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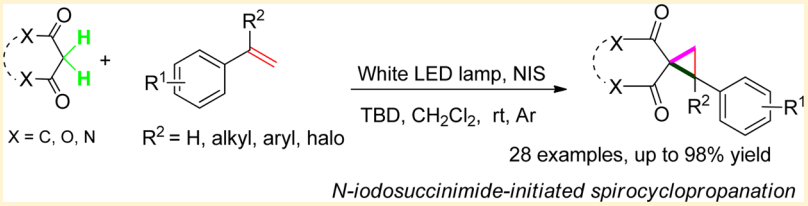
N-Iodosuccinimide-Initiated Spirocyclopropanation of Styrenes with 1,3-Dicarbonyl Compound for the Synthesis of Spirocyclopropanes

Ping Qian,[†] Bingnan Du,[†] Ruichun Song,[†] Xiaodong Wu,[‡] Haibo Mei,[†] Jianlin Han,*[,†] and Yi Pan[†]

[†]School of Chemistry and Chemical Engineering, State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing 210093, China

[‡]MaAnShan High-Tech Research Institute of Nanjing University, MaAnShan 238200, China

Supporting Information



N-iodosuccinimide-initiated spirocyclopropanation

ABSTRACT: Herein is reported an *N*-iodosuccinimide-initiated spirocyclopropanation reaction of styrenes with 1,3-dicarbonyl compounds in the presence of white LED light. The reaction proceeds via two C−H and two C−I bond cleavage event, along with two C−C bond formation event, and formation of quaternary centers. These reactions could be carried out at room temperature and tolerated a wide range of substrates, resulting in good to excellent chemical yields. This developed radical reaction provides easy and practical access to spiro[2.4]heptane-4,7-dione derivatives.

INTRODUCTION

The spirocyclopropanes represent an important class of organic compounds in the field of organic chemistry, which show a diverse range of biological activities, such as anti-inflammatory, antibiotic, analgesic, anticancer, and cytotoxic activity.[1] This spirocyclopropane functionality is also a unique structure occurring in a number of natural products (Figure 1).[2]

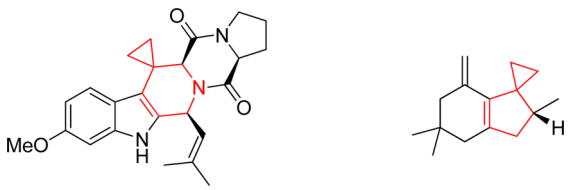


Figure 1. Natural products containing spirocyclopropane unit.

Furthermore, the spirocyclopropanes could be used as versatile tools for the preparation of natural and other organic compounds.[3] For example, the Carreira group reported the total synthesis of Gelsemoxonine by using the spirocyclopropane isoxazolidine ring contraction as a key step.[4] Among the various types of spirocyclopropanes skeletons, the spiro[2.4]-heptane-4,7-dione derivatives play an important role and have been demostrated to show antimicrobial and nematicidal activities.[5] Thus, there is a compelling interest in the development of efficient synthetic methodologies to access such a privileged structure. However, there have been only a few examples reported for the synthesis of spiro[2.4]heptane-4,7-dione derivatives until now.[5] In 2000, a rhodium acetate-catalyzed cyclopropanation reaction of 2-diazo-1-indanone with various substituted styrenes was developed for the construction of spiro[2.4]heptane-4,7-dione derivatives (Scheme 1a).[6] The Barba group reported an electrochemical reduction synthetic method by using 2,2-dibromo-1,3-indandione and styrene as substrates (Scheme 1a).[7] The Bavantula group reported a one-pot two-step tandem reaction starting from pyridine, 4-chloro phenacyl bromide, 1,3-indandione, and aromatic aldehydes using triethylamine as catalyst for the synthesis of polysubstituted spirocyclopropane derivatives (Scheme 1b).[5] Recently, the Yakura group also reported a synthetic method for cyclopentane-1,3-dione-2-spirocyclopropanes from 1*H*-indene-1,3(2*H*)-dione and (1-aryl-2-bromoethyl)dimethylsulfonium bromides in the presence of K_2CO_3 (Scheme 1b).[8] In 2009, the Wang group reported the oxidative addition reaction of various aldehydes with 5,5-dimethylcyclohexane-1,3-dione and 1,3-indanedione to selectively afford spirocyclopropane derivatives, promoted by molecular iodine and dimethylaminopyridine under mechanical milling conditions (Scheme 1b).[9] Such spirocyclopropane also could be prepared from 2-arylmethylideneindan-1,3-diones with α-monohalogenated active methylene compounds via a base-promoted MIRC (Michael-induced ring closure) approach[10] or bromine-containing zinc enolates intermediate[11] (Scheme 1c). However, these methods generally require the pregeneration of reagents or harsh reaction conditions, which lowers the synthetic efficiency and limits the practical application. Thus, developing an efficient method for the preparation of spiro[2.4]heptane-4,7-dione derivatives

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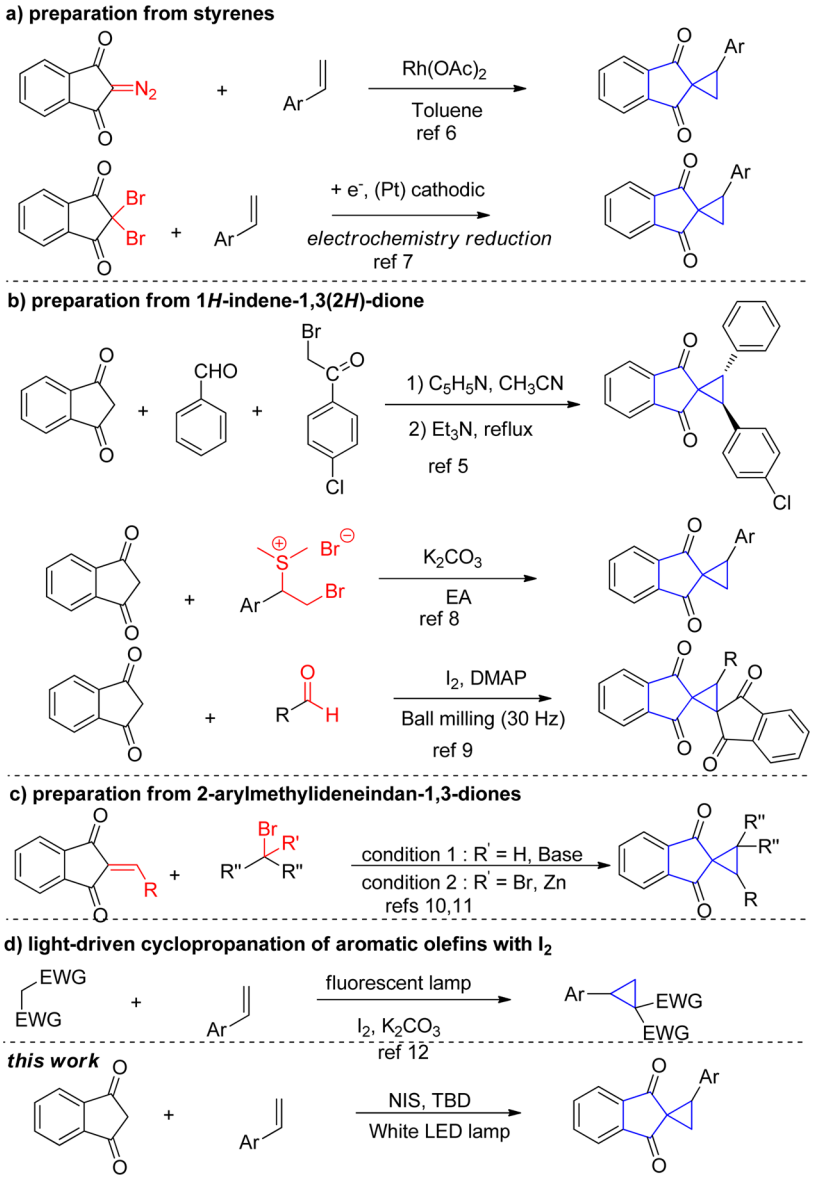
Scheme 1. Preparation of Spiro[2.4]heptane-4,7-dione Derivatives and Light-Driven Cyclopropanation



from simple and available starting materials under convenient condition still remains desirable.

Very recently, the Itoh group developed a light-driven intermolecular cyclopropanation of aromatic olefins with activated methylene compounds using molecular iodine, which provides cyclopropanes as products in good chemical yields (Scheme 1d).[12] Taking advantage of this work[12] and recent works in C−H functionalization,[13] direct sp^3 C−H functionalization of simple 1,3-dicarbonyl compound, subsequent coupling with styrene, and following cyclization under mild condition would be an ideal pathway for synthesis of spiro[2.4]heptane-4,7-dione derivatives. Notably, Sutherland and other groups have reported elegant works on iodination with NIS (*N*-iodosuccinimide) as precursor.[14] Also, several groups developed relevant cyclopropanation methodologies to give substituted cyclopropanes with the use of molecular iodine in recent years.[15] However, to the best of our knowledge, NIS-promoted spirocyclopropanes of 1,3-dicarbonyl compounds with styrenes via C−H bond cleavage, iodination, and intramolecular spirocyclization to assemble spiro[2.4]heptane has never been explored. Herein, we report an efficient pathway for the synthesis of spiro[2.4]heptane-4,7-dione derivatives via NIS-initiated spirocyclopropanation reaction of styrenes with 1,3-dicarbonyl compound in the presence of white LED light. This reaction could be carried out under simple conditions with readily available NIS as promoter. Furthermore, this process demonstrates a multistep radical reaction for functionalization of 1,3-dicarbonyl compounds and also represents easy access to spirocyclopropane.

RESULTS AND DISCUSSION

Initial examination of reactivity between 2*H*-indene-1,3-dione **2a** and styrenes **1a** was conducted at room temperature using ethyl acetate as a solvent (Table 1).[16] As shown in entries 1−5, the corresponding spiro[2.4]heptane-4,7-dione **3aa** was generated in up to 56% yield with the use of inorganic bases. Application of different organic bases (entries 6−8) was also examined in this reaction, and the best results were obtained in the case of sterically bulky base TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene), allowing preparation of **3aa**

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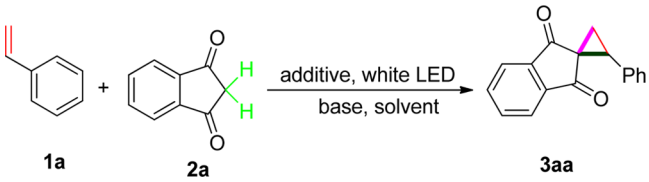
Table 1. Optimization of Reaction Conditions[a]



entry	additive (equiv)	base	time (h)	solvent	yield (%)[b]
1	NIS (2)	K_2CO_3	10	EA[c]	0
2	NIS (2)	KOH	10	EA	20
3	NIS (2)	CH_3ONa	10	EA	48
4	NIS (2)	*t*-BuONa	10	EA	56
5	NIS (2)	DABCO	10	EA	6
6	NIS (2)	TEA	10	EA	23
7	NIS (2)	DBU	10	EA	61
8	NIS (2)	TBD	10	EA	87
9	NIS (2)	TBD	10	DMF	87
10	NIS (2)	TBD	10	DMSO	80
11	NIS (2)	TBD	10	THF	62
12	NIS (2)	TBD	10	CH_3CN	91
13	NIS (2)	TBD	10	$CHCl_3$	88
14	NIS (2)	TBD	10	DCM	95
15	NIS (2)	TBD	2	DCM	98
16	NIS (1)	TBD	2	DCM	41
17	NIS (2)	TBD	2	DCM	91[d]
18	NIS (2)	TBD	2	DCM	68[e]
19	NBS (2)	TBD	10	DCM	21
20	I_2 (2)	TBD	10	DCM	10
21	NIS (2)	TBD	2	DCM	84[f]
22	NIS (2)	TBD	2	DCM	88[g]

[a]Reaction conditions: **1a** (0.9 mmol), **2a** (0.3 mmol), additive, base (1 equiv), white LED lamp, solvent (3 mL), rt, under argon atmosphere. [b]Ethyl acetate. [c]Isolated yield. [d]2 equiv of **1a**. [e]Reaction was carried out in the dark. [f]Yellow LED lamp was used. [g]Blue LED lamp was used.

with 87% yield (entry 8). The reaction media was found to have a significant effect on the reaction efficiency. The cyclopropanation reactions performed in DMF (entry 9), DMSO (entry 10), and $CHCl_3$ (entry 13) gave the product **3aa** with a similar yield to that observed in ethyl acetate (entry 8). An excellent yield of **3aa** was obtained when the reaction was carried out in acetonitrile (entry 12). CH_2Cl_2 was the best choice, resulting in an increased yield of 95% (entry 14). It is desireable that the reaction could be completed within 2 h, with an almost quantitative yield of **3aa** (98%, entry 15). Further scan showed that decreasing the loading amount of NIS to 1 equiv led to a dramatically lower yield (41%, entry 16). On the other hand, decreasing the use of **1a** to 2 equiv gave a slightly lower yield of product **3aa** (entry 17). It should be mentioned that the reaction performed in the dark also could proceed, however, with significantly less efficiency (68% yield, entry 18). Other additives, such as NBS (entry 19) and iodine (entry 20), were tried for this reaction instead of NIS, and the results clearly suggested that NIS might be considered as the best choice. Finally, the reactions in the presence of a yellow LED lamp (entry 21) and blue LED lamp (entry 22) were examined, and the reactions could also proceed smoothly with 84% and 88% yield, respectively.

Then examination of the substrate scope for this NIS-initiated spirocyclopropanation reaction of styrenes was performed. As shown in Scheme 2, a variety of styrenes efficiently coupled with 2*H*-indene-1,3-dione **2a** under standard reaction conditions to produce the corresponding spirocyclopropanes **3** in good yields. The presence of a substituent on the phenyl ring of styrenes **1** had almost no effect on chemical yields. The substituents, including alkyl (**1b**, **1c**, and **1f**), methoxyl (**1d**), and halo (**1g**–**i**, **1m**) groups, were well tolerated and successfully cyclized, even for the strong electron-withdrawing groups (nitro **1j**, cyano **1k**). Very interestingly, the substrates with naphthyl (**1n**) or pyridinyl substituent (**1o**) could also work well, and the products **3na** and **3oa** were isolated in excellent yields (87% and 80%, respectively). Notably, allylbenzene (**1p**) also was tried as substrate in this reaction, which was transformed into benzyl-substituted product in a low yield (15%, **3pa**). Finally, substrates with substituents on the C–C double bond of styrenes were tried to investigate the steric effect, and the results indicate that steric hindrance had almost no effect on this reaction. For example, the reaction with methyl- or phenyl-substituted olefins could work well, affording products with yields of 70% (**3sa**) and 71% (**3ta**), respectively. However, the electronegativity of the substituents showed a significant effect on this reaction, and iodo- (**1q**) and bromo- (**1r**) substituted styrenes gave obviously lower chemical yields of corresponding products along with a complex mixture.

As the next goal of the substrate study on cyclopropanation reaction, several other types of 1,3-dicarbonyl compounds were selected as substrates for this reaction (Scheme 3). First, several Meldrum's acid derivatives (**2b**–**d**) were chosen to react with styrenes **1a**. As shown in Scheme 3, the reactions with Meldrum's acid and its analogs (1,5-dioxaspiro[5.5]undecane-2,4-dione **2c** and 6,10-dioxaspiro[4.5]decane-7,9-dione **2d**) could proceed very well under the standard condition, affording the corresponding product with 84–89% yields (**3ab**–**ad**). Then several barbituric acid derivatives were examined. For example, 1,3-dimethylbarbituric acid **2e** and 1,3-dicyclohexylbarbituric acid **2f** could be smoothly transferred into the desired product with good yield (**3ae** and **3af**). Finally, the substrate with a variation to the sulfur atom, 1,3-dibutyl-2-thiobarbituric acid **2g**, was used in this reaction. Unfortunately, almost no desired product **3ag** was observed under the standard condition.

To investigate the details of the mechanism for this spirocyclization reaction, several control experiments were carried out (Scheme 4). First, 2,2-diiodo-1*H*-indene-1,3(2*H*)-dione **4a**, instead of 2*H*-indene-1,3-dione **2a**, was used to react with styrene **1a** under the standard condition. No desired product **3aa** was obtained, which indicates that 2-iodo-1*H*-indene-1,3(2*H*)-dione radical generated from the light-promoted C–I bond cleavage is not the reaction intermediate (Scheme 4a). The reaction does not happen at all without addition of base TBD (Scheme 4b). Also, it is found that in the absence of NIS, the reaction gives no desired product **3aa** (Scheme 4c). A reaction of **1a** and **2a** with the addition of radical-trapping reagent 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or butylated hydroxytoluene (BHT) under the standard condition was performed, and the formation of desired product **3aa** was suppressed, which suggests the radical nature of the mechanism.

On the basis of the control experiments and the previous reports,[12] a possible mechanism was proposed in Scheme 5. Initially, 2*H*-indene-1,3-dione **2a** in the presence of TBD undergoes deprotonation and is converted into anion **A**. Subsequently, anion **A** reacts with NIS to form the 2-iodo-1*H*-

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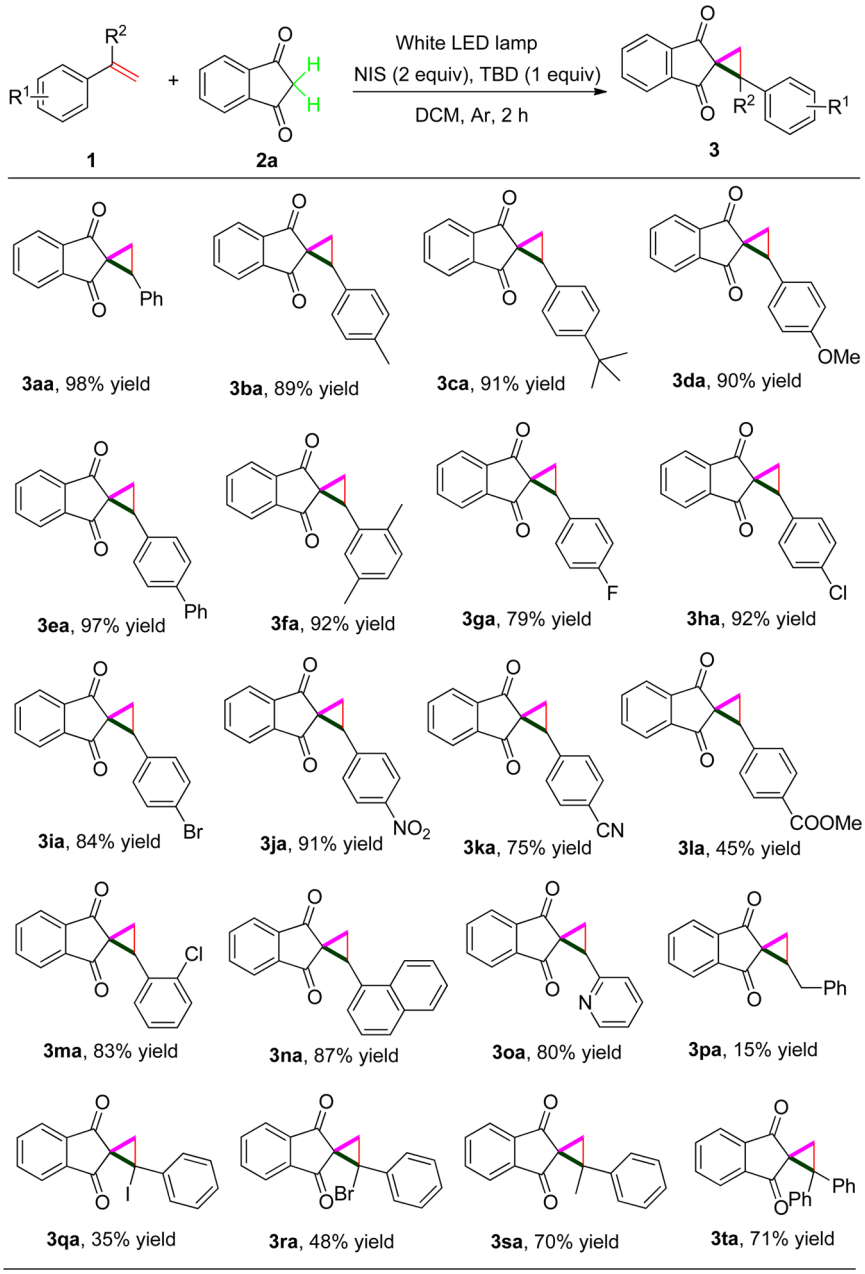
Scheme 2. Substrate Study with Variation of Styrenes[a,b]



[a]Reaction conditions: **1** (0.9 mmol), **2a** (0.3 mmol), NIS (2 equiv) based on **2a**, TBD (1 equiv), white LED lamp 2 h, rt, under argon atmosphere. [b]Isolated yield.

indene-1,3(2*H*)-dione **B** along with regeneration of TBD by succinimide anion. The intermediate **B** proceeds through C−I bond cleavage with irradiation of light to generate intermediate **C**. Then **C** couples with styrene **1a**, affording the intermediate **D**, which undergoes the second C−I bond formation with another equivalent of NIS. This is accounting for the necessity of 2 equiv of NIS. The second deprotonation happens on the intermediate **E** with the aid of base TBD, giving the intermediate **F**. Finally, intramolecular nucleophilic attack of **F** happens via the second C−I bond cleavage to give the corresponding product **3aa**.

The synthetic value of this new reaction was further demonstrated by the successful spirocyclopropanation of *p*-quinone methide **1u** with 2*H*-indene-1,3-dione **2a**. Under the standard reaction condition, the reaction between **1u** and **2a** proceeds smoothly to produce the corresponding product **3ua** in excellent yield (91%) (Scheme 6). Such spiro[2.5]octa-4,7-dien-6-one core is a privileged structure found in many natural products.[17] However, the previous literature method has to use 2-halo 1,3-dicarbonyl compound as starting material.[18] Thus, this developed reaction represents a straightforward method to prepare valuable spiro[2.5]octa-4,7-dien-6-one compounds from the readily available 2*H*-indene-1,3-dione.

CONCLUSION

In summary, we developed an efficient cascade spirocyclopropanation reaction between 1,3-dicarbonyl compounds and styrenes, which proceeded through cleavage of a sp^3 C−H bond

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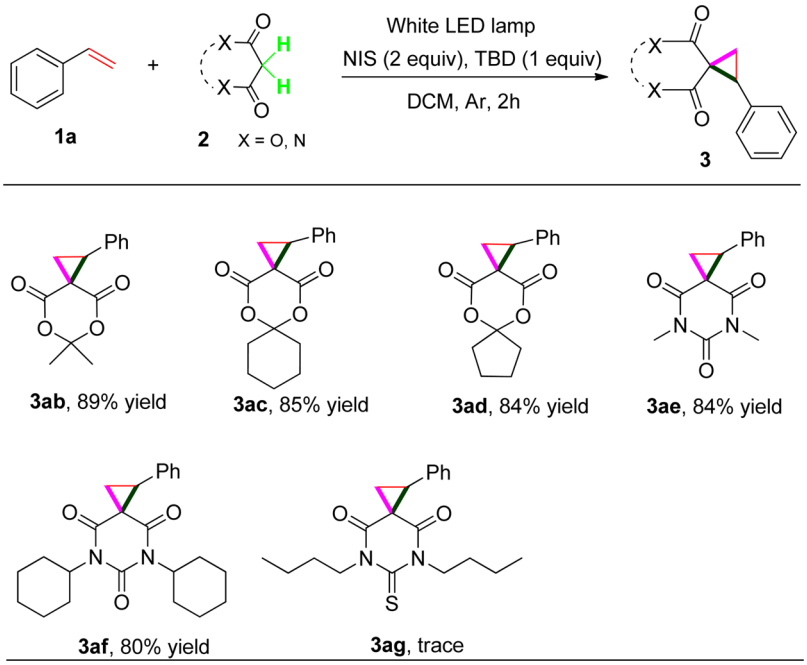
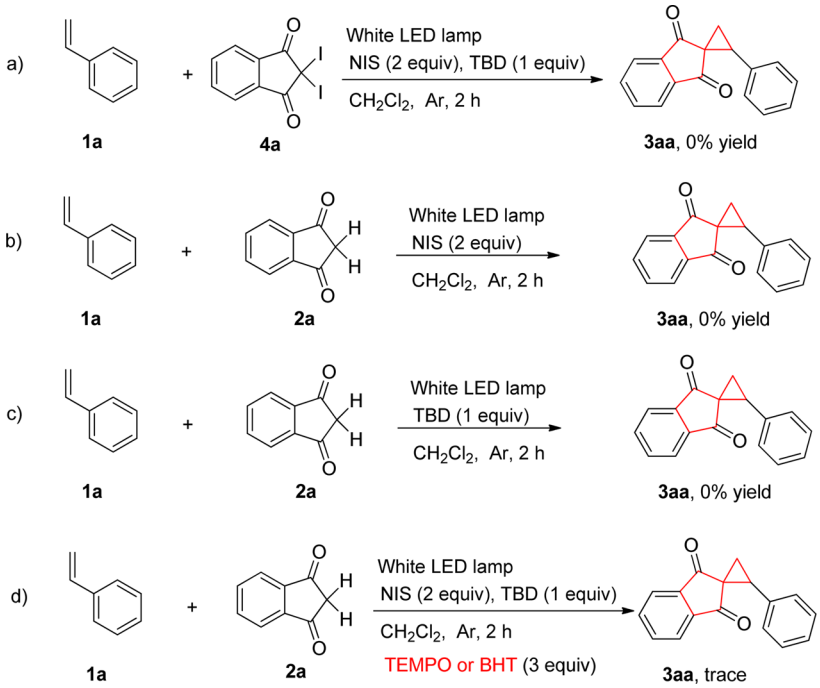
Scheme 3. Substrate Study with Variation of 1,3-Dicarbonyl Compounds[a,b]



[a]Reaction conditions: **1a** (0.9 mmol), **2** (0.3 mmol), NIS (2 equiv) based on **2**, TBD (1 equiv), white LED lamp 2 h, rt, under argon atmosphere. [b]Isolated yield.

Scheme 4. Investigation of the Mechanism Conditions



of 2*H*-indene-1,3-dione, iodination, coupling with styrene, second iodination, and intramolecular cyclization. These reactions could be carried out at room temperature and tolerated a wide range of substrates, resulting in good to excellent chemical yields. This process demonstrates a multistep radical reaction for functionalization of 1,3-dicarbonyl compounds and also represents a new strategy for preparation of spirocyclopropane. Further studies directly toward the development of new coupling partners for the construction of spirocyclobutane are currently underway in our lab.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of Spirocyclopropanes between Styrenes with 1,3-Dicarbonyl Compounds. Into an oven-dried reaction vial flushed with argon was added 1*H*-indene-1,3(2*H*)-dione (**2a**) (0.3 mmol), styrene (**1a**, 0.9 mmol), NIS (0.6 mmol), TBD (0.3 mmol), and DCM (3 mL). Then the reaction mixture was stirred for 2 h at room temperature under argon

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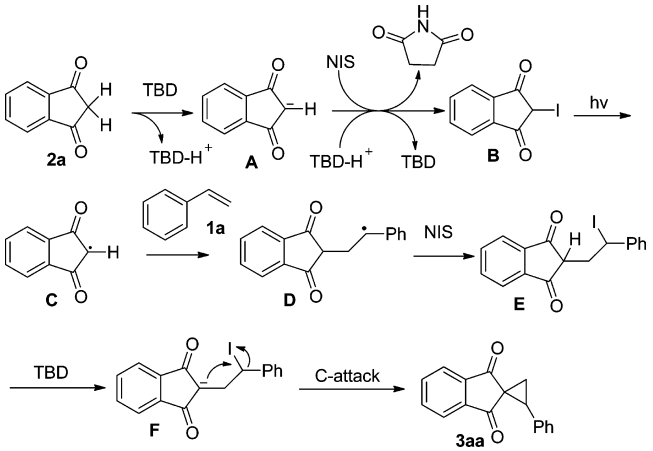
Scheme 5. Proposed Mechanism



atmosphere in the presence of white LED light. After the reaction was complete, the mixture was poured into H_2O (20 mL) and extracted with DCM three times. The combined organic layer was dried with anhydrous Na_2SO_4 and evaporated under vacuum. The crude mixture was charged onto silica gel and purified by flash chromatography (petroleum ether:ethyl acetate = 6:1) to furnish the corresponding product **3aa**. Other compounds **3** were obtained with similar reaction conditions.

*2-Phenylspiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3aa**).* Light yellow solid (72.9 mg, 98% yield), mp 126−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.88 (m, 1H), 7.75−7.64 (m, 3H), 7.24−7.16 (m, 5H), 3.38 (t, J = 8.9 Hz, 1H), 2.41 (dd, J = 8.8, 4.3 Hz, 1H), 2.23 (dd, J = 9.0, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 196.0, 142.8, 141.7, 135.0, 134.7, 133.7, 129.3, 128.2, 127.9, 122.6, 122.6, 42.8, 41.3, 22.3. IR (attenuated total reflection, cm^{-1}): ν 1967, 1381, 1330, 1320, 1310, 1287, 1216, 1061, 1040, 1027, 998, 942, 745, 706, 593. HRMS (TOF MS ESI): calcd for $C_{17}H_{13}O_2^+$ [M + H]$^+$ 249.0916, found 249.0911.

*2-(p-Tolyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ba**).* Light yellow solid (70.0 mg, 89% yield), mp 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 6.4, 1.3 Hz, 1H), 7.72−7.60 (m, 3H), 7.04 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 3.33 (t, J = 8.9 Hz, 1H), 2.37 (dd, J = 8.8, 4.2 Hz, 1H), 2.21(s, 3H), 2.22−2.18 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 196.0, 142.7, 141.6, 137.6, 134.8, 134.6, 130.6, 129.6, 129.1, 128.9, 122.5, 122.4, 42.9, 41.4, 22.3, 21.3, 21.1. IR (attenuated total reflection, cm^{-1}): ν 1696, 1350, 1334, 1309, 1289, 1223, 1162, 1045, 816, 757, 721. HRMS (TOF MS ESI): calcd for $C_{18}H_{15}O_2^+$ [M + H]$^+$ 263.1072, found 263.1066.

*2-(4-(tert-Butyl)phenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ca**).* White solid (83.0 mg, 91% yield), mp 85−87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 6.3, 1.4 Hz, 1H), 7.73−7.60 (m, 3H), 7.24−7.14 (m, 4H), 3.32 (t, J = 9.0 Hz, 1H), 2.38 (dd, J = 8.9, 4.2 Hz, 1H), 2.20 (dd, J = 9.1, 4.2 Hz, 1H), 1.20 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 196.0, 150.7, 142.8, 141.6, 134.8, 134.6, 130.6, 128.9, 125.1, 122.5, 122.5, 43.0, 41.4, 34.6, 31.4, 22.6. IR (attenuated total reflection, cm^{-1}): ν 1700, 1381, 1354, 1334, 1310, 1289, 1225, 1064, 1040, 1009, 824, 760, 744. HRMS (TOF MS ESI): calcd for $C_{21}H_{21}O_2^+$ [M + H]$^+$ 305.1542, found 305.1538.

*2-(4-Methoxyphenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione(**3da**).* White solid (75.1 mg, 90% yield), mp 148−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (t, J = 7.1 Hz, 1H), 7.82−7.69 (m, 3H), 7.22 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H), 3.41 (t, J = 8.9 Hz, 1H), 2.45 (dd, J = 8.8, 4.3 Hz, 1H), 2.29 (dd, J = 9.0, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 196.0, 159.2, 142.7, 141.6, 134.8, 134.6, 130.4, 125.5, 122.4, 122.4, 113.6, 55.3, 55.2, 43.1, 41.4, 22.4. IR (attenuated total reflection, cm^{-1}): ν 1697, 1520, 1333, 1256, 1224, 1187, 1150, 1045, 1024, 1008, 841, 756, 686. HRMS (TOF MS ESI): calcd for $C_{18}H_{15}O_3^+$ [M + H]$^+$ 279.1021, found 279.1015.

*2-([1,1′-Biphenyl]-4-yl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione(**3ea**).* Light yellow solid (94.31 mg, 97% yield), mp 169−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.79 (m, 1H), 7.65−7.63 (m, 1H), 7.56−7.51 (m, 2H), 7.42−7.37 (m, 4H), 7.26−7.21 (m, 4H), 7.17−7.13 (m, 1H), 3.33 (t, J = 8.9 Hz, 1H), 2.35 (dd, J = 8.8, 4.3 Hz, 1H), 2.17 (dd, J = 9.0, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.2, 196.0, 142.8, 141.7, 140.8, 140.7, 135.0, 134.8, 132.8, 129.7, 128.8, 127.4, 127.2, 127.0, 122.6, 122.6, 43.0, 41.2, 22.5. IR (attenuated total reflection, cm^{-1}): ν 1700, 1601, 1380, 1334, 1311, 1225, 1194, 1064, 1044, 1007, 843, 768, 729. HRMS (TOF MS ESI): calcd for $C_{23}H_{17}O_2^+$ [M + H]$^+$ 325.1229, found 325.1219.

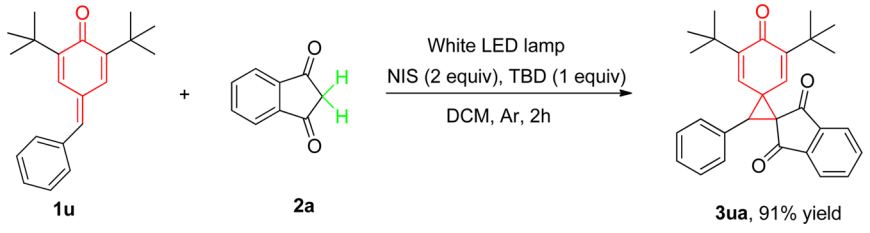
*2-(2,5-Dimethylphenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3fa**).* White solid (76.2 mg, 92% yield), mp 128−129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−7.93 (m, 1H), 7.85−7.71 (m, 3H), 7.16 (s, 1H), 7.01 (d, J = 8.0 Hz, 1H), 6.96 (d, J = 7.7 Hz, 1H), 3.29 (t, J = 8.8 Hz, 1H), 2.47 (dd, J = 8.8, 4.0 Hz, 1H), 2.36 (s, 3H), 2.28 (dd, J = 8.8, 4.0 Hz, 1H), 1.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 195.6, 142.3, 141.4, 135.1, 134.9, 134.8, 134.7, 132.4, 129.7, 129.6, 128.8, 122.5, 122.4, 42.0, 39.7, 22.5, 21.2, 19.1. IR (attenuated total reflection, cm^{-1}): ν 1700, 1375, 1330, 1311, 1285, 1196, 1042, 820, 561, 556. HRMS (TOF MS ESI): calcd for $C_{19}H_{17}O_2^+$ [M + H]$^+$ 277.1229, found 277.1223.

*2-(4-Fluorophenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ga**).* Light yellow solid (63.1 mg, 79% yield), mp 150−151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 6.2, 1.3 Hz, 1H), 7.75−7.62 (m, 3H), 7.21−7.13 (m, 2H), 6.92−6.86 (m, 2H), 3.32 (t, J = 8.9 Hz, 1H), 2.33 (dd, J = 8.7, 4.3 Hz, 1H), 2.21 (dd, J = 9.1, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0, 195.9, 163.6 ($^1J_{C-F}$ = 248.5 Hz), 142.7, 141.7, 135.0, 134.8, 130.9, 130.9, 129.4, 129.4, 122.6, 122.6, 115.3 ($^2J_{C-F}$ = 22.2 Hz), 42.6, 40.2, 22.4. IR (attenuated total reflection, cm^{-1}): ν 1700, 1513, 1334, 1306, 1287, 1219, 1191, 1161, 1152, 1037, 1109, 844, 762, 726. HRMS (TOF MS ESI): calcd for $C_{17}H_{11}FO_2Na^+$ [M + Na]$^+$ 289.0641, found 289.0635.

*2-(4-Chlorophenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione-(**3ha**).* Light yellow solid (77.8 mg, 92% yield), mp 165−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, J = 8.6, 4.2 Hz, 1H), 7.83−7.73 (m, 3H), 7.29−7.20 (m, 4H), 3.39 (t, J = 8.9 Hz, 1H), 2.42 (dd, J = 8.7, 4.3 Hz, 1H), 2.29 (dd, J = 9.0, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 195.8, 142.6, 141.6, 135.0, 134.9, 133.7, 132.2, 130.6, 128.4, 122.6, 122.6, 42.5, 40.1, 22.3. IR (attenuated total reflection, cm^{-1}): ν 1700, 1594, 1363, 1344, 1336, 1310, 1198, 1091, 768, 727. HRMS (TOF MS ESI): calcd for $C_{17}H_{12}ClO_2^+$ [M + H]$^+$ 283.0526, found 283.0521.

*2-(4-Bromophenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ia**).* White solid (82.1 mg, 84% yield), mp 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dt, J = 7.9, 3.8 Hz, 1H), 7.76−7.64 (m, 3H), 7.36−7.30 (m, 2H), 7.08 (d, J = 8.4 Hz, 2H), 3.29 (t, J = 8.9 Hz,

Scheme 6. Spirocyclopropanation Reaction of *p*-Quinone Methide



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1H), 2.33 (dd, J = 8.7, 4.4 Hz, 1H), 2.21 (dd, J = 9.0, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 195.8, 142.6, 141.6, 135.1, 134.9, 132.7, 131.3, 130.9, 122.6, 122.6, 121.9, 42.5, 40.1, 22.2. IR (attenuated total reflection, cm^{-1}): ν 1697, 1334, 1314, 1289, 1260, 1219, 1091, 1076, 1067, 1008, 750, 721, 691. HRMS (TOF MS ESI): calcd for $C_{17}H_{11}BrO_2Na^+$ [M + Na]$^+$ 348.9840, found 348.9834.

2-(4-Nitrophenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ja**). Light yellow solid (80.0 mg, 91% yield), mp 169−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.7, 2H), 7.91 (dd, J = 12.2, 5.6 Hz, 1H), 7.78−7.68 (m, 3H), 7.40 (d, J = 8.7 Hz, 2H), 3.38 (t, J = 8.8 Hz, 1H), 2.40 (dd, J = 8.6, 4.5 Hz, 1H), 2.28 (dd, J = 8.9, 4.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 195.6, 147.4, 142.5, 141.6, 141.4, 135.4, 135.2, 130.2, 123.4, 122.9, 122.8, 42.4, 39.0, 22.2. IR (attenuated total reflection, cm^{-1}): ν 1698, 1507, 1314, 1289, 1226, 1041, 1009, 871, 766, 689. HRMS (TOF MS ESI): calcd for $C_{17}H_{11}NO_4Na^+$ [M + Na]$^+$ 316.0586, found 316.0581.

4-(1′,3′-Dioxo-1′,3′-dihydrospiro[cyclopropane-1,2′-inden]-2-yl)-benzonitrile (**3ka**). Light yellow solid (61.4 mg, 75% yield), mp 206−208 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.98 (m, 1H), 7.85−7.76 (m, 3H), 7.63−7.58 (m, 2H), 7.42 (d, J = 8.1 Hz, 2H), 3.42 (t, J = 8.8 Hz, 1H), 2.45 (dd, J = 8.7, 4.5 Hz, 1H), 2.33 (dd, J = 9.0, 4.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 195.7, 142.6, 141.7, 139.3, 135.4, 135.2, 132.0, 130.1, 122.9, 122.8, 118.8, 111.7, 42.4, 39.5, 22.1. IR (attenuated total reflection, cm^{-1}): ν 2227, 1700, 1593, 1333, 1286, 1218, 1093, 1063, 1009, 853, 763, 736. HRMS (TOF MS ESI): calcd for $C_{18}H_{12}NO_2^+$ [M + H]$^+$ 274.0868, found 274.0872.

Methyl 4-(1′,3′-Dioxo-1′,3′-dihydrospiro[cyclopropane-1,2′-inden]-2-yl)benzoate (**3la**). White solid (41.3 mg, 45% yield), mp 205−207 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.86 (m, 3H), 7.76−7.65 (m, 3H), 7.30 (d, J = 8.2 Hz, 2H), 3.86−3.78 (s, 3H), 3.37 (dd, J = 10.9, 6.8 Hz, 1H), 2.41 (dd, J = 8.7, 4.4 Hz, 1H), 2.25 (dd, J = 9.0, 4.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 195.7, 166.9, 142.7, 141.7, 139.0, 135.2, 135.0, 129.6, 129.5, 129.4, 122.7, 122.7, 52.2, 42.6, 40.2, 22.2. IR (attenuated total reflection, cm^{-1}): ν 1715, 1700, 1430, 1278, 1260, 1220, 1177, 1108, 1041, 1020, 800, 776. HRMS (TOF MS ESI): calcd for $C_{19}H_{15}O_4^+$ [M + H]$^+$ 307.0970, found 307.0965.

2-(2-Chlorophenyl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ma**). White solid (70.2 mg, 83% yield), mp 176−177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.89 (m, 1H), 7.75−7.62 (m, 3H), 7.35 (d, J = 7.6 Hz, 1H), 7.25−7.10 (m, 3H), 3.27 (t, J = 8.7 Hz, 1H), 2.29 (dd, J = 8.7, 4.2 Hz, 1H), 2.21 (dd, J = 8.8, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.2, 195.7, 142.4, 141.6, 136.0, 134.9, 134.7, 132.7, 130.7, 129.2, 129.0, 126.7, 122.5, 122.5, 41.4, 38.1, 22.0. IR (attenuated total reflection, cm^{-1}): ν 1700, 1594, 1377, 1336, 1313, 1287, 1219, 1039, 1009, 770, 749, 734. HRMS (TOF MS ESI): calcd for $C_{17}H_{12}ClO_2^+$ [M + H]$^+$ 283.0526, found 283.0520.

2-(Naphthalen-1-yl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3na**). Light yellow solid (77.8 mg, 87% yield), mp 155−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.02 (d, J = 7.6 Hz, 1H), 7.79−7.72 (m, 3H), 7.66−7.59 (m, 2H), 7.56−7.55 (m, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 3.78 (t, J = 8.7 Hz, 1H), 2.61 (dd, J = 8.6, 4.0 Hz, 1H), 2.41 (dd, J = 8.7, 4.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 195.4, 142.5, 141.6, 135.1, 134.7, 133.5, 132.9, 130.2, 129.0, 128.8, 127.0, 126.5, 125.8, 125.3, 122.8, 122.6, 122.6, 42.3, 38.4, 22.4. IR (attenuated total reflection, cm^{-1}): ν 1700, 1593, 1362, 1344, 1335, 1309, 1291, 1198, 1148, 1091, 1045, 999, 768, 727. HRMS (TOF MS ESI): calcd for $C_{21}H_{15}O_2^+$ [M + H]$^+$ 299.1072, found 299.1067.

2-(Pyridin-2-yl)spiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3oa**). Light yellow oil (59.8 mg, 80% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52−8.51 (m, 1H), 7.99−7.96 (m, 1H), 7.86−7.62 (m, 4H), 7.37 (d, J = 7.9 Hz, 1H), 7.18 (m, 1H), 3.59 (t, J = 8.8 Hz, 1H), 2.59 (dd, J = 8.6, 4.2 Hz, 1H), 2.31 (dd, J = 9.0, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 196.2, 153.8, 149.3, 142.6, 141.8, 136.2, 135.0, 134.9, 123.7, 122.7, 122.6, 122.5, 41.8, 41.2, 21.8. IR (attenuated total reflection, cm^{-1}): ν 1696, 1591, 1433, 1333, 1311, 1289, 1222, 1039, 787, 748, 704. HRMS (TOF MS ESI): calcd for $C_{16}H_{12}NO_2^+$ [M + H]$^+$ 250.0868, found 250.0866.

2-Benzylspiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3pa**). Light yellow oil (11.8 mg, 15% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.90 (m, 2H), 7.80−7.75 (m, 2H), 7.25−7.18 (m, 2H), 7.18−7.07 (m, 3H), 3.18−3.07 (m, 2H), 2.55−2.47 (m, 1H), 2.05 (dd, J = 8.7, 3.6 Hz, 1H), 1.92 (dd, J = 8.3, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.1, 198.7, 142.7, 141.6, 140.1, 134.9, 134.8, 128.6, 128.4, 126.4, 122.6, 122.4, 40.0, 38.2, 32.6, 26.2. IR (attenuated total reflection, cm^{-1}): ν 1702, 1597, 1454, 1387, 1335, 1314, 1285, 1205, 1157, 1098, 1021, 743, 721, 697. HRMS (TOF MS ESI): calcd for $C_{18}H_{15}O_2^+$ [M + H]$^+$ 263.1072, found 263.1063.

2-Iodo-2-phenylspiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3qa**). White solid (39.3 mg, 35% yield), mp 65−67 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−7.97 (m, 1H), 7.82−7.70 (m, 3H), 7.25−7.11 (m, 5H), 2.71 (d, J = 5.7 Hz, 1H), 2.35 (d, J = 5.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.4, 193.6, 142.4, 142.4, 142.3, 135.4, 128.6, 128.6, 123.3, 122.9, 42.8, 32.2, 16.3. IR (attenuated total reflection, cm^{-1}): ν 1707, 1353, 1254, 1165, 1064, 1051, 1039, 1020, 1010, 936, 853, 751. HRMS (TOF MS ESI): calcd for $C_{17}H_{12}IO_2^+$ [M + H]$^+$ 374.9882, found 374.9888.

2-Bromo-2-phenylspiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ra**). White solid (46.9 mg, 48% yield), mp 95−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.04 (m, 1H), 7.88−7.76 (m, 3H), 7.36−7.25 (m, 5H), 2.80 (d, J = 6.0 Hz, 1H), 2.60 (d, J = 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 193.6, 142.8, 142.3, 138.7, 135.4, 135.2, 129.1, 129.0, 128.7, 123.3, 123.0, 46.6, 44.3, 29.1. IR (attenuated total reflection, cm^{-1}): ν 1709, 1354, 1256, 1066, 1057, 752, 716, 607. HRMS (TOF MS ESI): calcd for $C_{17}H_{12}BrO_2^+$ [M + H]$^+$ 327.0021, found 327.0021.

2-Methyl-2-phenylspiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3sa**). Light yellow oil (55.0 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.94 (m, 1H), 7.80−7.71 (m, 3H), 7.33−7.24 (m, 3H), 7.20−7.12 (m, 2H), 2.53 (d, J = 4.2 Hz, 1H), 2.18 (d, J = 4.2 Hz, 1H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 196.1, 142.6, 142.4, 140.6, 134.7, 134.6, 128.6, 128.5, 127.5, 122.4, 122.3, 49.3, 46.1, 29.0, 22.0. IR (attenuated total reflection, cm^{-1}): ν 1702, 1597, 1350, 1249, 1220, 1158, 1132, 1069, 1027, 758, 698. HRMS (TOF MS ESI): calcd for $C_{18}H_{14}O_2Na^+$ [M + Na]$^+$ 285.0891, found 285.0894.

2,2-Diphenylspiro[cyclopropane-1,2′-indene]-1′,3′-dione (**3ta**). White solid (69.0 mg, 71% yield), mp 176−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.89 (m, 2H), 7.80−7.77 (m, 2H), 7.31−7.29 (m, 5H), 7.27−7.24 (m, 3H), 7.22−7.18 (m, 2H), 2.71 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.4, 142.6, 139.7, 134.9, 129.2, 128.7, 127.6, 122.8, 56.2, 46.2, 27.5. IR (attenuated total reflection, cm^{-1}): ν 1740, 1706, 1490, 1446, 1358, 1238, 1156, 1061, 819, 773. HRMS (TOF MS ESI): calcd for $C_{23}H_{17}O_2^+$ [M + H]$^+$ 325.1229, found 325.1223.

6,6-Dimethyl-1-phenyl-5,7-dioxaspiro[2.5]octane-4,8-dione (**3ab**). Light yellow solid (65.7 mg, 89% yield), mp 130−131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.29 (m, 5H), 3.45 (t, J = 9.4 Hz, 1H), 2.69 (dd, J = 9.3, 4.8 Hz, 1H), 2.55 (dd, J = 9.5, 4.8 Hz, 1H), 1.73 (d, J = 1.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 163.6, 131.2, 129.6, 128.8, 128.5, 105.0, 44.7, 33.2, 28.1, 27.8, 23.0. IR (attenuated total reflection, cm^{-1}): ν 1731, 1331, 1287, 1175, 1035, 959, 718, 658. HRMS (TOF MS ESI): calcd for $C_{14}H_{14}O_4Na^+$ [M + Na]$^+$ 269.0790, found 269.0782.

1-Phenyl-5,12-dioxadispiro[2.2.5^6.2.3^3]tridecane-4,13-dione (**3ac**). White solid (73.0 mg, 85% yield), mp 146−148 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.27 (m, 5H), 3.43 (t, J = 9.4 Hz, 1H), 2.67 (dd, J = 9.3, 4.7 Hz, 1H), 2.52 (dd, J = 9.5, 4.7 Hz, 1H), 2.08−1.86 (m, 4H), 1.82−1.33 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 163.6, 131.4, 129.5, 128.7, 128.4, 105.8, 44.3, 37.2, 36.2, 33.3, 24.1, 23.0, 22.3, 21.8. IR (attenuated total reflection, cm^{-1}): ν 1735, 1366, 1340, 1298, 1268, 1252, 1221, 1180, 1108, 1058, 971, 836, 697. HRMS (TOF MS ESI): calcd for $C_{17}H_{18}O_4Na^+$ [M + Na]$^+$ 309.1103, found 309.1101.

1-Phenyl-5,11-dioxadispiro[2.2.4^6.2.3^3]dodecane-4,12-dione (**3ad**). White solid (68.6 mg, 84% yield), mp 137−138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 5H), 3.40 (t, J = 9.4 Hz, 1H), 2.67 (dd, J = 9.3, 4.9 Hz, 1H), 2.53 (dd, J = 9.5, 4.9 Hz, 1H), 2.28−2.10 (m,

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3H), 1.94−1.71 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 164.1, 131.2, 129.5, 128.8, 128.4, 114.2, 44.6, 39.8, 38.4, 33.9, 24.3, 22.8, 22.5. IR (attenuated total reflection, cm^{-1}): ν 1739, 1700, 1338, 1216, 977, 698, 650. HRMS (TOF MS ESI): calcd for $C_{16}H_{16}O_4Na^+$ $[M + Na]^+$ 295.0946, found 295.0956.

*5,7-Dimethyl-1-phenyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (**3ae**).* Light yellow solid (65.0 mg, 84% yield), mp 87−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.24 (m, 5H), 3.52 (t, J = 9.3 Hz, 1H), 3.37 (s, 3H), 3.12 (s, 3H), 2.59 (dd, J = 9.2, 4.0 Hz, 1H), 2.45 (dd, J = 9.4, 4.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 165.0, 152.0, 132.6, 129.8, 128.3, 128.2, 46.4, 36.0, 28.9, 28.6, 24.7. IR (attenuated total reflection, cm^{-1}): ν 1672, 1413, 1368, 1283, 1127, 1057, 787, 749, 691. HRMS (TOF MS ESI): calcd for $C_{14}H_{15}N_2O_3^+$ $[M + H]^+$ 259.1083, found 259.1079.

*5,7-Dicyclohexyl-1-phenyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (**3af**).* White solid (94.6 mg, 80%), 144−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.25 (m, 3H), 7.24−7.17 (m, 2H), 4.70−4.63 (m, 1H), 4.41−4.33 (m, 1H), 3.37 (t, J = 9.1 Hz, 1H), 2.54 (dd, J = 9.0, 4.1 Hz, 1H), 2.38 (dd, J = 9.3, 4.1 Hz, 1H), 2.37−2.23 (m, 2H), 2.17−2.06 (m, 1H), 1.91−1.78 (m, 3H), 1.72−1.66 (m, 5H), 1.55−1.52 (m, 1H), 1.45−1.32 (m, 3H), 1.27−1.02 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 165.1, 151.4, 133.0, 129.7, 128.2, 128.1, 55.7, 55.5, 46.0, 36.8, 29.6, 29.5, 29.1, 28.4, 26.6, 26.5, 26.4, 26.3, 25.4, 25.1, 22.8. IR (attenuated total reflection, cm^{-1}): ν 1681, 1663, 1404, 1364, 1428, 1264, 894, 821, 754. HRMS (TOF MS ESI): calcd for $C_{24}H_{31}N_2O_3$ $[M + H]^+$ 395.2335, found 395.2331.

***3ua**.* Light yellow solid (119.7 mg, 91% yield), mp 208−210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (m, 1H), 7.96−7.89 (m, 1H), 7.88−7.77 (m, 2H), 7.39−7.29 (m, 3H), 7.23 (d, J = 2.7 Hz, 1H), 7.18 (d, J = 2.7 Hz, 1H), 7.12−7.03 (m, 2H), 4.30 (s, 1H), 1.29 (s, 9H), 1.19 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 193.2, 186.2, 150.2, 150.0, 143.0, 141.5, 135.7, 135.6, 135.4, 133.7, 131.6, 130.3, 128.4, 128.2, 123.1, 123.1, 51.9, 49.2, 46.9, 35.9, 35.6, 29.5, 29.4. IR (attenuated total reflection, cm^{-1}): ν 2920, 2160, 2031, 1710, 1610, 1610, 1380, 1255, 1220, 1148, 1005, 914, 743, 534. HRMS (TOF MS ESI): calcd for $C_{30}H_{31}O_3^+$ $[M + H]^+$ 439.2273, found 439.2270.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01163.

^{1}H NMR and ^{13}C NMR spectra for compounds **3** (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hanjl@nju.edu.cn.

Notes

The authors declare no competing financial interest.

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