Solvent-Free Iridium(III)-Catalyzed [2+2+2] Cycloaddition Providing Access to Fused Arenes: Isoindolines, Dihydroisobenzofurans and Indanes

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Abstract: A practical and convenient solvent-free iridium-catalyzed [2+2+2] cycloaddition of α,ω-diynes and alkynes to prepare fused arenes has been developed. The method has shown high efficiency as isoindolines, dihydroisobenzofurans and indanes have been synthesized in good to excellent yields.

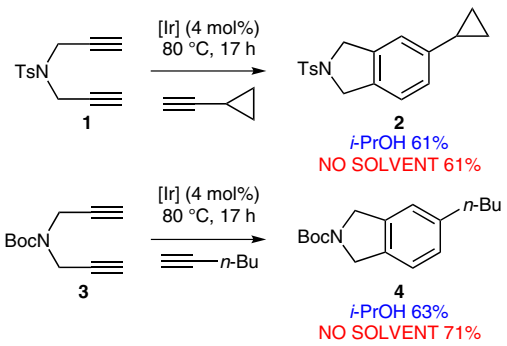
Keywords: cycloadditions, iridium, atom economy, solvent-free conditions, benzannulation

The development of solvent-free reactions has attracted much interest due to environmental concerns.[1] As one of the most important and effective carbon–carbon bond-forming processes, and in terms of atom economy, benzannulation is widely used in both academia and industry due to the diverse functional group tolerance.[2] In addition, this transformation provides a practical and easy access to the formation of complex structures in a single step. Transition metals have proven their synthetic utility in the construction of complex and heavily substituted benzene-derived systems from relatively simple starting materials. The most useful cobalt, nickel, rhodium and ruthenium catalysts offer the possibility of catalyzing [2+2+2] cycloadditions, leading to aromatic compounds;[3] however, iridium catalysis has been less studied with regard to [2+2+2] cycloaddition[4] which prompted us to investigate the potential of an iridium(III) complex. Recently, we reported that [{Ir(H)[*rac*-binap]}$_2$(μ-I)$_3$]I complex[5] is able to catalyze the [2+2+2] cycloaddition of α,ω-diynes to provide isoindolines, useful building blocks for pharmaceutical purposes.[6] In line with the 12 principles of green chemistry,[7] one key point of our study was to use a simple, easy-to-handle and air-stable catalyst that would operate under environmentally friendly conditions. As benzannulation reactions are always performed in the presence of organic solvent, the challenge was to explore the method and expand the scope of the reaction using solvent-free conditions. As far as the solvent-free [2+2+2]-cycloaddition reaction is concerned, only one example of tandem double A^3-coupling and [2+2+2]-cycloaddition reactions in the presence of rhodium and copper as catalysts has been reported so far.[8]

In this paper, we describe our preliminary results on iridium-catalyzed [2+2+2]-cycloaddition reactions under solvent-free conditions leading to functionalized N-protected isoindolines, dihydroisobenzofurans and indanes.

We first compared the reaction under our general conditions using isopropyl alcohol, as previously reported, with the same reaction under solvent-free conditions. The results are depicted in Scheme 1. In both cases, the cycloaddition run with diyne **1** and cyclopropylacetylene provided compound **2** in 61% yield. Pleasingly, the cycloaddition carried out with diyne **3** and *n*-hex-1-yne afforded the desired isoindoline **4** with yield improvement when run under solvent-free conditions. We could therefore assume that the solvent-free conditions provide a potential route to access fused arenes efficiently in a greener fashion.

We then turned our attention to investigation of the reactivity of alternative alkynes as precursors of a series of functionalized isoindoline derivatives. The scope of the reaction is highlighted in Table 1. Pleasingly, the cycloaddition was successful with several alkynes bearing an alcohol or a chloride substituent, and provided the corresponding isoindolines **7**–**13** in good yields (Table 1, entries 1–7). The reaction conditions are compatible with both the tosyl- and Boc-protected diynes **1** and **3**. The reaction was also successful with the functionalized alkyne 1-methyl-4-(prop-2-yn-1-yl)piperazine (Table 1, entry 8). Compound **14** was isolated in 49% yield and is of particular significant importance as it is a key intermediate in the synthesis of a biologically active compound.[9] We also wanted to extend the scope of the reaction to include terminally disubstituted diynes, thus targeting highly func-



Scheme 1 Comparative results of [2+2+2] cycloaddition under isopropyl alcohol and solvent-free conditions

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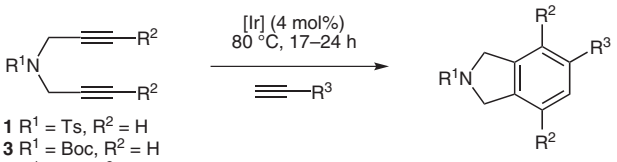
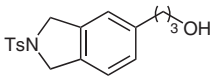
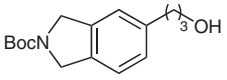
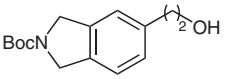
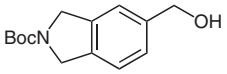
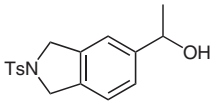
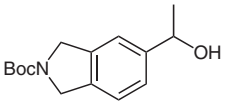
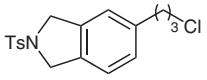
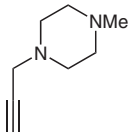
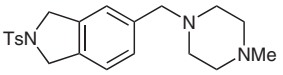
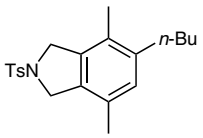
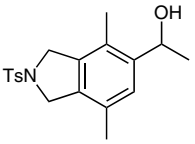
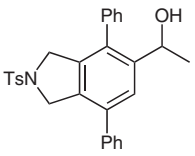
Table 1 Scope of the Iridium-Catalyzed [2+2+2] Cycloaddition: Synthesis of Isoindolines[a]



1 R^1 = Ts, R^2 = H
3 R^1 = Boc, R^2 = H
5 R^1 = Ts, R^2 = Me
6 R^1 = Ts, R^2 = Ph

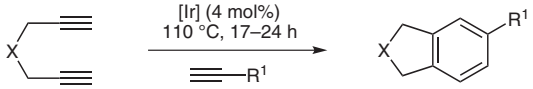
Entry	Starting material	Alkyne	Product	Yield[b] (%)
1	**1**		**7**		59
2	**3**		**8**		60
3	**3**		**9**		85
4	**3**		**10**		77
5	**1**		**11**		75
6	**3**		**12**		68
7	**1**		**13**		59
8	**1**		**14**		49
9[c,d]	**5**		**15**		43
10[c]	**5**		**16**		62
11[c]	**6**		**17**		60

[a] Reaction conditions: diyne (1 equiv), alkyne (3 equiv), [{Ir(H)[*rac*-binap]}$_2$(μ-I)$_3$]I (4 mol%), 80 °C, 17–24 h.
[b] Isolated yield.
[c] 110 °C.
[d] Using 10 equivalents of alkyne.

tionalized aromatic systems (Table 1, entries 9–11). Promising results were observed using diyne **5** with *n*-hex-1-yne which provided the corresponding isoindoline **15** in 43% yield (Table 1, entry 9). To our delight, the yield of the reaction could be improved when using but-3-yn-2-ol as the alkyne partner, leading to compound **16** in 62% yield (Table 1, entry 10). Finally, the use of a more hindered diyne **6** gave a similar result, as isoindoline **17** was isolated in 60% yield (Table 1, entry 11).

We then examined the reactivity of diynes **18** and **19** with additional alkynes, which allows the preparation of indanes and dihydroisobenzofurans (Table 2). To our delight, the cycloaddition reactions were successful at 110 °C. The hydrocarbon *n*-hex-1-yne underwent cycloaddition to furnish the desired indane **20**[4a] (Table 2, entry 1) and dihydroisobenzofuran **21**[4a] (Table 2, entry 2) in good yields of 80% and 76%, respectively. We also turned our attention to alcohols as alkyne partners. The cycloaddition was fruitful with both the carbon- and oxygen-tethered diynes **18** and **19**, and provided the corresponding indanes **22** and **24** and dihydroisobenzofurans **23**[10] and **25** in good yields (Table 2, entries 3–6). It is noteworthy that variation of the length of the side chain was rewarding, with compounds **23** and **25** being obtained in similar yields (Table 2, entries 4 and 6). Other functional groups, such as cyclic alkynes, were tolerated. The reaction of cyclohex-1-enylacetylene led to the desired indane **26**[4a] and dihydroisobenzofuran **27** in 55% and 68% yield, respectively (Table 2, entries 7 and 8). Cyclopentylacetylene was also employed and provided the desired compounds **28** and **29** in satisfying yields (Table 2, entries 9 and 10). The reaction of diyne **19** with cyclohexylacetylene led to the formation of dihydroisobenzofuran **30** in 53% (Table 2, entry 11).

Table 2 Synthesis of Indanes and Dihydroisobenzofurans[a]



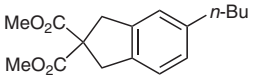
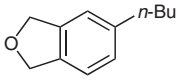
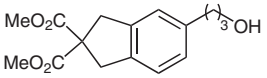
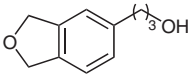
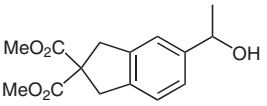
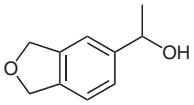
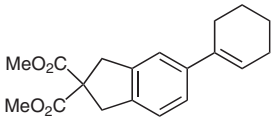
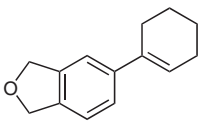
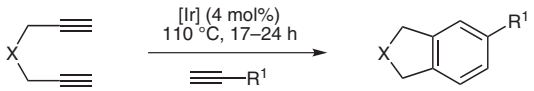
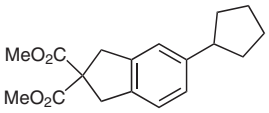
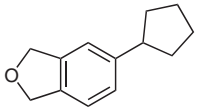
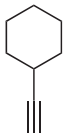
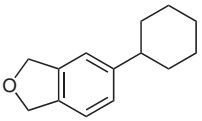
Entry	Starting material	Alkyne	Product	Yield[b] (%)
1[c]	**18**		**20** 	80
2[c]	**19**		**21** 	76
3	**18**		**22** 	70
4	**19**		**23** 	63
5	**18**		**24** 	52
6	**19**		**25** 	61
7	**18**		**26** 	55
8	**19**		**27** 	68

Table 2 Synthesis of Indanes and Dihydroisobenzofurans[a] (continued)



18 X = $C(CO_2Me)_2$
19 X = O

Entry	Starting material	Alkyne	Product		Yield[b] (%)
9[c]	**18**		**28**		44
10[c]	**19**		**29**		64
11[c]	**19**		**30**		53

[a] Reaction conditions: diyne (1 equiv), alkyne (3 equiv), [{Ir(H)[*rac*-binap]}$_2$(μ-I)$_3$]I (4 mol%), 110 °C, 17–24 h.
[b] Isolated yield.
[c] Using 10 equivalents of alkyne.

We have demonstrated that iridium-catalyzed [2+2+2] cycloaddition can be performed efficiently under solvent-free conditions. The value of this transformation has been highlighted via the functional group tolerance, the large substrate scope and the application of the method to the synthesis of a biorelevant intermediate target. The reaction conditions are compatible with mono- and disubstituted carbon-, nitrogen- and oxygen-tethered diynes, as well as with functionalized alkynes. Fused arenes are accessed in good to excellent yields in a practical, convenient and environmentally friendly manner.

All manipulations were carried out under an argon atmosphere. ^{1}H NMR and ^{13}C NMR were recorded on Bruker AV300 or AV400 instruments. All signals were expressed as ppm (δ) and internally referenced to residual protio solvent signals. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplicities. High-resolution mass spectra were performed at the University Pierre and Marie Curie (Paris). [{Ir(H)[*rac*-binap]}2(μ-I)$_3$]I was prepared according to the previously published procedure.[5a] All alkynes were commercially available, except **14**, which was prepared according to the literature.[9b]

Fused Arenes by Iridium-Catalyzed Cycloaddition; General Procedure

To a screw-cap tube was added [{Ir(H)[*rac*-binap]}$_2$(μ-I)$_3$]I (4 mol%), the diyne (1 equiv) was added, followed by addition of the alkyne (3 equiv or 10 equiv). The tube was purged with argon and capped and the reaction mixture was stirred overnight (17–24 h) at 80 °C or 110 °C. The crude reaction mixture was purified by flash chromatography over silica gel (cyclohexane–EtOAc).

3-(2-Tosylisoindolin-5-yl)propan-1-ol (7)

Yield: 40 mg (59%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71–1.80 (m, 2 H), 2.33 (s, 3 H), 2.50–2.62 (m, 2 H), 3.57 (t, *J* = 6.5 Hz, 2 H), 4.51 (s, 4 H), 6.93 (s, 1 H), 7.00 (br, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.69 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 31.8, 34.3, 53.5, 53.6, 62.0, 122.5, 127.6, 128.0, 129.8, 133.6, 136.3, 141.8, 143.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{21}O_3NSNa$: 354.1134; found: 354.1137.

***tert*-Butyl 5-(3-Hydroxypropyl)isoindoline-2-carboxylate (8)**

Yield: 43 mg (60%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (s, 9 H), 1.76–1.86 (m, 2 H), 2.62–2.67 (m, 2 H), 3.60 (t, *J* = 6.5 Hz, 2 H), 4.55–4.65 (m, 4 H), 6.99–7.13 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.5, 31.9, 34.4, 51.8, 51.9, 62.1, 79.6, 122.4, 122.7, 127.6, 134.5, 134.9, 137.2, 137.6, 141.1, 154.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{23}O_3NNa$: 300.1570; found: 300.1572.

***tert*-Butyl 5-(2-Hydroxyethyl)isoindoline-2-carboxylate (9)**

Yield: 58 mg (85%); white solid. Spectral data were in agreement with those reported in the literature.[6a]

***tert*-Butyl 5-(Hydroxymethyl)isoindoline-2-carboxylate (10)**

Yield: 50 mg (77%); colorless oil. Spectral data were in agreement with those reported in the literature.

1-(2-Tosylisoindolin-5-yl)ethanol (11)

Yield: 48 mg (75%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (d, *J* = 6.5 Hz, 3 H), 2.33 (s, 3 H), 4.51 (s, 4 H), 4.80 (q, *J* = 6.5 Hz, 1 H), 7.05 (d, *J* = 8.0 Hz, 1 H), 7.13–7.17 (m, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.68 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 25.4, 53.5, 53.6, 70.0, 119.6, 122.6, 125.1, 127.6, 129.8, 133.6, 135.2, 136.4, 143.7, 145.9.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{19}O_3NSNa$: 340.0978; found: 340.0980.

***tert*-Butyl 5-(1-Hydroxyethyl)isoindoline-2-carboxylate (12)**
Yield: 46 mg (68%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, *J* = 6.5 Hz, 3 H), 1.44 (s, 9 H), 4.56–4.58 (m, 4 H), 4.84 (q, *J* = 6.5 Hz, 1 H), 7.12 (d, *J* = 8.0 Hz, 1 H), 7.17–7.22 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.5, 28.5, 51.8, 51.9, 52.1, 52.7, 119.5, 119.7, 122.5, 122.7, 124.7, 136.2, 136.5, 137.3, 137.6, 145.4, 154.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{21}O_3NNa$: 286.1414; found: 286.1418.

5-(3-Chloropropyl)-2-tosylisoindoline (13)
Yield: 42 mg (59%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90–1.99 (m, 2 H), 2.32 (s, 3 H), 2.64–2.69 (m, 2 H), 3.41 (t, *J* = 6.5 Hz, 2 H), 4.51 (s, 4 H), 6.93 (s, 1 H), 6.97–7.03 (m, 2 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.69 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 32.5, 34.0, 44.0, 53.5, 53.6, 122.7, 127.6, 128.1, 129.8, 133.7, 134.0, 136.5, 140.6, 143.7.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{20}O_2NS^{35}ClNa$: 372.0796; found: 372.0799.

5-[(4-Methylpiperazin-1-yl)methyl]-2-tosylisoindoline (14)
Yield: 38 mg (49%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 2.31–2.47 (m, 11 H), 3.39 (s, 2 H), 4.52 (s, 4 H), 7.01–7.13 (m, 3 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 7.72 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 44.9, 52.0, 52.5, 52.6, 54.0, 61.6, 121.3, 122.2, 126.6, 127.7, 128.8, 132.7, 133.9, 135.2, 137.1, 142.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{28}O_2N_3S$: 386.1897; found: 386.1906.

5-Butyl-4,7-dimethyl-2-tosylisoindoline (15)
Yield: 27 mg (43%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.5 Hz, 3 H), 1.18–1.44 (m, 4 H), 2.01 (s, 3 H), 2.06 (s, 3 H), 2.33 (s, 3 H), 2.42–2.47 (m, 2 H), 4.47–4.49 (m, 4 H), 6.75 (s, 1 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.72 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 14.9, 18.2, 21.5, 22.7, 32.6, 33.0, 53.4, 53.8, 127.5, 127.6, 129.4, 129.8, 132.2, 133.9, 135.4, 141.0, 143.5.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{27}O_2NSNa$: 380.1655; found: 380.1658.

1-(4,7-Dimethyl-2-tosylisoindolin-5-yl)ethanol (16)
Yield: 39 mg (62%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (d, *J* = 6.5 Hz, 3 H), 2.05 (s, 3 H), 2.10 (s, 3 H), 2.34 (s, 3 H), 4.46–4.48 (m, 4 H), 5.05 (m, 1 H), 7.15 (s, 1 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 7.71 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 18.4, 21.5, 24.3, 53.4, 53.7, 66.5, 125.3, 126.0, 127.5, 129.8, 130.1, 133.7, 133.8, 135.5, 143.6, 143.7.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{23}O_3NSNa$: 368.1291; found: 368.1293.

1-(4,7-Diphenyl-2-tosylisoindolin-5-yl)ethanol (17)
Yield: 35 mg (60%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, *J* = 6.5 Hz, 3 H), 2.33 (s, 3 H), 4.24–4.25 (m, 2 H), 4.62–4.63 (m, 2 H), 4.72 (q, *J* = 6.5 Hz, 1 H), 7.31–7.42 (m, 12 H), 7.51 (br, 1 H), 7.60 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 25.1, 53.6, 53.9, 66.4, 125.6, 127.2, 127.6, 127.8, 127.9, 128.0, 128.4, 128.8, 129.8, 132.8, 133.6, 134.2, 136.1, 137.0, 137.4, 139.5, 143.6, 144.0.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{27}O_3NSNa$: 492.1604; found: 492.1604.

Dimethyl 5-(Butyl)indane-2,2-dicarboxylate (20)
Yield: 56 mg (80%); colorless oil. Spectral data were in agreement with those reported in the literature.[4a]

5-Butyl-1,3-dihydroisobenzofuran (21)
Yield: 71 mg (76%); colorless oil. Spectral data were in agreement with those reported in the literature.[4a]

Dimethyl 5-(3-Hydroxypropyl)indane-2,2-dicarboxylate (22)
Yield: 49 mg (70%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.86–1.91 (m, 2 H), 2.64–2.69 (m, 2 H), 3.56 (s, 4 H), 3.66 (t, *J* = 6.5 Hz, 2 H), 3.74 (s, 6 H), 6.99–7.03 (m, 2 H), 7.10 (d, *J* = 7.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.9, 34.4, 40.3, 40.6, 53.0, 60.5, 62.4, 124.2, 124.3, 127.3, 137.5, 140.2, 140.8, 172.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{20}O_5Na$: 315.1203; found: 315.1203.

3-(1,3-Dihydroisobenzofuran-5-yl)propan-1-ol (23)
Yield: 60 mg (63%); white solid. Spectral data were in agreement with those reported in the literature.[10]

Dimethyl 5-(1-Hydroxyethyl)indane-2,2-dicarboxylate (24)
Yield: 35 mg (52%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47 (d, *J* = 6.5 Hz, 3 H), 3.57–3.60 (m, 4 H), 3.74 (s, 6 H), 4.86 (q, *J* = 6.5 Hz, 1 H), 7.16 (br, 2 H), 7.22 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.3, 40.4, 40.6, 53.0, 60.5, 70.5, 121.3, 124.3, 124.5, 139.3, 140.3, 145.0, 172.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{18}O_5Na$: 301.1046; found: 301.1049.

1-(1,3-Dihydroisobenzofuran-5-yl)ethanol (25)
Yield: 53 mg (61%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50 (d, *J* = 6.5 Hz, 3 H), 4.93 (q, *J* = 6.5 Hz, 1 H), 5.09 (s, 4 H), 7.19–7.28 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 70.4, 73.4, 73.5, 118.0, 121.0, 124.8, 138.4, 139.6, 145.4.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{10}H_{11}O_2$: 163.0754; found: 163.0750.

Dimethyl 5-(Cyclohexenyl)indane-2,2-dicarboxylate (26)
Yield: 41 mg (55%); colorless oil. Spectral data were in agreement with those reported in the literature.[4a]

5-(Cyclohex-1-enyl)-1,3-dihydroisobenzofuran (27)
Yield: 72 mg (68%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.53–1.63 (m, 2 H), 1.67–1.75 (m, 2 H), 2.10–2.17 (m, 2 H), 2.30–2.35 (m, 2 H), 5.02 (s, 4 H), 6.00–6.04 (m, 1 H), 7.09 (d, *J* = 8.0 Hz, 1 H), 7.17–7.22 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1, 23.0, 25.8, 27.7, 73.4, 73.6, 117.5, 120.6, 124.3, 124.9, 136.5, 137.3, 139.2, 142.4.

HRMS (EI): *m*/*z* $[M + Na + O_2]^+$ calcd for $C_{14}H_{16}O_3Na$: 255.0991; found: 255.0992.

Dimethyl 5-Cyclopentylindane-2,2-dicarboxylate (28)
Yield: 32 mg (44%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45–1.74 (m, 6 H), 1.92–2.00 (m, 2 H), 2.81–2.93 (m, 1 H), 3.49–3.50 (s, 4 H), 3.67 (s, 6 H), 6.96–7.04 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 34.8, 40.3, 40.6, 45.8, 52.9, 60.4, 122.8, 123.8, 126.0, 137.1, 139.8, 145.5, 172.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{22}O_4Na$: 325.1410; found: 325.1411.

5-Cyclopentyl-1,3-dihydroisobenzofuran (29)
Yield: 64 mg (64%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45–1.77 (m, 6 H), 1.96–2.04 (m, 2 H), 2.88–2.99 (m, 1 H), 5.02 (s, 4 H), 7.05 (m, 1 H), 7.07–7.08 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 34.8, 45.8, 73.4, 73.5, 119.4, 120.6, 126.3, 136.5, 139.3, 145.9.

HRMS (ESI): *m*/*z* $[M - H_2O + O_2 + Na]^+$ calcd for $C_{13}H_{14}O_2Na$: 225.0885; found: 225.0886.

5-Cyclohexyl-1,3-dihydroisobenzofuran (30)
Yield: 57 mg (53%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18–1.37 (m, 5 H), 1.67–1.80 (m, 5 H), 2.40–2.47 (m, 1 H), 5.01 (s, 4 H), 7.02–7.07 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.1, 26.9, 34.7, 44.5, 73.4, 73.5, 119.2, 120.7, 126.1, 136.6, 139.2, 147.6.

HRMS (EI): *m*/*z* $[M - H]^+$ calcd for $C_{14}H_{17}O$: 201.1274; found: 201.1274.

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