JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

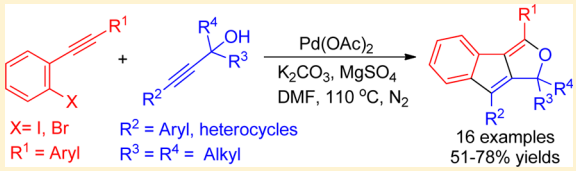
Synthesis of Indeno[1,2-*c*]furans via a Pd-Catalyzed Bicyclization of 2-Alkynyliodobenzene and Propargylic Alcohol

Jisong Jin, Yan Luo, Chao Zhou, Xiaopeng Chen, Qiaodong Wen, Ping Lu,* and Yanguang Wang*

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

Supporting Information

ABSTRACT: A general and efficient synthesis of indeno[1,2]furans via a Pd-catalyzed bicyclization reaction between 2-alkynyliodobenzenes and propargylic alcohols is described. The procedure furnishes indeno[1,2]furans with moderate to excellent yields (51%−78%) and a broad substrate scope. The cascade process combines the formation of one C−O bond and two C−C bonds in a single step.

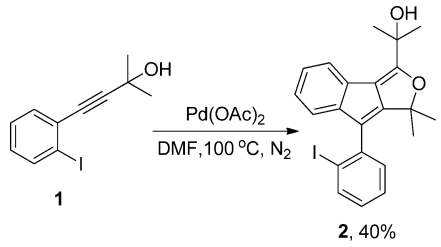


Fused heterocyclic compounds are important substructures in many natural products and drugs.[1−3] Among these fused heterocycles, O-containing heterocycles act in an important and indispensable role, such as the tricyclic indenofurans, which are key substructures of (−)-galiellalactone,[4] GR-24,[5] leucosceptroid A,[6,7] and ramelteon[8] as well. Due to their biological importance, a growing number of methods have been developed to prepare various indenofurans. Among these, there is only one publication related to the construction of the indeno[1,2-*c*]furan skeleton which started from *o*-lithiated aryloxiranes and *α,β*-unsaturated malonates *via* Micheal addition and a sequential ring opening of oxirane.[9]

Recently, synthesis of fused heterocyclic compounds through Pd-catalyzed bicyclization from alkyne has attracted significant attention.[10−15] These reactions construct fused-heterocycles in cascade approach with high atom efficiency and fit the basic requirements of green chemistry.[16−20] For instance, our group developed a cascade construction of 8*H*-acenaphtho[1,2-*c*]pyrroles from 1,8-diarenynyl naphthalenes and primary amines through an aminopalladation and a sequential carbopalladation over two triple bonds.[21] Wu and co-workers revealed that fused heterocycles containing an indene skeleton could be synthesized *via* a palladium-catalyzed bicyclization of amine, phenol, or amide across two triple bonds.[22−27] Nevertheless, to our knowledge, the preparation of indenofurans *via* this cascade process was never reported. Herein, we would like to report a palladium-catalyzed bicyclization between 2-alkynyliodobenzene and propargylic alcohol, which furnished the skeleton of indeno[1,2-*c*]furan in a single step.

Our initial effort focused on the palladium-catalyzed reaction between 4-(2-iodophenyl)-2-methyl-3-butyn-2-ol (**1**) and aniline to construct an indole or quinoline skeleton under a nitrogen atmosphere in DMF at 100 °C for 12 h (Scheme 1). To our surprise, we obtained **2** in a 40% yield along with a 50% recovery of **1**. Aniline did not participate in the reaction. The structure of **2** was confirmed by single crystal analysis (Figure S1). Compound **2** included a tricyclic indeno[1,2-*c*]furan substructure, resulting from a self-condensation of two molecules of **1** accompanied by an elimination of HI. Prompted by this result and the biological importance of indeno[1,2-*c*]furans, we tested the cross-condensation reaction between **3a** and **4a** under the same reaction conditions. In this manner, product **5a** was obtained in 38% yield.

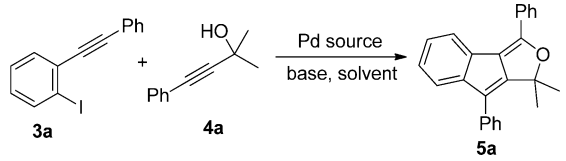
Scheme 1. Formation of 2 from 1



Then we focused our attention toward optimizing the reaction conditions, and the results are listed in Table 1. $Pd(OAc)_2$ presented the highest efficiency in comparison with $PdCl_2$, $Pd(PPh_3)_4$, and $PdCl_2(PPh_3)_2$ (Table1, entries 1−4). When $PdCl_2(PPh_3)_2$ was used, only a trace amount of **5a** was detected by TLC, which indicated that this could be a phosphine ligand free reaction. K_2CO_3 was found to be the best base additive (Table 1, entries 5−8). No desired product was detected when strong bases, such as DBU and KOH, were used which indicated that addition of a suitable base additive was critical to approach a practical reaction. The optimal solvent was determined to be DMF (Table 1, entries 9−14). Both lowering the reaction temperature to 90 °C and raising the reaction temperature to 130 °C would decrease the yield of **5a** (Table 1, entries 15 and 16). It was noticeable that this reaction could be conducted under air or by using 4 Å MS instead of anhydrous $MgSO_4$, but with slightly lower yields (Table 1, entries 17 and 18). The suitable reaction time was found to be 12 h. Shortening the reaction time would decrease the yield (entry 19), while extending the reaction time was not necessary.

Received: October 10, 2012
Published: November 30, 2012

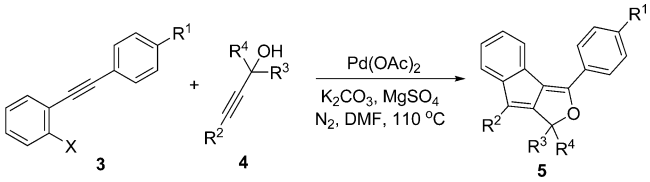
Table 1. Screening of Reaction Conditions for the Formation of 5a[a]



entry	[Pd]	base	solvent	temp (°C)	yield (%)[b]
1	$Pd(OAc)_2$	K_2CO_3	DMF	110	75
2	$PdCl_2(PPh_3)_2$	K_2CO_3	DMF	110	trace
3	$Pd(PPh_3)_4$	K_2CO_3	DMF	110	36
4	$PdCl_2$	K_2CO_3	DMF	110	72
5	$Pd(OAc)_2$	Na_2CO_3	DMF	110	45
6	$Pd(OAc)_2$	$Bu_4N^+OH^-$	DMF	110	15
7	$Pd(OAc)_2$	DBU	DMF	110	0
8	$Pd(OAc)_2$	KOH	DMF	110	0
9	$Pd(OAc)_2$	K_2CO_3	DMAc	110	35
10	$Pd(OAc)_2$	K_2CO_3	DMSO	110	29
11	$Pd(OAc)_2$	K_2CO_3	Et_3N	reflux	trace
12	$Pd(OAc)_2$	K_2CO_3	CH_3CN	reflux	trace
13	$Pd(OAc)_2$	K_2CO_3	CCl_4	reflux	trace
14	$Pd(OAc)_2$	K_2CO_3	toluene	110	31
15	$Pd(OAc)_2$	K_2CO_3	DMF	90	56
16	$Pd(OAc)_2$	K_2CO_3	DMF	130	52
17[c]	$Pd(OAc)_2$	K_2CO_3	DMF	110	63
18[d]	$Pd(OAc)_2$	K_2CO_3	DMF	110	56
19[e]	$Pd(OAc)_2$	K_2CO_3	DMF	110	58

[a]Reaction conditions: Reaction was conducted under N_2 with **3a** (0.5 mmol), **4a** (0.75 mmol), Pd catalyst (5 mol %, 0.025 mmol), base (1 mmol), and anhydrous $MgSO_4$ (2 mmol) in solvent (2 mL) for 12 h unless specially indicated. [b]Isolated yield. [c]Under air. [d]Using 4 Å MS instead of anhydrous $MgSO_4$. [e]8 h.

Table 2. Pd-Catalyzed Reaction of 2-Alkynyliodobenzenes 3 with Propargylic Alcohols 4[a]



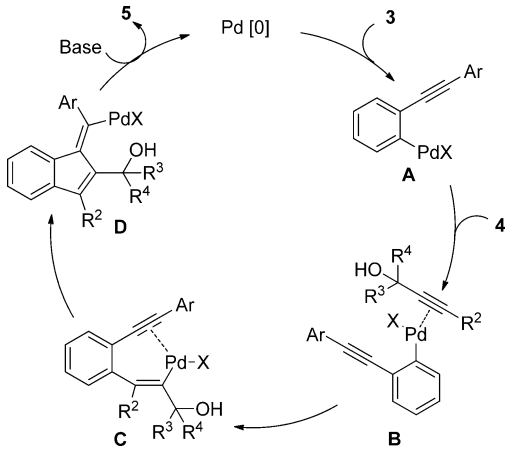
entry	**3** (R^1/X)	**4** (R^2/R^3/R^4)	**5**/yield (%)[b]
1	**3a** (H/I)	**4a** (Ph/Me/Me)	**5a**/75
2	**3a**	**4b** (*p*-MeC_6H_4/Me/Me)	**5b**/72
3	**3a**	**4c** (*p*-$MeOC_6H_4$/Me/Me)	**5c**/60
4	**3a**	**4d** (*p*-PhC_6H_4/Me/Me)	**5d**/65
5	**3a**	**4e** (*p*-$MeCOC_6H_4$/Me/Me)	**5e** /51
6	**3a**	**4f** (*p*-$NO_2C_6H_4$/Me/Me)	**5f**/61
7	**3a**	**4g** (3-thiophenyl/Me/Me)	**5g**/67
8	**3a**	**4h** (3-thiophenyl/-$(CH_2)_5$-)	**5h**/53
9	**3a**	**4i** (*o*-$MeOC_6H_4$/Me/Me)	–[c]
10	**3a**	**4j** (*m*-MeC_6H_4/Me/Me)	–[c]
11	**3a**	**4k** (1-naphthalenyl/Me/Me)	–[c]
12	**3a**	**4l** (Ph/Ph/Me)	–[c]
13	**3b** (Me/I)	**4a**	**5i**/56
14	**3c** (OMe/I)	**4a**	**5j**/62
15	**3d** (*n*-Bu/I)	**4a**	**5k**/55
16	**3e** (F/I)	**4a**	**5l** /78
17	**3f** (COMe/I)	**4a**	**5m**/66
18	**3g** (H/Br)	**4a**	**5a**/61
19	**3h** (OMe/Br)	**4a**	**5j**/57
20	**3i** (F/Br)	**4a**	**5l** /53

[a]Reaction conditions: **3** (0.5 mmol), **4** (0.75 mmol), $Pd(OAc)_2$ (5 mol %), K_2CO_3 (1 mmol), $MgSO_4$ (2 mmol), and DMF (2 mL) were mixed and reacted at 110 °C for 12 h under nitrogen. [b]Isolated yield. [c]Recovery of propargylic alcohol.

With optimized reaction conditions in hand, the substrate scope of this palladium-catalyzed tandem reaction was then investigated (Table 2). With respect to propargylic alcohols **4**, the yields were not apparently affected by either electron-donating or -withdrawing groups on the R^2 moiety. The desired products **4a**–**4f** were isolated in moderate yields ranging from 51% to 75% (Table 2, entries 1–6). Single crystal analysis of **5d** further supported the products containing an indeno[1,2-*c*]furan substructure. **4g** and **4h**, both with the thiophene, afforded the corresponding **5g** and **5h** in moderate yields, indicating that the thiophene ring tolerated this palladium-catalyzed bicyclization (Table 2, entries 7 and 8). However, the *o*-$MeOC_6H_4$ substituted **4i** did not react although **3a** was completely consumed as indicated by TLC (Table 2, entry 9). A similar result was observed for **4j**–**4l** (Table 2, entries 10–12). The possible reason might be the steric hindrance. We also tested the substituent effect of R^1 in **3** on this transformation. If the substituent was an electron-donating group, such as methyl, methoxy, and *n*-butyl, the yields decreased to 56%, 62%, and 55%, respectively (Table 2, entries 13–15). A slightly increased yield was obtained when the substituent group was fluorine (Table 2, entry 16). However, when we changed the $C_6H_4R^1$ group of **3** into alkyl, such as 1-(hept-1-yn-1-yl)-2-iodobenzene, no corresponding product was isolated with the recovery of two starting materials. By altering 1-iodo-2-(phenylethynyl)benzene (**3a**) to 1-bromo-2-(phenylethynyl)benzene (**3g**), we isolated **5a** in a relatively lower yield (61%, Table 2, entry 18). Similarly, 1-bromo-2-(phenylethynyl)benzenes **3h** (Table 2, entry 19) and **3i** (Table 2, entry 20) also gave lower yields of **5j** (57%) and **5l** (53%) because of the relative reactivity of C–X bonds for the oxidative addition of palladium. With further alternation of bromo in **3g** to chloro, the desired product **5a** was not detected with the recovery of two starting materials.

The plausible mechanism for this transformation is proposed in Scheme 2. First, oxidative addition of palladium into the C–X bond of **3** generates intermediate **A**. **A** cooperates with propargylic alcohol **4** to form complex **B**, which then undergoes

Scheme 2. Proposed Mechanism for the Formation of 5



dx.doi.org/10.1021/jo302223y | J. Org. Chem. 2012, 77, 11368–11371

a *syn*-carbopalladation to form complex **C**. Subsequently, a *syn*-carbopalladation occurs, resulting in the formation of **D**, in which palladium coordinated with the hydroxyl group. Finally, assisted by a proper base, a reductive elimination affords indeno[1,2-*c*]furan **5**. During this cascade progress, one C−O bond and two C−C bonds were formed in a single step. Compared with classic C−C and C−O bond formation, this strategy seems to be more effective and convenient as starting materials, 2-alkynyliodobenzene and propargylic alcohols, were easily prepared.[28]

In conclusion, we demonstrated a palladium-catalyzed bicyclization between 2-alkynylhalobenzene and propargylic alcohols, furnishing indeno[1,2-*c*]furans with moderate to excellent yields. A plausible mechanism for this cascade process is proposed, which involves the formation of one C−O bond and two C−C bonds in a single step. Regarding the biological importance of indenofurans, our palladium-catalyzed bicyclization would find applications in pharmaceutical chemistry.

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR spectra were recorded at 400 or 500 MHz using TMS as an internal standard and ^{13}C NMR spectra at 100, or 125 MHz using $CDCl_3$. High resolution mass spectra (HRMS) were performed on an electron ionization time-of-flight (EI-TOF) mass spectrometer. Melting points were measured with a micro melting point apparatus.

The 2-alkynyliodobenzenes **3** and propargylic alcohols **4** were prepared by the Sonogashira reaction according to the published methods.[29] Other materials were purchased from common commercial sources and used without additional purification.

Procedure for Synthesis of Compound 2. A 10 mL round-bottom flask was charged with 4-(2-iodophenyl)-2-methyl-3-butyn-2-ol (**1**) (0.5 mmol), $Pd(OAc)_2$ (0.025 mmol) and dry DMF (2 mL). The reaction mixture was stirred at 100 °C (oil bath) under N_2 for 12 h. After cooling to room temperature, the resultant mixture was added to 30 mL of water, extracted with DCM (3 × 5 mL), and dried over Na_2SO_4. The dichloromethane was evaporated under reduced pressure and the residue was purified by flash column chromatography on a silica gel to give the product **2**.

General Procedures for the Reaction of 2-Alkynyliodobenzene 3 with Propargylic Alcohol 4. A 10 mL round-bottom flask was charged with 2-alkynyliodobenzene **3** (0.5 mmol), propargylic alcohol **4** (0.75 mmol), K_2CO_3 (1 mmol), $MgSO_4$ (2 mmol), $Pd(OAc)_2$ (0.025 mmol) and dry DMF (2 mL). The reaction mixture was stirred at 110 °C (oil bath) under N_2 for 12 h. After cooling to room temperature, the resultant mixture was added to 30 mL of water, extracted with DCM (3 × 5 mL), and dried over Na_2SO_4. The dichloromethane was evaporated under reduced pressure and the residue was purified by flash column chromatography on a silica gel to give the products.

2-(8-(2-Iodophenyl)-1,1-dimethyl-1*H*-indeno[1,2-*c*]furan-3-yl)propan-2-ol (2). R_f = 0.2 (petroleum ether/DCM = 6:1). Yellow solid (89 mg, 40%), mp 169−171 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.7 Hz, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.33 (d, J = 7.5 Hz, 1H), 7.20 (dd, J = 12.8, 6.3 Hz, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.97 (d, J = 7.0 Hz, 1H), 2.46 (s, 1H), 1.71 (s, 6H), 1.56 (s, 3H), 1.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 152.3, 146.5, 140.7, 138.9, 131.3, 129.0, 127.7, 127.0, 126.4, 125.2, 123.7, 122.9, 120.1, 118.3, 101.3, 86.7, 71.4, 28.7, 26.8, 25.3. HRMS (EI) Calcd. for $[C_{22}H_{21}IO_2]$ ($[M]^+$): 444.0586, found: 444.0589.

1,1-Dimethyl-3,8-diphenyl-1*H*-indeno[1,2-*c*]furan (5a). R_f = 0.3 (petroleum ether/DCM = 10:1). Yellow solid (126 mg, 75%), mp 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15−8.07 (m, 2H), 8.00 (d, J = 7.2 Hz, 1H), 7.62−7.51 (m, 5H), 7.52−7.42 (m, 3H), 7.41−7.35 (m, 1H), 7.32−7.20 (m, 2H), 1.70 (d, J = 6.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 152.8, 147.2, 135.3, 131.0, 130.9, 129.2, 128.8, 128.45, 128.4, 127.6, 126.9, 125.8, 124.4, 123.2, 121.3, 120.7, 120.2, 86.7, 27.2. HRMS (EI) Calcd. for $[C_{25}H_{20}O]$ ($[M]^+$): 336.1514, found: 336.1510.

1,1-Dimethyl-3-phenyl-8-(*p*-tolyl)-1*H*-indeno[1,2-*c*]furan (5b). R_f = 0.3 (petroleum ether/DCM = 10:1). Yellow solid (126 mg, 72%), mp 145−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.1 Hz, 2H), 8.03 (d, J = 7.4 Hz, 1H), 7.63−7.55 (m, 3H), 7.47 (d, J = 7.8 Hz, 3H), 7.28 (m, 5H), 2.48 (s, 3H), 1.74 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 152.5, 147.4, 136.6, 132.3, 131.1, 130.8, 129.2, 129.1, 128.8, 128.4, 127.6, 125.7, 124.4, 123.2, 121.3, 120.8, 120.2, 86.6, 27.2, 21.4. HRMS (EI) Calcd. for $[C_{26}H_{22}O]$ ($[M]^+$): 350.1671, found: 350.1674.

8-(4-Methoxyphenyl)-1,1-dimethyl-3-phenyl-1*H*-indeno[1,2-*c*]furan (5c). R_f = 0.3 (petroleum ether/DCM = 8:1). Yellow solid (110 mg, 60%), mp 141−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 7.6 Hz, 2H), 8.01 (d, J = 7.4 Hz, 1H), 7.64−7.52 (m, 3H), 7.48 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 7.6 Hz, 1H), 7.26 (tt, J = 14.8, 7.3 Hz, 2H), 7.04 (d, J = 8.3 Hz, 2H), 3.91 (s, 3H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 158.6, 152.2, 147.4, 131.0, 130.7, 130.2, 128.7, 128.3, 127.6, 125.6, 123.9, 123.1, 121.2, 120.6, 120.0, 113.8, 86.5, 55.3, 27.1. HRMS (EI) Calcd. for $[C_{26}H_{22}O_2]$ ($[M]^+$): 366.1620, found: 366.1620.

8-([1,1′-Biphenyl]-4-yl)-1,1-dimethyl-3-phenyl-1*H*-indeno-[1,2-*c*]furan (5d). R_f = 0.2 (petroleum ether/DCM = 10:1). Yellow solid (134 mg, 65%), mp 155−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.6 Hz, 2H), 8.06 (d, J = 7.5 Hz, 1H), 7.75 (t, J = 6.1 Hz, 4H), 7.69−7.50 (m, 8H), 7.42 (t, J = 7.3 Hz, 1H), 7.37−7.25 (m, 2H), 1.78 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 152.9, 147.0, 140.8, 139.5, 134.3, 130.9, 130.9, 129.5, 128.8, 128.8, 128.4, 127.6, 127.3, 127.1, 127.0, 125.7, 123.9, 123.2, 121.3, 120.8, 120.2, 86.7, 27.1. HRMS (EI) Calcd. for $[C_{31}H_{24}O]$ ($[M]^+$): 412.1827, found: 412.1828.

1-(4-(1,1-Dimethyl-3-phenyl-1*H*-indeno[1,2-*c*]furan-8-yl)-phenyl)ethanone (5e). R_f = 0.2 (petroleum ether/DCM = 6:1). Yellow solid (96 mg, 51%), mp 183−184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.07 (m, 4H), 8.03 (d, J = 7.4 Hz, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.60 (q, J = 6.4 Hz, 3H), 7.48 (d, J = 7.4 Hz, 1H), 7.35−7.23 (m, 2H), 2.70 (s, 3H), 1.73 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 160.3, 154.0, 146.3, 140.6, 135.4, 131.1, 130.6, 129.1, 128.8, 128.6, 128.4, 127.5, 125.8, 123.4, 123.1, 121.3, 120.8, 119.9, 86.8, 27.0, 26.7. HRMS (EI) Calcd. for $[C_{27}H_{22}O_2]$ ($[M]^+$): 378.1620, found: 378.1624.

1,1-Dimethyl-8-(4-nitrophenyl)-3-phenyl-1*H*-indeno[1,2-*c*]furan (5f). R_f = 0.3 (petroleum ether/DCM = 6:1). Yellow solid (116 mg, 61%), mp 178−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.3 Hz, 2H), 8.13−8.07 (m, 2H), 8.02 (d, J = 7.4 Hz, 1H), 7.70 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 6.5 Hz, 3H), 7.44 (d, J = 7.5 Hz, 1H), 7.35−7.24 (m, 2H), 1.72 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 155.1, 146.4, 145.7, 142.7, 131.4, 130.4, 129.5, 128.9, 128.5, 127.4, 125.9, 123.9, 123.7, 121.9, 121.4, 120.9, 119.7, 86.9, 27.1. HRMS (EI) Calcd. for $[C_{25}H_{19}NO_3]$ ($[M]^+$): 381.1365, found: 381.1368.

1,1-Dimethyl-3-phenyl-8-(thiophen-3-yl)-1*H*-indeno[1,2-*c*]furan (5g). R_f = 0.2 (petroleum ether/DCM = 8:1). Yellow solid (115 mg, 67%), mp 173−175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 6.6 Hz, 2H), 8.02 (d, J = 7.5 Hz, 1H), 7.65−7.52 (m, 4H), 7.47 (s, 1H), 7.41 (s, 1H), 7.34 (dd, J = 16.9, 6.1 Hz, 2H), 7.29−7.22 (m, 1H), 1.76 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 152.7, 147.0, 135.3, 130.8, 128.8, 128.6, 128.5, 128.3, 127.5, 125.7, 125.4, 123.2, 122.0, 121.2, 120.5, 120.2, 118.8, 86.6, 26.7. HRMS (EI) Calcd. for $[C_{23}H_{18}OS]$ ($[M]^+$): 342.1078, found: 342.1077.

3′-Phenyl-8′-(thiophen-3-yl)spiro[cyclohexane-1,1′-indeno-[1,2-*c*]furan] (5h). R_f = 0.2 (petroleum ether/DCM = 8:1). Yellow solid (101 mg, 53%), mp 199−201 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 6.8 Hz, 2H), 8.01 (d, J = 7.5 Hz, 1H), 7.58 (dq, J = 10.2, 7.1 Hz, 3H), 7.52−7.44 (m, 2H), 7.39 (d, J = 1.8 Hz, 1H), 7.34−7.22(m, 3H), 2.01−1.74 (m, 9H), 1.35 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 153.2, 147.4, 135.5, 131.3, 130.8, 129.1, 128.8, 128.5, 127.5, 125.7, 125.3, 123.1, 122.4, 121.4, 120.9, 120.2, 118.7, 88.2, 35.7, 25.0, 22.9. HRMS (EI) Calcd. for $[C_{26}H_{22}OS]$ ($[M]^+$): 382.1391, found: 382.1393.

1,1-Dimethyl-8-phenyl-3-(*p*-tolyl)-1H-indeno[1,2-*c*]furan (5i). R_f = 0.3 (petroleum ether/DCM = 10:1). Yellow solid (98 mg,

dx.doi.org/10.1021/jo302223y | *J. Org. Chem.* 2012, 77, 11368−11371

56%), mp 142−143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.7 Hz, 3H), 7.59 (d, J = 7.9 Hz, 2H), 7.51 (dd, J = 12.8, 5.6 Hz, 3H), 7.42 (t, J = 8.5 Hz, 3H),7.34−7.25(m,, 2H), 2.52 (s, 3H), 1.75 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 152.9, 147.1, 141.4, 135.5, 129.5, 129.3, 128.5, 128.4, 128.2, 127.6, 126.8, 125.5, 123.9, 123.1, 121.3, 120.2, 120.1, 86.6, 27.2, 21.8. HRMS (EI) Calcd. for [$C_{26}H_{22}O$] ([M]$^+$): 350.1671, found: 350.1668.

3-(4-Methoxyphenyl)-1,1-dimethyl-8-phenyl-1*H*-indeno[1,2-*c*]furan (5j). R_f = 0.2 (petroleum ether/DCM = 8:1). Yellow solid (113 mg, 62%), mp 146−147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.3 Hz, 2H), 8.02 (d, J = 7.4 Hz, 1H), 7.56 (d, J = 7.9 Hz, 2H), 7.49 (t, J = 7.6 Hz, 3H), 7.38 (t, J = 7.2 Hz, 1H), 7.33−7.20 (m, 2H), 7.11 (d, J = 8.4 Hz, 2H), 3.93 (s, 3H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 159.6, 152.9, 146.8, 135.5, 130.2, 129.2, 128.4, 127.4, 126.7, 125.3, 123.4, 122.9, 121.1, 120.0, 119.3, 114.2, 86.5, 55.5, 27.2. HRMS (EI) Calcd. for [$C_{26}H_{22}O_2$] ([M]$^+$): 366.1620, found: 366.1619.

3-(4-Butylphenyl)-1,1-dimethyl-8-phenyl-1*H*-indeno[1,2-*c*]furan (5k). R_f = 0.2 (petroleum ether/DCM = 10:1). Yellow solid (108 mg, 55%), mp 113−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10−8.01 (m, 3H), 7.57 (d, J = 4.7 Hz, 2H), 7.54−7.45 (m, 3H), 7.42 (d, J = 6.3 Hz, 3H),7.31−7.25(m, 2H), 2.76 (t, J = 6.7 Hz, 2H), 1.72 (d, J = 2.9 Hz, 8H), 1.45 (dd, J = 12.8, 6.8 Hz, 2H), 1.08−0.96 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 152.9, 147.1, 146.4, 135.5, 129.3, 128.9, 128.4, 128.4, 128.4, 127.6, 126.8, 125.5, 123.9, 123.1 121.3, 120.2, 120.1, 86.6, 35.9, 33.5, 27.2, 22.4, 14.0. HRMS (EI) Calcd. for [$C_{29}H_{28}O$] ([M]$^+$): 392.2140, found: 392.2141.

3-(4-Fluorophenyl)-1,1-dimethyl-8-phenyl-1H-indeno[1,2-*c*]furan (5l). R_f = 0.3 (petroleum ether/DCM = 8:1). Yellow solid (138 mg, 78%), mp 143−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 8.5, 5.5 Hz, 2H), 7.96 (d, J = 7.4 Hz, 1H), 7.55 (d, J = 7.1 Hz, 2H), 7.53−7.43 (m, 3H), 7.40 (t, J = 7.2 Hz, 1H), 7.34−7.21 (m,4H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2 ($^1J_{C-F}$ = 200 Hz), 158.1, 152.7, 147.3, 135.2, 130.6 ($^3J_{C-F}$ = 7 Hz), 129.2, 128.5, 127.5, 127.3 ($^4J_{C-F}$ = 3 Hz), 127.0, 125.8, 124.5, 123.3, 121.1, 120.5, 120.3, 116.2 ($^2J_{C-F}$ = 21 Hz), 86.8, 27.2. HRMS (EI) Calcd. for [$C_{25}H_{19}OF$] ([M]$^+$): 354.1420, found: 354.1418.

1-(4-(1,1-Dimethyl-8-phenyl-1*H*-indeno[1,2-*c*]furan-3-yl)-phenyl)ethanone (5m). R_f = 0.2 (petroleum ether/DCM = 6:1). Yellow solid (124 mg, 66%), mp 180−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.12 (m, 4H), 7.98 (d, J = 7.5 Hz, 1H), 7.57−7.46 (m, 4H), 7.41 (dd, J = 16.8, 7.5 Hz, 2H), 7.33−7.24(m, 2H), 2.71 (s, 3H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 157.3, 152.5, 147.6, 138.2, 135.2, 135.0 129.1, 128.7, 128.5, 128.5, 127.4, 127.2, 126.3, 125.7, 123.6, 122.5, 121.5, 120.4, 86.8, 27.1, 26.8. HRMS (EI) Calcd. for [$C_{27}H_{22}O_2$] ([M]$^+$): 378.1620, found: 378.1618.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectra (^{1}H and ^{13}C) for **3a**-**3i**, **4a**-**4l**, **5a**-**5m** and crystallographic information (CIF files) for compounds **2** and **5d**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

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

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial support of the National Natural Science Foundation of China (Nos. 21272203 and 21032005).

■ REFERENCES

(1) Singh, S.; Bharti, N.; Mohapatra, P. P. *Chem. Rev.* **2009**, *109*, 1900.
(2) Li, W.-T.; Hwang, D.-R.; Chen, C.-P.; Shen, C.-W.; Huang, C.-L.; Chen, T.-W.; Lin, C.-H.; Chang, Y.-L.; Chang, Y.-Y.; Lo, Y.-K.; Tseng, H.-Y.; Lin, C.-C.; Song, J.-S.; Chen, H.-C.; Chen, S.-J.; Wu, S.-H.; Chen, C.-T. *J. Med. Chem.* **2003**, *46*, 1706.
(3) Xiao, Z.; Bastow, K. F.; Vance, J. R.; Sidwell, R. S.; Wang, H.-K.; Chen, M. S.; Shi, Q.; Lee, K.-H. *J. Med. Chem.* **2004**, *47*, 5140.
(4) Gidlöf, R.; Johansson, M.; Sterner, O. *Org. Lett.* **2010**, *12*, 5100.
(5) Thuring, J. W. J. F.; Nefkens, G. H. L.; Zwanenburg, B. *J. Agric. Food Chem.* **1997**, *15*, 1409.
(6) Uchikawa, O.; Fukatsu, K.; Tokunoh, R.; Kawada, M.; Matsumoto, K.; Imai, Y.; Hinuma, S.; Kato, K.; Nishikawa, H.; Hirai, K.; Miyamoto, M.; Ohkawa, S. *J. Med. Chem.* **2002**, *45*, 4222.
(7) Koike, T.; Hoashi, Y.; Takai, T.; Nakayama, M.; Yukuhiro, N.; Ishikawa, T.; Hirai, K.; Uchikawa, O. *J. Med. Chem.* **2011**, *54*, 3436.
(8) Xie, J.; Ma, Y.; Horne, D. A. *J. Org. Chem.* **2011**, *76*, 6169.
(9) Salomone, A.; Capriati, V.; Florio, S.; Luisi, R. *Org. Lett.* **2008**, *10*, 1947.
(10) Sugihara, T.; Copéret, C.; Owczarczyk, Z.; Harring, L. S.; Negishi, E. *J. Am. Chem. Soc.* **1994**, *116*, 7923.
(11) Kojima, A.; Takemoto, T.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1996**, *61*, 4876.
(12) Copéret, C.; Ma, S.; Sugihara, T.; Negishi, E. *Tetrahedron* **1996**, *52*, 11529.
(13) Roesch, K. R.; Larock, R. C. *Org. Lett.* **1999**, *1*, 1551.
(14) Zhang, H.; Larock, R. C. *Org. Lett.* **2002**, *4*, 3035.
(15) Yamamoto, Y.; Nagata, A.; Nagata, H.; Ando, Y.; Arikawa, Y.; Tatsumi, K.; Itoh, K. *Chem.—Eur. J.* **2003**, *9*, 2469.
(16) Wang, C.; Rakshit, S.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 14006.
(17) Wu, T.-C.; Tai, C.-C.; Tiao, H.-C.; Chang, Y.-T.; Liu, C.-C.; Li, C.-H.; Huang, C.-H.; Kuo, M.-Y.; Wu, Y.-T. *Chem.—Eur. J.* **2011**, *17*, 7220.
(18) Eversloh, C. L.; Avlasevich, Y.; Chen, L.; Müllen, K. *Chem.—Eur. J.* **2011**, *17*, 12756.
(19) Chen, T.-A.; Liu, R.-S. *Org. Lett.* **2011**, *13*, 4644.
(20) Zhu, S.; Wu, L.; Huang, X. *Org. Biomol. Chem.* **2012**, *10*, 3696.
(21) Chen, X.; Jin, J.; Wang, Y.; Lu, P. *Chem.—Eur. J.* **2011**, *17*, 9920.
(22) Luo, Y.; Hong, L.; Wu, J. *Chem. Commun.* **2011**, *47*, 5298.
(23) Luo, Y.; Pan, X.; Wu, J. *Org. Lett.* **2011**, *13*, 1150.
(24) Pan, X.; Luo, Y.; Wu, J. *Chem. Commun.* **2011**, *47*, 8967.
(25) Luo, Y.; Wu, J. *Chem. Commun.* **2011**, *47*, 11137.
(26) Pan, X.; Luo, Y.; Liu, G.; Pu, S.; Wu, J. *Adv. Synth. Catal.* **2012**, *354*, 171.
(27) Luo, Y.; Wu, J. *Org. Lett.* **2012**, *14*, 1592.
(28) Verma, A. K.; Kesharwani, T.; Singh, J.; Tandon, V.; Larock, R. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 1138.
(29) Cao, H.; McNamee, L.; Alper, H. *Org. Lett.* **2008**, *10*, 5281.