DOI: 10.1002/ejoc.201000604

Palladium-Catalyzed Bis-Functionalization of Isatylidenes: A Facile Route towards Spiro-Indol-2-ones

Sholly Clair George,[a] Jubi John,[a] Saithalavi Anas,[a] Joshni John,[a] Yoshinori Yamamoto,[b] Eringathodi Suresh,[c] and K. V. Radhakrishnan*[a]

Keywords: Nitrogen heterocycles / Spiro compounds / Palladium / Allylation / Ring closing metathesis

An effective protocol has been developed for the construction of 3,3-disubstituted indol-2-ones from isatylidenes by utilizing amphiphilic bis-π-allylpalladium and related intermediates. The developed strategy is a new method for the quaternization of position 3 of the indol-2-one towards disubstituted functionalized indol-2-ones. These products were subjected to ring-closing metathesis towards the synthesis of spiro[cyclohexene-1,3′-indol]-2′-ones and spiro[oxep-5-ene-2,3′-indol]-2′-ones, which are of biological interest.

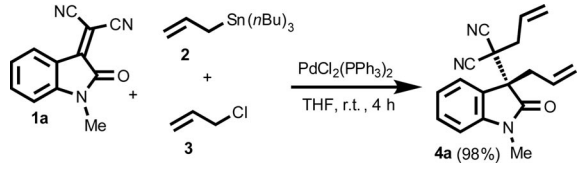
Introduction

Indol-2-ones incorporating a stereogenic center at C-3 are challenging targets for chemical synthesis, as they are common motifs in natural products[1] and pharmaceutically active compounds.[2] Moreover, 3,3-disubstituted indol-2-ones have shown promising biological activity.[1a,1e] Therefore a number of synthetic methods have been developed in pursuit of this structure, including intermolecular alkylations,[3] palladium-catalyzed reactions,[4] cycloadditions,[5] and sigmatropic rearrangements.[6] The extreme steric congestion makes the construction of all-carbon quaternary centers a formidable challenge for synthetic organic chemists.[7] Herein we introduce a new synthetic pathway towards spirocyclic indol-2-ones by a palladium catalyzed bis-allylation of isatylidenes generating a quaternary center which is followed by ring-closing metathesis using Grubbs' 2nd generation catalyst.

The functionalization of activated olefins by utilizing amphiphilic bis-π-allylpalladium or similar complex is becoming an important area of research.[8] These reactions generally proceed under milder conditions with high atom economy and have been exploited for the bis-allylation,[9] alkoxy-allylation,[10] cyano-allylation,[11] acetonation-allylation,[12] amino-allylation[13] and alkyl-allylation[14] of activated olefins to afford the corresponding α, β-functionalized products in high yields. In light of these reports, we were interested to investigate the reactivity of these amphiphilic complexes with different substituted isatylidenes, obtained by the Knoevenagel condensation of a commercially available isatin and malononitrile.

Results and Discussion

Our experiments started with the reaction of the *N*-methylisatylidene **1a** with allyltributyltin (**2**) and allyl chloride (**3**) under the same reaction condition adopted for the bis-allylation of benzylidenemalononitrile.[9] The reaction of these substrates in presence of the catalyst $PdCl_2(PPh_3)_2$ (5 mol-%) in THF at room temperature after four hours yielded the bis-allylated oxindole **4a** in 98% yield (Scheme 1).



Scheme 1. Pd-catalyzed bis-allylation reaction of the isatylidene **1a**.

The structure of the product **4a** was assigned based on spectroscopic analysis. The final confirmation of the structure was made with the help of X-ray crystallographic analysis (Figure 1).

The success in quaternizing C-3 of the oxindole moiety effectively made us extend the reaction to other substituted isatylidenes. The reaction was found to be general with a number of *N*-alkylated isatylidenes and the results are summarized in Table 1. The presence of electron withdrawing groups like $-NO_2$ in the substrate resulted in a slight decrease in the reaction yield (Table 1, entry 5 and 6). The

[a] National Institute for Interdisciplinary Science and Technology, CSIR (Formerly Regional Research Laboratory), Trivandrum 695019, Kerala, India
Fax: +91-471-2491712
E-mail: radhupreethi@rediffmail.com
[b] Department of Chemistry, Graduate School of Science Tohoku University, Sendai 980-8578, Japan
[c] Central Salt and Marine Chemicals Research Institute, Bhavnagar 364002, India
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000604.

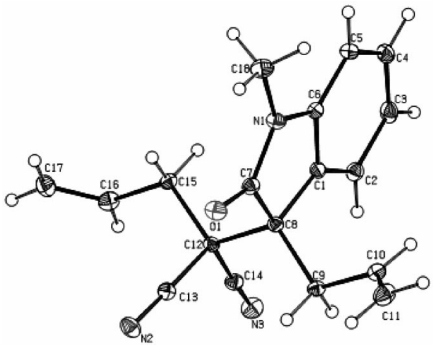
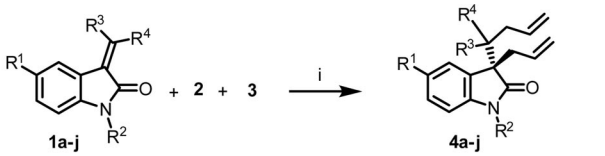


Figure 1. X-ray crystal structure of the bis-allylated oxindole **4a**.

isatylidene derived from ethyl cyanoacetate also showed similar reactivity towards the bis-π-allylpalladium complex and yielded the corresponding bis-allylated indol-2-ones **4i** and **4j** in good yields (Table 1, entry 9 and 10). But for this transformation $Pd(PPh_3)_4$ was found to be the suitable catalyst, as $PdCl_2(PPh_3)_2$ failed to deliver the expected bis-allylated oxindole.

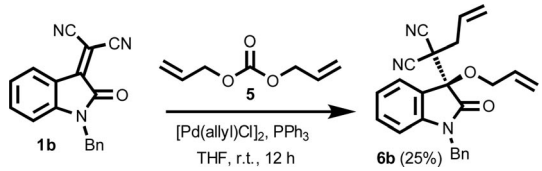
Table 1. Bis allylation reaction of various isatylidenes with bis-π-allylpalladium complex.[a]



Entry	Substrate	R^1	R^2	R^3	R^4	Product	Yield(%)
1	**1a**	H	CH_3	CN	CN	**4a**	98
2	**1b**	H	$CH_2C_6H_5$	CN	CN	**4b**	94
3	**1c**	H	C_2H_5	CN	CN	**4c**	90
4	**1d**	H	$CH_2C_6H_4NO_2$	CN	CN	**4d**	97
5	**1e**	NO_2	$CH_2C_6H_5$	CN	CN	**4e**	83
6	**1f**	NO_2	C_2H_5	CN	CN	**4f**	85
7	**1g**	Br	$CH_2C_6H_5$	CN	CN	**4g**	95
8	**1h**	Br	C_2H_5	CN	CN	**4h**	95
9	**1i**	H	CH_3	CN	CO_2Et	**4i**	78[b]
10	**1j**	H	$CH_2C_6H_5$	CN	CO_2Et	**4j**	73[b]

[a] Reaction conditions: i = isatylidene (1.0 equiv.), allyl chloride (2.0 equiv.), allyltributylstannane (2.0 equiv.), $PdCl_2(PPh_3)_2$ (5 mol-%), THF, room temp. 4 h. [b] $Pd(PPh_3)_4$ (5 mol-%), THF, room temp., 6 h.

Our success in the bis-allylation of substituted isatylidenes made us think to utilize other amphiphilic bis-π-allylpalladium complexes for quaternizing the C-3 position of oxindole skeleton. Hence we turned our attention towards the use of diallyl carbonate **5** for the allyloxy-allylation[10] of activated isatylidenes. In an initial attempt, 1.0 equiv. of the isatylidene **1b** was treated with 1.2 equiv. of diallyl carbonate **5** in the presence of 5 mol-% $[Pd(allyl)Cl]_2$ catalyst in THF which afforded the allylated-oxyallylated product **6b** in 25% yield (Scheme 2).



Scheme 2. Allyloxy-allylation reaction of the isatylidene **1b** with diallyl carbonate **5**.

The compound **6b** was recrystallized from a solvent mixture of acetone and chloroform. The structure and stereochemistry of the product **6b** was unambiguously confirmed by X-ray crystallographic analysis (Figure 2).

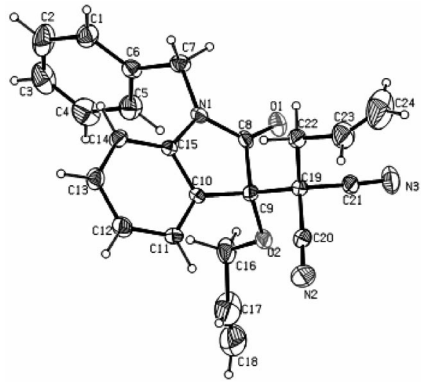
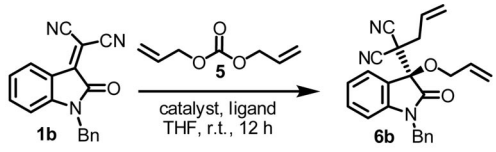


Figure 2. X-ray crystal structure of allyloxy-allylated oxindole **6b**.

Table 2 describes our effort towards optimizing various reaction parameters. Various catalysts such as $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $PdCl_2$, $Pd(OAc)_2$, $Pd_2dba_3{\cdot}CHCl_3$ and $[Pd(allyl)Cl]_2$, were screened from which $[Pd(allyl)Cl]_2$ gave the highest yield (Table 2, entry 1–7). The ligands examined were PPh_3, dppe, dppm, dppp and $P(OEt)_3$ from which PPh_3 was found to be the best ligand (Table 2, entry 7–11).

Table 2. Optimization studies for the reaction between **1b** and diallyl carbonate **5**.[a]

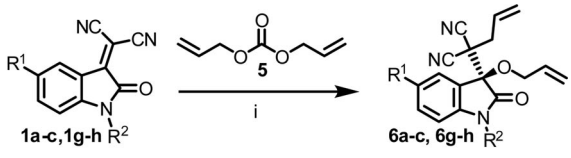


Entry	Catalyst	Ligand	Yield(%)
1	$Pd(PPh_3)_4$	-	75
2	$PdCl_2(PPh_3)_2$	-	No reaction
3	$PdCl_2(PPh_3)_2$	PPh_3	No reaction
4	$PdCl_2$	PPh_3	No reaction
5	$Pd(OAc)_2$	PPh_3	No reaction
6	$Pd_2dba_3.CHCl_3$	PPh_3	50
7	$[Pd(allyl)Cl]_2$	PPh_3	88
8	$[Pd(allyl)Cl]_2$	dppe	38
9	$[Pd(allyl)Cl]_2$	dppm	38
10	$[Pd(allyl)Cl]_2$	dppp	30
11	$[Pd(allyl)Cl]_2$	$P(OEt)_3$	No reaction

[a] Reaction conditions: isatylidene (1.0 equiv.), diallyl carbonate (2.5 equiv.), catalyst (5 mol-%), ligand (10–20 mol-%), THF, room temp., 3 h.

Under this optimized condition [1.0 equiv. of isatylidenes, 2.5 equiv. of diallyl carbonate, 5 mol-% of [Pd(allyl)Cl]$_2$, 20 mol-% of PPh_3 in THF] the reaction was found to be general with different functionalized isatylidenes and the results are summarized in Table 3.

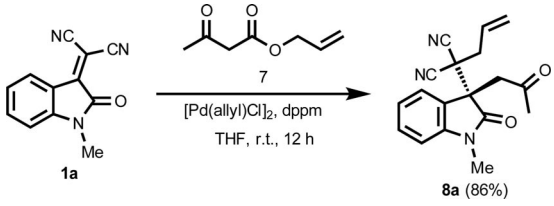
Table 3. Reaction of different isatylidenes with diallyl carbonate **5**.[a]



Entry	Substrate	R^1	R^2	Product	Yield(%)
1	**1a**	H	CH_3	**6a**	88
2	**1b**	H	$CH_2C_6H_5$	**6b**	73
3	**1c**	H	C_2H_5	**6c**	76
4	**1g**	Br	$CH_2C_6H_5$	**6g**	70
5	**1h**	Br	C_2H_5	**6h**	55

[a] Reaction conditions: i = isatylidene (1.0 equiv.), diallyl carbonate (2.5 equiv.), [Pd(allyl)Cl]$_2$ (5 mol-%), PPh_3 (20 mol-%), THF, room temp., 12 h.

In the last phase of the present bis-functionalization study, we decided to investigate the reactivity of oxa-π-allyl π-allylpalladium intermediate[12] generated from allyl acetoacetate **7** as an unsymmetric and functionalized version of amphiphilic bis-π-allylpalladium complex. A test reaction of **1a** with **7** in the presence of catalyst [Pd(allyl)Cl]$_2$ and ligand dppm in THF afforded the β-acetonation α-allylation product **8a** in good yield (Scheme 3).



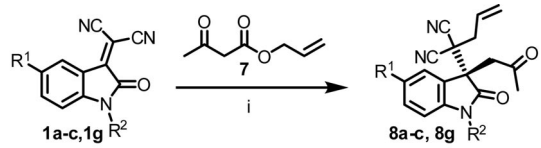
Scheme 3. Acetonation–allylation reaction of isatylidene **1a** with allyl acetoacetate **7**.

Under the optimized conditions [1.0 equiv. of isatylidenes, 1.2 equiv. of allylacetoacetate, 5 mol-% of [Pd(allyl)Cl]$_2$, 10 mol-% of dppm in THF] the reaction of allyl acetoacetate **7** was repeated with different isatylidenes and the results are summarized in Table 4.

Thus amphiphilic bis-π-allylpalladium and related intermediates were effectively utilized for the quaternization of C-3 position of oxindole towards the synthesis of disubstituted functionalized indol-2-ones. The C-3 position was quaternized by introducing different substituents like allyl, oxy-allyl and acetonyl groups and it is to be noted that these latent functional groups can be easily manipulated towards the synthesis of biologically relevant spiro-indol-2-ones.

In the next phase of the work, we decided to exploit the synthetic potential of these bis-allylated products towards the synthesis of spirocycles. The ring-closing metathesis[15]

Table 4. Reaction of various isatylidenes with allylacetoacetate **7**.[a]



Entry	Substrate	R^1	R^2	Product	Yield(%)
1	**1a**	H	CH_3	**8a**	86
2	**1b**	H	$CH_2C_6H_5$	**8b**	78
3	**1c**	H	C_2H_5	**8c**	63
4	**1g**	Br	$CH_2C_6H_5$	**8g**	84

[a] Reaction conditions: i = isatylidene (1.0 equiv.), allylacetoacetate (1.2 equiv.), [Pd(allyl)Cl]$_2$ (5 mol-%), dppm (10 mol-%), THF, room temp., 12 h.

of **4a** in presence of Grubbs' 2nd generation catalyst resulted in the formation of the spiro[cyclohexene-1,3′-indol]-2′-one **9a** in excellent yield (Table 5, entry 1). The generality of these cyclization reactions is presented in Table 5.

Table 5. RCM of different bis-allylated indol-2-ones towards spiro-[cyclohexene-1,3′-indol]-2′-ones.[a]

Entry	Substrate	R^1	R^2	R^3	R^4	Product	Yield(%)
1	**4a**	H	CH_3	CN	CN	**9a**	90
2	**4b**	H	$CH_2C_6H_5$	CN	CN	**9b**	95
3	**4g**	Br	$CH_2C_6H_5$	CN	CN	**9g**	80
4	**4h**	Br	C_2H_5	CN	CN	**9h**	90
5	**4i**	H	CH_3	CN	CO_2Et	**9i**	85

[a] Reaction conditions: bis allylated isatylidene (1.0 equiv.), Grubbs' 2nd generation catalyst (5 mol-%), CH_2Cl_2, room temp., 2 h.

Finally the structure and stereochemistry of the spiro-oxindole **9h** was confirmed by X-ray crystallographic analysis (Figure 3).

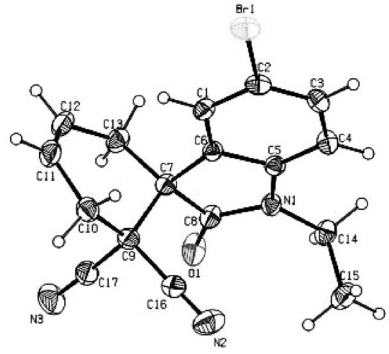
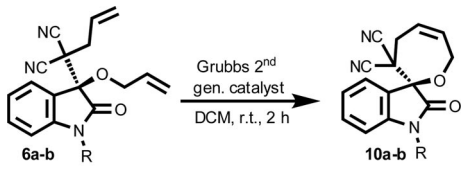


Figure 3. X-ray crystal structure of spiro-indol-2-one **9h**.

We then carried out the ring-closing metathesis of the substrates **6a** and **6b** with Grubbs' 2nd generation catalyst and synthesized the corresponding spirooxepane-fused oxindole **10a** and **10b** in good yields. A survey of literature showed that apart from the methodology reported by Panek et al. which elaborated the stereo-controlled synthesis of spiro-indol-2-ones,[16] there is no other report on the synthesis of oxepane-fused spiro-indol-2-ones. These results are shown in Scheme 4.

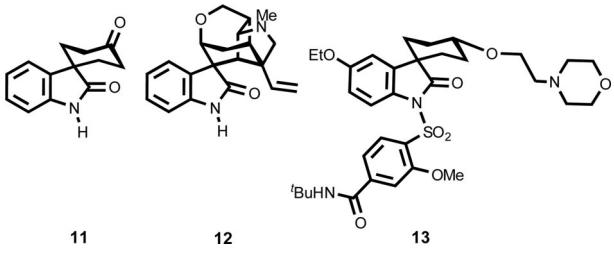


6a, **R** = CH_3; Yield = 61% (**10a**)
6b, **R** = $CH_2C_6H_5$; Yield = 87% (**10b**)

Scheme 4. Synthesis of oxepanes **10a** and **10b**.

Conclusions

In summary, we have described an efficient synthesis of 3,3-disubstituted indol-2-ones from isatylidenes by utilizing the amphiphilic bis-π-allylpalladium and related intermediates. The ring-closing metathesis of the resulting products afforded the corresponding spiro[cyclohexene-1,3′-indol]-2′-ones and spiro[oxep-5-ene-2,3′-indol]-2′-ones in excellent yields. The synthesized spirocyclohexene compound exactly has the core structure of biologically important molecules like the ketone **11**[17], which is active against *Mycobacterium tuberculosis* H37Rv, gelsemine (**12**),[18] the main component of *Gelsemium sempervirenes* and SR 121463 A (**13**),[19] an antagonist of vasopressin receptors (Figure 4).



11 **12** **13**

Figure 4. Spirocyclic indol-2-ones of biological interest.

Therefore this methodology offers a simple and high yielding three step synthesis of various functionalized spirocyclohexenyl and spiro[oxep-5-ene-2,3′-indol]-2′-ones from commercially available isatins. Further work to explore the possible applications of this strategy is underway in our laboratory.

Experimental Section

General Methods: All reactions were conducted in oven dried glassware. Solvents used for the experiments were distilled or dried as specified. All reactions were monitored by TLC (Silica gel 60 F_{254}, 0.25 mm, Merck), visualization was done with UV, by staining with alkaline $KMnO_4$ solution. Gravity column chromatography was done using 100–200 mesh silica gel and appropriate mixture of petroleum ether and ethyl acetate for elution. The solvents were removed by using a Büchi rotary evaporator.

Melting points was determined with a Büchi melting point apparatus. The IR spectra were taken on Nicolet impact 400d FT-IR spectrophotometer. NMR spectra were recorded at 300 and 500 (^{1}H) and 75 and 125 (^{13}C) MHz, respectively, on a Bruker DPX-300 and 500 MHz FT-NMR spectrophotometer. NMR spectra were obtained using $CDCl_3$ as the solvent. Chemical shifts are given in δ scale with TMS as internal standard. Abbreviations used in ^{1}H NMR are s: singlet, d: doublet, dd: double doublet, t: triplet, m: multiplet. Mass spectra were recorded by FAB ionization technique using JEOL JMS 600H mass spectrophotometer.

General Procedure for the Bis-π-Allylation of Isatylidenes: To a degassed solution of catalyst (5 mol-%) in dry THF (2 mL) in a Schlenk tube, allyltributyltin (2.0 equiv.) was added followed by allyl chloride (2.0 equiv.). To this isatylidene derivative (50 mg, 1.0 equiv.) was added (in THF) and stirred at room temperature for further 4 h. After the completion of the reaction (TLC), the solvent was evaporated in vacuo and the residue on silica gel (60–120 mesh) column chromatography using 15% ethyl acetate in hexane afforded the products in excellent yields.

2-Allyl-2-(3-allyl-1-methyl-2-oxoindolin-3-yl)malononitrile (4a): Isatylidene **1a** (50 mg, 0.24 mmol), allyltributyltin (**2**; 0.15 mL, 0.48 mmol) and allyl chloride (**3**; 0.04 mL, 0.48 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4a** was obtained as a white solid (68 mg, 98%) R_f = 0.33 (hexane/ethyl acetate, 7:3); m.p. 84–86 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3434, 2923, 1722, 1612, 1492, 1471, 1374, 1259, 993, 932, 754 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.67 (d, J = 7.6 Hz, 1 H, Ar-H), 7.45–7.40 (m, 1 H, Ar-H), 7.19 (t, J = 7.6 Hz, 1 H, Ar-H), 6.90 (d, J = 7.9 Hz, 1 H, Ar-H) 5.92–5.87 (m, 1 H), 5.39–5.27 (m, Ar-H 2 H), 5.10 (d, J = 3.5 Hz, 1 H), 4.94 (dd, J_1 = 8.9, J_2 = 2.9 Hz, 1 H), 3.23 (s, 3 H, N-Me), 3.10–3.06 (m, 1 H), 3.04–2.99 (m, 1 H), 2.47 (d, J = 7.1 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 144.2, 130.7, 129.4, 128.8, 124.9, 123.9, 123.5, 121.5, 113.8, 112.9, 110.8, 54.4, 44.7, 38.4, 37.0, 28.0 ppm. HRMS (EI): calcd.for $C_{18}H_{17}N_3O$, M^+: 291.1372; found 291.1383.

2-Allyl-2-(3-allyl-1-benzyl-2-oxindolin-3-yl)malononitrile (4b): Isatylidene **1b** (50 mg, 0.175 mmol), allyltributyltin (**2**; 0.10 mL, 0.35 mmol) and allyl chloride (**3**; 0.03 mL, 0.35 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4b** was obtained as a white solid (60 mg, 94%; m.p. 78–80 °C. R_f = 0.47 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3439, 3071, 2924, 1715, 1640, 1611, 1488, 1468, 1432, 1367, 1294, 1226, 1181, 1113, 1078, 991, 934, 866, 755, 698 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.67 (d, J = 7.5 Hz, 1 H, Ar-H), 7.34–7.25 (m, 6 H, Ar-H), 7.15 (t, J = 7.5 Hz, 1 H, Ar-H), 6.82 (d, J = 7.8 Hz, 1 H, Ar-H), 5.89–5.78 (m, 1 H), 5.37–5.25 (m, 2 H), 5.16–5.12 (m, 2 H), 5.07–4.93 (m, 2 H), 4.80 (d, J = 15.5 Hz, 1 H), 3.19–2.99 (m, 2 H), 2.46 (d, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.8, 143.3, 134.9, 130.3, 129.3, 128.8, 128.5, 128.0, 127.6, 124.8, 124.6, 123.7, 123.3, 121.6, 113.5, 112.6, 109.8, 54.0, 44.7, 44.3, 38.3, 36.7 ppm. HRMS (EI): calcd.for $C_{24}H_{21}N_3O$, M^+: 367.1685; found 367.1676.

2-Allyl-2-(3-allyl-1-ethyl-2-oxoindolin-3-yl)malononitrile (4c): Isatylidene **1c** (50 mg, 0.22 mmol), allyltributyltin (**2**; 0.14 mL,

0.44 mmol) and allyl chloride (**3**; 0.04 mL, 0.44 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4c** was obtained as a white solid (57 mg, 90%; m.p. 64–66 °C. R_f = 0.40 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3406, 3087, 2983, 1715, 1640, 1611, 1489, 1469, 1372, 1349, 1234, 1097, 990, 932, 754, 685 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.68 (d, J = 7.7 Hz, 1 H, Ar-H), 7.43–7.38 (m, 1 H, Ar-H), 7.18 (t, J = 7.7 Hz, 1 H, Ar-H), 6.90 (d, J = 7.4 Hz, 1 H, Ar-H), 5.91–5.82 (m, 1 H), 5.40–5.29 (m, 2 H), 5.16–5.12 (m, 2 H), 4.95–4.91 (m, 1 H), 3.79–3.74 (m, 2 H, N-CH_2CH_3), 3.14–3.07 (m, 1 H), 2.99–2.94 (m, 1 H), 2.52–2.48 (m, 2 H), 1.25 (t, J = 7.3 Hz, 3 H, N-CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.3, 143.2, 130.4, 129.2, 128.6, 125.0, 123.5, 121.3, 113.5, 112.7, 108.9, 53.8, 44.6, 38.1, 36.6, 12.6 ppm. HRMS (EI): calcd.for $C_{19}H_{19}N_3O$, M^+: 305.1528; found 305.1616.

2-Allyl-2-[3-allyl-1-(4-nitrobenzyl)-2-oxoindolin-3-yl]malononitrile (4d): Isatylidene **1d** (50 mg, 0.15 mmol), allyltributyltin (**2**; 0.09 mL, 0.30 mmol) and allyl chloride (**3**; 0.025 mL, 0.30 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4d** was obtained as a pale yellow solid (60 mg, 97%; m.p. 178–182 °C. R_f = 0.26 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3862, 3564, 3071, 2933, 2862, 1728, 1612, 1514, 1467, 1345, 1262, 1180, 1111, 990, 938, 858, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.10 (d, J = 8.7 Hz, 2 H, Ar-H), 7.65 (d, J = 7.4 Hz, 1 H, Ar-H), 7.41 (d, J = 8.6 Hz, 2 H, Ar-H), 7.27 (t, J = 7.7 Hz, 1 H, Ar-H), 7.19–7.04 (m, 1 H, Ar-H), 6.67 (d, J = 7.8 Hz, 1 H, Ar-H), 5.87–5.78 (m, 1 H), 5.34–5.17 (m, 2 H), 5.09–5.02 (m, 3 H), 4.92–4.80 (m, 2 H, N-CH_2-4-$NO_2C_6H_4$), 3.06–2.98 (m, 2 H), 2.60–2.48 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 147.7, 142.5, 142.0, 130.6, 129.3, 128.4, 128.3, 125.1, 124.7, 124.2, 124.1, 123.9, 123.5, 121.8, 113.2, 112.6, 109.4, 54.2, 44.6, 43.6, 37.9, 36.5 ppm. HRMS (EI): calcd.for $C_{24}H_{20}N_4O_3$, M^+: 412.1535; found 412.1530.

2-Allyl-2-(3-allyl-1-benzyl-5-nitro-2-oxoindolin-3-yl)malononitrile (4e): Isatylidene **1e** (50 mg, 0.15 mmol), allyltributyltin (**2**; 0.09 mL, 0.30 mmol) and allyl chloride (**3**; 0.025 mL, 0.30 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4e** was obtained as a pale yellow solid (52 mg, 83%; m.p. 124–126 °C. R_f = 0.28 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3439, 2934, 2857, 1730, 1615, 1446, 1337, 1262, 1171, 1111, 1072, 828, 735 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.50–8.39 (m, 1 H), 8.23–8.20 (m, 1 H), 7.27–7.19 (m, 5 H), 6.86–6.82 (m, 1 H), 5.87–5.76 (m, 1 H), 5.37–4.78 (m, 7 H), 3.16–3.02 (m, 1 H), 2.88–2.75 (m, 2 H), 2.65–2.46 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.7, 148.3, 144.4, 133.8, 129.3, 128.6, 128.3, 127.6, 127.4, 126.1, 124.0, 123.1, 122.7, 120.8, 119.8, 110.1, 109.5, 54.3, 52.2, 45.0, 39.2, 37.6 ppm. HRMS (EI): calcd.for $C_{24}H_{20}N_4O_3$, M^+: 412.1535; found 412.1540.

2-Allyl-2-(3-allyl-1-ethyl-5-nitro-2-oxindolin-3-yl)malononitrile (4f): Isatylidene **1f** (50 mg, 0.186 mmol), allyltributyltin (**2**; 0.12 mL, 0.37 mmol) and allyl chloride (**3**; 0.03 mL, 0.37 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4f** was obtained as a pale yellow solid (55 mg, 85%; m.p. 80–84 °C. R_f = 0.19 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3780, 3082, 2983, 1729, 1615, 1524, 1489, 1443, 1338, 1275, 1234, 1116, 1089, 994, 937, 839 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.57 (d, J = 2.1 Hz, 1 H, Ar-H), 8.42–8.39 (m, 1 H, Ar-H), 7.04 (d, J = 8.7 Hz, 1 H, Ar-H), 5.92–5.81 (m, 1 H), 5.45–5.36 (m, 2 H), 5.21–5.11 (m, 2 H), 5.01–4.97 (m, 1 H), 3.86 (q, J = 7.3 Hz, 2 H, N-CH_2CH_3), 3.13–3.11 (m, 2 H), 3.05–3.04 (m, 1 H), 2.74–2.67 (m, 1 H), 2.61–2.54 (m, 1 H), 1.29 (t, J = 7.2 Hz, 3 H, N-CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.6, 148.6, 143.8, 128.2, 128.0, 127.4, 125.9, 124.0, 122.5, 120.8, 112.7, 112.2, 108.6, 53.8, 44.2, 37.5, 36.4, 35.7, 12.5 ppm. HRMS (EI): calcd.for $C_{19}H_{18}N_4O_3$, M^+: 350.1379; found 350.1374.

2-Allyl-2-(3-allyl-1-benzyl-5-bromo-2-oxoindolin-3-yl)malononitrile (4g): Isatylidene **1g** (50 mg, 0.14 mmol), allyltributyltin (**2**; 0.09 mL, 0.28 mmol) and allyl chloride (**3**; 0.02 mL, 0.37 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4g** was obtained as a white solid (58 mg, 95%; m.p. 138–140 °C. R_f = 0.44 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3840, 3444, 2930, 2862, 1727, 1604, 1454, 1347, 1262, 1176, 993, 814 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.78 (d, J = 1.8 Hz, 1 H, Ar-H), 7.44 (dd, J_1 = 8.4, J_2 = 1.8 Hz, 1 H, Ar-H), 7.32–7.26 (m, 5 H, Ar-H), 6.69 (d, J = 8.4 Hz, 1 H, Ar-H), 5.93–5.79 (m, 1 H), 5.41–5.36 (m, 2 H), 5.16–5.10 (m, 2 H), 5.01–4.96 (m, 2 H), 4.78 (d, J = 15.5 Hz, 1 H), 3.18–3.00 (m, 2 H), 2.55–2.49 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.3, 142.3, 134.3, 133.4, 128.9, 128.8, 128.3, 128.2, 127.9, 127.6, 126.7, 123.6, 122.0, 116.5, 113.2, 112.4, 111.3, 54.1, 44.4, 38.2, 36.6, 27.9 ppm. HRMS (EI): calcd.for $C_{24}H_{20}BrN_3O$, M^+: 445.0790; found 445.0792.

2-Allyl-2-(3-allyl-5-bromo-1-ethyl-2-oxoindolin-3-yl)malononitrile (4h): Isatylidene **1h** (50 mg, 0.165 mmol), allyltributyltin (**2**; 0.1 mL, 0.33 mmol) and allyl chloride (**3**; 0.03 mL, 0.33 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 85:15), compound **4h** was obtained as a white solid (60 mg, 95%); m.p. 80–82 °C. R_f = 0.37 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3423, 3076, 2935, 1715, 1643, 1604, 1428, 1467, 1361, 1345, 1235, 1200, 1146, 1115, 992, 934, 883, 815, 666, 567 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.84 (d, J = 1.8 Hz, 1 H), 7.61 (dd, J_1 = 8.3, J_2 = 1.8 Hz, 1 H, Ar-H), 6.86 (d, J = 8.4 Hz, 1 H, Ar-H), 5.99–5.86 (m, 1 H), 5.47–5.38 (m, 2 H), 5.28–5.17 (m, 2 H), 5.04–5.00 (m, 1 H), 3.84–3.80 (m, 2 H), 3.15 (dd, J_1 = 10.6, J_2 = 3.3 Hz, 1 H), 2.99 (dd, J_1 = 13.4, J_2 = 3.0 Hz, 1 H), 2.63–2.55 (m, 2 H), 1.29 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.7, 142.2, 133.4, 128.7, 128.3, 128.0, 126.9, 123.6, 121.8, 116.1, 113.1, 112.4, 110.3, 53.9, 44.3, 37.9, 36.5, 35.2, 13.6 ppm. HRMS (EI): calcd.for $C_{19}H_{18}BrN_3O$, M^+: 383.0633; found 383.0633.

Ethyl 2-(3-Allyl-1-methyl-2-oxoindolin-3-yl)-2-cyanopent-4-enoate (4i): Isatylidene **1i** (50 mg, 0.19 mmol), allyltributyltin (**2**; 0.12 mL, 0.37 mmol) and allyl chloride (**3**; 0.03 mL, 0.38 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 80:20), compound **4i** was obtained as colorless viscous liquid (55 mg, 78%). R_f = 0.43 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3062, 2927, 2856, 1867, 1745, 1735, 1710, 1639, 1608, 1490, 1463, 1361, 1244, 1178, 1101, 1012, 997, 931, 856, 815, 694 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.70 (d, J = 7.5 Hz, 1 H, Ar-H), 7.33–7.29 (m, 1 H, Ar-H), 7.09 (t, J = 7.5 Hz, 1 H, Ar-H), 6.78 (d, J = 7.8 Hz, 1 H, Ar-H), 5.85–5.72 (m, 1 H), 5.30–5.20 (m, 2 H), 5.18–4.97 (m, 2 H), 4.88–4.84 (m, 1 H), 3.84–3.81 (m, 2 H, $CO_2CH_2CH_3$), 3.57–3.48 (m, 1 H), 3.18 (s, 3 H, N-Me), 2.98–2.95 (m, 2 H), 2.87–2.80 (m, 1 H), 0.93 (t, J = 7.3 Hz, 3 H, $CO_2CH_2CH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.2, 165.9, 143.9, 141.1, 130.8, 130.3, 126.9, 124.6, 122.6, 121.1, 120.2, 117.2, 107.8, 62.3, 56.9, 53.4, 37.7, 35.2, 27.7, 13.5 ppm. HRMS (EI): calcd.for $C_{20}H_{22}N_2O_3$, M^+: 338.1630; found 338.1627.

Ethyl 2-(3-Allyl-1-benzyl-2-oxoindolin-3-yl)-2-cyanopent-4-enoate (4j): Isatylidene **1j** (50 mg, 0.15 mmol), allyltributyltin (**2**; 0.09 mL, 0.30 mmol) and allyl chloride (**3**; 0.03 mL, 0.30 mmol) were treated according to the general method. After purification by column chromatography (hexane/EtOAc, 80:20), compound **4j** was obtained as pale yellow viscous liquid (46 mg, 73%). R_f = 0.54 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3003, 2958, 2926, 2872, 2854, 1739, 1712, 1610, 1490, 1367, 1238, 1180, 1078, 995, 931, 858, 698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.72 (d, J = 7.1 Hz, 1 H, Ar-H), 7.34–7.24 (m, 5 H, Ar-H), 7.16–7.13 (m, 1 H, Ar-H), 7.06–7.04 (m, 1 H, Ar-H), 6.61 (d, J = 7.7 Hz, 1 H, Ar-H), 5.74–5.70 (m, 1 H), 5.33–5.22 (m, 2 H), 5.11–5.06 (m, 2 H), 4.99 (d, J = 15.6 Hz, 1 H), 4.88–4.84 (m, 1 H), 4.75 (d, J = 15.7 Hz, 1 H), 3.84–3.79 (m, 2 H, $CO_2CH_2CH_3$), 3.57 (dd, J_1 = 13.9, J_2 = 8.1 Hz, 1 H), 3.03–3.01 (m, 2 H), 2.89 (dd, J_1 = 13.8, J_2 = 8.1 Hz, 1 H), 0.80 (t, J = 7.1 Hz, 3 H, $CO_2CH_2CH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.4, 165.9, 143.1, 135.5, 130.8, 130.3, 129.3, 128.6, 127.7, 127.6, 127.2, 124.7, 122.7, 121.5, 120.7, 117.4, 109.2, 62.5, 56.8, 53.3, 44.3, 38.1, 35.2, 14.2 ppm. MS (FAB): calcd.for $C_{26}H_{26}N_2O_3$, M^+: 414.1943; found 414.1931.

General Experimental Procedure for the Reaction of Isatylidenes with Diallyl Carbonate: Isatylidene (1.0 equiv.), PPh_3 (10 mol-%), and $[Pd(allyl)Cl]_2$ (5 mol-%) were taken in a Schlenk tube, degassed and diallyl carbonate (2.5 equiv.) was added followed by 2 mL THF. Argon gas is purged into the reaction mixture and stirred at room temperature. After the completion of the reaction (TLC), the solvent was evaporated in vacuo and the residue on silica gel (100–200 mesh) column chromatography using 10% ethyl acetate in hexane afforded the products in excellent yields.

(*S*)-2-Allyl-2-[3-(allyloxy)-1-methyl-2-oxoindolin-3-yl]malononitrile (6a): Isatylidene **1a** (30 mg, 0.14 mmol) and diallyl carbonate (**5**; 0.05 mL, 0.36 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 90:10), compound **6a** was obtained as a white solid (32 mg, 73%); m.p. 82–86 °C. R_f = 0.39 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 2926, 2856, 2003, 1708, 1610, 1467, 1355, 1284, 1222, 1122, 1001, 921, 852, 761 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.77 (d, J = 7.5 Hz, 1 H, Ar-H), 7.50 (t, J = 7.8 Hz, 1 H, Ar-H), 7.26–7.21 (m, 1 H, Ar-H), 6.93 (d, J = 7.9 Hz, 1 H), 5.91–5.77 (m, 2 H), 5.41–5.35 (m, 2 H), 5.21–5.12 (m, 2 H), 3.77–3.73 (m, 2 H), 3.26 (s, 3 H, N-Me), 2.98–2.86 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 144.3, 132.7, 132.3, 129.2, 126.0, 123.9, 123.1, 121.7, 118.2, 112.2, 112.1, 80.7, 68.1, 46.3, 35.0, 29.2 ppm. HRMS (EI): calcd.for $C_{18}H_{17}N_3O_2$, M^+: 307.1321; found 307.1333.

(*S*)-2-Allyl-2-[3-(allyloxy)-1-benzyl-2-oxoindolin-3-yl]malononitrile (6b): Isatylidene **1b** (30 mg, 0.11 mmol) and diallyl carbonate (**5**; 0.04 mL, 0.26 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 90:10), compound **6b** was obtained as a white solid (35 mg, 88%); m.p. 132–134 °C. R_f = 0.38 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3066, 2954, 2924, 2850, 2316, 1888, 1728, 1610, 1485, 1361, 1296, 1182, 1130, 1095, 989, 943, 804, 756, 732 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.78 (d, J = 7.5 Hz, 1 H, Ar-H), 7.39–7.19 (m, 7 H), 6.83 (d, J = 7.9 Hz, 1 H), 5.90–5.80 (m, 2 H), 5.41–5.35 (m, 2 H), 5.22–5.10 (m, 2 H), 4.93 (d, J = 4.4 Hz, 2 H, N-CH_2Ph), 3.80–3.72 (m, 2 H), 2.98–2.91 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 143.6, 134.6, 132.5, 132.3, 129.1, 128.9, 128.3, 127.6, 126.1, 124.1, 123.3, 121.5, 118.3, 112.6, 112.4, 110.3, 80.5, 67.9, 46.4, 35.3, 32.0 ppm. HRMS (EI): calcd.for $C_{24}H_{21}N_3O_2$, M^+: 383.1634; found 383.1632.

(*S*)-2-Allyl-2-[3-(allyloxy)-1-ethyl-2-oxoindolin-3-yl]malononitrile (6c): Isatylidene **1c** (30 mg, 0.13 mmol) and diallyl carbonate (**5**; 0.04 mL, 0.34 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 90:10), compound **6c** was obtained as a white solid (32 mg, 76%); m.p. 76–78 °C. R_f = 0.40 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3425, 2956, 1724, 1612, 1467, 1371, 1288, 1224, 1122, 1097, 991, 937, 837, 804, 752 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.77 (d, J = 7.0 Hz, 1 H), 7.49–7.46 (m 1 H), 7.26–7.19 (m, 1 H), 6.95 (d, J = 7.9 Hz, 1 H), 5.91–5.86 (m, 2 H), 5.42–5.37 (m, 2 H), 5.23–5.12 (m, 2 H), 3.89–3.67 (m, 4 H), 3.00–2.91 (m, 2 H), 1.31 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.0, 143.4, 132.6, 132.3, 129.0, 126.2, 123.8, 123.2, 121.7, 118.2, 112.4, 109.2, 80.4, 67.9, 46.4, 35.3, 35.1, 12.4 ppm. HRMS (EI): calcd.for $C_{19}H_{19}N_3O_2$, M^+: 321.1477; found 321.1453.

(*S*)-2-Allyl-2-[3-(allyloxy)-1-benzyl-5-bromo-2-oxoindolin-3-yl]-malononitrile (6g): Isatylidene **1g** (30 mg, 0.08 mmol) and diallyl carbonate (**5**; 0.03 mL, 0.20 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 90:10), compound **6g** was obtained as a white solid (26 mg, 70%); m.p. 140–142 °C. R_f = 0.45 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 2978, 1730, 1608, 1479, 1427, 1340, 1238, 1180, 1105, 987, 941, 823, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.21 (d, J = 8.5 Hz, 2 H), 7.82 (d, J = 7.5 Hz, 1 H), 7.53 (d, J = 8.4 Hz, 2 H), 7.42 (t, J = 7.7 Hz, 1 H), 7.28–7.23 (m, 1 H), 6.75 (d, J = 7.8 Hz, 1 H), 5.94–5.81 (m, 2 H), 5.45–5.40 (m, 2 H), 5.22–5.13 (m, 3 H), 4.92–4.86 (m, 1 H), 3.77 (d, J = 3.7 Hz, 2 H), 3.15–2.83 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 147.9, 143.0, 141.7, 132.5, 132.4, 129.2, 129.1, 128.9, 128.3, 126.4, 124.6, 124.3, 124.1, 123.4, 121.6, 118.6, 112.5, 112.3, 109.8, 80.6, 68.1, 46.4, 44.0, 35.2 ppm. HRMS (EI): calcd.for $C_{24}H_{20}BrN_3O_2$, M^+: 461.0739; found 461.0743.

(*S*)-2-Allyl-2-[3-(allyloxy)-5-bromo-1-ethyl-2-oxoindolin-3-yl]-malononitrile (6h): Isatylidene **1h** (30 mg, 0.10 mmol) and diallyl carbonate (**5**; 0.035 mL, 0.24 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 90:10), compound **6b** was obtained as a white solid (22 mg, 55%); m.p. 124–130 °C. R_f = 0.49 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3689, 2929, 1710, 1606, 1483, 1429, 1346, 1213, 1118, 1099, 993, 925, 769, 754, 723, 667 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.52–7.26 (m, 2 H), 6.68 (d, J = 8.4 Hz, 1 H), 5.94–5.83 (m, 2 H), 5.46–5.32 (m, 2 H), 5.02–4.89 (m, 2 H), 3.74–3.67 (m, 2 H), 2.69–2.61 (m, 2 H), 2.56–2.50 (m, 2 H), 1.18 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.7, 133.7, 133.3, 131.7, 130.7, 128.2, 126.7, 123.4, 119.3, 117.3, 114.7, 110.2, 109.3, 80.3, 64.3, 40.9, 37.2, 34.6, 12.8 ppm. HRMS (EI): calcd.for $C_{19}H_{18}BrN_3O_2$, M^+: 399.0582; found 399.0584.

General Experimental Procedure for the Reaction of Isatylidenes with Allyl Acetoacetate: Isatylidene (1.0 equiv.), dppm (10 mol-%), and $[Pd(allyl)Cl]_2$ (5 mol-%) were taken in a Wheaton reactor, and allyl acetoacetate was added. The mixture was stirred at room temperature for 12 h. After the completion of the reaction (TLC), the solvent was evaporated in vacuo and the residue on silica gel (60–120 mesh) column chromatography using 30% ethyl acetate in hexane afforded the products in excellent yields.

(*R*)-2-Allyl-2-[1-methyl-2-oxo-3-(2-oxopropyl)indolin-3-yl]malononitrile (8a): Isatylidene **1a** (30 mg, 0.14 mmol) and diallyl carbonate (**5**; 0.024 mL, 0.17 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **8a** was obtained as a white crystalline solid (38 mg, 86%); m.p. 140–144 °C. R_f = 0.28 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3055, 2933, 2245, 1903, 1782, 1643,

1614, 1494, 1471, 1433, 1421, 1404, 1369, 1344, 1309, 1251, 1170, 1097, 999, 943, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.48–7.39 (m, 2 H), 7.12 (t, J = 7.6 Hz, 1 H), 6.93 (d, J = 7.8 Hz, 1 H), 5.86–5.75 (m, 1 H), 5.39–5.27 (m, 2 H), 3.60 (d, J = 10.5 Hz, 2 H), 3.31 (s, 3 H, N-Me), 2.40 (dd, J_1 = 13.5, J_2 = 7.3 Hz, 1 H), 2.31–2.24 (m, 1 H), 2.08 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 201.4, 172.9, 145.3, 130.6, 128.3, 124.7, 123.6, 123.3, 113.2, 112.3, 109.0, 50.6, 47.2, 44.8, 35.6, 30.0, 26.9 ppm. HRMS (EI): calcd.for $C_{18}H_{17}N_3O_2$: M^+: 307.1321; found 307.1331.

(*R*)-2-Allyl-2-[1-benzyl-2-oxo-3-(2-oxopropyl)indolin-3-yl]malononitrile (8b): Isatylidene **1b** (30 mg, 0.1 mmol) and diallyl carbonate (**5**; 0.02 mL, 0.13 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **8b** was obtained as a white crystalline solid (31 mg, 78%); m.p. 132–134 °C. R_f = 0.40 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3455, 2933, 2245, 1904, 1762, 1643, 1611, 1484, 1468, 1433, 1421, 1369, 1344, 1309, 1251, 1170, 1097, 999, 943, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.47–7.42 (m, 3 H), 7.37–7.25 (m, 4 H), 7.10–7.05 (m, 1 H), 6.81 (d, J = 7.8 Hz, 1 H), 5.86–5.72 (m, 1 H), 5.38–5.23 (m, 2 H), 4.99 (s, 2 H), 3.65 (d, J = 12.1 Hz, 2 H), 2.42–2.26 (m, 2 H), 2.10 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 201.2, 173.0, 144.5, 135.1, 130.5, 128.9, 128.3, 127.9, 127.6, 124.6, 123.6, 123.3, 113.1, 112.3, 110.0, 50.6, 47.1, 45.1, 44.9, 35.6, 29.9 ppm. HRMS (EI) calcd.for $C_{24}H_{21}N_3O_2$: M^+: 383.1643; found 383.1632.

(*R*)-2-Allyl-2-[1-ethyl-2-oxo-3-(2-oxopropyl)indolin-3-yl]malononitrile (8c): Isatylidene **1c** (30 mg, 0.14 mmol) and diallyl carbonate (**5**; 0.024 mL, 0.17 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **8c** was obtained as a white crystalline solid (27 mg, 63%); m.p. 122–124 °C. R_f = 0.35 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3406, 3087, 2983, 1903, 1715, 1643, 1614, 1611, 1489, 1469, 1372, 1349, 1234, 1097, 990, 932, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.45 (d, J = 7.5 Hz, 1 H), 7.41–7.35 (m, 1 H), 7.12–7.07 (m, 1 H), 5.83–5.77 (m, 1 H), 5.39–5.28 (m, 2 H), 3.93–3.75 (m, 2 H), 3.63–3.49 (m, 2 H), 2.39–2.25 (m, 2 H), 2.07 (s, 3 H, $COCH_3$), 1.34 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.7, 172.3, 144.5, 130.5, 128.6, 125.2, 123.5, 123.0, 113.0, 112.2, 108.9, 50.4, 47.1, 44.8, 35.6, 35.4, 29.9, 12.0 ppm. HRMS (EI) calcd.for $C_{19}H_{19}N_3O_2$, M^+: 321.1477; found 321.1462.

(*R*)-2-Allyl-2-[5-bromo-1-ethyl-2-oxo-3-(2-oxopropyl)indolin-3-yl]-malononitrile (8g): Isatylidene **1g** (30 mg, 0.10 mmol) and diallyl carbonate (**5**; 0.017 mL, 0.12 mmol) were treated according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **8g** was obtained as a white crystalline solid (29 mg, 74%); m.p. 142–146 °C. R_f = 0.38 (hexane/ethyl acetate, 7:3). IR (KBr): $\tilde{\nu}_{max}$ = 3423, 3076, 2935, 1892, 1715, 1643, 1604, 1428, 1467, 1361, 1345, 1235, 1200, 1146, 1115, 992, 934, 883, 815, 660 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.55 (d, J = 1.8 Hz, 1 H), 7.42–7.25 (m, 6 H), 6.67 (d, J = 8.4 Hz, 1 H), 5.88–5.75 (m, 1 H), 5.41–5.28 (m, 2 H), 4.97 (s, 2 H), 3.73–3.54 (m, 2 H), 2.41–2.30 (m, 2 H), 2.14 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 201.6, 172.6, 143.5, 134.5, 133.5, 129.0, 128.1, 128.0, 127.6, 126.7, 126.5, 123.9, 116.0, 112.2, 111.5, 50.7, 47.2, 45.0, 35.5, 29.9 ppm. HRMS (EI) calcd.for $C_{24}H_{20}BrN_3O_2$, M^+: 461.0734; found 461.0721.

General Experimental Procedure for the Preparation of Spiro-Indolone and Spiro-Oxepane Derivatives: To the bis allylated or allylated-oxyallylated compound (1.0 equiv.) in 5 mL DCM, the Grubbs' 2nd generation catalyst (5 mol-%) was added and stirred at room temperature for 2 h. Completion of reaction was monitored by Thin Layer Chromatography. After the completion of the reaction (TLC), the solvent was evaporated in vacuo and the residue on silica gel (60–120 mesh) column chromatography using 40% ethyl acetate in hexane afforded the products in excellent yields.

(*R*)-1′-Methyl-2′-oxospiro[cyclohex-3-ene-1′,3′-indoline]-6,6-dicarbonitrile (9a): Compound **4a** (30 mg, 0.10 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **9a** was obtained as a white crystalline solid (24 mg, 90%); m.p. 160–162 °C. R_f = 0.29 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3433, 2923, 1715, 1613, 1489, 1471, 1423, 1371, 1267, 1089, 1023, 834, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.50 (d, J = 7.5 Hz, 1 H), 7.43 (t, J = 7.8 Hz, 1 H), 7.17–7.12 (m, 1 H), 6.01 (d, J = 11.7 Hz, 1 H), 5.92 (d, J = 11.7 Hz, 1 H), 3.35 (d, J = 17.7 Hz, 1 H), 3.28 (s, 3 H), 2.96 (d, J = 17.4 Hz, 1 H), 2.73 (d, J = 18.9 Hz, 1 H), 2.55 (d, J = 18.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.2, 143.6, 130.6, 126.7, 125.2, 124.3, 123.5, 121.0, 113.7, 113.2, 108.9, 48.3, 36.2, 32.4, 30.1, 26.5 ppm. HRMS (EI): calcd.for $C_{16}H_{13}N_3O$, M^+: 263.1059; found 263. 1049.

(*R*)-1′-Benzyl-2′-oxospiro[cyclohex-3-ene-1,3′-indoline]-6,6′-dicarbonitrile (9b): Compound **4b** (30 mg, 0.08 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **9b** was obtained as a white crystalline solid (26 mg, 95%); m.p. 96–98 °C. R_f = 0.41 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3435, 2923, 1715, 1611, 1484, 1468, 1432, 1367, 1264, 1204, 1174, 1017, 965, 831, 755, 694 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 745 (d, J = 7.5 Hz, 1 H), 7.26–7.18 (m, 6 H), 7.04 (t, J = 7.6 Hz, 1 H), 6.73 (d, J = 7.8 Hz, 1 H), 5.97–5.84 (m, 2 H), 4.98 (d, J = 15.7 Hz, 1 H), 4.80 (d, J = 15.7 Hz, 1 H), 3.36 (d, J = 17.7 Hz, 1 H), 2.96–2.89 (m, 1 H), 2.72–2.51 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5, 142.7, 134.7, 130.5, 128.9, 127.9, 127.3, 126.8, 125.1, 124.4, 123.6, 121.2, 113.8, 113.4, 110.1, 48.2, 44.3, 36.2, 32.6, 30.8 ppm. HRMS (EI): calcd.for $C_{22}H_{17}N_3O$, M^+: 339.1372; found 339.1379.

(*R*)-1′-Benzyl-5′-bromo-2′-oxospiro[cyclohex-3-ene-1,3′-indoline]-6,6′-dicarbonitrile (9g): Compound **4g** (30 mg, 0.07 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **9g** was obtained as a white crystalline solid (23 mg, 80%); m.p. 146–148 °C. R_f = 0.40 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3435, 2923, 1715, 1611, 1484, 1468, 1432, 1367, 1264, 1204, 1174, 1017, 965, 831, 755, 694 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 758 (d, J = 1.6 Hz, 1 H), 7.43–7.40 (m, 1 H), 7.35–7.16 (m, 5 H), 6.67 (d, J = 8.4 Hz, 1 H), 6.05–5.93 (m, 2 H), 5.04 (d, J = 15.7 Hz, 1 H), 4.85 (d, J = 15.7 Hz, 1 H), 3.39 (d, J = 17.9 Hz, 1 H), 3.00 (d, J = 17.9 Hz, 1 H), 2.80 (d, J = 18.9 Hz, 1 H), 2.55 (d, J = 18.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.0, 141.8, 134.2, 133.5, 129.2, 128.9, 128.7, 128.4, 128.1, 127.7, 127.4, 127.3, 124.9, 121.3, 116.3, 113.5, 113.1, 48.4, 44.5, 35.9, 32.6, 30.7 ppm. MS (FAB): calcd.for $C_{22}H_{16}BrN_3O$, M^+: 417.0477; found (M + 1): 418.07.

(*R*)-5′-Bromo-1′-ethyl-2′-oxospiro[cyclohex-3-ene-1,3′-indoline]-6,6-dicarbonitrile (9h): Compound **4h** (30 mg, 0.08 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **9h** was obtained as a white crystalline solid (25 mg, 90%); m.p. 208–210 °C. R_f = 0.31 (hexane/ethyl

acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3435, 2923, 1715, 1611, 1484, 1468, 1432, 1367, 1264, 1204, 1174, 1017, 965, 831, 755, 694 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.58–7.55 (m, 2 H), 6.87 (d, J = 8.5 Hz, 1 H), 6.06–6.03 (m, 1 H, CH=CH), 5.97–5.94 (m, 1 H, CH=CH), 3.97 (q, J = 4.2 Hz, 1 H, N-CH_2), 3.66 (q, J = 4.2 Hz, 1 H, N-CH_2), 3.37–3.33 (m, 1 H), 3.01–2.97 (m, 1 H), 2.77–2.71 (m, 1 H), 2.53–2.49 (m, 1 H), 1.34–1.31 (m, 3 H, N-CH_2CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.4, 141.9, 133.5, 128.8, 127.8, 125.1, 121.1, 116.0, 113.3, 112.9, 110.4, 48.1, 36.0, 35.4, 32.5, 29.9, 12.3 ppm. HRMS (EI): calcd.for $C_{17}H_{14}BrN_3O$, M^+: 355.0320; found (M + 2): 357.0113.

Ethyl 2-Cyano-1′-methyl-2′-oxo-1′,2′-dihydrospiro[cyclohex-4-ene-1,3′-indole]-2-carboxylate (9i): Compound **4i** (30 mg, 0.09 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **9i** was obtained as a white crystalline solid (23 mg, 85%); m.p. 104–108 °C. R_f = 0.29 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 2958, 2926, 2247, 1743, 1712, 1612, 1494, 1471, 1375, 1352, 1267, 1240, 1328, 1132, 1093, 1041, 970, 852, 794, 688 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.71 (d, J = 7.4 Hz, 1 H), 7.35–7.26 (m, 1 H), 7.11–7.08 (m, 1 H), 6.81 (d, J = 7.8 Hz, 1 H), 5.95–5.88 (m, 2 H, CH=CH), 4.00 (q, J = 7.1 Hz, 2 H, $CO_2CH_2CH_3$), 3.52–3.47 (m, 1 H), 3.20 (s, 3 H, N-Me), 2.86–2.79 (m, 1 H), 2.71–2.63 (m, 1 H), 2.37–2.29 (m, 1 H), 1.00 (t, J = 7.1 Hz, 3 H, $CO_2CH_2CH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.4, 166.2, 142.7, 132.3, 131.3, 126.9, 123.3, 123.1, 117.6, 115.4, 109.4, 63.0, 48.6, 46.7, 32.9, 29.7, 28.0, 13.7 ppm. MS (FAB): calcd.for $C_{18}H_{18}N_2O_3$, M^+: 310.1317; found 310.15.

(*S*)-1-Methyl-2-oxo-3′*H*-spiro[indoline-3,2′-oxepine]-3,3′-(4′*H*,7′*H*)-dicarbonitrile (10a): Compound **6a** (30 mg, 0.10 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **10a** was obtained as a white crystalline solid (24 mg, 87%); m.p. 144–148 °C. R_f = 0.29 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 2926, 2856, 2003, 1708, 1610, 1467, 1355, 1284, 1222, 1122, 1001, 918, 842, 781 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.76 (d, J = 7.5 Hz, 1 H), 7.48 (t, J = 7.7 Hz, 1 H), 7.26–7.18 (m, 1 H), 6.93 (d, J = 7.8 Hz, 1 H), 6.18–6.16 (m, 1 H, CH=CH), 5.97–5.95 (m, 1 H, CH=CH), 5.14–5.09 (m, 1 H), 4.33–4.26 (m, 1 H), 4.01–3.95 (m, 1 H), 3.25 (s, 3 H, N-Me), 2.92–2.84 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.5, 143.0, 134.0, 131.8, 126.0, 125.6, 124.0, 112.8, 112.7, 109.1, 79.3, 63.5, 42.5, 32.2, 26.4 ppm. HRMS (EI): calcd.for $C_{16}H_{13}N_3O_2$, M^+: 279.1008; found 279.1005.

(*S*)-1-Benzyl-2-oxo-3′*H*-spiro[indoline-3,2′-oxepine]-3,3′-(4′*H*,7′*H*)-dicarbonitrile (10b): Compound **6b** (30 mg, 0.08 mmol) was treated with Grubbs' 2nd generation catalyst according to the general procedure. After purification by column chromatography (hexane/EtOAc, 70:30), compound **10b** was obtained as a white crystalline solid (17 mg, 61%); m.p. 54–56 °C. R_f = 0.38 (hexane/ethyl acetate, 6:4). IR (KBr): $\tilde{\nu}_{max}$ = 3066, 2954, 2924, 2850, 2316, 1888, 1728, 1610, 1485, 1361, 1296, 1182, 1140, 1075, 989, 943, 804 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.77 (d, J = 7.5 Hz, 1 H, Ar-H), 7.32–7.26 (m, 6 H, Ar-H), 7.19–7.14 (m, 1 H), 6.78 (d, J = 7.8 Hz, 1 H), 6.20–6.17 (m, 1 H, CH=CH), 5.99–5.97 (m, 1 H, CH=CH), 5.11–5.04 (m, 2 H, CH_2-Ph), 4.94–4.83 (m, 1 H), 4.39–4.31 (m, 1 H), 4.05–4.00 (m, 1 H), 2.97–2.89 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.8, 142.4, 134.3, 133.8, 131.8, 129.0, 128.0, 127.5, 127.2, 125.6, 125.4, 125.2, 123.9, 112.9, 110.3, 79.2, 63.9, 44.3, 42.5, 32.5 ppm. HRMS (EI): calcd.for $C_{22}H_{17}N_3O_2$, M^+: 355.1321; found 355.1228.

CCDC-751478 (for **4a**), -751228 (for **6b**) and -751229 (for **9h**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra for all the compounds.

Acknowledgments

Financial assistance from Department of Science and Technology (DST) No: SR/S1/OC-78/2009) and Council of Scientific and Industrial Research, New Delhi are greatly acknowledged. S. C. G. acknowledges the University Grants Commission (UGC) for a research fellowship.

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Received: May 1, 2010
Published Online: August 4, 2010

