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Palladium-catalyzed chemoselective synthesis of indane-1, 3-dione derivatives via *tert*-butyl isocyanide insertion

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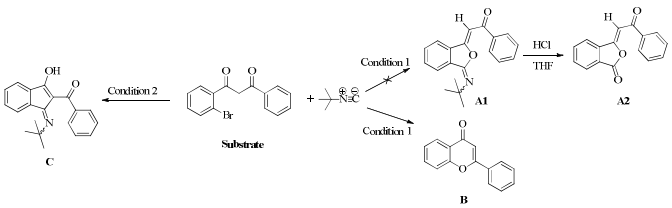
A simple and efficient strategy for the synthesis of indane-1, 3-dione derivatives through a palladium (0)-catalyzed reaction incorporating with *tert*-butyl isocyanide has been developed. In addition, by applying this protocol as the key step, indenopyrazole derivatives can be easily synthesized in high yields in a one-pot procedure. The methodology is tolerant of a wide range of substrates and applicable to library synthesis.

Introduction

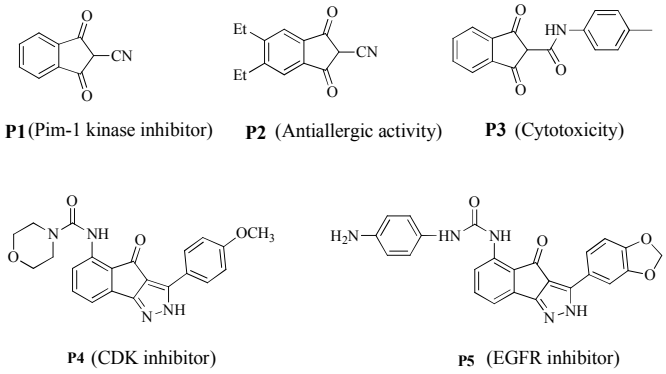
During the past few decades, isocyanides insertion has emerged as an effective strategy in modern synthetic organic chemistry, since the pioneering work of Passerini[1] and Ugi[2] and subsequently related isocyanide-based two-component reactions[3] with isocyanides insertion into palladium-carbon bond and evolutionary multicomponent reactions (MCRs).[4] Recently, a wide range of organic compounds including isocoumarins, phthalides,[5] quinazolinones,[6] 6*H*-isoindolo[2,1-*a*]indol-6-ones, indenoindolones,[7] alkynones,[8] diarylketones,[9] arylaldehydes[10] have been synthesized via the insertion of isocyanides to form C-N , C-O or C-C bonds by our group. However, the work about chemoselective insertion of isocyanides to form C-C bond has been rarely reported, especially when insertion of isocyanides to form C-O bond was also a choice at the same time.



Scheme1. An unexpected synthetic pathway

Condition 1： $Pd(OAc)_2$, DPEPhos, K_2CO_3, DMF, 120 °C; Condition 2： $PdCl_2(PPh_3)_2$, LiO*t*Bu, dioxane, 120 °C

In 2012, our group reported palladium-catalyzed synthesis of isocoumarins and phthalides via *tert*-butyl isocyanide insertion by forming C-O bond.[5] In a continuation to our interest, we tried to synthesis (Z)-3-(2-oxo-2-phenylethylidene)isobenzofuran-1(3*H*)-one (Scheme 1, **A2**) with 1-(2-bromophenyl)-3-phenylpropane-1,3-dione as the substrate by applying the same reaction condition from the above literature.[5] It was surprised that *tert*-butyl isocyanide was not inserted, and the major product (yield = 86%) was 2-phenyl-4*H*-chromen-4-one (Scheme 1, **B**). We suspected that there was a competing reaction under the special condition. It was coincident with Fu group's report.[11] We varied the reaction condition in order to insert *tert*-butyl isocyanide into the substrate. To our delight, *tert*-butyl isocyanide was successfully coupled with carbon atom of the active methylene between the two carbonyls. So new C-C bond was formed, not C-O bond and (1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(phenyl)methanone (Scheme 1, **C**) was synthesized.



P1 (Pim-1 kinase inhibitor) **P2** (Antiallergic activity) **P3** (Cytotoxicity)

P4 (CDK inhibitor) **P5** (EGFR inhibitor)

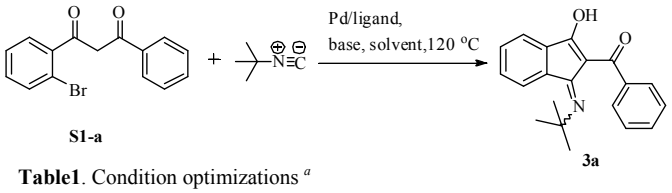
Figure1. Bioactive indane-1, 3-dione derivatives

Indane-1, 3-diones are important building blocks in organic synthesis, especially for the preparation of many natural products and pharmaceuticals.[12] Indane-1, 3-dione derivatives have many biological activities, including Pim-1 kinase inhibitor (**P1**),[13] antiallergic activity (**P2**),[14] cytotoxicity (**P3**),[15] CDK inhibitor (**P4**),[16] and EGFR inhibitor (**P5**)[17]. Due to the importance of indane-1, 3-dione derivatives (Fig.1), some synthetic methodologies have been reported. 1) Decomposition of 2-diazo-l,3-indandione by rhodium(II) acetate in substituted benzene resulted in overall carbon-hydrogen insertion to give 2-substituted indane-1, 3-diones.[18] 2) The reaction of α-diazo ketones and aldehydes in the presence of tin(II) chloride gave indane-1, 3-diones.[19] 3) Furthermore, another alternative approach was via oxidation and cyclization of 2-(2-arylethynylphenyl) acetonitrile with palladium(II) chloride.[20] It is necessary to explore mild and high regioselective methods for the

preparation of indane-1, 3-dione derivatives from commercially available simple starting materials. Herein we report a chemoselective synthesis pathway for these valuable derivatives.

Results and discussion

According to our previous work,[5] the reaction of **S1-a** (1.0 equiv) with *tert*-butyl isocyanide (1.2 equiv) was examined in DMF at 120 °C in the presence of $Pd(OAc)_2$ (5 mol %) and DPEPhos (10 mol %) with K_2CO_3 (2.0 equiv) as base. *tert*-Butyl isocyanide was not inserted and 2-phenyl-4*H*-chromen-4-one(Scheme 1, **B**) was the major product in 86% yield (Table 1, entry 1). We suspected that the reaction selectivity may be affected by base, so we varied base from K_2CO_3 to KO*t*Bu (Table 1, entry 2). The solvent choice was critical for the reaction (Table 1, entries 3-7). It was interesting that the major product was also 2-phenyl-4*H*-chromen-4-one when DMF or CH_3CN was used as solvent. However, (1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl) (phenyl)methanone (**3a**) was synthesized in 62% yield with dioxane as solvent. When the base was switched to LiO*t*Bu, the yield of **3a** was improved to 72% (Table 1, entries 8-11). $Pd(OAc)_2$ or $Pd(dba)_2$ was selected as the Pd resource (Table 1, entries 12-13), and the yield of **3a** decreased. Then, several phosphorus ligands were tested in this reaction (Table 1, entries 14-16), the yield of **3a** did not be improved. When the reaction temperature varied from 120 °C to 100 °C, the yield of **3a** decreased from 72% to 63% (Table 1, entry17). To our delight, 84% yield of **3a** was obtained when 3 equiv LiO*t*Bu was used (Table 1, entry18). Thus, the optimal reaction was performed with **S1-a** (1.0 mmol) in 2.0 mL of dioxane at 60 °C for 0.5 h, then *tert*-butyl isocyanide (1.2 mmol), $PdCl_2(PPh_3)_2$ (0.05mmol) and LiO*t*Bu (3.0 mmol) were added, the reaction was kept at 120 °C for another 2 h.



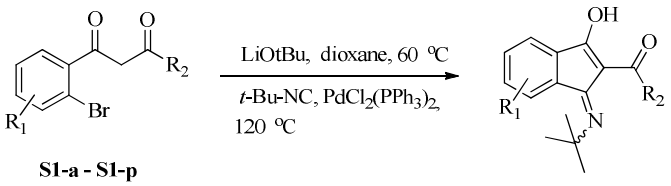
S1-a **3a**

Table1. Condition optimizations [a]

Entry	Catalyst/ligand	Base	Solvent	Yield [b](%)
1	$Pd(OAc)_2$/ DPEPhos	K_2CO_3	DMF	0[c]
2	$PdCl_2(PPh_3)_2$	KO*t*Bu	DMF	0[c]
3	$PdCl_2(PPh_3)_2$	KO*t*Bu	CH_3CN	0[c]
4	$PdCl_2(PPh_3)_2$	KO*t*Bu	THF	41%
5	$PdCl_2(PPh_3)_2$	KO*t*Bu	dioxane	62%
6	$PdCl_2(PPh_3)_2$	KO*t*Bu	toluene	trace
7	$PdCl_2(PPh_3)_2$	KO*t*Bu	anisole	43%
8	$PdCl_2(PPh_3)_2$	LiO*t*Bu	dioxane	72%
9	$PdCl_2(PPh_3)_2$	NaO*t*Bu	dioxane	60%
10	$PdCl_2(PPh_3)_2$	LiHMDS	dioxane	36%
11	$PdCl_2(PPh_3)_2$	K_3PO_4	dioxane	trace
12	$Pd(OAc)_2$/ PPh_3	LiO*t*Bu	dioxane	63%
13	$Pd(dba)_2$/ PPh_3	LiO*t*Bu	dioxane	66%
14	$PdCl_2$/ PCy_3	LiO*t*Bu	dioxane	62%
15	$PdCl_2$/DPPF	LiO*t*Bu	dioxane	58%
16	$PdCl_2$/DPEPhos	LiO*t*Bu	dioxane	52%
17	$PdCl_2(PPh_3)_2$	LiO*t*Bu	dioxane	63%[d]
18	$PdCl_2(PPh_3)_2$	LiO*t*Bu	dioxane	84%[e]

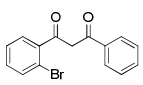
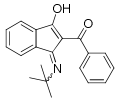
[a] Reaction conditions: All reactions were performed with **S1-a** (1.0 mmol), *tert*-butyl isocyanide (1.2 mmol), catalyst system (0.05mmol) and base (2.0 mmol) in 2.0 mL of solvent at 120 °C for 2 h. DPPF = 1,1′-bis (diphenyl phosphino)ferrocene, DPEPhos = bis [(2-diphenylphosphino) phenyl]ether. PCy_3 = tricyclohexylphosphine, PPh_3 = triphenylphosphine, $Pd(dba)_2$ = bis (dibenzylideneacetone) palladium. [b] Isolated yield. [c] The major product was 2-phenyl-4*H*-chromen-4-one. [d] Reaction at 100 °C for 2 h. [e] The reaction was performed with **S1-a** (1.0 mmol) in 2.0 mL of solvent at 60 °C for 0.5 h. Then *tert*-butyl isocyanide (1.2 mmol), $PdCl_2(PPh_3)_2$ (0.05mmol) and LiO*t*Bu (3.0 mmol) were added, the reaction was kept at 120 °C for another 2 h.

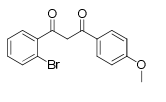
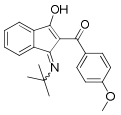
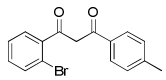
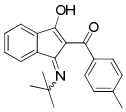
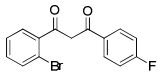
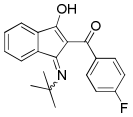
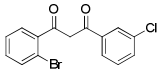
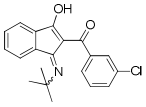
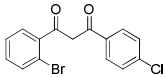
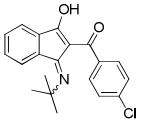
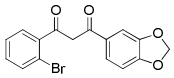
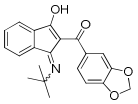
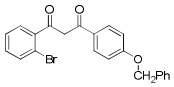
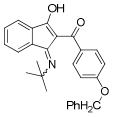
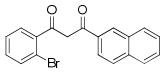
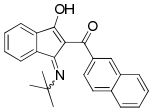
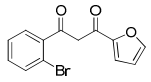
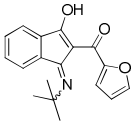
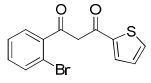
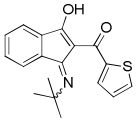
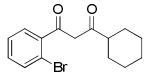
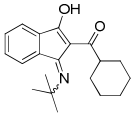
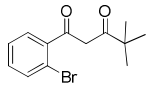
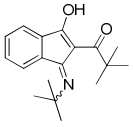
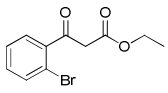
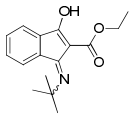
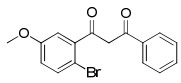
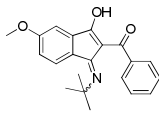
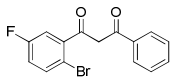
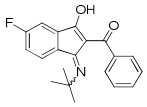
With the optimized reaction conditions in hand, we then tested the scope and generality of this method. Various substitutes in R_2, including aryl (Table 2, entries 1-9), heteroaryl (Table 2, entries 10-11) and alkyl (Table 2, entries 12-13), were well tolerated. Substrates with electron rich and electron deficient functional groups both gave good yields (Table 2, entries 1-8). Good yields were also obtained when $R_2$was a naphthalene or heteroaryl group (Table 2, entries 9-11). In addition, when R_2 was an aliphatic group or OEt (Table 2, entries 12-14), the moderate yields were also obtained. While R_1 was OCH_3 or F (Table 2, entries 15-16), it resulted in a decreased yields of 56% or 54%. It seemed that R_1 was closely correlative with the reaction yield. From the NMR spectra of compounds **3a-3p**, we found that there was a ketone-enol isomerization phenomenon.



S1-a - S1-p **3a-3p**

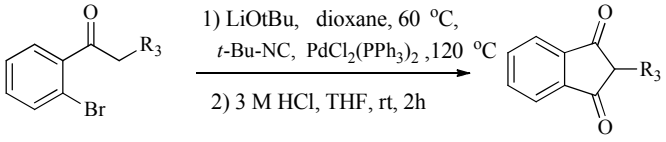
Table2. Synthesis of indane-1, 3-dione derivatives[a]

Entry	Substrate	Product	Yield(%)[b]
1	 **S1-a**	 **3a**	84

2		**S1-b**		**3b**	65
3		**S1-c**		**3c**	68
4		**S1-d**		**3d**	71
5		**S1-e**		**3e**	63
6		**S1-f**		**3f**	61
7		**S1-g**		**3g**	72
8		**S1-h**		**3h**	69
9		**S1-i**		**3i**	86
10		**S1-j**		**3j**	76
11		**S1-k**		**3k**	72
12		**S1-l**		**3l**	53
13		**S1-m**		**3m**	68
14		**S1-n**		**3n**	62
15		**S1-o**		**3o**	56
16		**S1-p**		**3p**	54

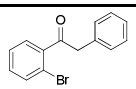
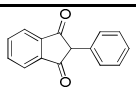
[a]All reactions were performed under N_2 on a 1.0 mmol scale, using LiO*t*Bu (3.0 mmol) in dioxane (2.0 mL) at 60 °C for 0.5 h. Then $PdCl_2(PPh_3)_2$ (0.05mmol) and *ter*t-butyl isocyanide (1.2 mmol) were added, the reactions were kept at 120 °C for another 2 h. [b] Isolated yield.

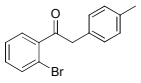
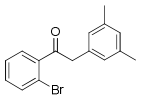
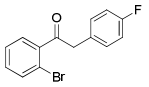
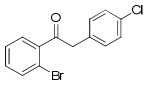
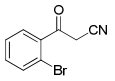
To further evaluate this practical approach, a variety of substrates with active methylene group were investigated, and the results were summarized in Table 3.When R_3 was phenyl, the insertion reaction of 1-(2-bromophenyl)-2-phenylethanone with *tert*-butyl isocyanide successfully delivered the desired products. And 2-phenyl-1*H*-indene-1,3(2*H*)-dione was synthesized via hydrochloric acid hydrolysis in the yield of 66% (Table 3, entry 1). Electron-donating as well as electron-withdrawing substitutes of benzene ring were well tolerated, and yields of the former were higher than those of the latter (Table 3, entries 2-5). In addition, as for aliphatic substitutes, the desired products were obtained in good yields (Table 3, entries 6-7). To our delight, the substrate with sensitive functional group such as CN was also converted smoothly in the moderate yield (Table 3, entry8). It was interesting that when (2-bromophenyl) (cyclohexyl) methanone was employed as the substrate, *tert*-butyl isocyanide was coupled with oxygen atom of enolic form by carbonyl tautomerism and *N*-(3-cyclohexylideneisobenzofuran-1(3*H*)-ylidene)-2-methyl propan-2-amine (Scheme 2, 4i) was generated in 74% yield, which might due to the steric hindrance. Similarly, 1-(2-bromophenyl) propan-2-one afforded 3-methyl-1*H*-isochromen-1-one (Scheme 2, 5a) with further hydrochloric acid hydrolysis. It suggested that in the optimized conditions, reaction selectivity was determined by the structure of substrate.



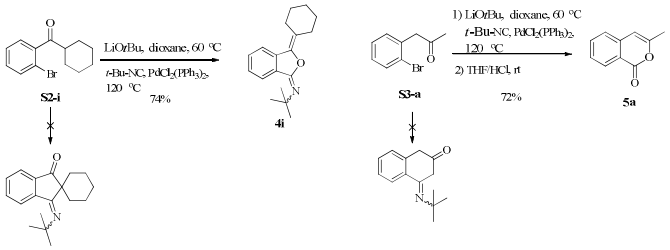
S2-a - S2-h **4a-4h**

Table3. Synthesis of indane-1, 3-diones [a]

Entry	Substrate	Product	Yield(%)[b]
1	 **S2-a**	 **4a**	66

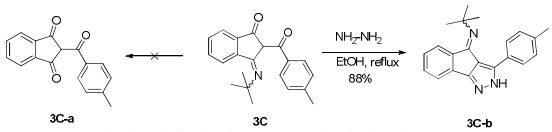
2		**S2-b**	**4b**	75
3		**S2-c**	**4c**	73
4		**S2-d**	**4d**	62
5		**S2-e**	**4e**	61
6		**S2-f**	**4f**	76
7		**S2-g**	**4g**	63
8		**S2-h**	**4h**	61[c]

[a] All reactions were performed under N_2 on a 1.0 mmol scale, using LiO*t*Bu (3.0 mmol) in dioxane (2.0 mL) at 60 °C for 0.5 h. Then $PdCl_2(PPh_3)_2$ (0.05mmol) and *ter*t-butyl isocyanide (1.2 mmol) were added, the reactions were at 120 °C for another 2 h, followed by hydrolysis in THF/hydrochloric acid at r.t. for 2 h. [b] Isolated yield. [c] No hydrolysis.



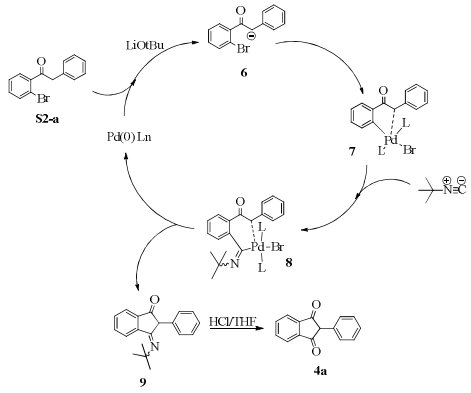
Scheme2. Examples of forming C-O bond

We tried to get compound **3C-a** from **3C** with the assistance of hydrochloric acid or Lewis acid ($AlCl_3$, $FeCl_3$ or $BF_3{\cdot}Et_2O$), but the desired product was not obtained, which might result from the decomposition of compound **3C.** Compound **3C** (1 mmol) was coupled with hydrazine (3 mmol) in refluxing ethanol (10 mL) for 2 hours and the product **3C-b** was afforded in 88% yield. Compound **3C-b** was the prodrug of tyrosine kinase inhibitor 3-(*p*-tolyl)indeno[1,2-*c*]pyrazol-4(2*H*)-one.[16-17] The biology activity evaluation of Compound **3C-b** is underway in our laboratory.



Scheme3. Synthesis of the indenopyrazole derivative **3C-b**

On the basis of the above experimental results and the related literature,[5] a plausible mechanism for this reaction is outlined in Scheme 4. With the assistance of LiO*t*Bu, the intermediate **6** is generated from **S2-a**. Oxidative addition of **6** to the Pd(0) catalyst leads to a Pd(Ⅱ) complex **7**, followed by *tert*-butyl isocyanide insertion to form **8**. Reductive elimination of **8** gives the intermediate **9**，which yields product **4a** by acid hydrolysis.



Scheme4. Plausible mechanism for the synthesis of **4a**

Conclusions

In summary, we have developed a simple and efficient strategy for chemoselective synthesis of indane-1,3-dione derivatives from easily accessible substrates and *tert*-butyl isocyanide. This approach, which provides one of the easiest pathways for this class of valuable compounds, uses $PdCl_2(PPh_3)_2$ as the catalyst system and LiO*t*Bu as base. Furthermore, indenopyrazole derivatives can be easily synthesized in high yields in a one-pot procedure by applying this protocol as the key step. Characterized by mild reaction conditions and moderate to excellent yields, this method may be very attractive in synthetic organic and medicinal chemistry.

Experimental

General experimental section

All chemicals were commercially available. All anhydrous solvents used in the reactions were dried and freshly distilled. Progresses of reactions were monitored by Thin Layer Chromatography on silica $HSGF_{254}$ plates while purification was performed using silica gel column chromatography. Melting points were recorded on an electrothermal digital melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were obtained from a solution in $CDCl_3$or d_6-DMSO with TMS as internal standard using a 400/101 MHz ($^1H/^{13}C$) spectrometer. Chemical shifts (δ) are given in ppm and J in Hz. High resolution mass spectra were carried out on a chemical ionization (CI) apparatus using time-of-flight (TOF) mass spectrometry.

Typical experimental procedure

In a 15 mL sealed tube equipped with a magnetic stirring bar were added the substrate (1.0 mmol) and LiO*t*Bu (240 mg, 3.0 mmol) in anhydrous dioxane (2.0 mL) at 60 °C for 0.5 h; Then $PdCl_2(PPh_3)_2$ (22 mg, 0.05 mmol) and *ter*t-butyl isocyanide (135 μL, 1.2 mmol) were added; The tube was purged with N_2, and the contents were stirred at 120 °C for another 2 h; After completion of the reaction as indicated by TLC, the mixture was filtered through neutral aluminum oxide and the solvent was removed under vacuum.{Then, the residue was stirred in THF (8 mL) and hydrochloric acid (3 M, 3

mL) at r.t. for 2 h. The mixture was extracted with EtOAc, dried with Na_2SO_4 and evaporated.)}[21] The residue was purified on a silica gel column using petroleum ether/EtOAc as the eluent to give the pure target product.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(phenyl)methanone(3a). Yellow solid (256 mg, 84%); m.p.: 139-141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.13(s, 1H), 7.91 (d, J = 4.0Hz, 1H), 7.71 (d, J = 4.0Hz, 1H), 7.65-7.67(m, 2H), 7.54-7.63(m, 2H), 7.40-7.49 (m, 3H), 1.77(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 186.4, 173.0, 140.1, 138.8, 133.5, 132.6, 131.6, 130.8, 128.6, 127.5, 126.9, 123.0, 104.8, 54.6, 30.5; HRMS-CI (m/z) calcd. for $C_{20}H_{20}NO_2[M+H]^+$: 306.1494; found: 306.1495.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(4-methoxyphenyl) methanone (3b).Yellow solid (227 mg, 65%); m.p.: 146-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 4.0Hz, 2H), 7.47-7.63 (m, 3H), 6.95 (d, J = 4.0Hz, 2H), 6.58(s, 1H),5.74(s, 1H), 3.87(s, 3H), 1.37(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 184.9, 163.5, 137.3, 135.3, 133.4, 132.6, 131.5, 130.7, 129.6, 129.5, 128.2, 128.1, 127.2, 114.0, 96.5, 55.6, 52.0, 28.6; HRMS-CI (m/z) calcd. for $C_{21}H_{22}NO_3[M+H]^+$: 336.1600; found: 336.1581.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(p-tolyl)methanone (3c). Yellow solid (217 mg, 68%); m.p.: 121-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 4.0Hz, 2H), 7.63-7.65 (m, 1H), 7.55-7.56 (m, 1H), 7.48-7.50 (m, 2H), 7.25-7.27 (m, 1H), 6.61 (s, 1H), 5.70 (s, 1H), 2.41 (s, 3H), 1.37(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ188.4, 184.6,168.5, 143.6, 137.6, 135.5, 131.9, 130.8, 129.7, 129.5, 128.7, 128.2, 128.1, 127.3, 96.7, 52.1, 28.5, 21.8(CH_3); HRMS-CI (m/z) calcd. for $C_{21}H_{22}NO_2[M+H]^+$: 320.1651; found: 320.1635.

(1-(*tert*-butylimino)-3-hydroxy-1H-inden-2-yl)(4-fluorophenyl) methanone (3d).Yellow solid (229 mg, 71%); m.p.: 144-146 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.98 (m, 2H), 7.64-7.66 (m, 1H), 7.48-7.53 (m, 3H), 7.14 (t, J = 4.0 Hz, 1H), 6.60 (s, 1H), 5.68 (s, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 183.8,168.7,167.2, 137.6, 135.3, 131.2, 129.9, 129.8,129.7, 128.3, 128.2, 116.1, 97.1, 52.3, 28.7; HRMS-CI (m/z) calcd. for $C_{20}H_{19}FNO_2[M+H]^+$: 324.1400; found: 324.1386.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(3-chlorophenyl) methanone (3e).Yellow solid (214 mg, 63%); m.p.: 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.93 (m, 1H), 7.80 (d, J = 4.0 Hz, 1H), 7.65-7.67(m, 1H), 7.50-7.54 (m, 3H), 7.40 (t, J = 8.0 Hz, 1H), 6.61 (s, 1H), 5.68 (s, 1H), 1.39(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 182.4,168.5, 137.6, 136.5, 135.3, 135.0, 132.5, 131.2, 130.0, 129.7, 128.2, 128.1, 127.3, 125.3, 97.3, 52.2, 28.6; HRMS-CI (m/z) calcd. for $C_{20}H_{19}ClNO_2[M+H]^+$: 340.1101; found: 340.1105.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(4-chlorophenyl) methanone (3f).Yellow solid (207 mg, 61%); m.p.: 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 4.0 Hz, 2H), 7.64-7.66(m, 1H), 7.49-7.53 (m, 2H), 7.45 (s, 1H), 7.42 (s, 1H), 6.62(s,1H), 5.67 (s, 1H), 1.38(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9, 182.9,168.6, 139.0, 137.5, 135.3, 133.1, 129.7, 129.1, 128.6, 128.2, 128.1, 97.1, 52.1, 28.5; HRMS-CI (m/z) calcd. for $C_{20}H_{19}ClNO_2[M+H]^+$: 340.1101; found: 340.1098.

benzo[*d*][1,3]dioxol-5-yl(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl) methanone (3g).Yellow solid (264 mg, 72%); m.p.: 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.64 (m, 1H), 7.53-7.56(m, 2H), 7.47-7.50(m, 1H), 7.42 (d, J = 2.0Hz, 1H), 6.86 (d, J = 4.0Hz, 1H), 6.53 (s, 1H), 6.05 (s, 2H), 5.69 (s, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 184.9, 168.6, 151.8, 148.4, 137.5, 135.2, 130.9, 129.8, 129.4, 128.2, 123.5, 108.4,107.4, 102.0, 96.8, 52.2, 28.7; HRMS-CI (m/z) calcd. for $C_{21}H_{22}NO_5[M+H_3O]^+$: 368.1498; found: 368.1509.

(4-(benzyloxy)phenyl)(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl) methanone(3h).Yellow solid (283 mg, 69%); m.p.: 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93(d, J = 4.0Hz, 2H), 7.63-7.65 (m, 1H), 7.53-7.56(m, 2H), 7.55-7.57(m, 1H), 7.35-7.50(m, 6H), 7.03(d, J = 4.0Hz, 2H), 6.58 (s, 1H), 5.71 (s, 1H), 5.13 (s, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1, 184.7, 168.6, 162.6, 137.3, 136.2, 135.3, 130.8, 129.6, 129.5, 128.7, 128.3, 128.1, 127.6, 127.5, 114.9, 96.5, 70.2(OCH_2), 52.1, 28.6; HRMS-CI (m/z) calcd. for $C_{27}H_{26}NO_3[M+H]^+$: 412.1913; found: 412.1910.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(naphthalen-2-yl) methanone (3i). Yellow solid (305 mg, 86%); m.p.: 235-237°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.21(s, 1H), 8.22 (s, 1H,), 7.92 (d, J = 4.0Hz, 2H), 7.86 (d, J = 4.0Hz, 2H), 7.72-7.77(m, 2H), 7.46-7.63(m, 4H), 1.78(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 186.4, 173.0, 138.8, 137.5, 134.8, 133.5, 132.6, 132.5, 131.7, 129.4, 129.2, 127.8, 127.1, 126.9, 126.8, 126.0, 125.8, 123.0, 105.0, 54.6, 30.5; HRMS-CI (m/z) calcd. for $C_{24}H_{22}NO_2[M+H]^+$: 356.1651; found: 356.1629.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(furan-2-yl)methanone (3j).Yellow solid (224 mg, 76%); m.p.: 133-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.66 (m, 2H), 7.59 (s, 1H), 7.52-7.55(m, 1H), 7.47-7.54 (m, 2H), 7.21 (d, J = 2.0 Hz, 1H), 6.57(s, 1H), 6.53(s, 1H), 5.68 (s, 1H), 1.39(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.7, 176.6, 168.4, 150.4, 146.5, 137.6, 134.2, 131.0, 129.6, 128.3, 128.2, 116.4,112.7, 96.7, 52.1, 28.5; HRMS-CI (m/z) calcd. for $C_{18}H_{20}NO_4[M+H_3O]^+$: 314.1392; found: 314.1380.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(thiophen-2-yl) methanone (3k).Yellow solid (224 mg, 72%); m.p.: 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 2.0 Hz, 1H), 7.64(d, J = 4.0 Hz, 2H), 7.48-7.55 (m, 2H), 7.13-7.15 (m, 1H), 6.50 (s, 1H), 5.67 (s, 1H),1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 181.8, 168.0, 141.0, 137.0, 133.3, 132.6, 130.5, 129.1, 127.9, 127.8, 127.6, 96.8, 51.6, 28.1; HRMS-CI (m/z) calcd. for $C_{18}H_{20}NO_3S$ $[M+H_3O]^+$: 330.1164; found:330.1154.

(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)(cyclohexyl)methanone (3l).Yellow solid (165mg, 53%); m.p.: 141-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.54(m, 2H), 7.42-7.47 (m, 2H), 5.93 (s, 1H), 2.24-2.28 (m, 1H), 1.90 (d, J = 4.0 Hz, 2H), 1.80 (d, J = 4.0 Hz, 2H), 1.69 (d, J = 4.0 Hz, 1H), 1.44(s, 1H), 1.41(s, 9H), 1.20-1.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 187.7, 168.4,137.2, 135.2, 130.6, 129.5, 128.1, 128.0, 98.5, 52.0, 46.8, 29.5, 28.6, 25.8, 25.7; HRMS-CI (m/z) calcd. for $C_{20}H_{28}NO_3[M+H_3O]^+$: 330.2069; found: 330.2063.

1-(1-(*tert*-butylimino)-3-hydroxy-1*H*-inden-2-yl)-2,2-dimethylpropan-1-one(3m).Yellow solid (194 mg, 68%); m.p.: 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.54(m, 2H), 7.44-7.49 (m, 2H), 6.04 (s, 1H), 1.41(s, 9H), 1.21(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 188.3, 168.3, 137.2, 135.5, 130.6, 129.6, 128.1, 128.0, 96.2, 52.0, 39.5, 28.6, 27.3; HRMS-CI (m/z) calcd. for $C_{18}H_{24}NO_2[M+H]^+$:286.1807; found: 286.1801.

ethyl 1-(*tert*-butylimino)-3-hydroxy-1*H*-indene-2-carboxylate (3n). Yellow solid (170 mg, 62%); m.p.: 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.96 (s, 1H), 7.80 (d, J = 4.0 Hz, 1H)， 7.68 (d, J = 4.0 Hz, 1H)，7.53 (t, J = 8.0 Hz, 1H),7.46 (t, J = 8.0 Hz, 1H),4.33(q, J = 8.0 Hz, 2H), 1.70(s, 9H), 1.39 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ186.0, 172.1, 168.3, 138.5, 132.9, 132.8, 131.0, 126.4, 122.5, 95.4, 59.8, 54.2, 30.8, 14.7; HRMS-CI (m/z) calcd. for $C_{16}H_{20}NO_3[M+H]^+$:274.1443; found: 274.1441.

(1-(*tert*-butylimino)-3-hydroxy-5-methoxy-1*H*-inden-2-yl)(phenyl) methanone (3o).Yellow solid (188 mg, 56%); m.p.: 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.05(s, 1H), 7.80 (d, J = 4.0Hz, 1H), 7.65-7.67(m, 2H), 7.40-7.46(m, 3H), 7.24 (d, J = 2.0 Hz, 1H)，6.98-7.01 (m, 1H), 3.90(s, 3H), 1.74(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 185.8, 164.3, 142.5, 140.2, 130.6, 128.7, 128.6, 127.5,123.8, 117.2, 107.9, 104.8, 56.0, 54.4, 30.3; HRMS-CI (m/z) calcd. for $C_{21}H_{22}NO_3[M+H]^+$: 336.1600; found: 336.1604.

(1-(*tert*-butylimino)-5-fluoro-3-hydroxy-1*H*-inden-2-yl)(phenyl) methanone (3p).Yellow solid (174 mg, 54%); m.p.: 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.95 (m, 2H), 7.54-7.59 (m, 2H), 7.47 (t, J = 8.0 Hz, 2H), 7.33 (t, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 1H)，6.62(s, 1H), 1.37(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9, 184.5, 172.9, 167.6, 164.2, 161.7, 138.0, 134.4, 133.6, 133.1, 130.6, 128.9, 127.5, 117.9, 115.2, 97.3, 52.3, 28.7; HRMS-CI (m/z) calcd. for $C_{20}H_{18}FNO_2[M+H]^+$: 323.1322; found: 323.1325.

2-phenyl-1*H*-indene-1,3(2*H*)-dione (4a).[22]Yellow solid (147 mg, 66%); m.p.: 165-167 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.09 (m, 2H), 7.90-7.93 (m, 2H), 7.31-7.38 (m, 3H), 7.18-7.20 (m, 2H), 4.27(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3,142.6,136.0,133.0, 129.0, 128.7, 127.8, 123.7, 59.8; HRMS-CI (m/z) calcd. for $C_{15}H_{11}O_2[M+H]^+$: 223.0759; found: 223.0763.

2-(*p*-tolyl)-1*H*-indene-1,3(2*H*)-dione (4b).[22]Yellow solid (177mg, 75%); m.p.: 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.07 (m, 2H), 7.88-7.91 (m, 2H), 7.16 (d, J = 4.0 Hz, 2H), 7.07 (d, J = 4.0 Hz, 2H), 4.18(s, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 142.7, 137.6,135.9, 130.2, 129.7, 128.6, 123.7, 65.9, 21.1; HRMS-CI (m/z) calcd. for $C_{16}H_{12}O_2[M+H]^+$: 237.0916; found:237.0919.

2-(3,5-dimethylphenyl)-1*H*-indene-1,3(2*H*)-dione(4c).Yellow solid (183 mg, 73%); m.p.: 271-273 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.89 (m, 2H), 7.72-7.74 (m, 2H), 6.97(s, 1H), 6.76(s,2H), 2.24(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 141.2, 136.9,135.6, 130.4, 130.1, 128.4, 123.9, 64.9, 21.5;HRMS-CI (m/z) calcd. for $C_{17}H_{15}O_2[M+H]^+$: 251.1072; found: 251.1077.

2-(4-fluorophenyl)-1*H*-indene-1,3(2*H*)-dione (4d).Yellow solid (149mg, 62%); m.p.: 248-250 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.91 (m, 2H), 7.77-7.79 (m, 2H), 7.14-7.18 (m, 2H), 6.93-6.97 (m, 2H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 197.5, 163.3, 141.0, 136.0, 132.4, 125.4, 124.0, 114.7, 63.5; HRMS-CI (m/z) calcd. for $C_{15}H_{10}O_2F$ $[M+H]^+$: 241.0665; found: 241.0672.

2-(4-chlorophenyl)-1*H*-indene-1,3(2*H*)-dione(4e). [22] Yellow solid (146 mg, 61%); m.p.: 244-246 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.91 (m, 2H), 7.77-7.79 (m, 2H), 7.26-7.32 (m, 2H), 7.11-7.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 163.1, 141.2, 136.4, 132.2, 125.1, 124.5, 114.3, 63.7; HRMS-CI (m/z) calcd. for $C_{15}H_{10}O_2Cl$ $[M+H]^+$: 257.0369; found: 257.0360.

1*H*-indene-1,3(2*H*)-dione (4f).Yellow solid (111 mg, 76%); m.p.: 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.98-8.00 (s, 2H), 7.84-7.86 (s, 2H), 3.26 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 143.7, 135.8, 124.3, 45.2; HRMS-CI (m/z) calcd. for $C_9H_7O_2$ $[M+H]^+$: 147.0446; found: 147.0447.

2-octyl-1*H*-indene-1,3(2*H*)-dione (4g).Yellow solid (162 mg, 63%); m.p.: 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 2H), 7.84 (s, 2H), 3.00 (s, 1H), 1.94 (brs, 2H), 1.21-1.37 (m, 11H), 0.85(brs, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 142.6, 135.7, 123.2, 53.6, 32.0, 29.8, 29.6, 29.4, 27.4, 26.5, 22.8, 14.2; HRMS-CI (m/z) calcd. for $C_{17}H_{23}O_2$[M+H]$^+$: 259.1698; found: 259.1703.

1-(*tert*-butylimino)-3-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile(4h). Yellow solid (138 mg, 61%); m.p.: 153-155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.66 (m, 1H), 7.50-7.56 (m, 2H), 7.37-7.39 (m, 1H), 6.34(s, 1H), 1.69(s, 9H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 189.6, 162.8, 137.3, 132.5, 132.4, 132.3, 121.7, 120.9, 118.6, 75.6, 55.0, 29.6; HRMS-CI(m/z) calcd. for $C_{14}H_{15}N_2O$ $[M+H]^+$:227.1184; found: 227.1181.

***N*-(3-cyclohexylideneisobenzofuran-1(3*H*)-ylidene)-2-methylpropan-2-amine (4i).** White solid (199 mg,74%); m.p.: 82-84 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J*=4.0Hz, 1H), 7.76 (d, *J* = 4.0Hz, 1H), 7.46(t, *J* = 8.0Hz,1H), 7.34(t, *J* = 8.0Hz, 1H), 2.66(t, *J* = 4.0Hz,2H), 2.59(t, *J* = 4.0Hz,2H), 1.66-1.70(m, 6H), 1.45(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 142.0, 135.6,132.7, 131.1, 127.8, 123.5, 122.3, 120.6, 53.9, 29.4,28.0, 27.6, 27.3, 26.4; HRMS-CI (m/z) calcd. for $C_{18}H_{23}NO[M]^+$: 269.1780; found: 269.1770.

3-methyl-1*H*-isochromen-1-one (5a).[23] White solid (115 mg,72%); m.p.:73-75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 4.0Hz, 1H), 7.67 (t, *J* = 8.0Hz, 1H), 7.45(t, *J* = 8.0Hz,1H), 7.34(d, *J* = 4.0Hz, 1H), 6.26(s, 1H), 2.29(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 154.1, 137.2, 134.3, 129.0, 127.1, 124.4, 119.4, 103.0, 19.3; HRMS-CI (m/z) calcd. for $C_{10}H_8O_2[M]^+$: 160.0524; found: 160.0528.

2-phenyl-4*H*-chromen-4-one(B).[11] Yellow solid (191 mg, 86%); m.p.: 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 4.0Hz, 1H), 7.93 (d, *J* = 4.0Hz, 2H), 7.71(t, *J* = 8.0Hz,1H), 7.57(d, *J* = 4.0Hz, 1H), 7.50-7.54 (m, 3H), 7.42(t, *J* = 4.0Hz,1H), 6.85(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6,163.6, 156.4, 133.9, 131.9, 131.8, 129.2, 126.4, 125.8, 125.4, 124.1, 118.2, 107.7; HRMS-CI (m/z) calcd. for $C_{15}H_{11}O_2$[M+H]$^+$: 223.0759; found: 223.0755.

2-methyl-*N*-(3-(p-tolyl)indeno[1,2-*c*]pyrazol-4(2*H*)-ylidene)propan-2-amine (3C-b). Yellow solid (277 mg, 88%); m.p.: 185-187 °C; ^{1}H NMR (400 MHz, d_6-DMSO) δ 13.2 (d, *J* = 4.0 Hz, 1H)，7.86-7.89(m, 1H), 7.60-7.64 (m, 2H), 7.24-7.49 (m, 5H), 6.82(s, 1H), 2.33(s, 3H),1.32(s, 9H, CH_3×3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 138.1, 131.2, 130.1, 129.8, 129.2, 128.9,128.3, 128.1, 127.5, 127.0, 125.2, 101.7, 51.1, 29.0, 21.1; HRMS-CI (m/z) calcd. for $C_{21}H_{23}N_3O$ $[M+H_2O]^+$:333.1841; found: 333.1847.

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Electronic Supplementary Information (ESI) available: NMR copies of the target products are provided.

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