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Acetyl Bromide Promoted Sequence *via* Allene Intermediates: Metal-Free Construction of 2,3-Dihydroindenes and Isoindolines

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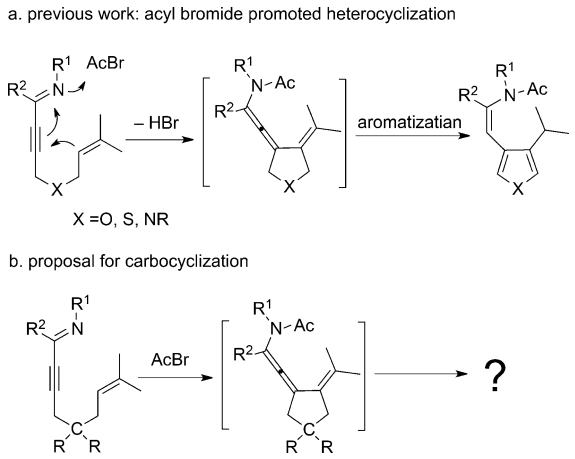
Abstract: 2,3-Dihydroindenes and isoindolines are important skeletons present in medicinal and synthetic chemistry. In this paper, an acetyl bromide promoted metal-free construction of 2,3-dihydroindenes and isoindolines with high synthetic efficiency is developed.

Keywords: 2,3-dihydroindene; acetyl bromide; isoindoline; metal-free

Introduction

During the last decade, allene chemistry has attracted much attention in the organic community and numerous reports on this area have been published.[1] However, compared with the alkynyl analogues of allenes, the preparation of highly functionalized allenes remains a challenging task for organic chemists, because of their high reactivity. A viable alternative might be use of readily available alkynyl compounds to generate in situ allene intermediates and trigger the subsequent reactions.[2]

During our recent studies on cyclization reactions *via* in situ generated allenes,[3] we reported an acetyl bromide promoted heterocyclization, using methylcrotyloxy/thio/amino propargyl imines as the substrates, which underwent a cyclization/heteroaromatization process due to the heteroatom effect (Scheme 1a).[3a] We reasonably anticipated that replacement of the heteroatom by a carbon moiety might offer totally different results (Scheme 1b).

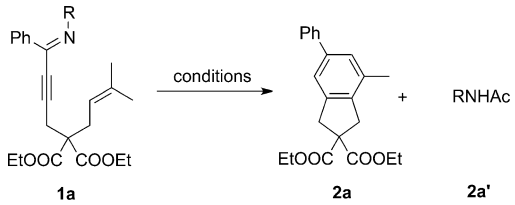


Scheme 1. Proposal of acetyl bromide promoted cyclization.

Results and Discussion

On the basis of this proposal, we chose **1a** as the starting material, which could be prepared readily *via* the Sonogashira coupling of diethyl 2-(3-methylcrotyl)-2-propargyl malonate with *N*-phenylbenzimidoyl chloride.[4] Our study was initiated by the treatment of **1a** with acetyl bromide in dichloromethane at room temperature. After work up, we isolated **2a** and acetanilide in yields of 78% and 80%, respectively (Table 1, Entry 1). Subsequent screening of solvents showed that the use of other common solvents, such as chloroform, 1,2-dichloroethane, or toluene, did not improve the yield (entries 1–4). Replacement of the phenyl group adjacent to nitrogen of **1a** by 4-chlorophenyl (**1a-Cl**), *p*-tolyl (**1a-Me**) and 4-methoxyphenyl (**1a-OMe**) groups, respectively, gave slightly different yields (entries 5–7). Thus the following reaction conditions were chosen for all subsequent reactions: 0.2 mmol of **1** (**1-OMe** in some cases), 0.24 mmol of acetyl bromide and 2 mL of dichloromethane were stirred at room temperature under N_2 atmosphere.

Table 1. Optimization of the reaction conditions[a]



R = phenyl, 4-chlorophenyl, *p*-tolyl or 4-methoxyphenyl

Entry	Substrate	Solvent	Yield of **2a**/**2a'** (%)
1	**1a**	**dichloromethane**	**78/80**
2	**1a**	chloroform	52/51
3	**1a**	dichloroethane	62/63
4	**1a**	toluene	complex
5	**1a-Cl**	dichloromethane	72/70
6	**1a-Me**	dichloromethane	75/74
7	**1a-OMe**	**dichloromethane**	**79/76**

[a] All reactions were conducted on a 0.2 mmol scale at room temperature and monitored by TLC.

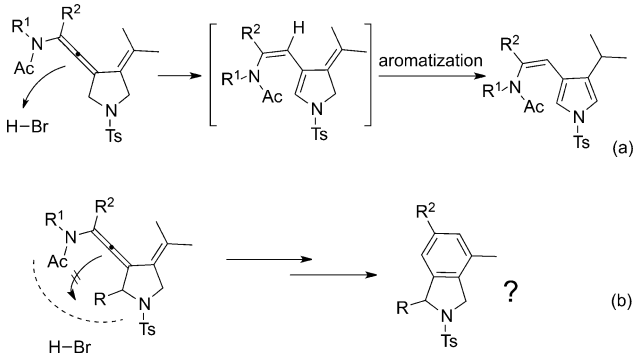
With these results in hand, the scope of the reaction was examined and 2,3-dihydro-1*H*-indenes were obtained in good yields (Table 2). Notably, this strategy was successful for the one-pot construction of fused polycyclic skeletons (**2h**–**2i**) and spirocyclic skeletons (**2j**–**2k**) in satisfactory yields.

In the preliminary publication about heterocyclization,[3a] control experiments demonstrated that the assistance of hydrogen bromide is essential to the hetero-aromatization of the allene intermediate (Scheme 2a). We hypothesized that increasing steric hindrance might prevent the trapping of hydrogen bromide and give isoindolines as the products (Scheme 2b).

Stimulated by this idea, we prepared **3** as the starting material and treated it under the standard conditions. As expected 2,3-dihydroisoindolines (**4**) were obtained in good yields, and the scope of this reaction was further investigated (Table 3).

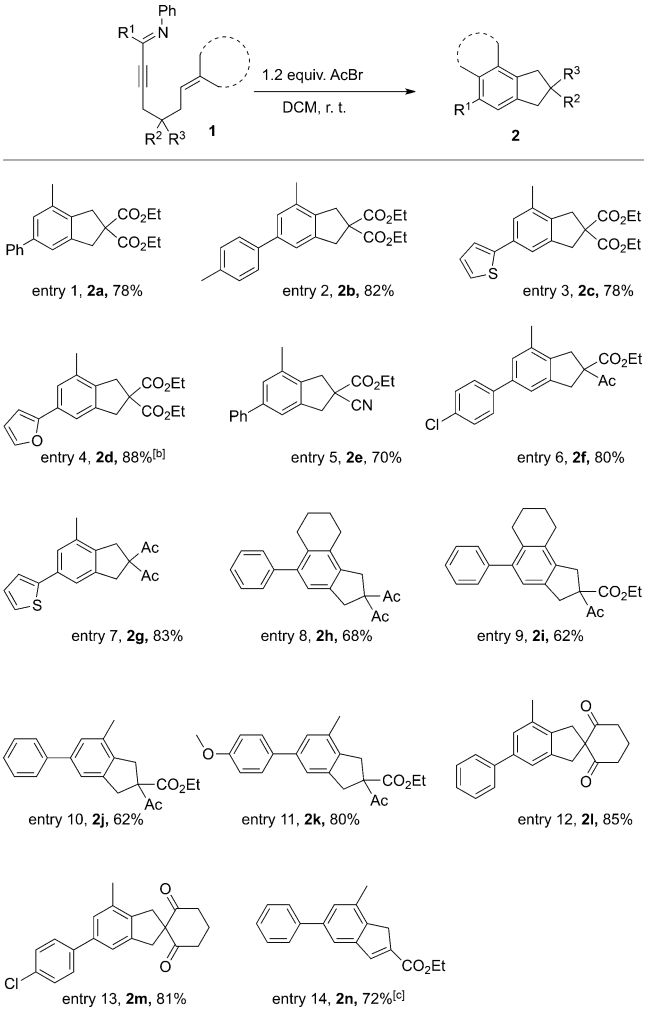
As a convenient and simple operating procedure, the usefulness of this protocol should be demonstrated on a multi-gram scale preparation. We thus conducted the cyclization of **1a** on a 4 gram scale and obtained **2a** in 75% yield (Scheme 3).

In order to demonstrate the potential synthetic application of the new reaction, we explored transfor-



Scheme 2. Hypothesis of the access to isoindolines.

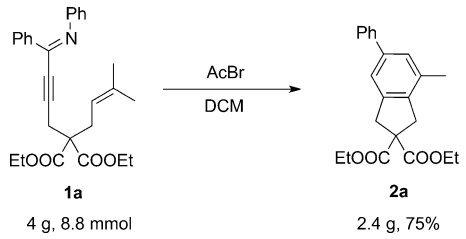
Table 2. Synthesis of 2,3-dihydro-1*H*-indenes.[a]



[a] The reaction was carried out using **1** (0.2 mmol) and acetyl bromide (0.24 mmol) in dichloromethane (2 mL) under N_2 at room temperature.

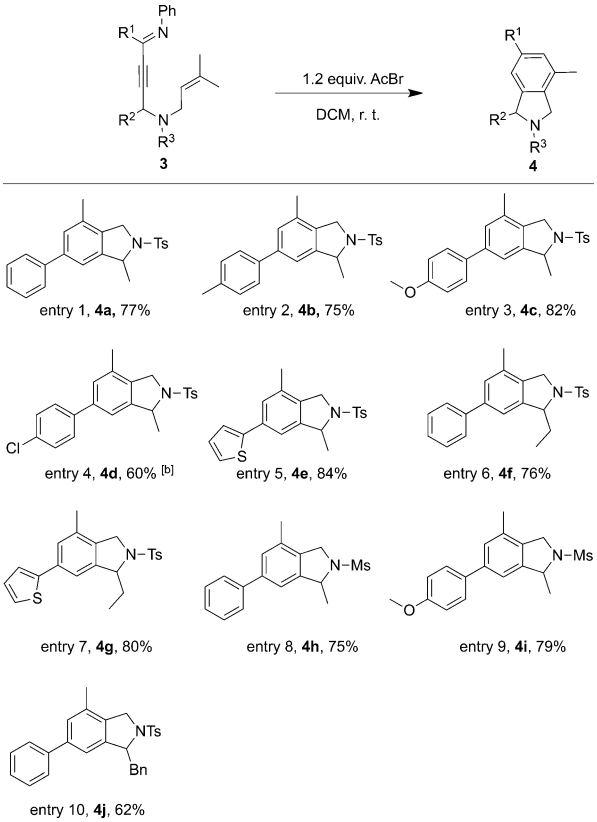
[b] **1d-OMe** was used.

[c] R^2 was phenylsulfonyl and eliminated in the reaction; the structure was confirmed by NOESY experiments.



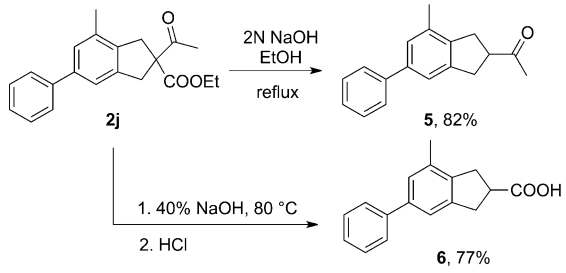
Scheme 3. Multi-gram scale preparation of **2a**.

Table 3. Synthesis of 2,3-dihydroisoindolines.[a]



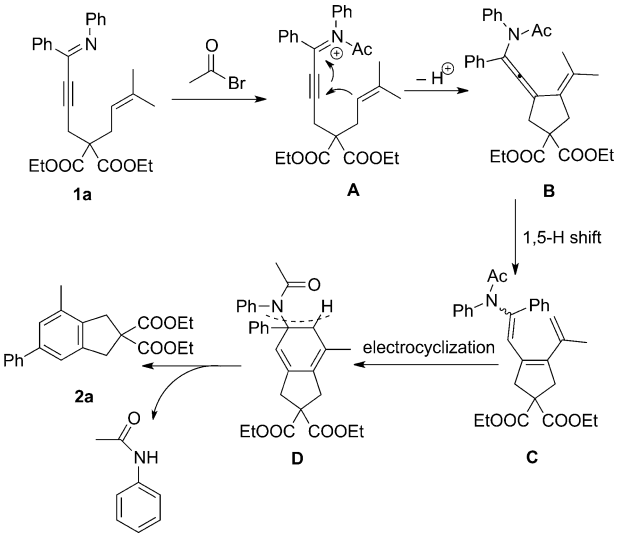
[a] The reaction was carried out using **3** (0.2 mmol) and acetyl bromide (0.24 mmol) in dichloromethane (2 mL) under N_2 at room temperature.
[b] **1d-OMe** was used.

mations of the 2,3-dihydroindene with the model product **2j** (Scheme 4). The cleavage of the ester group and acyl group were achieved under alkaline conditions to obtain the corresponding product **5** and **6** in good yields.



Scheme 4. Transformation of 2,3-dihydroindene.

We propose a plausible pathway as shown in Scheme 5. First, addition of acetyl bromide to **1a** produces propargylic acetyliminium/amidoallenylium **A**, which undergoes the first cyclization to give eneallene intermediate **B**.[5] The intermediate **B** experiences a 1,5-H shift offering triene intermediate **C**,[6] in



Scheme 5. Plausible pathway.

which a 6π-electrocyclization occurs to achieve the second ring closure and generate **D**.[6a,b,7] The elimination of a molecule of acetanilide finishes the last aromatization to produce **2a** (Scheme 5).

Conclusions

Construction of the benzenoid aromatic compounds might be arguably one of the most frequently encountered tasks for synthetic organic chemists. Direct functionalization to benzene, however, might encounter difficulty in some cases, because of the effect of the substituent(s). Herein, we developed an efficient construction of a new benzene ring to access 2,3-dihydroindenes[8] and isoindolines,[9] which are important in medicinal and synthetic chemistry.[10,11] As a result of readily available starting materials and simple operation, the protocol presented here should have potential utility in organic synthesis.

Experimental Section

General: Dichloromethane was dried with CaH_2 and distilled freshly before use. Toluene was dried with sodium and distilled freshly before use. Other materials and solvents were purchased from commercial suppliers and used without additional purification. NMR spectra were measured in $CDCl_3$, operating for ^1H NMR at 400 MHz and for ^{13}C NMR at 100 MHz. Chemical shifts are expressed in ppm and J values are given in Hz. Mass spectroscopy data of the products were collected with an HRMS-TOF instrument. Melting points were measured on an apparatus with microscope and are uncorrected.

Diethyl 4-methyl-6-phenyl-1*H*-indene-2,2(3*H*)-dicarboxylate (2a). Typical Procedure. To a solution of **1a** (89 mg, 0.2 mmol) in dichloromethane (2 mL) was added acetyl bro-

mide (30 mg, 0.24 mmol, 1.2equiv) under argon. The resulting mixture was stirred at room temperature and the reaction was monitored by TLC until completion. Then the reaction was quenched with 10 mL of water, extracted with dichloromethane (3×10 mL), dried with anhydrous Na_2SO_4. After evaporation, chromatography on silica gel (eluent: hexane/ethyl acetate = 5:1) of the reaction mixture afforded **2a**: yellow oil, 55 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.2 Hz, 2H), 7.40 (t, J = 15.2 Hz, 2H), 7.33–7.29 (m, 1H), 7.24 (s, 1H), 7.21 (s, 1H), 4.25–4.20 (m, 4H), 3.66 (s, 2H), 3.55 (s, 2H), 2.32 (s, 3H), 1.27 (t, J = 14.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 141.5, 140.7, 140.4, 138.1, 134.0, 128.6, 127.2, 127.1, 127.0, 120.4, 61.8, 60.0, 40.7, 39.2, 19.2, 14.1; IR (neat) 2980, 1731, 1098 cm^{-1}; HRMS (TOF) calcd for $C_{24}H_{24}O_4$ 352.1675, found 352.1671.

Diethyl 4-methyl-6-(p-tolyl)-1*H*-indene-2,2(3*H*)-dicarboxylate (2b). Yellow oil, 60 mg, 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.42 (s, 1H), 7.21 (s, 2H), 7.19 (s, 2H), 4.24–4.19 (m, 4H), 3.65 (s, 2H), 3.55 (s, 2H), 2.37 (s, 3H), 2.31 (s, 3H), 1.26 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 140.6, 140.4, 138.6, 137.9, 136.7, 133.9, 129.4, 127.0, 126.9, 120.2, 61.7, 60.1, 40.7, 39.2, 21.1, 19.2, 14.1; IR (neat) 2982, 1729, 1083 cm^{-1}; HRMS (TOF) calcd for $C_{23}H_{26}O_4$ 366.1831, found 366.1830.

Diethyl 4-methyl-6-(thiophen-2-yl)-1*H*-indene-2,2(3*H*)-dicarboxylate (2c). Yellow oil, 56 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.25–7.21 (m, 3H), 7.05–7.03 (m, 1H), 4.24–4.19 (m, 4H), 3.62 (s, 2H), 3.52 (s, 2H), 2.28 (s, 3H), 1.26 (t, J = 12.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 144.8, 140.6, 138.5, 134.1, 133.7, 127.9, 125.9, 124.3, 122.7, 119.2, 61.8, 60.0, 40.6, 39.2, 19.0, 14.0; IR (neat) 2980, 1729, 1096 cm^{-1}; HRMS (TOF) calcd for $C_{20}H_{22}O_4S$ 358.1239, found 358.1239.

Diethyl 6-(furan-2-yl)-4-methyl-1*H*-indene-2,2(3*H*)-dicarboxylate (2d). Yellow oil, 60 mg, 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.40 (m, 1H), 7.33 (s, 1H), 7.31 (s, 1H), 6.56 (d, J = 3.3 Hz, 1H), 6.43 (dd, J = 3.3, 1.8 Hz, 1H), 4.24–4.18 (m, 4H), 3.62 (s, 2H), 3.51 (s, 2H), 2.28 (s, 3H), 1.26 (t, J = 14.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 154.3, 141.6, 140.3, 138.4, 134.0, 130.2, 123.6, 117.1, 111.5, 104.4, 61.7, 60.0, 40.6, 39.2, 19.1, 14.0; IR (neat) 2982, 1728, 1068 cm^{-1}; HRMS (TOF) calcd for $C_{20}H_{22}O_5$ 342.1467, found 342.1467.

Ethyl 2-cyano-4-methyl-6-phenyl-2,3-dihydro-1*H*-indene-2-carboxylate (2e). Yellow oil, 43 mg, 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 6.8 Hz, 2H), 7.41 (t, J = 15.2 Hz, 2H), 7.36–7.29 (m, 1H), 7.26 (s, 2H), 4.34–4.28 (m, 2H), 3.77–3.52 (m, 4H), 2.31 (s, 3H), 1.35 (t, J = 14.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 141.5, 141.0, 138.7, 136.3, 134.4, 128.8, 127.9, 127.3, 127.2, 120.8, 120.6, 63.3, 47.2, 43.4, 41.9, 19.2, 14.0; IR (neat) 3032, 2361, 1743, 1233 cm^{-1}; HRMS (TOF) calcd for $C_{20}H_{29}NO_2$ 305.1416, found 305.1413.

Ethyl 2-acetyl-6-(4-chlorophenyl)-4-methyl-2,3-dihydro-1*H*-indene-2-carboxylate (2f). Yellow oil, 57 mg, 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.42 (m, 2H), 7.38–7.33 (m, 2H), 7.18 (s, 1H), 7.16 (s, 1H), 4.26–4.21(m, 2H), 3.65–3.51 (m, 2H), 3.47 (s, 2H), 2.31 (s, 3H), 2.25 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 172.4, 140.5, 139.8, 139.4, 138.4, 134.2, 133.1, 128.8, 128.3, 126.9, 120.3, 66.5, 61.9, 39.2, 37.6, 26.1, 19.2, 14.1; IR (neat) 2924, 1714, 1236 cm^{-1}; HRMS (TOF) calcd for $C_{21}H_{21}ClO_3$ 356.1179, found 356.1175.

1,1′-(4-Methyl-6-(thiophen-2-yl)-2,3-dihydro-1*H*-indene-2,2-diyl)diethanone (2g). Yellow oil, 50 mg, 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.24 (s, 2H), 7.23–7.22 (m, 1H), 7.06–7.04 (m, 1H), 3.54 (s, 2H), 3.42 (s, 2H), 2.30 (s, 3H), 2.19 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 144.5, 140.3, 138.2, 134.4, 133.8, 127.9, 126.0, 124.4, 122.8, 119.4, 74.4, 37.7, 36.2, 26.5, 19.1; IR (neat) 2919, 1697, 1146 cm^{-1}; HRMS (TOF) calcd for $C_{18}H_{18}O_2S$ 298.1028, found 298.1026.

1,1′-(5-Phenyl-2,3,6,7,8,9-hexahydro-1*H*-cyclopenta[a]-naphthalene-2,2-diyl)diethanone (2h). Amorphous solid, 45 mg, 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, J = 7.3 Hz, 2H), 7.31 (d, J = 7.2 Hz, 1H), 7.27–7.23 (m, 2H), 6.90 (s, 1H), 3.52 (s, 2H), 3.41 (s, 2H), 2.70 (t, J = 6.3 Hz, 2H), 2.53 (t, J = 5.9 Hz, 2H), 2.20 (s, 6H), 1.85–1.77 (m, 2H), 1.70–1.64 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.90, 141.16, 140.55, 136.64, 135.26, 132.39, 132.28, 128.19, 126.95, 125.62, 121.81, 76.35, 76.23, 76.03, 75.71, 73.50, 36.56, 35.22, 27.43, 26.31, 25.53, 22.11, 21.66; IR (neat) 2923, 1670, 1190 cm^{-1}; HRMS (TOF) calcd for $C_{23}H_{24}O_2$ 332.1776, found 332.1780.

Ethyl 2-acetyl-5-phenyl-2,3,6,7,8,9-hexahydro-1*H*-cyclopenta[*a*]naphthalene-2-carboxylate (2i). Amorphous solid, 45 mg, 62%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, J = 7.4 Hz, 2H), 7.33–7.28 (m, 1H), 7.26 (s, 1H), 7.24 (s, 1H), 6.89 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.54 (q, J = 16.6 Hz, 2H), 3.43 (d, J = 8.9 Hz, 2H), 2.69 (t, J = 6.2 Hz, 2H), 2.53 (t, J = 5.8 Hz, 2H), 2.25 (s, 3H), 1.85–1.77 (m, 2H), 1.70–1.63 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.79, 172.64, 142.29, 141.45, 137.81, 136.40, 133.28, 133.16, 129.26, 127.94, 126.59, 122.71, 66.56, 61.83, 39.00, 37.69, 28.47, 27.31, 26.11, 23.16, 22.70, 14.06; IR (neat) 2935, 1722, 1245 cm^{-1}; HRMS (TOF) calcd for $C_{24}H_{26}O_3$ 362.1882, found 362.1885.

Ethyl 2-acetyl-4-methyl-6-phenyl-2,3-dihydro-1*H*-indene-2-carboxylate (2j). Amorphous solid, 50 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 2H, J = 8 Hz), 7.40 (t, 2H, J = 8 Hz), 7.30 (t, 1H, J = 8 Hz), 7.23 (s, 1H), 7.20 (s, 1H), 4.23 (q, 2H, J = 8 Hz), 3.59 (dd, 2H, J = 12 Hz, 4 Hz), 3.48 (s, 2H), 2.32 (s, 3H), 2.25 (s, 3H), 1.28 (t, 3H, J = 8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 172.5, 141.4, 140.7, 140.2, 137.9, 134.0, 128.6, 127.1, 127.0, 120.4, 66.5, 61.9, 39.2, 37.6, 26.1, 19.2, 14.0; IR (neat) 3461, 1714, 1233 cm^{-1}; HRMS (TOF) Calcd for $C_{21}H_{22}O_3$ 322.1569; Found, 322.1574.

Ethyl 2-acetyl-6-(4-methoxyphenyl)-4-methyl-2,3-dihydro-1*H*-indene-2-carboxylate (2k). Amorphous solid, 56 mg, 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, 2H, J = 8 Hz), 7.18 (s, 1H), 7.16 (s, 1H), 6.93 (d, 2H, J = 8 Hz), 4.23 (dd, 2H, J = 12 Hz, 4 Hz), 3.82 (s, 3H), 3.57 (dd, 2H, J = 24 Hz, 8 Hz), 3.46 (d, 2H, J = 4 Hz), 2.30 (s, 3H), 2.24 (s, 3H), 1.27 (t, 3H, J = 8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 172.5, 158.9, 140.3, 140.2, 137.3, 134.0, 133.9, 128.1, 126.7, 120.0, 114.0, 66.5, 61.9, 55.3, 39.2, 37.5, 26.1, 19.2, 14.1; IR (neat) 3455, 1712, 1242 cm^{-1}; HRMS (TOF) Calcd for $C_{22}H_{24}O_4$ 352.1675; Found, 352.1680.

4′-Methyl-6′-phenyl-1′,3′-dihydrospiro[cyclohexane-1,2′-indene]-2,6-dione (2l). Yellow solid, mp 55–57 °C, 52 mg, 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 7.2 Hz,

2H), 7.39 (t, J=15.2 Hz, 2H), 7.34–7.27 (m, 1H), 7.20 (s, 2H), 3.53 (s, 2H), 3.42 (s, 2H), 2.89–2.73 (m, 4H), 2.30 (s, 3H), 2.10–1.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 141.4, 140.8, 139.7, 137.7, 134.0, 128.7, 127.2, 127.1, 127.0, 120.4, 72.1, 39.1, 37.6, 37.1, 19.2, 17.8; IR (neat) 2919, 1695, 1316 cm^{-1}; HRMS (TOF) calcd for $C_{21}H_{20}O_2$ 304.1463, found 304.1466.

6′-(4-Chlorophenyl)-4′-methyl-1′,3′-dihydrospiro[cyclohexane-1,2′-indene]-2,6-dione (2m). Yellow solid, mp 65–68 °C, 55 mg, 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J=8.3 Hz, 2H), 7.34 (d, J=8.5 Hz, 2H), 7.14 (s, 2H), 3.51 (s, 2H), 3.40 (s, 2H), 2.77 (t, J=6.7 Hz, 4H), 2.28 (s, 3H), 2.08–1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.69, 139.95, 139.84, 139.47, 138.04, 134.13, 132.97, 128.74, 128.31, 126.93, 120.16, 71.96, 38.97, 37.54, 37.13, 19.15, 17.73; IR (neat) 2925, 1698, 1336 cm^{-1}; HRMS (TOF) Calcd for $C_{21}H_{19}ClO_2$ 338.1074, Found, 338.1079.

Ethyl 7-methyl-5-phenyl-1*H*-indene-2-carboxylate(2n). Amorphous solid, 40 mg, 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (t, 1H, J=4 Hz), 7.60–7.56 (m, 3H), 7.45–7.42 (m, 2H), 7.38 (s, 1H), 7.36–7.32 (m, 1H), 4.33 (dd, 2H, J=12 Hz, 8 Hz), 3.62 (d, 2H, J=4 Hz), 2.44 (s, 3H), 1.38 (t, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 143.1, 142.6, 141.3, 140.7, 137.7, 133.8, 128.7, 127.9, 127.3, 127.2, 119.7, 60.5, 37.1, 18.8, 14.4; IR (neat) 3464, 1705, 763 cm^{-1}; HRMS (TOF) Calcd for $C_{19}H_{18}O_2$ 278.1307; Found, 278.1308.

1,4-Dimethyl-6-phenyl-2-tosylisoindoline (4a). Amorphous solid, 58 mg, 77%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J=8.0 Hz, 2H), 7.50 (d, J=6.8 Hz, 2H), 7.41 (t, J=15.2 Hz, 2H), 7.35 –7.33 (m, 1H), 7.30 (s, 1H), 7.28 (s, 1H), 7.23 (s, 1H), 7.11 (s, 1H), 4.99 –4.95 (m, 1H), 4.73–4.68 (m, 1H), 4.51 (d, J=13.6 Hz, 1H), 2.39 (s, 3H), 2.25 (s, 3H), 1.71 (d, J=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 142.2, 141.8, 140.8, 134.7, 133.1, 132.8, 129.8, 128.8, 127.8, 127.6, 127.4, 127.1, 118.4, 62.3, 53.1, 24.0, 21.5, 18.7; IR (neat) 3406, 1607, 1179 cm^{-1}; HRMS (TOF) calcd for $C_{23}H_{23}NO_2S$ 377.1449, found 377.1448.

1,4-Dimethyl-6-(*p*-tolyl)-2-tosylisoindoline (4b). Amorphous solid, 59 mg, 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J=8.3 Hz, 2H), 7.39 (d, J=8.1 Hz, 2H), 7.29 (d, J=8.0 Hz, 2H), 7.22 (d, J=2.0 Hz, 2H), 7.20 (s, 1H), 7.09 (s, 1H), 5.07–4.84 (m, 1H), 4.72–4.68 (m, 1H), 4.50 (d, J=13.8 Hz, 1H), 2.38 (s, 3H), 2.37 (s, 3H), 2.24 (s, 3H), 1.70 (d, J=6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 142.1, 141.7, 137.9, 137.3, 134.6, 132.8, 132.8, 129.8, 129.5, 127.6, 127.6, 126.9, 118.2, 62.3, 53.1, 24.0, 21.5, 21.1, 18.7; IR (neat) 3408, 1610, 1183 cm^{-1}; HRMS (TOF) calcd for $C_{24}H_{25}NO_2S$ 391.1606, found 391.1609.

6-(4-Methoxyphenyl)-1,4-dimethyl-2-tosylisoindoline(4c). Amorphous solid, 67 mg, 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 2H, J=8 Hz), 7.36 (d, 2H, J=12 Hz), 7.21 (d, 2H, J=8 Hz), 7.11 (s, 1H), 6.99 (s, 1H), 6.87 (d, 2H, J=12 Hz), 4.88 (d, 1H, J=4 Hz), 4.62 (dd, 1H, J=12 Hz, 8 Hz), 4.42 (d, 1H, J=16 Hz), 3.75 (s, 3H), 2.31 (s, 3H), 2.16 (s, 3H), 1.63 (d, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 143.5, 142.1, 141.3, 134.5, 133.2, 132.7, 132.4, 129.8, 128.1, 127.5, 127.3, 117.9, 114.2, 62.2, 55.3, 53.0, 24.0, 21.5, 18.7; IR (neat) 3414, 1619, 1186 cm^{-1}; HRMS (TOF) Calcd for $C_{24}H_{25}NO_3S$ 407.1555; Found, 407.1554.

6-(4-Chlorophenyl)-1,4-dimethyl-2-tosylisoindoline(4d). Amorphous solid, 49 mg, 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, 2H, J=8 Hz), 7.42–7.35 (m, 4H), 7.28 (d, 2H, J=8 Hz), 7.18 (s, 1H), 7.05 (s, 1H), 4.95 (d, 1H, J=8 Hz), 4.69 (d, 1H, J=16 Hz, 4 Hz), 4.49 (d, 1H, J=16 Hz), 2.38 (s, 3H), 2.24 (s, 3H), 1.69 (d, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 142.3, 140.4, 139.2, 134.5, 133.5, 133.4, 133.0, 129.8, 128.9, 128.3, 127.5, 127.5, 118.2, 62.2, 53.0, 24.0, 21.5, 18.7; IR (neat) 3476, 1619, 1163 cm^{-1}; HRMS (TOF) Calcd for $C_{23}H_{22}ClNO_2S$ 411.1060; Found, 411.1056.

1,4-Dimethyl-6-(thiophen-2-yl)-2-tosylisoindoline(4e). Amorphous solid, 64 mg, 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2H, J=8 Hz), 7.28 (d, 2H, J=8 Hz), 7.24–7.21 (m, 3H), 7.11 (s, 1H), 7.04 (dd, 1H, J=8 Hz, 4 Hz), 4.92 (dd, 1H, J=12 Hz, 8 Hz), 4.66 (dd, 1H, J=16 Hz, 12 Hz), 4.46 (d, 1H, J=16 Hz), 2.37 (s, 3H), 2.21 (s, 3H), 1.68 (d, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 143.6, 142.3, 134.6, 134.5, 133.3, 133.0, 129.8, 128.0, 127.5, 126.5, 124.9, 123.2, 117.2, 62.1, 53.0, 24.0, 21.5, 18.6; IR (neat) 3475, 1620, 1190 cm^{-1}; HRMS (TOF) Calcd for $C_{21}H_{21}NO_2S_2$ 383.1014; Found, 383.1021.

1-Ethyl-4-methyl-6-phenyl-2-tosylisoindoline(4f). Amorphous solid, 59 mg, 76%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2H, J=8 Hz), 7.51–7.48 (m, 2H), 7.42–7.38 (m, 2H), 7.34–7.32 (m, 1H), 7.26 (d, 2H, J=8 Hz), 7.22 (s, 1H), 7.09 (s, 1H), 5.06–5.05 (m, 1H), 4.65 (dd, 1H, J=16 Hz, 4 Hz), 4.56 (d, 1H, J=8 Hz), 2.36 (s, 3H), 2.33–2.24 (m, 1H), 2.24 (s, 3H), 1.97–1.91 (m, 1H), 0.79 (t, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 141.5, 140.8, 140.1, 134.8, 134.2, 132.6, 129.7, 128.8, 127.6, 127.4, 127.4, 127.1, 118.4, 66.9, 53.5, 29.0, 21.5, 18.8, 7.5; IR (neat) 3415, 1620, 1187 cm^{-1}; HRMS (TOF) Calcd for $C_{24}H_{25}NO_2S$ 391.1606; Found, 391.1606.

1-Ethyl-4-methyl-6-(thiophen-2-yl)-2-tosylisoindoline(4g). Amorphous solid, 64 mg, 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, 2H, J=8 Hz), 7.26 (s, 1H), 7.24–7.22 (m, 4H), 7.10 (s, 1H), 7.05–7.02 (m, 1H), 5.02–5.01 (m, 1H), 4.61 (dd, 1H, J=16 Hz, 4 Hz), 4.52 (d, 1H, J=12 Hz), 2.36 (s, 3H), 2.30–2.20 (m, 1H), 2.20 (s, 3H), 1.94–1.88 (m, 1H), 0.77 (t, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 143.5, 140.2, 134.8, 134.5, 134.5, 132.8, 129.7, 128.0, 127.3, 126.4, 124.8, 123.1, 117.2, 66.8, 53.5, 29.1, 21.5, 18.6, 7.4; IR (neat) 3415, 1622, 1130 cm^{-1}; HRMS (TOF) Calcd for $C_{22}H_{23}NO_2S_2$ 397.1170; Found, 397.1176.

1,4-Dimethyl-2-(methylsulfonyl)-6-phenylisoindoline(4h). Amorphous solid, 45 mg, 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.73 (m, 2H), 7.45–7.41 (m, 2H), 7.37–7.35 (m, 1H), 7.31 (s, 1H), 7.20 (s, 1H), 5.08 (q, 1H, J=8 Hz), 4.67–4.66 (m, 2H), 2.87 (s, 3H), 2.31 (s, 3H), 1.64 (d, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 142.0, 140.7, 133.1, 133.0, 128.8, 128.0, 127.5, 127.1, 118.5, 62.3, 52.8, 35.7, 23.8, 18.8; IR (neat) 3476, 1620, 1158 cm^{-1}; HRMS (TOF) Calcd for $C_{17}H_{19}NO_2S$ 301.1136; Found, 301.1140.

6-(4-Methoxyphenyl)-1,4-dimethyl-2-(methylsulfonyl)-isoindoline(4i). Amorphous solid, 52 mg, 79%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.46 (m, 2H), 7.27 (s, 1H), 7.15 (s, 1H), 6.96 (d, 2H, J=8 Hz), 5.08–5.04 (m, 1H), 4.69–4.61 (m, 2H), 3.84 (s, 3H), 2.86 (s, 3H), 2.30 (s, 3H), 1.63 (d, 3H, J=8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 142.1, 141.6, 133.2, 132.9, 132.5, 128.2, 127.6, 118.0, 114.2, 62.4, 55.4, 52.8,

35.6, 23.8, 18.8; IR (neat) 3413, 1619, 1189 cm^{-1}; HRMS (TOF) Calcd for $C_{18}H_{21}NO_3S$ 331.1242; Found, 331.1245.

1-Benzyl-4-methyl-6-phenyl-2-tosylisoindoline(4j). Amorphous solid, 56 mg, 62%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, 2H, $J=8$ Hz), 7.38–7.37 (m, 4H), 7.34–7.27 (m, 3H), 7.24–7.19 (m, 3H), 7.16 (s, 1H), 7.12–7.10 (m, 2H), 6.72 (s, 1H), 5.25 (d, 1H, $J=8$ Hz), 4.44 (d, 1H, $J=16$ Hz), 4.31–4.27 (m, 1H), 3.50–3.46 (dd, 1H, $J=12$ Hz, 8 Hz), 3.23 (q, 1H, $J=8$ Hz), 2.36 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 140.7, 140.6, 139.7, 136.6, 134.2, 132.5, 130.4, 129.8, 128.7, 128.0, 127.6, 127.3, 127.2, 126.9, 126.5, 119.2, 67.1, 52.9, 43.5, 21.5, 18.7; IR (neat) 3465, 1638, 699 cm^{-1}; HRMS (TOF) Calcd for $C_{29}H_{27}NO_2S$ 453.1762; Found, 453.1765.

1-(4-Methyl-6-phenyl-2,3-dihydro-1*H*-inden-2-yl)ethanone(5). To a solution of **2j** (160 mg, 0.5 mmol) in ethanol (6 mL) was added 2N NaOH (2 mL). The mixture was allowed to reflux overnight. After cooling, water (5 mL) and EtOAc (10 mL) were added and the mixture was separated. The organic layer was dried over Na_2SO_4. After evaporation, chromatography on silica gel (eluent: hexane/ethyl acetate = 5:1) afforded **5**. Amorphous solid, 102 mg, 82%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, 2H, $J=4$ Hz), 7.43–7.40 (m, 2H), 7.34–7.30 (m, 1H), 7.27 (s, 1H), 7.22 (s, 1H), 3.53–3.44 (m, 1H), 3.26–3.24 (m, 2H), 3.14 (d, 2H, $J=8$ Hz), 2.33 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.4, 141.9, 141.5, 140.4, 139.6, 134.2, 128.7, 127.1, 127.0, 126.8, 120.6, 51.6, 35.2, 33.4, 28.6, 19.3; IR (neat) 3458, 1709, 733 cm^{-1}; HRMS (TOF) Calcd for $C_{18}H_{18}O$ 250.1358; Found, 250.1362.

4-Methyl-6-phenyl-2,3-dihydro-1*H*-indene-2-carboxylic acid(6). To a solution of **2j** (160 mg, 0.5 mmol) was added 40% NaOH (3 mL). The mixture was stirred at 80°C for 2 h. After cooling, concentrated hydrochloric acid was added at 0°C until pH 1~2. Dichloromethane (10 mL) was added and the mixture was separated. The organic layer was dried over Na_2SO_4, After evaporation, chromatography on silica gel (eluent: hexane/ethyl acetate = 1:1) afforded **6**. Amorphous solid, 97 mg, 77%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, 2H, $J=8$ Hz), 7.43–7.40 (m, 2H), 7.34–7.30 (m, 1H), 7.28 (s, 1H), 7.23 (s, 1H), 3.43 (q, 1H, $J=8$ Hz), 3.36–3.30 (m, 2H), 3.24 (d, 2H, $J=8$ Hz), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.7, 141.8, 141.4, 140.5, 139.4, 134.1, 128.6, 127.1, 127.0, 126.8, 120.5, 43.0, 36.2, 34.5, 19.2; IR (neat) 3458, 1704, 762 cm^{-1}; HRMS (TOF) Calcd for $C_{17}H_{16}O_2$ 252.1150; Found, 252.1154.

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