]-3'-one (**2d**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 87% Yield (58 mg); White solid, mp

232-233 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.48-7.38 (m, 3H), 7.28 (d, J = 7.5 Hz, 2H), 7.11 (d, J = 8.0 Hz, 1H), 6.99 (d, J = 7.0 Hz, 1H), 6.84 (s, 1H), 6.36 (s, 1H), 6.09 (s, 1H), 2.42 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 146.8, 146.7, 146.1, 140.0, 138.8, 137.4, 132.6, 131.84, 131.81, 131.7, 129.7, 129.5, 128.7, 127.6, 124.3, 124.0, 122.1, 121.4, 72.4, 21.6, 21.5; IR (film): 3391, 3226, 3068, 2921, 1694, 1468, 1311, 909, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{19}NO$ 337.1467; found 337.1467.

6-Fluoro-3-(4-fluorophenyl)spiro[indene-1,1'-isoindolin]-3'-one ***(2e)***. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 65% Yield (45 mg); Brown solid, mp 207-208 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.85 (m, 1H), 7.64-7.56 (m, 2H), 7.52-7.40 (m, 3H), 7.22-7.13 (m, 2H), 7.06-6.97 (m, 2H), 6.92 (s, 1H), 6.75 (dd, J = 7.8, 2.2 Hz, 1H), 6.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 163.2 (d, $^1J_{CF}$ = 247 Hz), 162.8 (d, $^1J_{CF}$ = 247 Hz), 148.4 (d, $^3J_{CF}$ = 8 Hz), 145.8, 145.2, 138.2 (d, $^4J_{CF}$ = 3 Hz), 133.1 (d, $^4J_{CF}$ = 3 Hz), 132.9, 131.7, 130.2 (d, $^4J_{CF}$ = 3 Hz), 129.5 (d, $^3J_{CF}$ = 8 Hz), 129.1, 124.5, 122.3 (d, $^3J_{CF}$ = 8 Hz), 122.0, 116.2 (d, $^2J_{CF}$ = 22 Hz), 115.7 (d, $^2J_{CF}$ = 23 Hz), 111.4 (d, $^2J_{CF}$ = 24 Hz), 72.2 (d, $^4J_{CF}$ = 2 Hz); IR (film): 3407, 3218, 3072, 1698, 1607, 1506, 1476, 1344, 1226, 1159, 909, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}F_2NO$ 345.0965; found 345.0964.

6-Bromo-3-(4-bromophenyl)spiro[indene-1,1'-isoindolin]-3'-one ***(2f)***. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 63% Yield (59 mg); Brown solid, mp 277-278 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96-7.90 (m, 1H), 7.65-7.60 (m, 2H), 7.55-7.44 (m, 5H), 7.36 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 1.6 Hz, 1H), 7.00 (d,

J = 6.8 Hz, 1H), 6.21 (s, 1H), 6.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 147.9, 145.3, 145.2, 141.0, 134.1, 133.0, 132.7, 132.4, 132.2, 131.6, 129.33, 129.30, 126.8, 124.7, 123.3, 122.7, 122.1, 121.9, 72.2; IR (film): 3409, 3208, 3074, 1698, 1485, 1464, 1398, 1337, 1315, 1263, 1070, 1010, 908, 823, 731 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}Br_2NO$ 464.9364; found 464.9363.

*3-(4-Chlorophenyl)spiro[indene-1,1'-isoindolin]-3'-one (**2g**)*. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 94% Yield (64 mg); oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 6.6, 1.4 Hz, 1H), 7.60-7.54 (m, 2H), 7.51-7.39 (m, 5H), 7.34 (td, *J* = 7.6, 0.8 Hz, 1H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.98 (dd, *J* = 6.4, 1.2 Hz, 1H), 6.64 (s, 1H), 6.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 146.1, 145.8, 145.7, 142.1, 134.7, 134.0, 132.8, 132.7, 131.9, 129.2, 129.1, 129.0, 128.9, 127.5, 124.4, 123.3, 122.0, 121.4, 72.6; IR (film): 3400, 3218, 3069, 1694, 1610, 1489, 1314, 1086, 909, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}ClNO$ 343.0764; found 343.0760.

*3-(4-Nitrophenyl)spiro[indene-1,1'-isoindolin]-3'-one (**2h**)*. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 79% Yield (56 mg); Pale brown solid, mp 244-245 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39-8.33 (m, 2H), 7.92 (dd, *J* = 6.4, 1.2 Hz, 1H), 7.85-7.80 (m, 2H), 7.53-7.43 (m, 3H), 7.39 (td, *J* = 7.6, 0.8 Hz, 1H), 7.25 (t, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 6.8 Hz, 1H), 6.60 (s, 1H), 6.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 148.1, 145.64, 145.61, 145.0, 141.4, 140.9, 136.5, 132.9, 131.8, 129.4, 129.2, 128.7, 128.1, 124.6, 124.4, 123.6, 122.0, 121.3, 72.6; IR (film): 3399, 3196, 3069, 1694, 1599, 1516, 1464, 1347, 1315, 1107,

909, 735 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}N_2O_3$ 354.1004; found 354.1007.

6-Methyl-3-phenylspiro[indene-1,1'-isoindolin]-3'-one ***(2ia)*** *and 3-p-tolylspiro[indene-1,1'-isoindolin]-3'-one* ***(2ib)***. The mixture (**2ia**:**2ib** = 2.2:1) was purified on silica gel using PE/EA = 6/1 as eluent; 92% Yield (89 mg); Yellow solid. ^1H NMR (400 MHz, $CDCl_3$), Major isomer (**2ia**): δ 7.94 - 7.88 (m, 1H), 7.64 (dd, J = 8.1, 1.3 Hz, 2H), 7.57 - 7.52 (m, 1H), 7.51 - 7.40 (m, 3H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.05 - 6.97 (m, 2H), 6.85 (s, 1H), 6.26 (s, 1H), 6.14 (s, 1H), 2.27 (s, 3H); Minor isomer (**2ib**): δ 7.94 - 7.88 (m, 1H), 7.57 - 7.52 (m, 1H), 7.51 - 7.40 (m, 8H), 7.36 - 7.33 (m, 1H), 7.18 (dd, J = 7.5, 1.0 Hz, 1H), 6.24 (s, 1H), 6.16 (s, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 146.92, 146.87, 146.7, 146.5, 146.1, 145.9, 142.8, 139.9, 139.0, 137.6, 134.6, 132.81, 132.77, 132.4, 131.9, 131.8, 131.5, 129.8, 129.6, 129.07, 129.05, 128.94, 128.88, 128.86, 127.8, 127.7, 127.4, 124.4, 124.1, 123.2, 122.2, 122.1, 121.7, 121.4, 72.6, 72.5, 21.7, 21.6; IR (film): 3234, 2246, 1695, 1610, 1510, 1492, 1467, 1445, 1378, 1342 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{17}NO$ 323.1310; found: 323.1313.

6-Methoxy-3-phenylspiro[indene-1,1'-isoindolin]-3'-one ***(2ja)*** *and 3-(4-methoxyphenyl)spiro[indene-1,1'-isoindolin]-3'-one* ***(2jb)***. The mixture (**2ja**:**2jb** = 1:1) was purified on silica gel using PE/EA = 6/1 as eluent; White solid; Yield: 89mg, 88%; ^1H NMR (400 MHz, $CDCl_3$), Major isomer (**2ja**): δ 7.92 (m, 2H), 7.61 - 7.57 (m, 2H), 7.55 (d, J = 7.6 Hz, 1H), 7.50 - 7.40 (m, 4H), 7.34 (td, J = 7.6, 1.1 Hz,

1H), 7.05 - 6.97 (m, 1H), 6.85 (dd, J = 8.4, 2.4 Hz, 1H), 6.31 (s, 1H), 6.09 (s, 1H), 3.87 (s, 3H); Minor isomer (**2jb**): 7.65 - 7.61 (m, 2H), 7.50 - 7.40 (m, 4H), 7.17 (td, *J* = 7.5, 1.0 Hz, 1H), 7.05 - 6.97 (m, 4H), 6.60 (d, *J* = 2.4 Hz, 1H), 6.26 (s, 1H), 6.13 (s, 1H), 3.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 160.3, 159.8, 147.8, 146.8, 146.7, 146.6, 146.4, 145.9, 142.8, 135.1, 134.7, 132.9, 132.8, 132.1, 131.8, 131.7, 131.2, 129.09, 129.07, 129.0, 128.94, 128.91, 128.87, 127.8, 127.4, 126.9, 124.4, 123.2, 122.3, 122.2, 122.1, 121.7, 114.5, 114.2, 109.6, 72.6, 72.4, 55.9, 55.7; IR (film): 3232, 3346, 1649, 1613, 1510, 1467, 1344, 1303, 1258, 1178; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{17}NO_2$ 339.1259; found 339.1259.

*4'-Fluoro-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**2k**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 94% Yield (61 mg); White solid, mp 132-134 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.0 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.47-7.32 (m, 3H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.08 (t, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.49 (s, 1H), 6.19 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.2, 159.3 (d, $^1J_{CF}$ = 260 Hz), 149.3 (d, $^4J_{CF}$ = 2 Hz), 147.3, 145.5, 142.5, 134.7 (d, $^3J_{CF}$ = 8 Hz), 134.2, 132.9, 129.2, 129.1, 127.8, 127.6, 123.1, 121.8, 119.1 (d, $^2J_{CF}$ = 13 Hz), 118.1 (d, $^3J_{CF}$ = 4 Hz), 116.1 (d, $^2J_{CF}$ = 19 Hz), 72.3; IR (film): 3396, 3219, 3070, 1699, 1623, 1483, 1304, 1260, 1074, 910, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}FNO$ 327.1059; found 327.1060.

*5'-Bromo-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**2l**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 91% Yield (70 mg); White solid, mp 239-240 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, *J* = 2.0 Hz, 1H), 7.65-7.60 (m,

2H), 7.57-7.52 (m, 2H), 7.52-7.47 (m, 2H), 7.47-7.42 (m, 1H), 7.35 (td, *J* = 7.5, 1.0 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.46 (s, 1H), 6.17 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.6, 147.4, 145.2, 142.5, 135.7, 134.2, 133.9, 132.7, 129.3, 129.1, 127.8, 127.6, 127.5, 123.8, 123.2, 122.9, 121.8, 72.4; IR (film): 3395, 3227, 3064, 1698, 1462, 1428, 1304, 909, 734 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}BrNO$ 387.0259; found 387.0255.

*5'-Nitro-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**2m**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 82% Yield (58 mg); Yellow solid, mp 223-224 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (d, *J* = 2.0 Hz, 1H), 8.30 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.65 (d, *J* = 7.0 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.54-7.44 (m, 3H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.67 (s, 1H), 6.20 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.6, 152.9, 149.1, 148.4, 144.5, 142.5, 133.9, 133.4, 131.6, 129.7, 129.4, 129.2, 127.9, 127.81, 127.77, 123.4, 123.2, 122.2, 120.1, 72.6; IR (film): 3391, 3233, 3073, 1714, 1616, 1531, 1346, 910, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}N_2O_3$ 354.1004; found 354.1006.

*5'-Methoxy-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**2n**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 82% Yield (56 mg); White solid, mp 229-230 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.60 (m, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.51-7.40 (m, 3H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.32 (td, *J* = 7.4, 1.0 Hz, 1H), 7.18 (td, *J* = 7.4, 1.0 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 7.00 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.33 (s, 1H), 6.18 (s, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 171.1, 160.7, 146.6, 145.9, 142.5, 138.1, 134.4, 133.6, 133.2, 129.04, 128.96, 128.9, 127.8, 127.4, 123.1, 123.0, 121.6, 121.2, 107.0, 72.2, 56.0; IR (film): 3398, 3217, 3064, 2836, 1694, 1488, 1328, 1247, 909, 759 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{17}NO_2$ 339.1259; found 339.1258.

*3-Phenyl-6'-(trifluoromethyl)spiro[indene-1,1'-isoindolin]-3'-one (**2o**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 96% Yield (72 mg); Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68-7.63 (m, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.53-7.42 (m, 3H), 7.37 (td, *J* = 7.4, 1.1 Hz, 1H), 7.24 (s, 1H), 7.20 (td, *J* = 7.4, 0.53 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.85 (s, 1H), 6.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 147.8, 147.1, 144.8, 142.6, 135.1, 134.7 (q, $^2J_{CF}$ = 32 Hz), 134.0, 132.2, 129.4, 129.2, 129.1, 127.8, 127.7, 126.3 (q, $^3J_{CF}$ = 4 Hz), 125.0, 123.7 (q, $^1J_{CF}$ = 271 Hz), 123.2, 122.0, 119.4 (q, $^3J_{CF}$ = 4 Hz), 72.6; IR (film): 3393, 3231, 3071, 1704, 1492, 1431, 1325, 1251, 1131, 909, 734 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{14}F_3NO$ 377.1027; found 377.1026.

*7'-Fluoro-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**2p**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 84% Yield (55 mg); Pale brown solid, mp 188-189 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 7.2 Hz, 1H), 7.65-7.60 (m, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.52-7.40 (m, 4H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.14-7.06 (m, 2H), 6.26-6.20 (m, 1H), 6.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 157.0 (d, $^1J_{CF}$ = 253 Hz), 147.9, 143.8, 142.9, 135.1 (d, $^3J_{CF}$ = 3 Hz), 134.4, 132.3 (d, $^2J_{CF}$ = 16 Hz), 131.2 (d, $^3J_{CF}$ = 7 Hz), 130.7, 129.3, 129.04, 128.99, 127.8, 127.4, 122.9, 121.8, 120.2 (d, $^4J_{CF}$ = 4 Hz), 119.8 (d, $^2J_{CF}$ = 19 Hz), 70.6 (d,

$^3J_{CF}$ = 1.7 Hz); IR (film): 3393, 3226, 3070, 1698, 1599, 1485, 1346, 1250, 909, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}FNO$ 327.1059; found 327.1060.

5'-Bromo-6-chloro-3-(4-chlorophenyl)spiro[indene-1,1'-isoindolin]-3'-one ***(2q)***. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 79% Yield (72 mg); Yellow solid, mp 225-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 1.6 Hz, 1H), 7.59-7.52 (m, 3H), 7.49-7.44 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.06 (b, 1H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.87 (dd, *J* = 8.0, 0.4 Hz, 1H), 6.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 147.0, 145.5, 144.2, 140.5, 136.0, 135.2, 134.0, 133.8, 133.3, 132.1, 129.5, 129.4, 129.0, 127.7, 123.9, 123.7, 123.3, 122.4, 72.1; IR (film): 3407, 3222, 3070, 1698, 1489, 1462, 1428, 1304, 1089, 1015, 908, 824, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{12}BrCl_2NO$ 454.9479; found 454.9474.

6-Chloro-3-(4-chlorophenyl)-5'-methoxyspiro[indene-1,1'-isoindolin]-3'-one ***(2r)***. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 46% Yield (37 mg); oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.51 (m, 2H), 7.49-7.43 (m, 2H), 7.42-7.37 (m, 2H), 7.31 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.05-7.00 (m, 2H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.36 (b, 1H), 6.19 (s, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 161.0, 147.8, 144.9, 140.6, 137.0, 135.1, 134.3, 133.8, 133.1, 132.4, 129.4, 129.2, 129.0, 123.9, 123.0, 122.3, 121.5, 107.2, 71.9, 56.0; IR (film): 3408, 3220, 3068, 2935, 1698, 1489, 1464, 1330, 1249, 1089, 1015, 908, 823, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{15}Cl_2NO_2$ 407.0480; found 407.0480.

General Procedure for the Synthesis of 3 and 4. To a stirred solution of **1** (0.2

mmol) in DCE (4 mL) was added concentrated H_2SO_4 (12.8 μL, 0.24 mmol). The reaction mixture was stirred at 83 ^oC for 30 min. After the reaction completed, NXS (0.2 mmol) was added. The reaction mixture was stirred for 30 min and then concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane/ AcOEt as the eluent to give **3**. When 0.6 mmol of NIS was used, products **4** were isolated.

*2-Iodo-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**3a**).* Purified on silica gel with hexane/ AcOEt (8:1, v/v) as the eluent. 86% Yield (75 mg); White solid, mp 112-113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 6.4, 1.2 Hz, 1H), 7.62-7.56 (m, 2H), 7.55-7.43 (m, 5H), 7.30-7.22 (m, 2H), 7.15-7.05 (m, 2H), 6.94 (dd, *J* = 6.4, 1.2 Hz, 1H), 6.65 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 150.5, 146.1, 144.6, 143.3, 134.2, 133.0, 132.3, 129.3, 129.2, 129.1, 128.94, 128.88, 127.2, 124.3, 123.8, 121.7, 121.0, 107.3, 76.7; IR (film): 3400, 3218, 3067, 1694, 1611, 1464, 1308, 1263, 1082, 909, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}INO$ 435.0120; found 435.0117.

*6-Chloro-3-(4-chlorophenyl)-2-iodospiro[indene-1,1'-isoindolin]-3'-one (**3b**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 65% Yield (65 mg); Yellow solid, mp 263-264 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 6.8 Hz, 1H), 7.59-7.48 (m, 6H), 7.30-7.25 (m, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 6.94 (d, *J* = 6.8 Hz, 1H), 6.30 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 148.8, 146.4, 145.3, 141.4, 135.4, 133.8, 133.4, 132.2, 132.1, 130.3, 129.8, 129.6, 129.4, 124.7, 124.6, 121.74, 121.67, 108.1, 76.4; IR (film): 3411, 3212, 3079, 1704,

1610, 1487, 1460, 1398, 1308, 1262, 1089, 1015, 907, 836, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{12}Cl_2INO$ 502.9341; found 502.9343.

2-Iodo-6-methyl-3-(p-tolyl)spiro[indene-1,1'-isoindolin]-3'-one (**3c**). Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 86% Yield (80 mg); Pale brown solid, mp 192-193 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 6.8 Hz, 1H), 7.55-7.44 (m, 4H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 6.8 Hz, 1H), 6.91 (s, 1H), 6.32 (b, 1H), 2.44 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 150.4, 146.5, 144.8, 140.8, 139.0, 137.4, 133.0, 132.2, 131.3, 129.7, 129.6, 129.2, 128.8, 124.6, 124.3, 121.9, 120.8, 105.1, 76.5, 21.7, 21.5; IR (film): 3392, 3223, 3078, 2920, 2859, 1701, 1611, 1467, 1309, 1263, 1141, 1085, 909, 827, 731 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{18}INO$ 463.0433; found 463.0430.

*3-(4-Chlorophenyl)-2-iodospiro[indene-1,1'-isoindolin]-3'-one (**3d**)*. Purified on silica gel with hexane/ AcOEt (8:1, v/v) as the eluent. 76% Yield (71 mg); Yellow solid, mp 228-229 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 6.8 Hz, 1H), 7.57-7.45 (m, 6H), 7.29 (td, *J* = 7.6, 1.2 Hz, 1H), 7.24 (d, *J* = 6.8 Hz, 1H), 7.15 (td, *J* = 7.4, 1.2 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 6.8 Hz, 1H), 6.46 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 149.5, 146.0, 144.6, 143.0, 135.1, 133.2, 132.6, 132.2, 130.4, 129.4, 129.35, 129.28, 127.4, 124.5, 124.0, 121.7, 120.8, 108.0, 76.8; IR (film): 3398, 3214, 3070, 1701, 1610, 1487, 1398, 1308, 1264, 1089, 1015, 908, 836, 729 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}ClINO$ 468.9730; found 468.9727.

*2-Iodo-3-(4-nitrophenyl)spiro[indene-1,1'-isoindolin]-3'-one (**3e**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 44% Yield (42 mg); Yellow solid, mp 300-301 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.97 (s, 1H), 8.45 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.8 Hz, 2H), 7.81 (dd, J = 6.2, 1.4 Hz, 1H), 7.60-7.49 (m, 2H), 7.39-7.32 (m, 1H), 7.27-7.17 (m, 2H), 7.10 (d, J = 7.2 Hz, 1H), 7.03 (d, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.9, 147.4, 147.3, 145.4, 144.9, 142.1, 140.8, 132.72, 132.67, 130.2, 129.2, 129.0, 127.1, 124.1, 123.5, 123.4, 121.6, 120.1, 112.5, 76.5; IR (film): 3399, 3207, 3075, 2925, 1703, 1599, 1519, 1462, 1347, 1312, 1266, 1181, 1105, 909 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}IN_2O_3$ 479.9971; found 479.9964.

*5'-Bromo-2-iodo-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**3f**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 90% Yield (92 mg); Yellow solid, mp 243-244 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 1.6 Hz, 1H), 7.60-7.45 (m, 6H), 7.31-7.26 (m, 2H), 7.18-7.12 (m, 1H), 7.09 (d, J = 7.2 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 6.45 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 151.0, 145.0, 144.0, 143.3, 136.1, 134.3, 134.0, 129.5, 129.3, 129.0, 128.9, 127.6, 127.4, 123.8, 123.5, 123.4, 121.2, 106.2, 76.6; IR (film): 3395, 3231, 3065, 1704, 1592, 1461, 1427, 1301, 1099, 908, 731 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}BrINO$ 512.9225; found 512.9221.

*2-Iodo-3-phenyl-6'-(trifluoromethyl)spiro[indene-1,1'-isoindolin]-3'-one (**3g**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 94% Yield (95 mg); White solid, mp 225-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.0 Hz, 1H),

7.80 (d, J = 8.0 Hz, 1H), 7.63-7.58 (m, 2H), 7.58-7.47 (m, 3H), 7.35-7.28 (m, 2H), 7.22-7.13 (m, 2H), 7.10 (d, J = 7.2 Hz, 1H), 6.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 151.4, 146.9, 143.6, 143.4, 135.5, 135.1 (q, $^2J_{CF}$ = 32 Hz), 133.8, 129.7, 129.4, 129.0, 128.9, 127.6, 126.8 (q, $^3J_{CF}$ = 4 Hz), 125.1, 123.9, 123.7 (q, $^1J_{CF}$ = 272 Hz), 121.4, 119.1 (q, $^3J_{CF}$ = 4 Hz), 105.6, 76.8; IR (film): 3393, 3226, 3069, 1712, 1602, 1490, 1431, 1325, 1254, 1171, 1132, 1054, 909, 733 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{23}H_{13}F_3INO$ 502.9994; found 502.9992.

*2-Bromo-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**3h**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 83% Yield (64 mg); Pale yellow solid, mp 229-230 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, J = 6.6, 1.4 Hz, 1H), 7.67-7.60 (m, 2H), 7.57-7.44 (m, 5H), 7.37-7.27 (m, 2H), 7.18 (td, J = 7.4, 1.3 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.99 (dd, J = 6.4, 1.2 Hz, 1H), 6.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 145.6, 144.0, 143.5, 142.6, 133.1, 132.5, 132.2, 129.4, 129.2, 129.0, 128.9, 127.5, 127.4, 124.4, 123.5, 121.8, 121.1, 74.9; IR (film): 3399, 3224, 3078, 1703, 1610, 1491, 1466, 1340, 1307, 1264, 1143, 1081, 909, 749 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{14}BrNO$ 387.0259; found 387.0257.

*2-Bromo-6-chloro-3-(4-chlorophenyl)spiro[indene-1,1'-isoindolin]-3'-one (**3i**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 73% Yield (66 mg); Pale yellow solid, mp 258-259 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, J = 6.6, 1.4 Hz, 1H), 7.59-7.48 (m, 6H), 7.30 (dd, J = 8.4, 2.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 1.6 Hz, 1H), 6.97 (dd, J = 6.4, 1.4 Hz, 1H), 6.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 145.3, 144.7, 142.2, 140.7, 135.4, 133.8, 133.3, 132.1,

130.5, 130.3, 129.8, 129.7, 129.4, 128.4, 124.6, 124.3, 121.8, 121.7, 74.7; IR (film): 3411, 3218, 3081, 1704, 1611, 1488, 1462, 1399, 1338, 1309, 1264, 1089, 1016, 908, 829 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{12}BrCl_2NO$ 454.9479; found 454.9482.

*2-Bromo-6-methyl-3-(p-tolyl)spiro[indene-1,1'-isoindolin]-3'-one (**3j**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 84% Yield (70 mg); Pale yellow solid, mp 211-212 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 6.4, 1.6 Hz, 1H), 7.55-7.45 (m, 4H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.99 (dd, *J* = 6.2, 1.4 Hz, 1H), 6.88 (s, 1H), 6.31 (s, 1H), 2.44 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 146.0, 143.9, 143.7, 140.1, 139.1, 137.5, 133.0, 132.2, 129.8, 129.7, 129.6, 129.3, 128.9, 125.6, 124.3, 121.8, 120.9, 74.8, 21.7, 21.5; IR (film): 3391, 3226, 3079, 2920, 1704, 1612, 1507, 1468, 1337, 1308, 1264, 1142, 909, 828 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{18}BrNO$ 415.0572; found 415.0576.

*2-Bromo-3-(4-chlorophenyl)spiro[indene-1,1'-isoindolin]-3'-one (**3k**).* Purified on silica gel with hexane/ AcOEt (6:1, v/v) as the eluent. 87% Yield (73 mg); Pale yellow solid, mp 246-247 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 6.4, 1.2 Hz, 1H), 7.61-7.55 (m, 2H), 7.55-7.45 (m, 4H), 7.35-7.27 (m, 2H), 7.22-7.16 (m, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.97 (dd, *J* = 6.6, 1.0 Hz, 1H), 6.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 145.4, 143.5, 142.9, 142.2, 135.1, 133.1, 132.2, 130.9, 130.4, 129.52, 129.50, 129.3, 128.2, 127.6, 124.5, 123.7, 121.7, 120.9, 74.9; IR (film): 3400, 3234, 3079, 1704, 1611, 1488, 1466, 1399, 1309, 1264, 1088, 1015, 908, 730 cm^{-1}; HRMS

(EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}BrClNO$ 420.9869; found 420.9878.

*2,6-Diiodo-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**4a**).* Purified on silica gel with hexane/ AcOEt (10:1, v/v) as the eluent. 77% Yield (86 mg); Yellow solid, mp 251-252 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.90 (m, 1H), 7.61 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.58-7.44 (m, 7H), 7.42 (d, *J* = 1.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.97-6.93 (m, 1H), 6.91 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 149.9, 146.7, 145.4, 142.8, 138.3, 133.7, 133.3, 132.8, 132.2, 129.6, 129.3, 129.0, 128.9, 124.5, 122.5, 121.7, 107.8, 92.7, 76.5; IR (film): 3407, 3208, 3078, 1704, 1609, 1489, 1456, 1398, 1309, 1262, 1086, 908, 823, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}I_2NO$ 560.9087; found 560.9086.

*3-(4-Chlorophenyl)-2,6-diiodospiro[indene-1,1'-isoindolin]-3'-one (**4b**).* Purified on silica gel with hexane/ AcOEt (10:1, v/v) as the eluent. 64% Yield (76 mg); Yellow solid, mp 294-295 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.2 Hz, 1H), 7.64 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.60-7.45 (m, 6H), 7.43 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 7.2 Hz, 1H), 6.20 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 149.0, 146.6, 145.2, 142.5, 138.5, 135.4, 133.4, 133.0, 132.1, 132.0, 130.3, 129.8, 129.4, 124.7, 122.3, 121.8, 108.4, 92.9, 76.4; IR (film): 3408, 3231, 3077, 2925, 1704, 1609, 1487, 1467, 1398, 1306, 1261, 1089, 1015, 908, 731 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{12}ClI_2NO$ 594.8697; found 594.8702.

Typical Procedure for the Preparation of Substrates 5. To a stirred suspension of $PdCl_2(PPh_3)_2$ (0.1 mmol), CuI (0.1 mmol), 2-iodobenzamide (2 mmol), and *i*-Pr_2NH (6 mL) in THF (10 mL) under N_2 atmosphere was added

1,1-diphenylpropyn-1-ol (2.2 mmol in 4 mL of THF) via a syringe. The reaction mixture was stirred at 50 ^{o}C for 3 hours and then concentrated in vacuo. The residue was washed with saturated NH_4Cl solution (5 mL) and extracted with AcOEt (20 mL). The organic layer was washed with brine and dried over Na_2SO_4. After filtered and concentrated, the residue was purified by column chromatography over silica gel with hexane/ AcOEt as the eluent to give pure **5a**.

*2-(3-Hydroxy-3,3-diphenylprop-1-yn-1-yl)benzamide (**5a**)*. Purified on silica gel with hexane/ AcOEt (2:1, v/v) as the eluent. 88% Yield (576 mg); White solid, mp 146-147 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02-7.94 (m, 1H), 7.65-7.59 (m, 4H), 7.58-7.54 (m, 1H), 7.46-7.38 (m, 2H), 7.38-7.32 (m, 4H), 7.32-7.26 (m, 2H), 7.01 (b, 1H), 5.64 (b, 1H), 3.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 144.5, 135.0, 133.8, 131.2, 130.5, 129.5, 128.7, 128.3, 126.3, 119.6, 98.5, 85.8, 75.1; IR (film): 3352, 1661, 1488, 1451, 1388, 1269, 1172, 1046, 754 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}NO_2Na$ 350.1151; found 350.1142.

*2-(3,3-Bis(4-fluorophenyl)-3-hydroxyprop-1-yn-1-yl)benzamide (**5b**)*. Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 92% Yield (668 mg); Pale yellow solid, mp 173-174 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90-7.84 (m, 1H), 7.61-7.51 (m, 5H), 7.47-7.38 (m, 2H), 7.06-6.97 (m, 4H), 6.86 (b, 1H), 5.97 (b, 1H), 4.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 162.6 (d, $^{1}J_{CF}$ = 246 Hz), 140.5 (d, $^{4}J_{CF}$ = 3 Hz), 135.4, 133.8, 131.2, 129.9, 129.5, 128.1 (d, $^{3}J_{CF}$ = 8 Hz), 119.6, 115.5 (d, $^{2}J_{CF}$ = 22 Hz), 97.7, 85.7, 74.1; IR (film): 3351, 1662, 1602, 1504, 1391, 1227, 1159, 1052, 837, 756 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for

$C_{22}H_{15}F_2NO_2Na$ 386.0963; found 386.0952.

*2-(3,3-Bis(4-chlorophenyl)-3-hydroxyprop-1-yn-1-yl)benzamide (**5c**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 95% Yield (750 mg); Pale yellow solid, mp 166-167 ^oC; ^1H NMR (400 MHz, $(CD_3)_2SO$): δ 7.96 (b, 1H), 7.77-7.68 (m, 5H), 7.62-7.52 (m, 2H), 7.51-7.45 (m, 2H), 7.45-7.38 (m, 4H), 7.21 (s, 1H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ 169.4, 145.1, 139.6, 132.6, 132.0, 129.6, 128.7, 128.1, 127.6, 127.5, 119.5, 95.6, 84.4, 72.5; IR (film): 3335, 2974, 1661, 1587, 1486, 1398, 1271, 1173, 1091, 1049, 996, 812, 757 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{15}Cl_2NO_2Na$ 418.0372; found 418.0378.

*2-(3,3-Bis(4-bromophenyl)-3-hydroxyprop-1-yn-1-yl)benzamide (**5d**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 89% Yield (860 mg); White solid, mp 163-164 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.2 Hz, 1H), 7.60-7.34 (m, 11H), 6.79 (b, 1H), 6.11 (b, 1H), 4.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 143.6, 135.5, 133.8, 131.8, 131.3, 129.7, 129.6, 128.0, 122.4, 119.5, 97.1, 85.9, 74.2; IR (film): 3337, 2973, 1660, 1586, 1482, 1395, 1270, 1171, 1048, 1001, 809, 756 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{15}Br_2NO_2Na$ 505.9362; found 505.9386.

*2-(3-Hydroxy-3,3-bis(4-methoxyphenyl)prop-1-yn-1-yl)benzamide (**5e**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 69% Yield (534 mg); Yellow solid, mp 137-138 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01-7.94 (m, 1H), 7.57-7.46 (m, 5H), 7.45-7.37 (m, 2H), 7.10 (b, 1H), 6.89-6.82 (m, 4H), 5.88 (b, 1H), 3.96 (b, 1H), 3.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 159.2, 137.2, 134.9, 133.7,

131.1, 130.1, 129.1, 127.6, 119.9, 113.8, 99.1, 85.0, 74.2, 55.5; IR (film): 3354, 2971, 1663, 1606, 1507, 1457, 1387, 1250, 1172, 1035, 753 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{21}NO_4Na$ 410.1363; found 410.1364.

*2-(3-Hydroxy-3,3-di-p-tolylprop-1-yn-1-yl)benzamide (**5f**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 87% Yield (618 mg); White solid, mp 171-172 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.06-8.00 (m, 1H), 7.60-7.55 (m, 1H), 7.49 (d, *J* = 8.0 Hz, 4H), 7.45-7.40 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 4H), 7.08 (b, 1H), 5.66 (b, 1H), 3.50 (s, 1H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 141.7, 138.1, 134.9, 133.8, 131.2, 130.5, 129.4, 126.2, 119.7, 98.8, 85.6, 74.9, 21.3; IR (film): 3342, 2921, 1662, 1585, 1509, 1386, 1266, 1170, 1051, 755 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{21}NO_2Na$ 378.1465; found 378.1465.

*2-(3-Hydroxy-3-phenylbut-1-yn-1-yl)benzamide (**5g**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 85% Yield (451 mg); Brown oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.67-7.61 (m, 2H), 7.45 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.38-7.21 (m, 6H), 6.55 (s, 1H), 4.94 (b, 1H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 145.4, 135.0, 133.7, 131.0, 130.0, 128.9, 128.6, 127.9, 125.1, 120.0, 99.7, 82.8, 70.2, 33.2; IR (film): 3339, 2984, 1658, 1587, 1385, 1265, 1141, 1091, 759 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{17}H_{15}NO_2$ 265.1103; found 265.1108.

*2-(3-Hydroxy-3-phenylprop-1-yn-1-yl)benzamide (**5h**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 75% Yield (377 mg); White solid, mp 124-125 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00-7.92 (m, 1H), 7.60-7.54 (m, 2H), 7.53-7.47

(m, 1H), 7.44-7.30 (m, 5H), 7.18 (b, 1H), 6.20 (b, 1H), 5.70 (d, J = 4.8 Hz, 1H), 3.94 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 140.3, 135.2, 133.8, 131.2, 130.1, 129.3, 129.0, 128.8, 126.9, 119.8, 96.0, 84.9, 65.1; IR (film): 3345, 2922, 1656, 1587, 1451, 1389, 1276, 1189, 1021, 964, 757 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{16}H_{13}NO_2$ 251.0946; found 251.0948.

*2-(3-Hydroxy-3-methylbut-1-yn-1-yl)benzamide (**5i**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 63% Yield (256 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05-7.95 (m, 1H), 7.50-7.30 (m, 4H), 6.35 (b, 1H), 3.46 (b, 1H), 1.63 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 135.0, 133.7, 131.2, 130.2, 129.0, 120.1, 100.9, 80.8, 65.7, 31.3; IR (film): 3347, 2980, 1658, 1589, 1378, 1265, 1164, 964, 757 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{12}H_{13}NO_2$ 203.0946; found 203.0943.

General Procedure for the Synthesis of 6. To a stirred solution of **5** (0.2 mmol) in toluene (4 mL) was added CF_3COOH (12 μL, 0.16 mmol). The reaction mixture was stirred at 110 ^{o}C. After the reaction completed, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane/ AcOEt as the eluent to give **6**.

*2-(3,3-Diphenylacryloyl)benzonitrile (**6a**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 91% Yield (56 mg); Yellow solid, mp 152-153 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, J = 7.8, 1.0 Hz, 1H), 7.52 (dd, J = 7.6, 1.2 Hz, 1H), 7.45-7.32 (m, 7H), 7.20-7.09 (m, 5H), 6.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 157.3, 142.8, 140.7, 138.6, 134.1, 132.2, 131.2, 130.5, 130.2, 129.9,

129.2, 129.1, 128.8, 128.3, 125.2, 118.0, 111.3; IR (film): 3059, 2226, 1652, 1591, 1570, 1445, 1350, 1266, 1213, 1030, 768 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{15}NO$ 309.1154; found 309.1158.

*2-(3,3-Bis(4-fluorophenyl)acryloyl)benzonitrile (**6b**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 98% Yield (68 mg); Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.57 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.52-7.34 (m, 4H), 7.15-7.03 (m, 4H), 6.93-6.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.4, 164.1 (d, $^1J_{CF}$ = 250 Hz), 163.2 (d, $^1J_{CF}$ = 249 Hz), 155.0, 142.5, 136.7 (d, $^4J_{CF}$ = 3 Hz), 134.3 (d, $^4J_{CF}$ = 3 Hz), 134.1, 132.4, 132.3 (d, $^3J_{CF}$ = 8 Hz), 131.5, 131.0 (d, $^3J_{CF}$ = 9 Hz), 129.8, 125.0, 117.9, 115.9 (d, $^2J_{CF}$ = 22 Hz), 115.5 (d, $^2J_{CF}$ = 22 Hz), 111.1; IR (film): 3071, 2225, 1661, 1597, 1505, 1411, 1349, 1228, 1160, 1021, 840, 759 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}F_2NO$ 345.0965; found 345.0968.

*2-(3,3-Bis(4-chlorophenyl)acryloyl)benzonitrile (**6c**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 95% Yield (72 mg); Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.60 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.54-7.43 (m, 2H), 7.38-7.29 (m, 4H), 7.20-7.15 (m, 2H), 7.10-7.04 (m, 2H), 6.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 154.6, 142.3, 138.8, 136.6, 136.5, 135.5, 134.2, 132.5, 131.7, 131.6, 130.3, 129.9, 129.2, 128.7, 125.3, 117.9, 111.2; IR (film): 3067, 2226, 1667, 1585, 1493, 1403, 1278, 1215, 1091, 1014, 832 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}Cl_2NO$ 377.0374; found 377.0372.

*2-(3,3-Bis(4-bromophenyl)acryloyl)benzonitrile (**6d**).* Purified on silica gel with

hexane/ AcOEt (3:1, v/v) as the eluent. 82% Yield (76 mg); Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68-7.63 (m, 1H), 7.62-7.58 (m, 1H), 7.54-7.44 (m, 4H), 7.37-7.31 (m, 2H), 7.28-7.22 (m, 2H), 7.03-6.98 (m, 2H), 6.96 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 154.8, 142.3, 139.2, 136.9, 134.3, 132.6, 132.2, 131.8, 131.74, 131.70, 130.5, 129.9, 125.3, 125.0, 123.9, 117.9, 111.2; IR (film): 3065, 2225, 1666, 1581, 1485, 1398, 1276, 1214, 1071, 1010, 826 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{22}H_{13}Br_2NO$ 464.9364; found 464.9371.

*2-(3,3-Bis(4-methoxyphenyl)acryloyl)benzonitrile (**6e**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 97% Yield (71 mg); Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.51 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.43-7.31 (m, 4H), 7.08-7.03 (m, 2H), 6.93-6.87 (m, 2H), 6.81 (s, 1H), 6.70-6.64 (m, 2H), 3.84 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 161.5, 160.5, 157.6, 143.5, 133.9, 133.4, 132.3, 132.1, 131.1, 130.9, 130.8, 129.7, 122.8, 118.1, 114.1, 113.7, 111.2, 55.6, 55.5; IR (film): 2934, 2838, 2225, 1645, 1605, 1506, 1463, 1353, 1290, 1174, 1030, 834 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{19}NO_3$ 369.1365; found 369.1363.

*2-(3,3-Di-p-tolylacryloyl)benzonitrile (**6f**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 76% Yield (51 mg); Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.52 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.43-7.32 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.88 (s, 1H), 2.38 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.0, 157.8, 143.0, 140.5, 139.2, 138.0, 135.8, 133.9, 132.1, 130.9, 130.5,

129.8, 129.4, 129.1, 128.9, 123.9, 118.0, 111.2, 21.5, 21.4; IR (film): 3026, 2921, 2225, 1664, 1589, 1508, 1443, 1348, 1296, 1209, 1115, 1021, 823 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{24}H_{19}NO$ 337.1467; found 337.1469.

*(E)-2-(3-Phenylbut-2-enoyl)benzonitrile (**6g**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 69% Yield (34 mg); Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.82 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.70 (td, *J* = 7.6, 1.3 Hz, 1H), 7.65-7.57 (m, 3H), 7.46-7.39 (m, 3H), 7.06 (q, *J* = 1.2 Hz, 1H), 2.69 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 159.1, 143.3, 142.5, 134.9, 132.8, 131.8, 129.9, 129.4, 128.9, 126.9, 122.0, 118.3, 111.3, 19.5; IR (film): 3063, 2225, 1660, 1593, 1446, 1278, 1215, 1046, 950, 761 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{17}H_{13}NO$ 247.0997; found 247.0997.

*2-Cinnamoylbenzonitrile (**6h**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 30% Yield (14 mg); Pale brown oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.85 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.79-7.71 (m, 2H), 7.69-7.61 (m, 3H), 7.47-7.40 (m, 3H), 7.37 (d, *J* = 16 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.0, 147.6, 142.0, 134.9, 134.5, 132.8, 132.0, 131.5, 129.5, 129.3, 129.0, 123.1, 117.9, 111.6; IR (film): 3063, 2226, 1667, 1600, 1449, 1334, 1301, 1218, 1020, 981, 761 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{16}H_{11}NO$ 233.0841; found 233.0844.

*2-(3-Methylbut-2-enoyl)benzonitrile (**6i**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 14% Yield (5 mg); Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.79 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.67 (td, *J* = 7.6, 1.6 Hz, 1H), 7.59 (td, *J* = 7.6, 1.2 Hz, 1H), 6.63 (m, 1H), 2.29 (d, *J* = 1.2 Hz, 3H), 2.06 (d, *J* =

1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.7, 161.2, 143.2, 134.9, 132.7, 131.6, 129.2, 121.7, 118.3, 111.4, 28.5, 21.9; IR (film): 2913, 2225, 1668, 1610, 1443, 1379, 1246, 1180, 1012, 772 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{12}H_{11}NO$ 185.0841; found 185.0839.

General Procedure for the Synthesis of 7. To a stirred mixture of $Pd(PPh_3)_4$ (0.01 mmol), Na_2CO_3 (0.2 mmol), **3** (0.2 mmol), phenylboronic acid (0.26 mmol) under N_2 atmosphere was added the solvent of DMF/ H_2O (4 mL, 2:1) via syringe at room temperature. The reaction mixture was stirred at 90 ^oC for about 12 hours. After cooled, the mixture was washed with H_2O, extracted with AcOEt, dried over Na_2SO_4, then filtered and concentrated. The residue was purified by column chromatography over silica gel with hexane/ AcOEt as the eluent to give **7**.

*2,3-Piphenylspiro[indene-1,1'-isoindolin]-3'-one (**7a**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 95% Yield (73 mg); Pale yellow solid, mp 221-222 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.82 (m, 1H), 7.48-7.42 (m, 2H), 7.40-7.28 (m, 7H), 7.18-7.09 (m, 2H), 7.06-6.93 (m, 4H), 6.72 (d, J = 7.2 Hz, 2H), 6.44 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 147.1, 145.0, 143.7, 143.5, 142.8, 134.2, 133.5, 132.9, 132.1, 129.5, 129.1, 129.0, 128.9, 128.8, 128.3, 128.2, 127.8, 127.3, 124.4, 122.8, 121.8, 121.5, 75.2; IR (film): 3395, 3210, 3062, 1694, 1611, 1466, 1338, 1311, 1263, 1079, 1029, 909, 730 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{28}H_{19}NO$ 385.1467; found 385.1468.

*3-Phenyl-2-(p-tolyl)spiro[indene-1,1'-isoindolin]-3'-one (**7b**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 93% Yield (74 mg); Pale yellow solid,

mp 119-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.82 (m, 1H), 7.47-7.42 (m, 2H), 7.40-7.26 (m, 7H), 7.16-7.08 (m, 2H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 2H), 6.42-6.35 (m, 1H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 147.2, 144.9, 143.8, 143.5, 142.3, 137.6, 134.4, 132.9, 132.1, 130.5, 129.5, 129.1, 129.0, 128.83, 128.81, 128.1, 127.1, 124.4, 122.8, 121.8, 121.4, 75.2, 21.3; IR (film): 3395, 3212, 3063, 1698, 1611, 1466, 1337, 1311, 1263, 1078, 909, 731 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{29}H_{21}NO$ 399.1623; found 399.1620.

*2-(4-Chlorophenyl)-3-phenylspiro[indene-1,1'-isoindolin]-3'-one (**7c**).* Purified on silica gel with hexane/ AcOEt (3:1, v/v) as the eluent. 91% Yield (76 mg); White solid, mp 251-252 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.82 (m, 1H), 7.48-7.43 (m, 2H), 7.41-7.27 (m, 7H), 7.15 (td, *J* = 7.4, 1.2 Hz, 1H), 7.12-7.06 (m, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.97-6.90 (m, 2H), 6.72 (s, 1H), 6.70-6.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 146.8, 144.8, 143.5, 142.1, 133.9, 133.7, 133.0, 132.1, 130.3, 129.5, 129.2, 129.01, 128.98, 128.6, 128.4, 127.5, 124.5, 122.8, 121.8, 121.7, 75.1; IR (film): 3395, 3207, 3068, 1694, 1611, 1487, 1465, 1338, 1311, 1264, 1091, 1014, 909, 840, 732 cm^{-1}; HRMS (EI-TOF) m/z: M^+ Calcd for $C_{28}H_{18}ClNO$ 419.1077; found 419.1078.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS Publications website at DOI:

^{1}H NMR and ^{13}C NMR spectra for all new compounds (PDF)

X-ray crystallography of **2a** (CIF)

X-ray crystallography of **3a** (CIF)

X-ray crystallography of **6a** (CIF)

AUTHOR INFORMATION

Corresponding authors

*E-mail: pinglu@zju.edu.cn.

*E-mail: orgwyg@zju.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENT

The authors thank the National Natural Science Foundation of China (Nos. 21632003 and 21472173) for the financial support.

REFERENCES

1 (a) Zhuang, Z.P.; Kung, M. P.; Mu, M.; Kung, H. F. *J. Med. Chem.* **1998**, *41*, 157. (b) De Clercq, E. *J. Med. Chem.* **1995**, *38*, 2491. (c) Wada, T.; Fukuda, N. *Psychopharmacology* **1991**, *103*, 314. (d) Li, E.; Jiang, L.; Guo, L.; Zhang, H.; Che, Y. *Bioorg. Med. Chem.* **2008**, *16*, 7894. (e)

Armoiry, X.; Aulagner, G.; Facon, T. *J. Clin. Pharm. Ther.* **2008**, *33*, 219. (f) Riedinger, C.; Noble, M. E.; Wright, D. J.; Mulks, F.; Hardcastle, I. R.; Endicott, J. A.; McDonnell, J. M. *Chem. Biol. Drug Des.* **2011**, *77*, 301.

2 (a) Egbertson, M. S.; Hartman, G. D.; Gould, R. J.; Bednar, R. A.; Cook, J. J.; Gaul, S. L.; Holahan, M. A.; Libby, L. A.; Lynch, J. J.; Sitko, G. R.; Stranieri, M. T.; Vassallo, L. M. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2519. (b) Boger, D. L.; Lee, J. K.; Goldberg, J.; Jin, Q. *J. Org. Chem.* **2000**, *65*, 1467.

3 (a) J. R. Fuchs, R. L. Funk, *Org. Lett.* **2001**, *3*, 3923. (b) P. Pigeon, B. Decroix, *Tetrahedron Lett.* **1997**, *38*, 2985.

4 Sharma, S.; Oh, Y.; Mishra, N. K.; De, U.; Jo, H.; Sachan, R.; Kim, H. S.; Jung, Y. H.; Kim, I. S. *J. Org. Chem.* **2017**, *82*, 3359.

5 Wrobel, J.; Dietrich, A.; Woolson, S. A.; Millen, J.; McCaleb, M.; Harrison, M. C.; Hohman, T. C.; Sredy, J.; Sullivan, D. *J. Med. Chem.* **1992**, *35*, 4613.

6 (a) Bao, X.; Shi, J.; Nie, X.; Zhou, B.; Wang, X.; Zhang, L.; Liao, H.; Pang, T. *Bioorg. Med. Chem.* **2014**, *22*, 4826. (b) Bao, X; Cao, X; Nie, X.; Xu, Y.; Guo, W; Zhou, B; Zhang, L; Liao, H.; Pang, T. *Sens. Actuators B: Chem.* **2015**, *208*, 54. (c) Yuan, L.; Lin, W.; Xie, Y.; Chen, B.; Zhu, S. *J. Am. Chem. Soc.* **2012**, *134*, 1305.

7 For selected examples, see: (a) Villuri, B. K.; Kotipalli, T.; kavala, V.; Ichake, S. S.; Bandi, V.; Kuo, C.-W.; Yao, C.-F. *RSC Adv.* **2016**, *6*, 74845.

(b) Suneja, A.; Bisai, V.; Singh, V. K. *J. Org. Chem.* **2016**, *81*, 4779. (c) Zhou, X. R.; Peng, Z. X.; Zhao, H. Y.; Zhang, Z. Y.; Lu, P.; Wang, Y. G. *Chem. Commun.* **2016**, 52, 10676. (d) Augner, D.; Gerbino, D. C.; Slavov, N.; Neudörfl, J.-M.; Schmalz, H.-G. *Org. Lett.* **2011**, *13*, 5374. (e) Bedford, R. B.; Bowen, J. G.; Méndez-Gálvez, C. *J. Org. Chem.* **2017**, *82*, 1719. (f) Kundu, A.; Pathak, S.; Debnath, K.; Pramanik, A. *Tetrahedron Lett.* **2014**, 55, 3960. (g) Bahajaj, A. A.; Vernon, J. M.; Wilson, G. D. *Tetrahedron* **2004**, *60,* 1247. (h) Butani, H. H.; Vachhani, D. D.; Bhoya, U. C.; Shah, A. K.; Van der Eycken, E. V. *Eur. J. Org. Chem.* **2014**, 6634. (i) Ghandi, M.; Zarezadeh, N.; Abbasi, A. *Org. Biomol. Chem.* **2015**, *13*, 8211.

8 For selected reviews, see: (a) Zhu, Y. X.; Sun, L.; Lu, P.; Wang, Y. G. *ACS Catal.* **2014**, *4*, 1911. (b) Wei, L. L.; Xiong, H.; Hsung, R. P. *Acc. Chem. Res.* **2003**, *36*, 773. (c) Ma, S. M. *Chem. Rev.* **2005**, *105*, 2829.

9 For the first example of Meyer-Schuster rearrangement, see: (a) Meyer, K. H.; Schuster, K. *Ber.* **1922**, *55B*, 819. For recent examples, see: (b) Han, Y. P.; Song, X. R.; Qiu, Y. F.; Hao, X. H.; Wang, J.; Wu, X. X.; Liu, X. Y.; Liang, Y. M. *J. Org. Chem.* **2015**, *80*, 9200. (c) Fang, Z. X.; Liu, J. Q.; Liu, Q.; Bi, X. H. *Angew. Chem. Int. Ed.* **2014**, *53*, 7209. (d) Li, Z. J.; Boyarskikh, V.; Hansen, J. H.; Autschbach, J.; Musaev, D. G.; Davies, H. M. L. *J. Am. Chem. Soc.* **2012**, *134*, 15497. (e) A Jo, K.; Maheswara, M.; Yoon, E.; Lee, Y. Y.; Yun, H.; Kang, E. J. *J. Org. Chem.* **2012**, *77*, 2924.

(f) Xu, C. F.; Xu, M.; Yang, L. Q.; Li, C. Y. *J. Org. Chem.* **2012**, *77*, 3010. (g) Shao, Y. S.; Zhu, K.; Qin, Z. C.; Li, E. D.; Li, Y. Z. *J. Org. Chem.* **2013**, *78*, 5731.

10 (a) Huang, K.; Sheng, G. R.; Lu, P.; Wang, Y. G. *J. Org. Chem.* **2017**, *82*, 5294. (b) Sun, L.; Zhu, Y. X.; Wang, J.; Lu, P.; Wang, Y. G. *Org. Lett.* **2015**, *17*, 242. (c) Yin, G. W.; Zhu, Y. X.; Wang, N. N.; Lu, P.; Wang, Y. G. *Tetrahedron* **2013**, *69*, 8353. (d) Zhang, L.; Zhu, Y. X.; Yin, G. W.; Lu, P.; Wang, Y. G. *J. Org. Chem.* **2012**, *77*, 9510. (e) Yin, G. W.; Zhu, Y. X.; Lu, P.; Wang, Y. G. *J. Org. Chem.* **2011**, *76*, 8922. (f) Zhu, Y. X.; Yin, G. W.; Hong, D.; Lu, P.; Wang, Y. G. *Org. Lett.* **2011**, *13*, 1024. (g) Zhu, Y. X.; Wen, S.; Yin, G. W.; Hong, D.; Lu, P.; Wang, Y. G. *Org. Lett.* **2011**, *13*, 3553.

11 Mao, C. L.; Barnish, I. T.; Hauser, C. R. *J. Heterocycle Chem.* **1969**, *6*, 475.

12 (a) Grigg, R.; Sridharan, V.; Stevenson, P.; Worakun, T. *J. Chem. Soc., Chem. Commun.* **1986**, *23*, 1697. (b) Grigg, R.; Sridharan, V.; Stevenson, P.; Sukirthalingam, *S. Tetrahedron* **1989**, *45*, 3557.

13 Nagamoto, M.; Nishimura, T. *Chem. Commun.* **2014**, *50*, 6274

14 CCDC 1037423 (**2a**), CCDC 1063023 (**3a**) and CCDC 1441341 (**6a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.