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One-Pot Synthesis of Polysubstituted Spirofluorene−Indene via Ru(II)-Catalyzed [3 + 2] Annulation and Intramolecular Friedel−Crafts Cyclization

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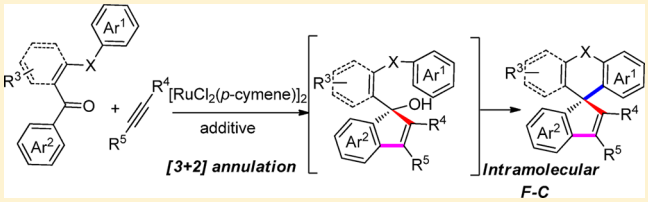
Supporting Information

ABSTRACT: Ru(II)-catalyzed one-pot synthesis of polysubstituted spirofluorene−indenes via [3 + 2] annulation and then intramolecular Friedel−Crafts alkylation has been achieved. The simple method provides a broad scope of aryl ketones and internal alkynes, achieving PAHs skeletons in moderate to good yields.

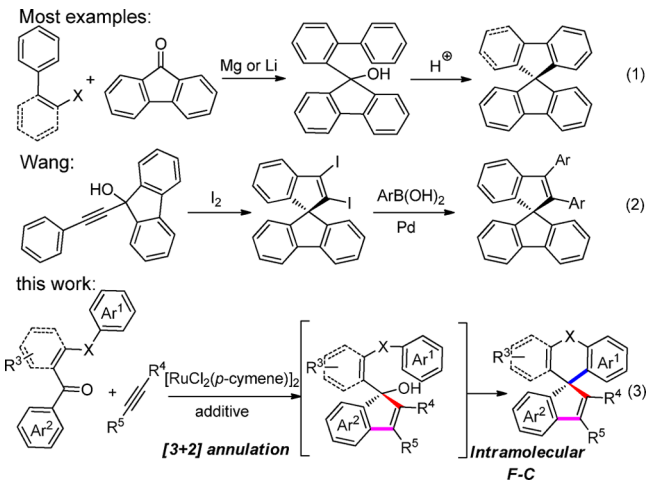


INTRODUCTION

Polycyclic aromatic hydrocarbons (PAHs) have emerged as an intriguing class of synthetic skeletons owing to the unique properties in material science.[1] In this respect, polysubstituted indenes are widely used in the chemical and pharmaceutical industries and in functionalized fluorenes.[2] Despite the widespread utility of these motifs, a limited number of efficient methods have been studied. For example, the classical methods for the synthesis of these compounds include intramolecular electrophilic alkylations promoted by Brønsted or Lewis acids with tertiary alcohols as starting materials, which were usually prepared from halides and fluorenone by Grignard reaction or halogen−lithium exchange (Scheme 1, eq 1).[2a,3] Wang has reported that l-diphenylene-2,3-diphenylindene possessing both fluorene and indene skeletons is constructed from the substituted 2,3-diiodoindenes via a Suzuki coupling reaction, which were obtained from substituted propargylic alcohols (Scheme 1, eq 2).[4] However, most of these approaches are associated with significant practical drawbacks including several transformations, limited substrate scope, and harsh reaction conditions. Therefore, development of a simple, practical, and efficient method for the synthesis of polysubstituted indene derivatives represents a highly desirable goal in organic synthesis.

Transition-metal-catalyzed functionalization of C−H bonds has been increasingly explored over the past decade due to its high efficiency.[5,6] Recently, various strategies toward substituted indenols have been reported via rhodium-catalyzed[7] or ruthenium-catalyzed[8] C−H activation and carbocyclization of aryl ketones and alkynes. Therefore, we envisioned that indenols generated in situ from aryl ketones and alkynes could be directly utilized in intramolecular Friedel−Crafts alkylation via a tandem process. Recently, tandem reactions following the first C−H bond activation have been well developed, furnishing efficient access to complex structures.[9] Herein, we report a highly efficient Ru(II)-catalyzed one-pot synthesis of polysubstituted spirofluorene−indenes via [3 + 2] annulation of aryl ketones with internal alkynes followed by intramolecular Friedel−Crafts alkylation (Scheme 1, eq 3).

Scheme 1. Strategies toward Polysubstituted Indene Derivatives



RESULTS AND DISCUSSION

The cascade reaction was first tested with [1,1′-biphenyl]-2-yl(4-methoxyphenyl)methanone **1a** and diphenylacetylene **2a** (Table 1). Using $[RuCl_2(p\text{-cymene})]_2$ as a catalyst, the corresponding polysubstituted indene product 5′-methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] **3aa** was isolated when $AgBF_4$ was added as an additive (entries 1−3). It is well-known that the Friedel−Crafts reaction could be catalyzed by Brønsted acids. Therefore, the effect of different protonic acids

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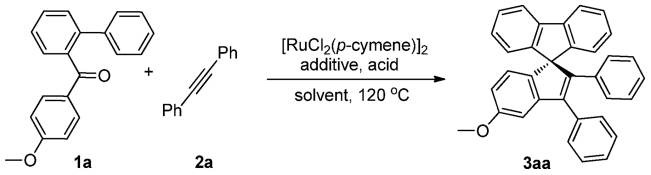
Table 1. Optimization of the Reaction Conditions[a]



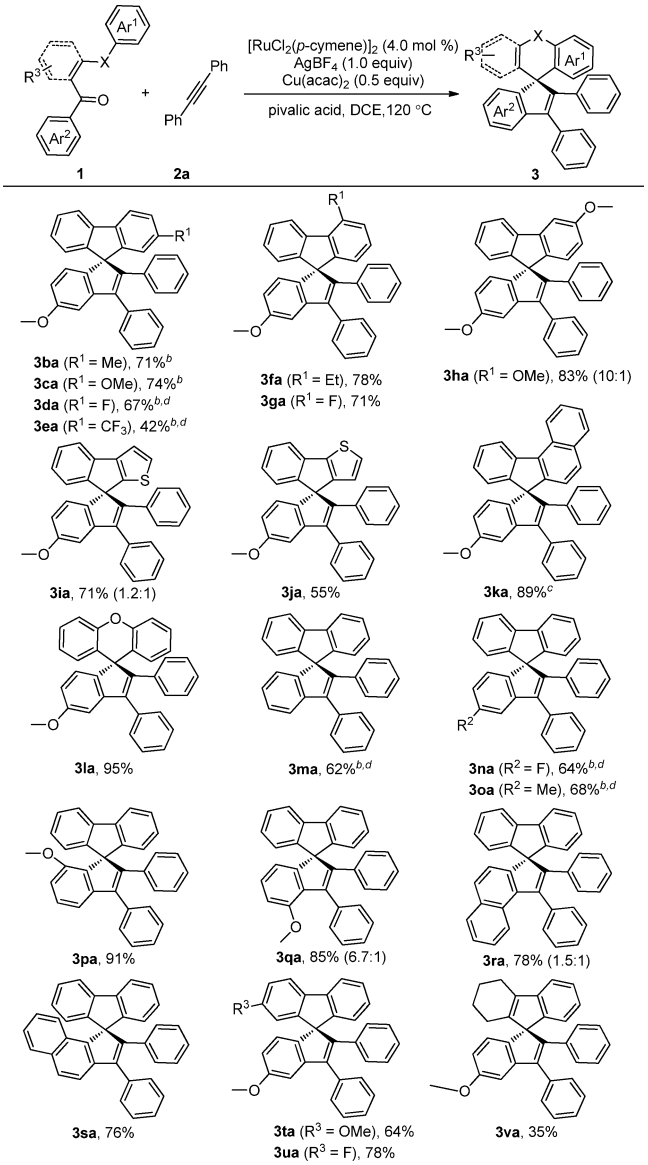
entry	additive	acid	solvent	yield[b] (%)
1	$Cu(OAc)_2$		DCE	trace
2	$Cu(acac)_2$		DCE	NR
3[c]	$AgBF_4$		DCE	26
4[c,d]	$AgBF_4$	pivalic acid	DCE	42
5[c,d]	$AgBF_4$	CH_3COOH	DCE	30
6[c,d]	$AgBF_4$	CF_3COOH	DCE	25
7[c,d]	$AgBF_4/Cu(acac)_2$	pivalic acid	DCE	63
8	$AgBF_4/Cu(acac)_2$	pivalic acid	DCE	73
9	$AgBF_4/Cu(OTf)_2$	pivalic acid	DCE	21
10	$AgBF_4/Cu(OAc)_2$	pivalic acid	DCE	trace
11	$AgBF_4/Cu(acac)_2$	pivalic acid	$CHCl_3$	55
12	$AgBF_4/Cu(acac)_2$	pivalic acid	THF	50
13	$AgBF_4/Cu(acac)_2$	pivalic acid	MeCN	NR
14[e]	$AgBF_4/Cu(acac)_2$	pivalic acid	DCE	**80**

[a]Reaction conditions unless otherwise specified: **1a** (0.04 mmol), **2a** (0.06 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4.0 mol %), silver salt (1.0 equiv), copper salt (0.5 equiv), acid (1.0 equiv), solvent (0.6 mL), 120 °C under Ar atmosphere, 24 h. [b]Isolated yield. [c]Silver salt (0.5 equiv). [d]Acid (0.5 equiv). [e]**2a** (0.04 + 0.032 mmol).

was explored on the reaction (entries 4−6). To our delight, the pivalic acid was more effective, giving the desired product **3aa** in 42% yield. Meanwhile, adding both $AgBF_4$ and $Cu(acac)_2$ in the presence of pivalic acid increased the reaction efficiency (entries 7−10). Screening of the solvents revealed that chloroform and THF were less effective, giving **3aa** in 55% and 50% yields, respectively, while MeCN was completely inert to the reaction process (entries 11−13). In the end, with an alteration of the addition mode of **2a**, the yield of **3aa** was dramatically improved to 80% (entry 14).

With the optimal reaction conditions in hand, we next explored the scope of aryl ketones via a Ru(II)-catalyzed cascade reaction with diphenylacetylene **2a** (Scheme 2). Substituents with different electronic properties at the *para*-position of Ar^1 ring were examined, and the electron-rich groups showed higher reactivity with **2a** albert with moderate to good yields (**3ba**−**ea**). Analogously, substituents at the *ortho*-position of the phenyl ring proceeded smoothly to afford the corresponding products in good yields (**3fa** and **3ga**). With high regioselectivity, treatment of **1h** with **2a** provided **3ha**, along with regioisomer **3ha′**, in good yield. In addition, substrates (**1i** and **1j**) bearing thiophene groups were also compatible under the optimal reactions. Meanwhile, 1-naphthyl-substituted **1k** was tolerated under the present catalytic system, giving **3ka** in 89% yield. Importantly, **1l** led to the product **3la** with six-membered heterocycle in 95% yield. Substitutions (**1n** and **1o**) bearing donating as well as withdrawing groups on the *para*-position of the Ar^2 ring exhibited similar reactivity as substrate **1m** to trigger the cascade reaction. In contrast, the *o*-OMe group on this ring occurred smoothly to furnish **3pa** in 91% yield. Selective C−H activation was even obtained at the more hindered position when the *m*-OMe group was introduced to the Ar^2 ring (**3qa**). Moreover, naphthyl-substituted benzophenone derivatives could participate in this reaction.

Scheme 2. Substrate Scope of Aryl Ketone[a]



[a]Reaction conditions unless otherwise specified: **1** (0.1 mmol), **2a** (0.1 + 0.08 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgBF_4$ (1.0 equiv), $Cu(acac)_2$ (0.5 equiv), pivalic acid (1.0 equiv), DCE (1 mL), 120 °C, 24 h, under Ar atmosphere. Yields are reported for the isolated products. Major isomers are shown. [b]**1** (0.08 mmol), **2a** (0.096 + 0.064 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4.0 mol %), DCE (0.6 mL), 24 h. [c]**1** (0.1 mmol), **2a** (0.1 mmol), 17 h. [d]130 °C, 36 h.

Compound **1r** afforded the isomers in 78% yield with poor regioselectivity, while the reaction of **1s** with **2a** proceeded effectively and gave **3sa** in 76% yield. Compounds **1t** and **1u** are also applicable, and the desired products were generated in good yields. Encouraged by the good tolerance toward diverse functional groups, we found that **1v** can also be utilized in the reaction, though **3va** was formed in only 35% yield. Furthermore, the structure of **3oa** was further confirmed by X-ray diffraction (Figure 1).[10]

To further investigate the scope of this transformation, we tested representative symmetrical and asymmetrical internal alkynes (Scheme 3). It is noteworthy that an array of different electrical properties of arylalkynes underwent the one-pot reaction to provide the corresponding products in moderate to

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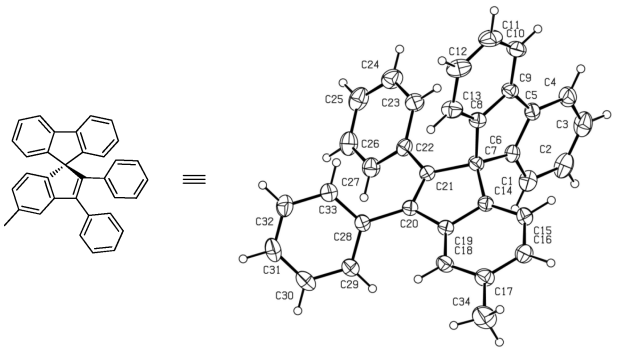
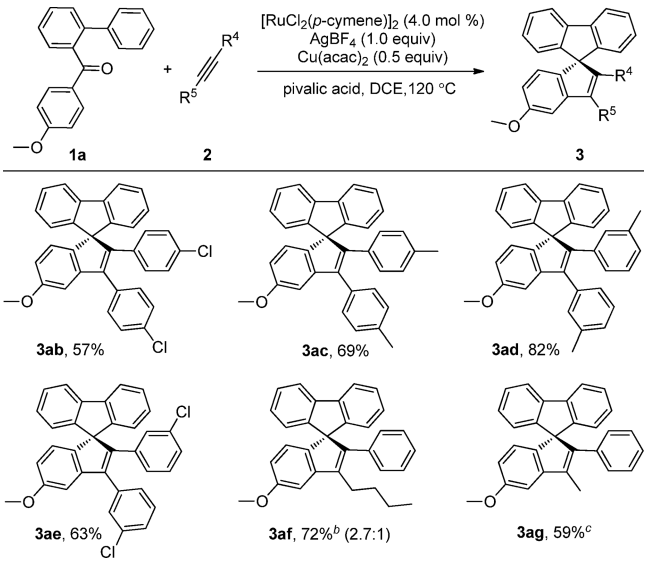


Figure 1. X-ray crystal structure of **3oa** (displacement ellipsoids are drawn at the 50% probability level).

Scheme 3. Substrate Scope of Alkynes[a]



[a]Reaction conditions unless otherwise specified: **1** (0.1 mmol), **2a** (0.1 + 0.08 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgBF_4$ (1.0 equiv), $Cu(acac)_2$ (0.5 equiv), pivalic acid (1.0 equiv), DCE (1 mL), 120 °C, 24 h, under Ar atmosphere. Yields are reported for the isolated products. Major isomers are shown. [b]**1a** (0.1 mmol), **2f** (0.12 + 0.12 mmol), 36 h. [c]**1a** (0.1 mmol), **2g** (0.12 + 3 mmol), 36 h.

good yields (**3ab**−**ae**). In contrast, electron-rich alkynes showed higher reactivity in this catalytic system. To examine the regioselectivity of the first C−H functionalization, disubstituted unsymmetrical alkynes were employed. 4-Butylphenylacetylene **2f** underwent the Ru(II)-catalyzed cascade reaction to deliver the isomers in 72% yield with poor regioselectivity. Fortunately, when unsymmetrical alkyne **2g** was treated with privileged substrate **1a**, a single regioisomeric product **3ag** was produced in 59% yield. It was found that terminal alkynes were not tolerated in the reaction.

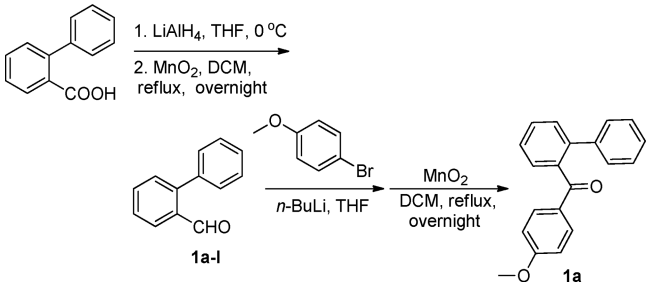
CONCLUSION

In summary, we have developed a highly efficient Ru(II)-catalyzed one-pot synthesis polysubstituted spirofluorene−indene derivatives via [3 + 2] annulation of aryl ketones with internal alkynes and then intramolecular Friedel−Crafts alkylation in moderate to excellent yields. Further applications of the approach to build biologically active molecules are being studied in our laboratory.

EXPERIMENTAL SECTION

ESI HRMS was recorded on a Q-ToF. [1,1′-Biaryl]-2-yl(aryl)-methanones were prepared according to the following general procedure. Alkynes were commercially available.

Preparation of [1,1′-Biaryl]-2-yl(aryl)methanones 1a,l−r. *General Procedure for Synthesis of [1,1′-Biphenyl]-2-carbaldehyde (1a-l).*



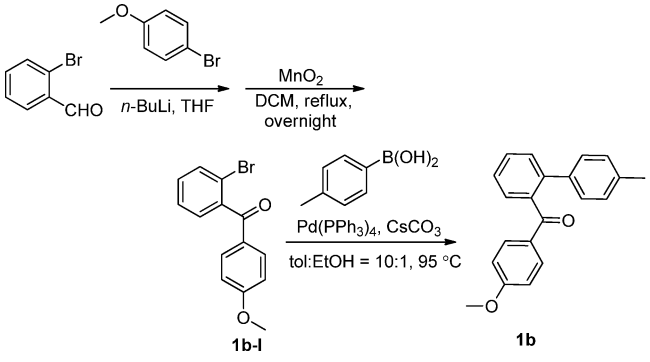
(1) [1,1′-Biphenyl]-2-carboxylic acid (5 g, 25.2 mmol) was dissolved in anhydrous THF (120 mL) under Ar atmosphere and cooled to 0 °C. $LiAlH_4$ (2.4 g, 63 mmol, 2.5 equiv) was added slowly to the solution. The reaction was allowed to warm to room temperature and stirred for 4 h. After the reaction was complete by TLC, it was quenched with aqueous NaOH solution (2 M, 50 mL). The reaction mixture was then poured into water (100 mL) and extracted with DCM (3 × 150 mL), the organic phase was dried over anhydrous Na_2SO_4, and the solution was evaporated in vacuo to give the crude alcohol product as colorless oil.

(2) Manganese dioxide (252 mmol, 10 equiv) was added to a solution of the above alcohol product in CH_2Cl_2. The resulting suspension was heated under reflux overnight. After cooling, the suspension was filtered through a pad of Celite and the organics were concentrated in vacuo. The residue was purified by flash chromatography, eluting with ethyl acetate and petroleum ether (1:50), to afford **1a-I** as a colorless oil (3.2 g, 69%).

General Procedure for Synthesis of [1,1′-Biphenyl]-2-yl(4-methoxyphenyl)methanone (1a). (1) To a solution of **1a-I** (3 mmol) in dried THF (5 mL), under Ar atmosphere at −78 °C, was slowly added a THF solution of organolithium reagent prepared from the *p*-bromoanisole (3.3 mmol, 1.1 equiv). The reaction mixture was stirred at this temperature for 1 h, and then the reaction mixture was allowed to reach room temperature and stirred for 3 h followed by quenching with saturated NH_4Cl. The solvent was removed in vacuo, and resulting reaction mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and filtered, and the solvent was removed in vacuo. The dried crude product was used without further purification.

(2) Manganese dioxide (30 mmol, 10 equiv) was added to a solution of above alcohol in CH_2Cl_2. The resulting suspension was heated under reflux overnight. After cooling, the suspension was filtered through a pad of Celite, and the organics were concentrated under vacuum. The residue was purified by flash chromatography, eluting with ethyl acetate and petroleum ether (1:50), to give the corresponding ketone product **1a** (670 mg, 77%).

Preparation of [1,1′-Biaryl]-2-yl(aryl)methanones 1b−j,s,t.



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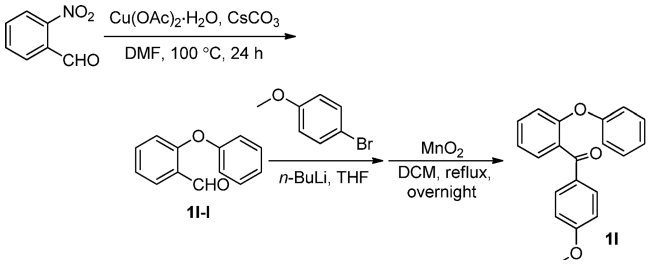
*General Procedure for Synthesis of (2-Bromophenyl)(4-methoxyphenyl)methanone (**1b-I**).* Diaryl ketone **1b-I** was prepared from 2-bromobenzaldehyde following the general procedures for synthesis of **1a**.

*General Procedure for Synthesis of (4-Methoxyphenyl)-(4′-methyl[1,1′-biphenyl]-2-yl)methanone (**1b**).* [1,1′-Biaryl]-2-yl-(aryl)methanone **1b** was prepared from **1b-I** according to the procedures reported in the literature.[11]

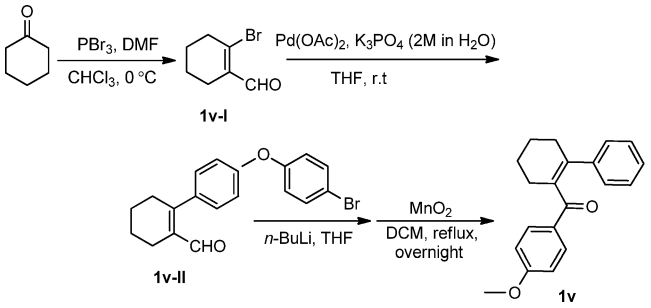
Preparation of (4-Methoxyphenyl)(2-phenoxyphenyl)-methanone (1l).



*General Procedure for Synthesis of 2-Phenoxybenzaldehyde (**1l-I**).* Compound **1l-I** was prepared from 2-nitrobenzaldehyde according to the procedures reported in the literature.[12]

*General Procedure for Synthesis of (4-Methoxyphenyl)-(2-phenoxyphenyl)methanone (**1l**).* Diaryl ketone **1l** was prepared from **1l-I** following the general procedures for synthesis of **1a**.

Preparation of (4-Methoxyphenyl)(3,4,5,6-tetrahydro[1,1′-biphenyl]-2-yl)methanone (1v).



*General Procedure for Synthesis of 3,4,5,6-Tetrahydro[1,1′-biphenyl]-2-carbaldehyde (**1v-II**).* **1v-II** was prepared from cyclohexanone according to the procedures reported in the literature.[13,14]

*General Procedure for Synthesis of (4-Methoxyphenyl)(3,4,5,6-tetrahydro[1,1′-biphenyl]-2-yl)methanone (**1v**).* Compound **1v** was prepared from **1v-II** following the general procedures for synthesis of **1a**.

*General Procedure for the Synthesis of Spirofluorene–Indene Derivatives (**3aa**).* [1,1′-Biphenyl]-2-yl(4-methoxyphenyl)methanone (**1a**) (28.8 mg, 0.1 mmol), diphenylacetylene **2a** (17.8 mg, 0.1 mmol), $[RuCl_2(p\text{-cymene})]_2$ (3.1 mg, 5 mol %), $AgBF_4$ (19.5 mg, 1.0 equiv), $Cu(acac)_2$ (13.1 mg, 0.5 equiv), and pivalic acid (10.2 mg, 1.0 equiv) was stirred in DCE (1.0 mL) under Ar atmosphere at 120 °C. After diphenylacetylene was completely consumed (monitored by TLC), additional **2a** (14.2 mg, 0.8 equiv) was subjected to the reaction mixture. After completion, the reaction mixture was purified by flash chromatography, eluting with ethyl acetate and petroleum ether (1:200), to give the product **3aa** as a yellow oil (35.9 mg, 80%). Recrystallization was performed with dichloromethane and petroleum ether (1:100) to give **3aa** as white solid (27.4 mg, 76%).

*[1,1′-Biphenyl]-2-yl(4-methoxyphenyl)methanone (**1a**):* white solid; 670 mg, 77% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.8 Hz, 2H), 7.58−7.53 (m, 1H), 7.49−7.42 (m, 3H), 7.29−7.26 (m, 2H), 7.24−7.15 (m, 3H), 6.76 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H); ESI HRMS calcd for $C_{20}H_{16}O_2$ $[M + Na]^+$ 311.1048, found 311.1043.

*(4-Methoxyphenyl)(4′-methyl[1,1′-biphenyl]-2-yl)methanone (**1b**):* white solid; 734 mg, 81%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 2H), 7.54−7.52 (m, 1H), 7.47−7.40 (m, 3H), 7.17 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 7.2 Hz, 2H), 6.78 (d, J = 7.8 Hz, 2H), 3.81 (s, 3H), 2.56 (s, 3H); ESI HRMS calcd for $C_{21}H_{18}O_2$ $[M + Na]^+$ 325.1204, found 325.1197.

*(4-Methoxyphenyl)(2-phenoxyphenyl)methanone (**1l**):* colorless oil; 375 mg, 76% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 7.8 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.25−7.18 (m, 3H), 7.03 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 7.8 Hz, 2H), 3.85 (s, 3H); ESI HRMS calcd for $C_{20}H_{16}O_3$ $[M + Na]^+$ 327.0997, found 327.0988.

*(4-Methoxyphenyl)(3,4,5,6-tetrahydro[1,1′-biphenyl]-2-yl)-methanone (**1v**):* colorless oil; 277 mg, 38% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.8 Hz, 2H), 7.12−7.01 (m, 5H), 6.71 (d, J = 8.4 Hz, 1H), 3.77 (s, 3H), 2.50−2.42 (m, 4H), 1.88−1.81 (m, 4H); ESI HRMS calcd for $C_{20}H_{20}O_2$ $[M + Na]^+$ 315.1361, found 315.1353.

*5′-Methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3aa**):* white solid; 35.9 mg, 80% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.8 Hz, 2H), 7.48 (d, J = 7.2 Hz, 2 Hz), 7.40 (t, J = 7.2 Hz, 2H), 7.36−7.32 (m, 3H), 7.17 (t, J = 7.8 Hz, 2H), 7.07 (d, J = 7.2 Hz, 2H), 6.98 (s, 1H), 6.89−6.87 (m, 1H), 6.81 (t, J = 7.8 Hz, 2H), 6.60−6.55 (m, 4H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 147.2, 146.7, 146.5, 142.6, 142.2, 140.9, 135.3, 135.0, 129.6, 128.7, 128.6, 127.7, 127.7, 127.5, 127.4, 126.8, 123.7, 123.0, 120.2, 111.6, 106.8, 69.6, 55.5; ESI HRMS calcd for $C_{34}H_{24}O$ $[M + H]^+$ 449.1905, found 449.1911.

*5′-Methoxy-2-methyl-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ba**):* white solid; 26.3 mg, 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.2 Hz, 2H), 7.41 (t, J = 8.0 Hz, 2H), 7.37−7.29 (m, 2H), 7.15−7.10 (m, 2H), 7.03 (d, J = 7.6 Hz, 1H) 6.97 (d, J = 2 Hz, 1H), 6.89−6.87 (m, 2H), 6.81 (t, J = 7.6 Hz, 2H), 6.61−6. 54 (m, 4H), 3.78 (s, 3H) 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 147.2, 146.7, 146.6, 146.4, 142.5, 142.2, 141.2, 139.6, 137.7, 135.4, 135.0, 129.7, 128.7, 128.7, 128.6, 127.6, 127.5, 127.4, 127.2, 126.8, 124.2, 123.6, 123.0, 119.9, 119.9, 111.6, 106.7, 69.4, 55.5, 21.7; ESI HRMS calcd for $C_{35}H_{26}O$ $[M + H]^+$ 463.2062, found 463.2058.

*2,5′-Dimethoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ca**):* white solid; 28.3 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H), 7.49−7.47 (m, 2 H), 7.42−7.26 (m, 4H), 7.10 (t, J = 7.6 Hz, 1H), 7.03−7.01 (m, 1H), 6.98−6.97 (m, 1H), 6.90−6.87 (m, 2H), 6.82 (t, J = 7.6 Hz, 2H), 6.60−6.56 (m, 5H), 3.78 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 159.4, 148.4, 147.2, 146.6, 146.0, 142.5, 142.1, 141.1, 135.3, 135.2, 135.0, 129.6, 128.7, 128.6, 127.6, 127.5, 127.5, 126.8, 126.6, 123.5, 123.0, 121.0, 119.4, 113.6, 111.6, 109.1, 106.8, 69.5, 55.5, 55.5; ESI HRMS calcd for $C_{35}H_{26}O_2$ $[M + H]^+$ 479.2011, found 479.2002.

*2-Fluoro-5′-methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3da**):* white solid; 27.0 mg, 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.47−7.26 (m, 7H), 7.18 (t, J = 7.6 Hz, 1H), 7.07- 6.89 (m, 4H), 6.82 (t, J = 7.6 Hz, 2H), 6.61−6.53 (m, 4H) 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 147.4 (d, J_{CF} = 205 Hz), 146.6, 146.4, 143.0, 141.0, 140.7, 140.0, 135.0, 134.7, 133.3, 129.6, 128.7, 128.6, 128.1, 128.0, 127.9, 127.7, 127.6, 126.9, 123.9, 123.7, 123.0, 121.1, 120.3, 111.8, 107.0, 69.4, 55.5; ESI HRMS calcd for $C_{34}H_{23}FO$ $[M + K]^+$ 505.1370, found 505.1375.

*5′-Methoxy-2′,3′-diphenyl-2-(trifluoromethyl)spiro[fluorene-9,1′-indene] (**3ea**):* white solid; 17.3 mg, 42% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (t, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 1H), 7.47−7.32 (m, 6H), 7.27−7.23 (m, 2H), 7.10 (d, J = 7.2 Hz, 1H), 6.99 (s, 1H), 6.91−6.88 (m, 1H), 6.80 (t, J = 7.6 Hz, 2H), 6.61−6.59 (m, 1H), 6.54−6.49 (m, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 147.2, 147.1, 146.7, 146.3, 143.2, 140.6, 139.5, 134.9, 134.6, 129.6, 129.0, 128.6, 128.6, 127.8 (q, J_{CF} = 31 Hz), 127.6, 127.0, 125.1 (q, J_{CF} = 3 Hz), 123.9, 121.7 (q, J_{CF} = 275 Hz), 121.0, 120.6 (q, J_{CF} = 4 Hz),, 111.9, 107.1, 69.5, 55.5; ESI HRMS calcd for $C_{35}H_{23}F_3O$ $[M + H]^+$ 517.1779, found 517.1772.

*4-Ethyl-5′-methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3fa**):* white solid; 37.2 mg, 78% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H), 7.47−7.46 (m, 2H), 7.39 (t, J = 7.2 Hz, 2H), 7.35−7.32 (m, 2H), 7.17−7.06 (m, 4H), 6.97−6.96 (m, 1H), 6.93−6.86 (m, 2H), 6.79 (t, J = 7.6 Hz, 2H), 6.59−6.52 (m, 4H),

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3.78 (s, 3H), 3.16−3.10 (m, 2H), 1.40 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 147.5, 146.8, 146.7, 146.7, 142.7, 142.4, 141.3, 139.6, 139.5, 135.4, 135.0, 129.6, 128.7, 128.6, 128.0, 127.6, 127.6, 127.5, 127.4, 127.0, 126.7, 123.6, 123.4, 122.9, 121.2, 111.6, 106.7, 69.4, 55.5, 27.1, 14.2; ESI HRMS calcd for $C_{36}H_{28}O$ $[M + H]^+$ 477.2218, found 477.2227.

*4-Fluoro-5′-methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ga**):* white solid; 33.1 mg, 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 1H), 7.47−7.34 (m, 6H), 7.20 (t, J = 7.6 Hz, 1H), 7.14−6.97 (m, 4H), 6.93−6.81 (m, 4H), 6.61−6.59(m, 4H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 158.4 (d, J_{CF} = 250 Hz), 149.4 (d, J_{CF} = 5 Hz), 146.6, 146.6, 145.9, 142.8, 140.3, 139.3 (d, J_{CF} = 3 Hz), 135.1, 134.8, 129.6, 129.3 (d, J_{CF} = 15 Hz), 128.9 (d, J_{CF} = 7 Hz), 128.7, 128.6, 128.0, 127.9, 127.6, 126.9, 123.7 (d, J_{CF} = 5 Hz), 123.4, 123.0, 119.4 (d, J_{CF} = 3 Hz), 114.8 (d, J_{CF} = 19 Hz), 111.7, 106.9, 69.9, 55.5; ESI HRMS calcd for $C_{34}H_{23}FO$ $[M + H]^+$ 467.1811, found 467.1813.

*(S)-3,5′-Dimethoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ha**). (R)-1,5′-Dimethoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ha′**):* (**3ha**:**3ha′** = 10:1); white solid; 39.8 mg, 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) 7.71 (d, J = 7.6 Hz, 1H, **3ha**), 7.47−7.45 (m, 2H, **3ha** and 1H 3**ha′**), 7.41−7.37 (m, 2H, **3ha** and 3H, **3ha′**), 7.35−7.30 (m, 2H, **3ha** and 4H, **3ha′**), 7.28−7.26 (m, 1H, **3ha** and 3H, **3ha′**), 7.18−7.14 (m, 1H, **3ha** and 2H, **3ha′**), 7.05 (d, J = 7.6 Hz, 1H, **3ha**), 6.98−6.96 (m, 2H, **3ha**), 6.91−6.88 (m, 1H, **3ha** and 1H, **3ha′**), 6.83−6.80 (m, 2H, **3ha** and 3H, **3ha′**), 6.75−6.72 (m, 1H, **3ha**), 6.60−6.55 (m, 4H, **3ha** and 1H, **3ha′**), 3.85 (s, 3H, **3ha**), 3.78 (s, 3H, **3ha** and 3H, **3ha′**), 3.56 (s, 3H, **3ha′**); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 159.3, 151.8, 147.3, 146.5, 143.5, 142.3, 142.0, 141.0, 138.1, 135.3, 135.1, 129.6, 128.6, 128.6, 128.5, 127.8, 127.5, 127.4, 126.7, 124.3, 123.6, 122.8, 120.1, 114.4, 111.6, 106.7, 105.3, 68.9, 55.5, 53.4; ESI HRMS (**3ha** + **3ha′**) calcd for $C_{35}H_{26}O_2$ $[M + H]^+$ 479.2011, found 479.2016.

*5-Methoxy-2,3-diphenylspiro[indene-1,8′-indeno[2,1-b]-thiophene] (**3ia**):* white solid; 14.7 mg, 71% yield (**3ia**:**3ia′** = 1.2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 7.2 Hz, 1H), 7.49−7.26 (m, 8H), 7.21 (d, J = 4.4 Hz, 1H), 7.16−7.14 (m, 3H), 7.09−7.03 (m, 3H), 6.69 (d, J = 8.0 Hz, 1H), 6.63−6.55 (m, 2H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 151.0, 150.3, 148.0, 144.9, 138.7, 136.4, 135.3, 134.7, 131.5, 129.8, 129.7, 129.2, 128.7, 128.0, 127.5, 127.2, 126.3, 125.8, 124.8, 124.3, 119.6, 118.4, 117.3, 111.7, 110.4, 86.0, 55.2; ESI HRMS calcd for $C_{32}H_{22}OS$ $[M + Na]^+$ 477.1289, found 477.1280.

*5-Methoxy-2,3-diphenylspiro[indene-1,8′-indeno[1,2-c]-thiophene] (**3ia′**).* white solid; 17.6 mg, 71% yield (**3ia**:**3ia′** = 1.2:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (d, J = 7.8 Hz, 1H), 7.44 (d, J = 7.2 Hz, 2H), 7.39−7.31 (m, 4H), 7.27−7.24 (m, 2H), 7.05 (t, J = 7.2 Hz, 1H), 6.99−6.91 (m, 3H), 6.85 (t, J = 8.4 Hz, 2H), 6.66−6.61 (m, 4H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 150.3, 148.1, 147.1, 146.4, 146.3, 142.3, 139.5, 139.3, 135.0, 134.6, 130.0, 129.5, 128.6, 128.6, 127.5, 127.5, 127.4, 126.9, 125.5, 123.0, 122.8, 119.5, 118.7, 111.7, 106.9, 67.4, 55.5; ESI HRMS calcd for $C_{32}H_{22}OS$ $[M + K]^+$ 493.1028, found 493.1030.

*5-Methoxy-2,3-diphenylspiro[indene-1,4′-indeno[1,2-b]-thiophene] (**3ja**):* white solid; 17.6 mg, 55% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.43 (m, 3H), 7.40−7.25 (m, 5H), 7.06−7.03 (m, 1H), 6.98−6.91 (m, 3H), 6.87−6.83 (m, 2H), 6.72−6.59 (m, 5H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 149.8, 149.3, 146.7, 145.8, 143.9, 142.4, 139.1, 138.3, 135.2, 134.9, 129.6, 128.6, 128.5, 128.1, 127.6, 127.5, 126.9, 125.9, 123.3, 122.3, 122.7, 121.4, 119.1, 111.6, 106.9, 67.1, 55.5; ESI HRMS calcd for $C_{32}H_{22}OS$ $[M + Na]^+$ 477.1289, found 477.1280.

*5′-Methoxy-2′,3′-diphenylspiro[benzo[c]fluorene-7,1′-indene] (**3ka**):* white solid; 44.3 mg, 89% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (d, J = 7.8 Hz, 1H), 8.37 (d, J = 7.2 Hz, 1H), 7.92 (d, J = 7.2 Hz, 1H), 7.70−7.67 (m, 2H), 7.55−7.37 (m, 7H), 7.26−7.19 (m, 3H), 7.02 (s, 1H), 6.85−6.75 (m, 3H), 6.60−6.51 (m, 4H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 147.1, 147.0, 146.4, 145.5, 143.3, 143.3, 139.8, 136.9, 135.4, 134.9, 134.1, 129.7, 129.7, 129.3, 128.9, 128.7, 128.6, 127.8, 127.6, 127.5, 126.9, 126.8, 126.7, 125.4, 123,8, 123.6, 123.2, 122.9, 121.7, 111.7, 107.0, 69.8, 55.5; ESI HRMS calcd for $C_{38}H_{26}O$ $[M + H]^+$ 499.2062, found 499.2067.

*5-Methoxy-2,3-diphenylspiro[indene-1,9′-xanthene] (**3la**):* white solid; 44.1 mg, 95% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.31 (m, 5H), 7.19−7.14 (m, 2 H), 7.07 (d, J = 8.0 Hz, 2H), 7.08−6.83 (m, 9H), 6.70−6.65 (m, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 153.9, 151.4, 150.1, 144.6, 140.0, 135.1, 134.9, 129.5, 129.4, 128.6, 128.2, 127.6, 127.6, 127.6, 127.0, 125.1, 123.3, 122.1, 116.9, 112.2, 106.8, 57.5, 55.5; ESI HRMS calcd for $C_{34}H_{24}O_2$ $[M + Na]^+$ 487.1674, found 487.1681.

*2′,3′-Diphenylspiro[fluorene-9,1′-indene] (**3ma**):* white solid; 20.7 mg, 62% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, J = 7.2 Hz, 2H), 7.48 (d, J = 7.2 Hz, 2H), 7.43−7.39 (m, 3H), 7.34 (t, J = 7.8 Hz, 3H), 7.27−7.24 (m, 1H), 7.17 (t, J = 7.2 Hz, 2H), 7.07−7.02 (m, 3H), 6.90−6.88 (m, 1H), 6.81 (t, J = 7.8 Hz, 2H), 6.63 (d, J = 7.2 Hz, 1H), 6.58 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 146.2, 145.7, 145.2, 142.8, 142.3, 135.4, 135.0, 129.7, 128.7, 128.6, 127.8, 127.7, 127.5, 127.1, 126.8, 126.3, 123.7, 122.4, 120.7, 120.3, 70.2; ESI HRMS calcd for $C_{33}H_{22}$ $[M + K]^+$ 457.1359, found 457.1364.

*5′-Fluoro-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3na**):* white solid; 22.3 mg, 64% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.77 (d, J = 7.6 Hz, 2H), 7.47−7.33 (m, 7H), 7.18 (t, J = 7.6 Hz, 2H), 7.14−7.11 (m, 1H), 7.06 (d, J = 7.6 Hz, 2H), 6.92−6.89 (m, 1H), 6.82 (t, J = 8.0 Hz, 2H), 6.74−6.70 (m, 1H), 6.58−6.56 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (d, J_{CF} = 242 Hz), 147.8, 147.2 (d, J_{CF} = 8 Hz), 145.7, 144.1 (d, J_{CF} = 2 Hz), 142.2, 142.0 (d, J_{CF} = 3 Hz), 134.8, 134.6, 129.5, 128.7, 128.6, 127.9, 127.8, 127.5, 127.0, 123.6, 123.4 (d, J_{CF} = 9 Hz), 120.4, 112.8 (d, J_{CF} = 23 Hz), 108.0 (d, J_{CF} = 24 Hz), 69.6; ESI HRMS calcd for $C_{33}H_{22}F$ $[M + H]^+$ 437.1706, found 437.1714.

*5′-Methyl-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3oa**).* white solid; 23.5 mg, 68% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, J = 7.8 Hz, 2H), 7.49−7.48 (m, 2H), 7.42 (t, J = 7.2 Hz, 2H), 7.37−7.33 (m, 3H), 7.23 (s, 1H), 7.17 (t, J = 7.2 Hz, 2H), 7.07 (d, J = 7.2 Hz, 2H), 6.90−6.86 (m, 2H), 6.82−6.79 (m, 2H), 6.59−6.57 (m, 2H) 6.54−6.53 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 146.1, 146.0, 145.4, 142.8, 142.2, 136.8, 135.6, 135.1, 129.7, 128.7, 128.6, 127.8, 127.7, 127.5, 127.5, 127.1, 126.7, 123.7, 122.1, 121.4, 120.2, 69.9, 21.6; ESI HRMS calcd for $C_{34}H_{24}$ $[M + H]^+$ 433.1956, found 433.1966.

*7′-Methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3pa**):* white solid; 40.8 mg, 91% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 7.2 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.38 (t, J = 7.2 Hz, 2H), 7.34−7.29 (m, 4H), 7.17 (t, J = 7.8 Hz, 2H), 7.13−7.10 (m, 3H), 6.89−6.87 (m, 1H), 6.81−6.79 (m, 2H), 6.65 (d, J = 7.8 Hz, 1H), 6.53 (d, J = 7.8 Hz, 2H), 3.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 147.4, 147.4, 144.7, 142.2,135.5, 135.5, 134.9, 129.7, 128.9, 128.8, 128.4, 127.3, 127.3, 127.2, 126.7, 123.1, 119.8, 113.8, 110.9, 69.1, 56.0; ESI HRMS calcd for $C_{34}H_{24}O$ $[M + Na]^+$ 471.1725, found 471.1732.

*4′-Methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3qa**). 6′-Methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene (**3qa′**):* (**3qa**:**3qa′** = 6.7:1); white solid; 38.1 mg, 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.72 (m, 2H, **3qa** and 2H, **3qa′**), 7.47−7.36(m, 2H, **3qa** and 2H, **3qa′**), 7.33−7.22 (m, 5H, **3qa** and 6H, **3qa′**), 7.16 (t, J = 7.6 Hz, 2H, **3qa**), 7.10−7.05 (m, 2H, **3qa** and 1H, **3qa′**), 6.97 (t, J = 8.0 Hz, 1H, **3qa**), 6.83−6.72 (m, 4H, **3qa** and 3H, **3qa′**), 6.54 (d, J = 7.2 Hz, 2H, **3qa′**), 6.53−6.48 (m, 2H, **3qa**), 6.25−6.18 (m, 1H, **3qa** and 1H, **3qa′**), 3.63 (s, 3H, **3qa**), 3.59 (s, 3H, **3qa′**); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.3, 151.0, 146.2, 145.1, 142.7, 142.2, 137.1, 135.1, 132.3, 130.3, 128.8, 127.7, 127.6, 127.4, 127.2, 127.2, 126.7, 126.3, 123.6, 120.2, 115.3, 110.7; ESI HRMS (**3qa** + **3qa′**): calcd for $C_{34}H_{24}O$ $[M + Na]^+$ 471.1725, found 471.1728.

*1,2-Diphenylspiro[cyclopenta[a]naphthalene-3,9′-fluorene] (**3ra**):* white solid; 21.9 mg, 78% yield; (**3ra**:**3ra′** = 1.5:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 7.2 Hz, 2H), 7.64 (d, J = 8.4 Hz, 1H), 7.51−7.41 (m, 8H), 7.34−7.25 (m, 5H), 7.12 (d, J = 7.8 Hz, 2H), 7.09−7.02 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 148.1, 139.8, 136.9, 135.7, 133.5, 132.6,

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131.9, 131.6, 131.1, 129.8, 129.2, 128.5, 127.9, 127.7, 127.4, 127.3, 126.2, 125.6, 125.5, 122.8, 120.2, 115.9, 87.5; ESI HRMS calcd for $C_{37}H_{24}$ $[M + H]^+$ 469.1956, found 469.1962.

*2,3-Diphenylspiro[cyclopenta[b]naphthalene-1,9′-fluorene] (**3ra′**):* white solid; 14.6 mg, 78% yield; (**3ra**:**3ra′** = 1.5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.80 (m, 4H), 7.57−7.52 (m, 3H), 7.46 (t, J = 7.6 Hz, 2H), 7.41−7.29 (m, 5H), 7.18 (t, J = 7.6 Hz, 2H), 7.11 (d, J = 7.2 Hz, 2H), 7.06 (s, 1H), 6.91−6.89 (m, 1H), 6.83 (t, J = 7.6 Hz, 2H), 6.61 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 147.0, 147.0, 144.1, 142.8, 142.2, 135.4, 134.9, 133.4, 132.8, 129.8, 128.8, 128.7, 128.1, 128.0, 127.8, 127.7, 127.5, 127.0, 125.5, 125.3, 124.0, 121.0, 120.3, 118.8, 69.5; ESI HRMS calcd for $C_{37}H_{24}$ $[M + K]^+$ 507.1515, found 507.1522.

*2,3-Diphenylspiro[cyclopenta[a]naphthalene-1,9′-fluorene] (**3sa**):* white solid; 35.6 mg, 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 1H), 7.83−7.80 (m, 3H), 7.70 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 7.2 Hz, 2H), 7.40−7.30 (m, 5H), 7.24−7.20 (m, 1H), 7.12 (t, J = 7.2 Hz, 2H), 7.02−6.98 (m, 3H), 6.91−6.87 (m, 1H), 6.80 (t, J = 7.6 Hz, 2H), 6.71 (d, J = 8.4 Hz, 1H), 6.47 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 145.8, 143.5, 142.6, 142.1, 142.0, 135.2, 134.8, 132.8, 129.8, 129.1, 128.7, 128.6, 128.5, 127.8, 127.8, 127.4, 127.3, 126.6, 124.5, 123.9, 123.0, 120.5, 119.6, 70.9; ESI HRMS calcd for $C_{37}H_{24}$ $[M + H]^+$ 469.1956, found 469.1949.

*(S)-2,6′-Dimethoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ta**):* white solid; 30.6 mg, 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.4 Hz, 2H), 7.47−7.45 (m, 2H), 7.41−7.24 (m, 4H), 7.08(t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 6.96 (s, 1H), 6.88−6.86 (m, 2H), 6.80 (t, J = 7.6 Hz, 2H), 6.59−6.54 (m, 5H), 3.77 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 159.4, 148.4, 147.2, 146.6, 146.1, 142.6, 142.1, 141.1, 135.3, 135.2, 135.0, 129.6, 128.7, 128.6, 127.6, 127.5, 127.5, 126.8, 126.6, 123.5, 123.0, 120.9, 119.4, 113.7, 116.7, 109.1, 106.8, 69.5, 55.5, 55.5; ESI HRMS calcd for $C_{35}H_{26}O_2$ $[M + H]^+$ 479.2011, found 479.2008.

*2-Fluoro-7′-methoxy-2′,3′-diphenylspiro[fluorene-9,1′-indene] (**3ua**):* white solid; 36.4 mg, 78% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.64 (m, 2H), 7.46−7.45 (m, 2H), 7.39 (t, J = 7.2 Hz, 2H), 7.35−7.30 (m, 2H), 7.15 (t, J = 7.2 Hz, 1H), 7.06−6.97 (m, 3H), 6.91−6.87 (m, 1H), 6.81 (t, J = 7.2 Hz, 2H), 6.75 (d, J = 8.4 Hz, 1H), 6.60−6.53 (m, 4H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, J_{CF} = 245 Hz), 159.6, 149.0 (d, J_{CF} = 8.0 Hz), 146.7, 146.6, 146.4 (d, J_{CF} = 2 Hz), 143.0, 141.3, 140.3, 138.1 (d, J_{CF} = 3 Hz), 135.1, 134.8, 129.6, 128.7, 128.7, 127.8, 127.7, 127.6, 127.5, 126.9, 123.7, 123.0, 121.2 (d, J_{CF} = 9 Hz), 119.9, 114.9 (d, J_{CF} = 23 Hz), 111.8, 111.0 (d, J_{CF} = 23 Hz), 107.0, 69.5 (d, J_{CF} = 2 Hz), 55.5; ESI HRMS calcd for $C_{34}H_{23}FO$ $[M + H]^+$ 467.1811, found 467.1819.

*5′-Methoxy-2′,3′-diphenyl-1,2,3,4-tetrahydrospiro[fluorene-9,1′-indene] (**3va**):* white solid; 15.8 mg, 35% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41−7.40 (m, 2H), 7.38−7.36 (m, 2H), 7.33−7.31 (m, 1H), 7.24−7.21 (m, 2H), 7.01−6.96 (m, 2H), 6.92−6.90 (m, 4H), 6.70 (d, J = 7.2 Hz, 2H), 6.62 (s, 2H), 3.77 (s, 3H), 2.56−2.43 (m, 2H), 1.90−1.73 (m, 4H), 1.64−1.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 147.3, 146.5, 145.9, 145.4, 144.3, 142.8, 138.4, 138.0, 135.6, 135.2, 129.6, 128.6, 128.3, 127.5, 127.4, 126.9, 126.7, 124.9, 122.1, 121.8, 117.9, 111.4, 106.5, 72.1, 55.4, 22.9, 22.6, 22.5, 22.1; ESI HRMS calcd for $C_{34}H_{28}O$ $[M + Na]^+$ 475.2038, found 475.2047.

*2′,3′-Bis(4-chlorophenyl)-5′-methoxyspiro[fluorene-9,1′-indene] (**3ab**):* white solid; 29.4 mg, 57% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.2 Hz, 2H), 7.38−7.33 (m, 6H), 7.17 (t, J = 7.6 Hz, 2H), 7.01 (d, J = 7.6 Hz, 2H), 6.92−6.91 (m, 1H), 6.79 (d, J = 8.4 Hz, 2H), 6.62−6.55 (m, 2H), 6.44 (d, J = 8.4 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 146.6, 146.0, 145.8, 142.2, 141.8, 140.6, 133.6, 133.4, 133.2, 132.8, 130.9, 129.8, 129.1, 128.0, 127.9, 127.9 123.6, 123.2, 120.4, 112.0, 106.7, 69.5, 55.5; ESI HRMS calcd for $C_{34}H_{22}Cl_2O$ $[M + Na]^+$ 539.0945, found 539.0950, 541.0929, 543.0929.

*5′-Methoxy-2′,3′-di-p-tolylspiro[fluorene-9,1′-indene] (**3ac**):* white solid; 32.9 mg, 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 2H), 7.38−7.31 (m, 4H), 7.21 (d, J = 7.6 Hz, 2H), 7.16 (t, J = 7.6 Hz, 2H), 7.05 (d, J = 7.6 Hz, 2H), 6.95 (d, J = 2.4 Hz, 1H), 6.62−6.46 (m, 6H), 3.77 (s, 3H), 2.40 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 147.0, 146.8, 146.5, 142.1, 140.9, 137.1, 136.3, 132.5, 132.1, 129.5, 129.4, 128.4, 128.2, 127.7, 127.5, 123.7, 122.8, 120.2, 111.5, 106.6, 69.4, 55.5, 21.4, 21.1; ESI HRMS calcd for $C_{36}H_{28}O$ $[M + H]^+$ 477.2218, found 477.2212.

*5′-Methoxy-2′,3′-di-m-tolylspiro[fluorene-9,1′-indene] (**3ad**):* white solid; 39.1 mg, 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 2H), 7.35−7.32 (m, 3H), 7.29−7.25 (m, 2H), 7.19−7.15 (m, 3H), 7.06 (d, J = 7.6 Hz, 2H), 6.97−6.96 (m, 1H), 6.70−6.68 (m, 2H), 6.59−6.53 (m, 2H), 6.38−6.36 (m, 2H), 3.78 (s, 3H), 2.37 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 146.9, 146.9, 146.7, 142.6, 142.1, 140.9, 138.1, 136.5, 135.4, 134.8, 130.1, 129.4, 128.5, 128.2, 127.7, 127.6, 127.5, 127.2, 126.7, 125.8, 123.7, 122.8, 120.1, 111.4, 106.9, 69.5, 55.5, 21.6, 21.2; ESI HRMS calcd for $C_{36}H_{28}O$ $[M + H]^+$ 477.2218, found 477.2217.

*2′,3′-Bis(3-chlorophenyl)-5′-methoxyspiro[fluorene-9,1′-indene] (**3ae**):* white solid; 32.5 mg, 63% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, J = 7.8 Hz, 2H), 7.48 (s, 1H), 7.37−7.32 (m, 4H), 7.30−7.29 (m, 1H), 7.19 (t, J = 7.8 Hz, 2H), 7.03 (d, J = 7.2 Hz, 2H), 6.95 (s, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.76 (t, J = 7.8 Hz, 1H), 6.63−6.58 (m, 2H), 6.49 (s, 1H), 6.42 (d, J = 8.4 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 146.7, 145.7, 145.5, 142.2, 141.9, 140.5, 136.6, 136.3, 134.5, 133.3, 130.0, 129.3, 128.8, 128.4, 128.0, 127.9, 127.8, 127.8, 127.2, 126.8, 123.5, 123.2, 120.3, 112.0, 106.9, 69.5, 55.5; ESI HRMS calcd for $C_{34}H_{22}Cl_2O$ $[M + H]^+$ 517.1126, found 517.1117, 519.1102.

*3′-Butyl-5′-methoxy-2′-phenylspiro[fluorene-9,1′-indene] (**3af**). 2′-Butyl-5′-methoxy-3′-phenylspiro[fluorene-9,1′-indene] (**3af′**):* (**3af**:**3af′** = 2.7:1); yellow oil; 30.8 mg, 72% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.6 Hz, 2H, **3af**), 7.47−7.26 (m, 3H, **3af** and 4H, **3af′**), 7.18−7.15 (m, 2H, **3af** and 2H, **3af′**), 7.13−6.91 (m, 5H, **3af** and 6H, **3af′**), 6.81−6.76 (m, 2H, **3af′**) 6.68 (d, J = 6.4 Hz, 2H, **3af**), 6.59−6.51 (m, 2H, **3af** and 2H, **3af′**), 3.89−3.85 (m, 3H, **3af** and 3H, **3af′**), 2.75−2.64 (m, 2H, **3af** and 2H, **3af′**), 1.78−1.70 (m, 2H, **3af**), 1.59−1.27 (m, 2H, **3af** and 4H, **3af′**), 1.01−0.90 (m, 3H, **3af** and 3H, **3af′**); ESI HRMS (**3af** + **3af′**) calcd for $C_{32}H_{28}O$ $[M + Na]^+$ 451.2038, found 451.2045.

*5′-Methoxy-3′-methyl-2′-phenylspiro[fluorene-9,1′-indene] (**3ag**):* white solid; 22.8 mg, 59% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (d, J = 8.4 Hz, 2H), 7.29 (t, J = 7.2 Hz, 2H), 7.13 (t, J = 7.8 Hz, 2H), 7.01−6.95 (m, 6H), 6.73−6.72 (m, 2H), 6.57−6.50 (m, 2H), 3.85 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 148.0, 146.6, 146.1, 142.1, 140.6, 137.4, 135.5, 128.3, 127.6, 127.5, 127.5, 126.8, 123.6, 122.5, 120.0, 111.1, 105.5, 69.5, 55.5, 12.2; ESI HRMS calcd for $C_{29}H_{22}O$ $[M + H]^+$ 387.1749, found 387.1741.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01517.

Crystallographic data for **3oa** (CIF)

Structural proofs and NMR spectra for the products (PDF)

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Notes

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REFERENCES

(1) For reviews, see: (a) Watson, M. D.; Fechtenkotter, A.; Mullen, K. *Chem. Rev.* **2001**, *101*, 1267. (b) Chandrasekhar, S.; Li, q. *Liq. Cryst.* **1993**, *14*, 3. (c) Pérez, D.; Guitián, E. *Chem. Soc. Rev.* **2004**, *33*, 274. (d) Buess, C. M.; Lawson, D. D. *Chem. Rev.* **1960**, *60*, 313. (e) Sergeyev, S.; Pisula, W.; Geerts, Y. H. *Chem. Soc. Rev.* **2007**, *36*, 1902.

(2) (a) Kowada, T.; Yamaguchi, S.; Ohe, K. *Org. Lett.* **2010**, *12*, 296. (b) Wu, C.-C.; Liu, T.-L.; Hung, W.-Y.; Lin, Y.-T.; Wong, K.-T.; Chen, R.-T.; Chen, Y.-M.; Chien, Y.-Y. *J. Am. Chem. Soc.* **2003**, *125*, 3710. (c) Jiang, Z.; Yao, H.; Zhang, Z.; Yang, C.; Liu, Z.; Tao, Y.; Qin, J.; Ma, D. *Org. Lett.* **2009**, *11*, 2607. (d) Fan, C.; Chen, Y.; Gan, P.; Yang, C.; Zhong, C.; Qin, J.; Ma, D. *Org. Lett.* **2010**, *12*, 5648. (e) Wu, R.; Schumm, J. S.; Pearson, D. L.; Tour, J. M. *J. Org. Chem.* **1996**, *61*, 6906. (f) Pei, J.; Ni, J.; Zhou, X.-H.; Cao, X.-Y.; Lai, Y.-H. *J. Org. Chem.* **2002**, *67*, 8104. (g) Franco, I.; Tretiak, S. *J. Am. Chem. Soc.* **2004**, *126*, 12130. (h) Steuber, F.; Staudigel, J.; Stössel, M.; Simmerer, J.; Winnacker, A.; Spreitzer, H.; Weissörtel, F.; Salbeck, J. *Adv. Mater.* **2000**, *12*, 130. (i) Wu, C.-C.; Lin, Y.-T.; Wong, K.-T.; Chen, R.-T.; Chien, Y.-Y. *Adv. Mater.* **2004**, *16*, 61. (j) Setayesh, S.; Grimsdale, A. C.; Weil, T.; Enkelmann, V.; Müllen, K.; Meghdadi, F.; List, E. J. W.; Leising, G. *J. Am. Chem. Soc.* **2001**, *123*, 946. (k) Poriel, C.; Ferrand, Y.; Le Maux, P.; Paul, C.; Raul-Berthelot, J.; Simonneaux, G. *Chem. Commun.* **2003**, 2308.

(3) (a) Yu, W.-L.; Pei, J.; Huang, W.; Heeger, A. J. *Adv. Mater.* **2000**, *12*, 828. (b) Wong, K.-T.; Ku, S.-Y.; Cheng, Y.-M.; Lin, X.-Y.; Hung, Y.-Y.; Pu, S.-C.; Chou, P.-T.; Lee, G.-H.; Peng, S.-M. *J. Org. Chem.* **2006**, *71*, 456. (c) Wu, C.-L.; Chen, C.-T.; Chen, C.-T. *Org. Lett.* **2014**, *16*, 2114. (d) Thiemann, F.; Piehler, T.; Haase, D.; Saak, W.; Lützen, A. *Eur. J. Org. Chem.* **2005**, *2005*, 1991. (e) Kim, Y.-H.; Shin, D.-C.; Kim, S.-H.; Ko, C.-H.; Yu, H.-S.; Chae, Y.-S.; Kwon, S.-K. *Adv. Mater.* **2001**, *13*, 1690. (f) Lee, H.; Oh, J.; Chu, Y.; Lee, J.-I.; Kim, S. H.; Yang, Y. S.; Kim, G. H.; Do, L.-M.; Zyung, T.; Lee, J.; Park, Y. *Tetrahedron* **2003**, *59*, 2773.

(4) Zhou, C.; Chen, X.-P.; Lu, P.; Wang, Y.-G. *Tetrahedron* **2012**, *68*, 2844.

(5) For selected reviews, see: (a) De Sarkar, S.; Liu, W.-P.; Kozhushkov, S. I.; Ackermann, L. *Adv. Synth. Catal.* **2014**, *356*, 1461. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (c) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (d) Davies, H. M. L.; Du Bois, J.; Yu, J.-Q. *Chem. Soc. Rev.* **2011**, *40*, 1855. (e) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (f) Baudoin, O. *Chem. Soc. Rev.* **2011**, *40*, 4902. (g) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (h) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (i) Zhao, D.; You, J.; Hu, C. *Chem. - Eur. J.* **2011**, *17*, 5466. (j) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (k) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (l) Li, B.-J.; Shi, Z.-J. *Chem. Soc. Rev.* **2012**, *41*, 5588. (m) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960. (n) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (o) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (p) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369. (q) Satoh, T.; Miura, M. *Chem. - Eur. J.* **2010**, *16*, 11212. (r) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651.

(6) For selected Pd-catalyzed C−H activation, see: (a) Curto, J. M.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2015**, *137*, 18. (b) Wang, C.; Rakshit, S.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 14006. (c) Gandeepan, P.; Parthasarathy, K.; Cheng, C.-H. *J. Am. Chem. Soc.* **2010**, *132*, 8569.

(7) (a) Patureau, F. W.; Besset, T.; Kuhl, N.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2154. (b) Muralirajan, K.; Parthasarathy, K.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2011**, *50*, 4169.

(8) (a) Zuo, Z. J.; Yang, X.; Liu, J. J.; Nan, J.; Bai, L.; Wang, Y. Y.; Luan, X. J. *J. Org. Chem.* **2015**, *80*, 3349. (b) Chinnagolla, R.-K.; Jeganmohan, M. *Eur. J. Org. Chem.* **2012**, *2012*, 417.

(9) (a) Zhang, L.; Zheng, L.-Y.; Guo, B.; Hua, R.-M. *J. Org. Chem.* **2014**, *79*, 11541. (b) Li, J.-H.; Benard, S.; Neuville, L.; Zhu, J.-P. *Org. Lett.* **2012**, *14*, 5980.

(10) Crystallographic data for **3oa**: CCDC 1400893, $C_{34}H_{24}$, M 432.53, space group: $P21/n$, cell: a = 10.4443(4) Å, b = 17.7411(8) Å, c = 12.8612(7) Å, α = 90, β = 92.330(4), γ = 90, T 293 K, calcd 1.207 mg/mm^3.

(11) Núñez, A.; Cuadro, A. M.; Alvarez-Builla, J.; Vaquero, J. J. *Org. Lett.* **2007**, *9*, 2977.

(12) Chen, J.-X.; Wang, X.-Y.; Zheng, X.-W.; Ding, J.-C.; Liu, M.-C.; Wu, H.-Y. *Tetrahedron* **2012**, *68*, 8905.

(13) Gogoi, J.; Gogoi, P.; Bezbaruah, P.; Boruah, R. C. *Tetrahedron Lett.* **2013**, *54*, 7136.

(14) Gogoi, P.; Bezboruah, P.; Boruah, R. C. *Eur. J. Org. Chem.* **2013**, *2013*, 5032.

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