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Palladium-catalyzed construction of poly-substituted indolizinones

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ABSTRACT

We have developed a highly efficient one-pot approach to poly-substituted indolizinones from tertiary propargylic alcohols by using a palladium-catalyzed domino reaction. This reaction is proposed to proceed via successive aminopalladation, reductive elimination, and 1,2-shift. While our previous effort to the same skeleton via 2-iodoindolizinones selected α,β-unsaturated esters, terminal acetylenes, or boronic acids as coupling partners, this strategy introduces new functional groups at the C2 position of indolizinone core with (hetero)aryl halides or diallyl carbonate, expanding the substrate scope for decoration at the C2 site. Furthermore, a new preparation route to tertiary propargylic alcohols for this study is described to rapidly diversify the molecular framework.

1. Introduction

Synthetic maneuvers with unsaturated double or triple bonds represent one of the main areas in organic chemistry owing to our capability to activate these bonds—in particular, unactivated ones—with the aid of either catalytic or stoichiometric amounts of reagents. A number of electrophilic reagents including halogens and transition metals have increasingly played a pivotal role in activating unsaturated chemical bonds, enabling us to make new chemical bonds with either internal or external reacting partners.[1]

In this vein we have investigated the facile construction of nitrogen-fused bicycles such as indolizines[2,3] and indolizinones[4,5] by employing electrophilic cyclization of alkenes or alkynes bearing a pyridine unit (Scheme 1). Thus, 2-iodoindolizines **2** and 2,3-disubstituted indolizines **4** were synthesized by 5-*endo-dig* iodocyclization and 5-*endo-trig* iodocyclization/dehydroiodination, respectively (Eqs. 1 and 2).[6,7] More recently, a similar strategy was applied to the synthesis of indolizinones by using subsequent 1,2-shift after ring closing event, resulting in excellent yields of 2-iodoindolizinones **6** and 2,3-disubstituted indolizinones **9** under mild conditions (Eqs. 3 and 4).[8] The utility of 2-iodoindolizinones **6** was further demonstrated by rapid construction of a diversity-oriented indolizinone library **7** via installation of various new functional groups at the C2 position of the core skeleton under palladium catalysis.[9]

In connection with our latter report, we hope to construct the same framework in a one-pot fashion by using the power of organopalladium species to activate unsaturated bonds, thereby facilitating smooth ring closure. Indeed, this idea was successfully realized to allow direct access to poly-substituted indolizinones (**7** from **5**), which was recently communicated (Scheme 2).[10,11] Here we wish to describe the full details of this work based on Pd-catalyzed domino process[12] including a new preparation method of tertiary propargylic alcohols, starting materials of this study.

2. Results and discussion

Palladium-catalyzed activation of alkenes or alkynes has served as a highly useful means for triggering a number of subsequent synthetic operations such as cyclization.[13] For instance, (hetero)aryl palladium intermediates formed in situ from oxidative addition of (hetero)aryl halides to Pd(0) indeed facilitate diverse modes of cyclization by intramolecularly tethered nucleophilic components through coordination to unsaturated bonds, giving rise to many useful carbo- or heterocycles very often with concomitant formation of multiple bonds.[14] Guided by this concept, we surmised that arylpalladium species would activate alkyne moiety of **5**, inducing smooth 5-*endo-dig* cyclization by the neighboring pyridine group as shown in Scheme 3. The resulting indolizinium salt **10** would undergo reductive elimination to give **11**.[15] Finally, 1,2-migration[16] of R^1 group would occur to furnish the desired indolizinone **7**.

To explore the feasibility of this strategy, we began our investigations with propargylic alcohol **12** and 1-iodo-4-nitrobenzene as substrates. To our delight, the desired product **13**

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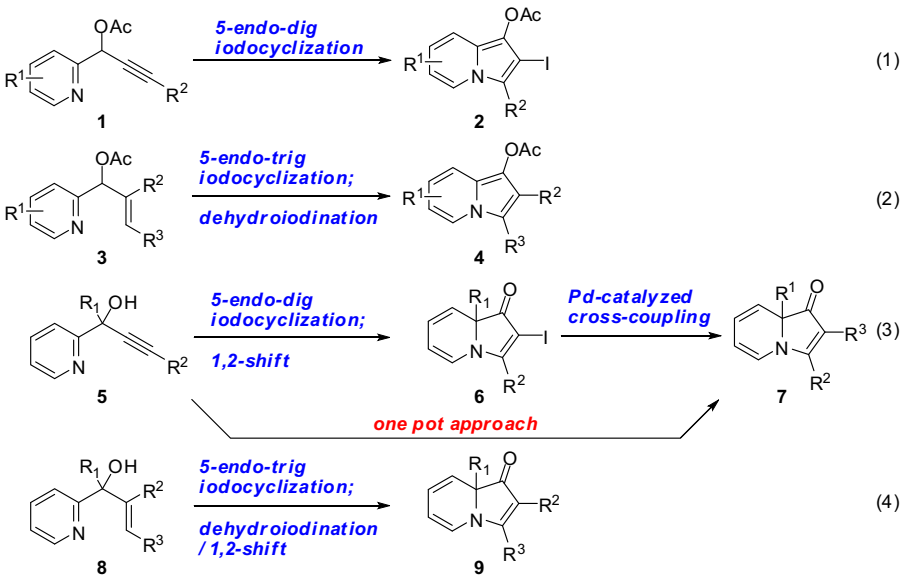
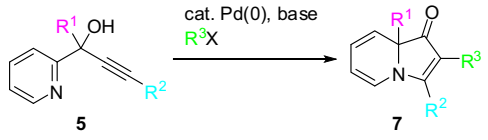


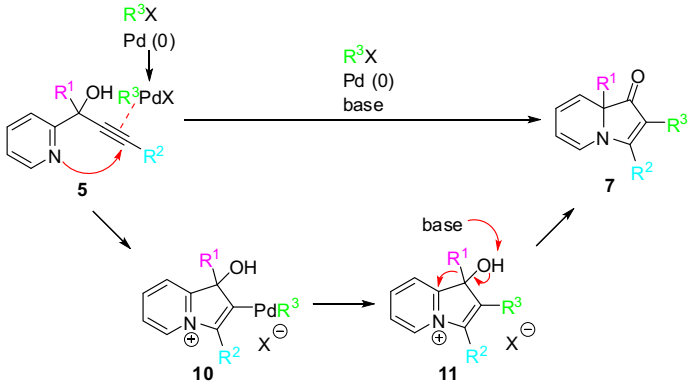
Scheme 1. Our approaches to highly substituted indolizines and indolizinones.



Scheme 2. Pd-catalyzed one-pot approach to poly-substituted indolizinones.

acids for installing new functional groups at the C2 site, this protocol used (hetero)aryl halides as coupling partner, expanding the substrate scope to decorate the C2 position of indolizinone.

To examine the reaction scope, we first reacted **12** with a variety of aryl iodides under optimized conditions (Table 2). Excellent yields of the desired products were obtained with aryl iodides containing electron-withdrawing groups (entries 1–6). Thus, phenyl group bearing 4-cyano-, 4-chloro-, 3-nitro-, 4-acetyl-, 4-ethoxycarbonyl-,

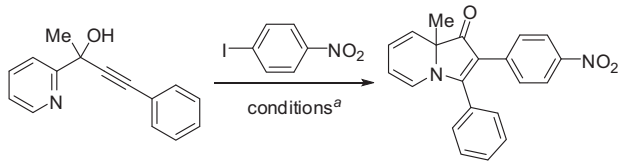


Scheme 3. Plausible mechanism.

was isolated in 69% yield from the reaction of **12** and 1-iodo-4-nitrobenzene (1.5 equiv) in acetonitrile in the presence of 10 mol % $Pd(PPh_3)_4$ and triethylamine (2.5 equiv) at 90 °C after 13 h (Table 1, entry 1). Switching the organic base to inorganic ones such as Na_2CO_3 and Cs_2CO_3 gave inferior results (entries 2 and 3). However, we were pleased to find that use of K_2CO_3 as base provided an excellent yield of **13** (entry 4). Catalyst loading can be reduced to 5 mol % without compromising the yield while decreased yield of **13** was obtained with 1 mol % of Pd(0) (entries 5 and 6). When the reaction was carried out in THF instead of acetonitrile, similar efficiency was observed (entry 7). Using dioxane or DMF as solvent, however, produced lower yield (entries 8 and 9). Other Pd(0) sources were tested to furnish the similar yield (entries 10 and 11). It is worth mentioning that compared with our previous approach toward the same skeleton via 2-iodoindolizinones, which utilized α,β-unsaturated esters, terminal acetylenes, or boronic or 3-trifluoromethyl moiety was successfully introduced at the C2 site of indolizinone. Furthermore, heterocycles such as thiophene and 2-chloropyridine were incorporated without any event by using the corresponding heteroaryl iodides (entries 11 and 12). On the other hand, the reactions with aryl iodides having electron-donating groups such as methoxyphenyl or tolyl gave the corresponding products in modest yields presumably due to the slower oxidative addition step (entries 7–10).

To demonstrate the generality of this process, several other tertiary propargylic alcohols containing different substituents at R^1 and R^2 sites (**26**–**37**) were then prepared and subjected to the identical reaction conditions with various (hetero)aryl iodides. As outlined in Table 3, to our delight, a diverse array of densely-functionalized indolizinones was readily constructed in good to excellent yields. Again, electronic nature of aryl iodides seemed to play a key role in determining isolated yield; electron-poor aryl

Table 1
Reaction optimization

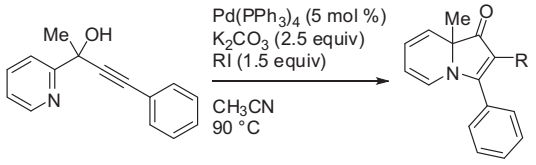


12 **13**

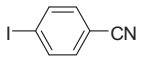
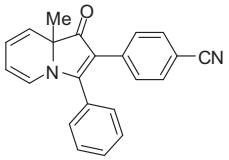
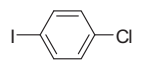
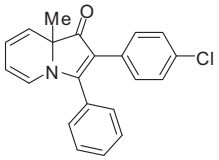
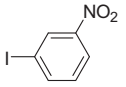
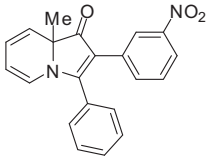
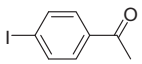
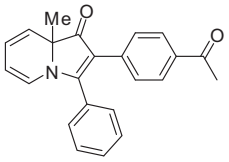
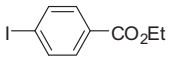
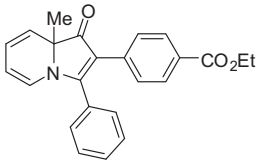
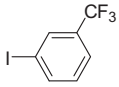
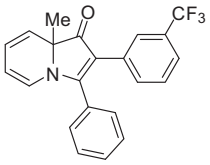
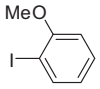
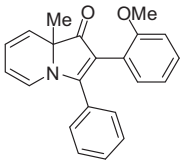
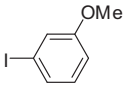
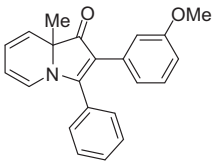
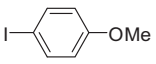
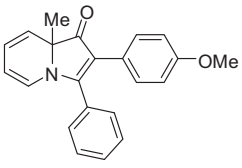
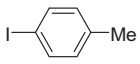
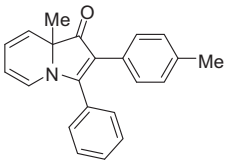
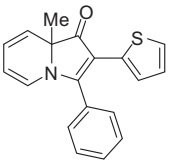
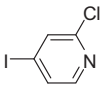
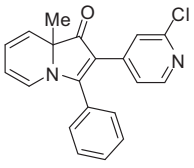
Entry	Pd(0)	Base	Solvent	Yield[f]
1	$Pd(PPh_3)_4$	Et_3N	CH_3CN	69
2	$Pd(PPh_3)_4$	Na_2CO_3	CH_3CN	50
3	$Pd(PPh_3)_4$	Cs_2CO_3	CH_3CN	56
4	$Pd(PPh_3)_4$	K_2CO_3	CH_3CN	96
5	$Pd(PPh_3)_4$[b]	K_2CO_3	CH_3CN	99
6	$Pd(PPh_3)_4$[c]	K_2CO_3	CH_3CN	80
7	$Pd(PPh_3)_4$	K_2CO_3	THF	98
8	$Pd(PPh_3)_4$	K_2CO_3	Dioxane	85
9	$Pd(PPh_3)_4$	K_2CO_3	DMF	52
10	$Pd_2(dba)_3+Ph_3P$[d]	K_2CO_3	CH_3CN	91
11	$Pd(OAc)_2+Ph_3P$[e]	K_2CO_3	CH_3CN	90

[a] A mixture of **12** (0.13 mmol), 1-iodo-4-nitrobenzene (1.5 equiv), Pd(0) (10 mol %), and base (2.5 equiv) in solvent (1 mL) was heated at 90 °C for 13 h unless otherwise stated.
[b] $Pd(PPh_3)_4$ of 5 mol %was used.
[c] $Pd(PPh_3)_4$ of 1 mol % was used.
[d] $Pd_2(dba)_3$ of 5 mol % and 10 mol % PPh_3 were used.
[e] $Pd(OAc)_2$ of 5 mol %and 10 mol % PPh_3 were used.
[f] Isolated yield (%).

Table 2
Synthesis of indolizinones from the reaction of **12** with various (hetero)aryl iodides



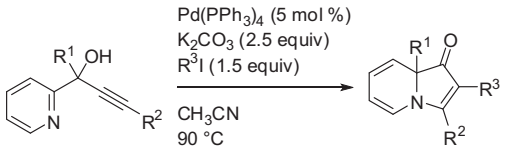
12 **14-25**

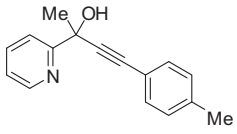
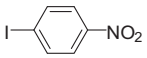
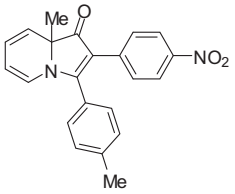
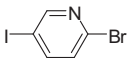
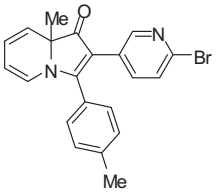
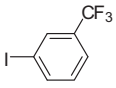
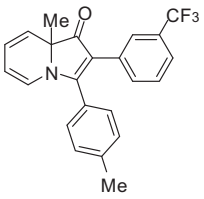
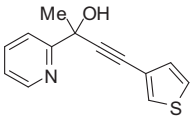
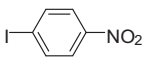
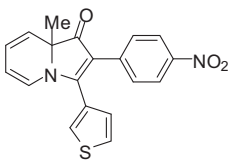
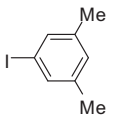
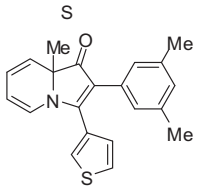
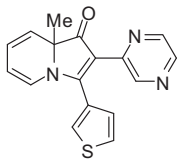
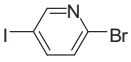
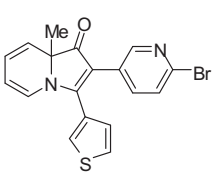
Entry	RI	Product		Yield[a]
1			**14**	100
2			**15**	86
3			**16**	82
4			**17**	95
5			**18**	78
6			**19**	92
7			**20**	47
8			**21**	55
9			**22**	53
10			**23**	45
11			**24**	77
12			**25**	95

[a] Isolated yield (%).

iodides furnished better yields of the products than electron-rich aryl iodides. Notably, because of the difference in reactivity under these conditions, reactions of **26** and **27** with 2-bromo-5-iodopyridine only afforded 2-bromopyridine-containing indolizinones, **39** and **44**, providing a functional handle for further coupling reactions (entries 2 and 7). Not only alkyl but also aryl groups including pyridine and 4-methoxyphenyl moiety smoothly move their position from propargylic sites to the ring junction of indolizinones.

Table 3
Synthesis of indolizinones from the reaction of diverse propargylic alcohols with various (hetero)aryl iodides



Entry	Starting material		R^3I	Product		Yield[a]
1		**26**			**38**	90
2		**26**			**39**	77
3		**26**			**40**	89
4		**27**			**41**	95
5		**27**			**42**	63
6		**27**			**43**	72
7		**27**			**44**	78

(*continued on next page*)

Table 3 (*continued*)

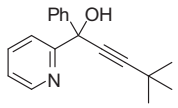
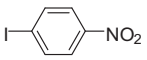
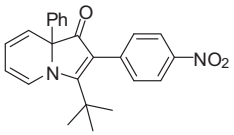
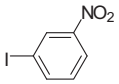
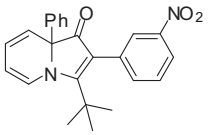
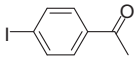
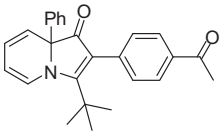
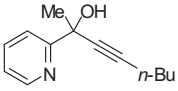
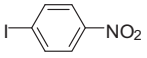
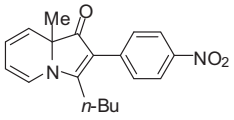
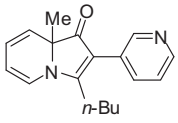
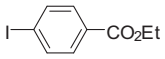
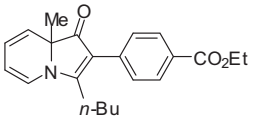
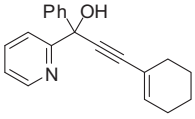
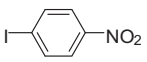
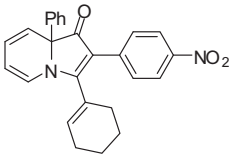
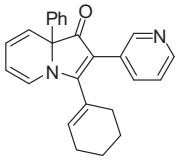
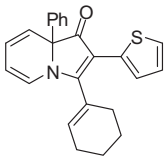
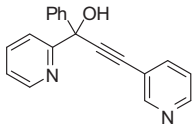
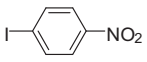
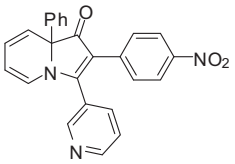
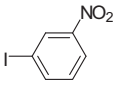
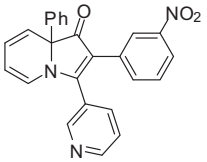
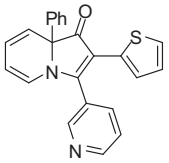
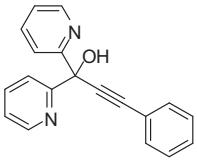
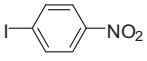
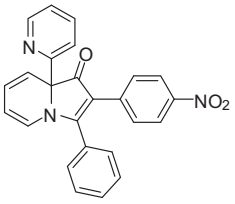
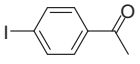
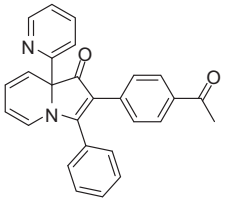
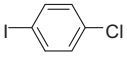
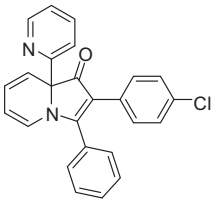
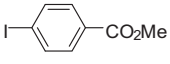
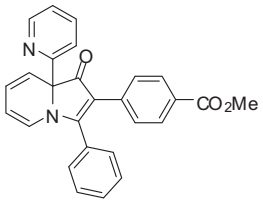
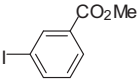
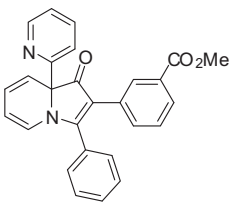
Entry	Starting material		R^3I	Product		Yield[a]
8		**28**			**45**	98
9		**28**			**46**	89
10		**28**			**47**	100
11		**29**			**48**	100
12		**29**			**49**	77
13		**29**			**50**	71
14		**30**			**51**	81
15		**30**			**52**	96
16		**30**			**53**	85

Table 3 (*continued*)

Entry	Starting material	R^3I	Product		Yield[a]
17		**31**			**54**	99
18		**31**			**55**	100
19		**31**			**56**	78
20		**32**			**57**	99
21		**32**			**58**	100
22		**32**			**59**	86
23		**32**			**60**	99
24		**32**			**61**	89

(*continued on next page*)

Table 3 (*continued*)

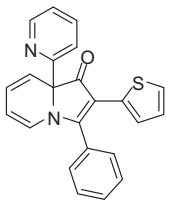
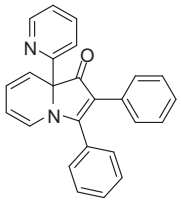
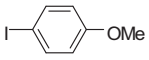
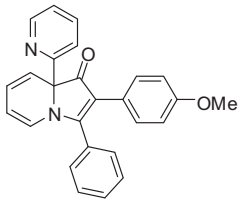
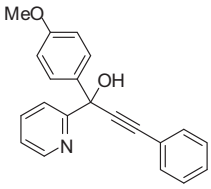
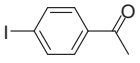
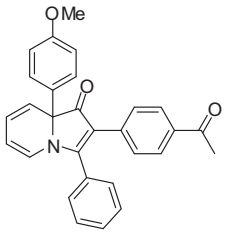
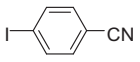
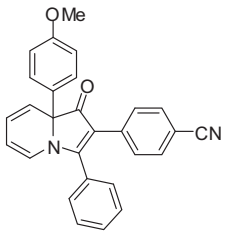
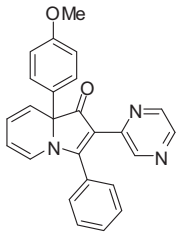
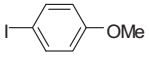
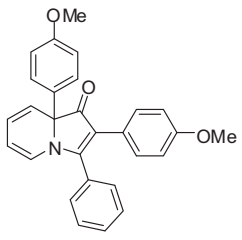
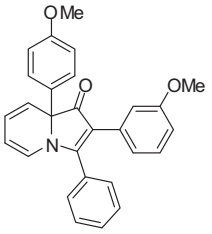
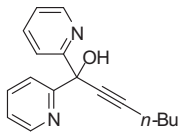
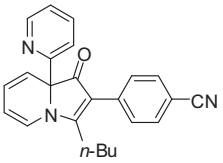
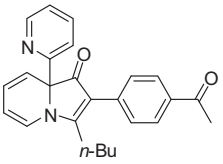
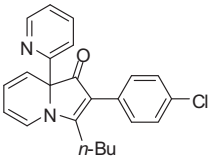
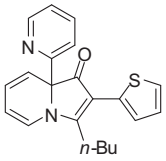
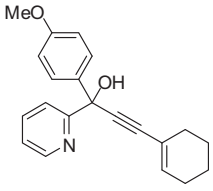
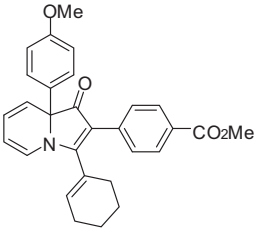
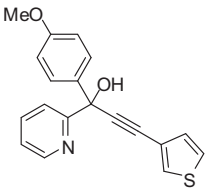
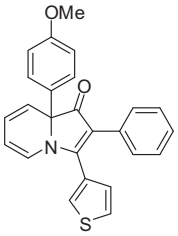
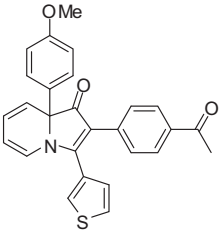
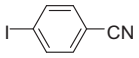
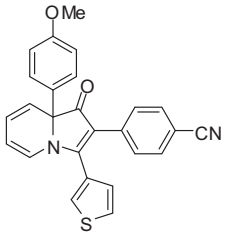
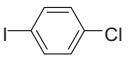
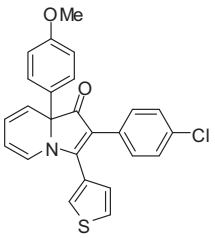
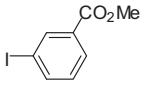
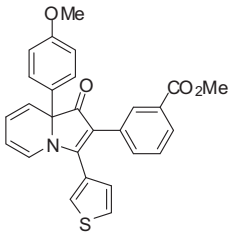
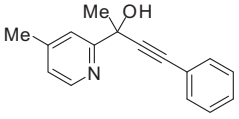
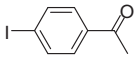
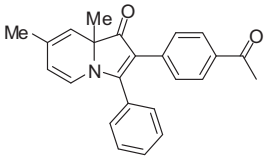
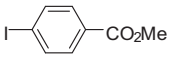
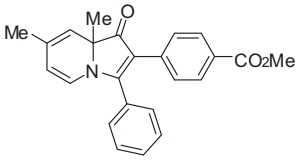
Entry	Starting material		R^3I	Product		Yield[a]
25		**32**			**62**	90
26		**32**			**63**	94
27		**32**			**64**	64
28		**33**			**65**	91
29		**33**			**66**	99
30		**33**			**67**	91
31		**33**			**68**	60

Table 3 (*continued*)

Entry	Starting material	R^3I	Product		Yield[a]
32		**33**		**69**	61
33		**34**		**70**	93
34		**34**		**71**	97
35		**34**		**72**	91
36		**34**		**73**	68
37		**35**		**74**	81
38		**36**		**75**	64
39		**36**		**76**	99

(*continued on next page*)

Table 3 (*continued*)

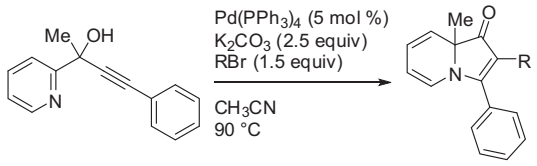
Entry	Starting material	R^3I	Product	Yield[a]
40	**36**		 **77**	99
41	**36**		 **78**	83
42	**36**		 **79**	100
43		**37**		 **80**	63
44	**37**		 **81**	86

[a] Isolated yield (%).

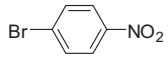
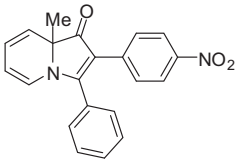
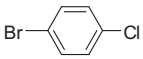
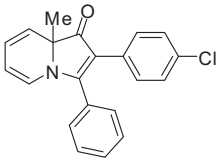
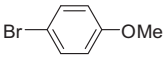
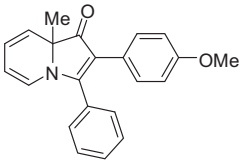
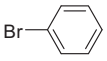
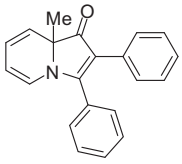
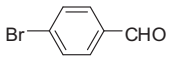
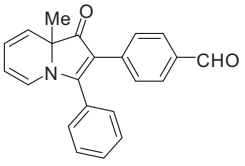
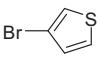
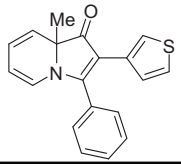
It turned out that aryl bromides are also suitable reaction partners of this cascade process with similar efficiency.[17] Thus, exposure of several aryl bromides to these reaction conditions delivered the corresponding indolizinones in good to excellent yields except 4-bromoanisole as shown in Table 4. Even 4-bromobenzaldehyde participated well in this reaction to afford indolizinone with 4-formylphenyl moiety at the C2 position in 68% yield (entry 5).

We also investigated the possibility of installing an allyl group at the C2 position of indolizinone by using π-allylpalladium complexes as alkyne activator (Table 5).[18] Our efforts began with the reaction of **12** with allyl bromide (10 equiv) in the presence of $Pd(PPh_3)_4$ (5 mol %) and K_2CO_3 (2.5 equiv) in THF at 80 °C, only leading to *O*-allylated product **86** in 58% yield (entry 1). When the catalytic system was switched to $Pd(OAc)_2$ (5 mol %) and xantphos (5 mol %) under identical conditions rather gave inferior result (entry 2). Employing allyl acetate (10 equiv) as an allyl source produced a complex mixture (entry 3). After extensive experimentation, we found that the desired *C*2-allylated product **85** was obtained by utilizing diallyl carbonate (10 equiv) in the presence of $Pd(PPh_3)_4$ (5 mol %) and K_2CO_3 (2.5 equiv) albeit in modest yield (entry 4). Under these conditions, *O*-allylated product **86** was initially formed as well but seemed to disappear after 18 h. Interestingly, *O*-allylated product was produced in high yield (84%) by use of $Pd(OAc)_2$ (5 mol %) and xantphos (5 mol %) instead of $Pd(PPh_3)_4$ (5 mol %) in the absence of K_2CO_3 (entry 5). Based on the previous reports where *O*- or *N*-allylated *o*-alkynylbenzenes delivered *C*-allylated products such as *C*2-allylated benzofurans or

Table 4
Synthesis of indolizinones from the reaction of **12** with various (hetero)aryl bromides



12 **13, 15, 22, 82, 83, 84**

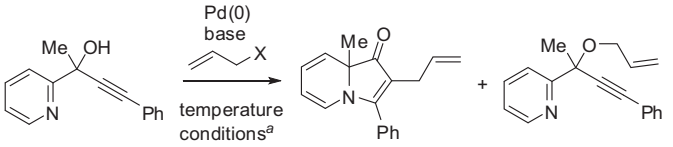
Entry	RI	Product		Yield[a]
1			**13**	95
2			**15**	84
3			**22**	28
4			**82**	68
5			**83**	68
6			**84**	86

[a] Isolated yield (%).

indoles under Pd catalysis,[18b,c,d,g] we expected that increased reaction temperature or prolonged heating of **86** might lead to the same type of cycloisomerization. However, only decreased yield of *O*-allylated product was observed, presumably, as a result of decomposition (entries 6 and 7).

In order to confirm that an allyl migration from O to C2 position of indolizinone does not occur in this system, we also subjected the pure **86** to $Pd(PPh_3)_4$ (5 mol %) and K_2CO_3 (2.5 equiv) in THF at 80 °C for 24 h, resulting in no formation of *C*2-allylated product. Starting material of 66% was recovered along with partial decomposition (Scheme 4).

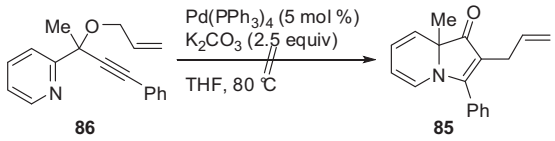
Table 5
Reaction optimization for the synthesis of *C*2-allylated indolizinone



12 **85** **86**

Entry	Pd(0)	Base	X	Temp (°C)	Product	Yield[e]
1	$Pd(PPh_3)_4$	K_2CO_3	Br	80	**86**	58
2	$Pd(OAc)_2$+xantphos[b]	K_2CO_3	Br	80	**86**	36
3	$Pd(OAc)_2$+xantphos	K_2CO_3	OAc	80	—	[c]
4	$Pd(PPh_3)_4$	K_2CO_3	$OCO_2CH_2CH{=}CH_2$	80	**85**	35
5	$Pd(OAc)_2$+xantphos	—	$OCO_2CH_2CH{=}CH_2$	80	**86**	84[d]
6	$Pd(OAc)_2$+xantphos	—	$OCO_2CH_2CH{=}CH_2$	120	**86**	35
7	$Pd(OAc)_2$+xantphos	K_2CO_3	$OCO_2CH_2CH{=}CH_2$	80	**86**	22

[a] A mixture of **12** (0.22 mmol), allylating reagent (10 equiv), Pd(0) (5 mol %), and base (2.5 equiv) in THF (2 mL) was heated at 80 °C for 18 h unless otherwise stated.
[b] Xantphos=4,5-bis(diphenylphosphino)-9,9-dimethylxanthene.
[c] Complex mixture.
[d] Reaction time=1.5 h.
[e] Isolated yield (%).

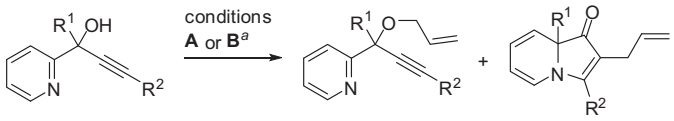


86 **85**

Scheme 4. Cycloisomerization attempts from **86** to **85**.

Table 6 further demonstrated that we were able to obtain *O*-allylated propargylic ethers or *C*2-allylated indolizinones depending on the reaction conditions.

Table 6
Synthesis of *O*-allylated propargylic alcohols or *C*2-allylated indolizinones

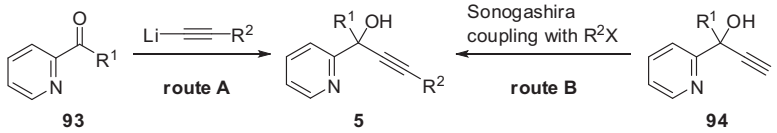


31, 32, 36 **87, 89, 91** **88, 90, 92**

Entry	Starting material	Conditions	Product	Yield[b]
1	**31**	**A**	**87**	90
2	**31**	**B**	**88**	28
3	**32**	**A**	**89**	73
4	**32**	**B**	**90**	68
5	**36**	**A**	**91**	80
6	**36**	**B**	**92**	43

[a] Conditions A: a mixture of propargylic alcohol (0.22 mmol), diallyl carbonate (10 equiv), $Pd(OAc)_2$ (5 mol %), xantphos (5 mol %) in THF (2 mL) was heated at 80 °C for 3 h. Conditions B: a mixture of propargylic alcohol (0.22 mmol), diallyl carbonate (10 equiv), $Pd(PPh_3)_4$ (5 mol %), and K_2CO_3 (2.5 equiv) in THF (2 mL) was heated at 80 °C for 18 h.
[b] Isolated yield (%).

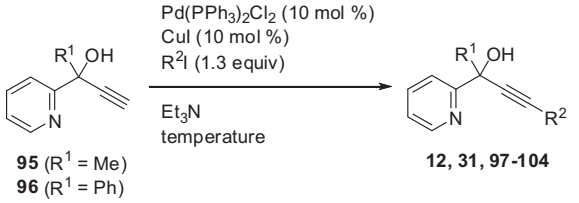
In the meantime, we sought to obtain the starting material, tertiary propargylic alcohols with more diverse R^2 group via a distinct route from conventional method through nucleophilic addition of appropriate terminal acetylides to pyridyl ketones **93** (Scheme 5, route A).[19] Although many terminal alkynes necessary for route A are commercially available or can be easily prepared, for example, by Corey–Fuchs protocol[20] or Ohira–Bestmann method,[21] we decided to assemble the same tertiary alcohols by way of Sonogashira cross-coupling[22] of terminal alkynes **94** with (hetero)aryl halides (route B), thereby extending the structural diversity more easily.

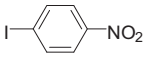
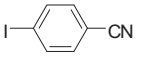
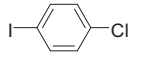
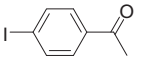
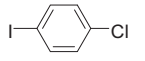
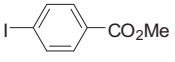
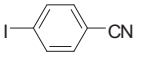


Scheme 5. Two routes to propargylic alcohols.

Our initial attempts in this line with **95** and 1-iodo-4-nitrobenzene (1.3 equiv) in the presence of $Pd(PPh_3)_2Cl_2$ (10 mol %), CuI (10 mol %), and Et_3N (5 equiv) in CH_3CN resulted in fast consumption of the starting material at room temperature. After column chromatographic purification, however, poor isolated yield (less than 10%) of the desired product was observed despite the relatively clean TLC pattern.[23] After some experimentation, we found that the desired transformation could be performed in reasonable yields with triethylamine as solvent. Thus, exposure of **95** to 1-iodo-4-nitrobenzene (1.3 equiv), $Pd(PPh_3)_2Cl_2$ (10 mol %), CuI (10 mol %), and Et_3N at room temperature led to **97** in 74% yield (Table 7, entry 2). Gentle heating was required to expedite the reaction in some cases. Under these conditions, reactions of **95** or **96** with several aryl iodides allowed direct access to several new propargylic alcohols such as **100** and **103**, which are difficult to obtain by other means although more optimization of this route needs to be done (entries 5 and 8).

Table 7
Preparation of tertiary propargylic alcohols via Sonogashira reaction



Entry	Starting material	R^2I	Temp (°C)	Product	Yield[a]
1	**95**		55	**12**	33
2	**95**		rt	**97**	74
3	**95**		rt	**98**	66
4	**95**		45	**99**	43
5	**95**		30	**100**	56
6	**96**		45	**101**	22
7	**96**		45	**102**	23
8	**96**		45	**103**	54
9	**96**		45	**104**	37
10	**96**		45	**31**	36

[a] Isolated yield (%).

3. Conclusions

In summary, we have described here that the power of organopalladium species to trigger intramolecular cyclization via alkyne activation was implemented to allow for facile construction of poly-substituted indolizinones from readily available tertiary propargylic alcohols in a domino fashion where aminopalladation and reductive elimination were successfully combined with 1,2-rearrangement for the first time. Some features of this highly efficient protocol include mild reaction conditions, ease of operation, high chemical yields, and a wide variety of functional-group tolerance. In addition, we introduced a new approach to tertiary propargylic alcohols containing a pyridine moiety, starting materials used for this study by employing Sonogashira coupling reaction. The chemistry described here should be useful for the rapid generation of a library of indolizinone derivatives for biological evaluation.[24]

4. Experimental section

4.1. General procedure for the synthesis of tertiary propargylic alcohols

To a stirred solution of terminal alkyne (1.2 equiv) in THF was added *n*-BuLi (1.1 equiv, 1.6 M solution in hexanes) at −78 °C. After 5 min, a solution of pyridinyl ketone **93** (1.0 equiv) in THF was slowly added to this mixture at −78 °C. After 15 min at −78 °C, the reaction mixture was quenched with saturated NH_4Cl. The reaction mixture was diluted with ethyl acetate and washed with aqueous NH_4Cl. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a crude mixture, which was purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to afford the propargylic alcohol.

*4.1.1. 4-Phenyl-2-(pyridin-2-yl)but-3-yn-2-ol (**12**).* Pale yellow solid, mp: 102.9–103.4 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J=4.5 Hz, 1H), 7.77 (td, J=1.5, 8.0 Hz, 1H), 7.69 (d, J=8.0 Hz, 1H), 7.49–7.44 (m, 2H), 7.31–7.24 (m, 4H), 5.62 (s, 1H), 1.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 147.5, 137.6, 131.9, 128.5, 128.3, 122.9, 122.8, 120.2, 92.4, 83.9, 69.1, 32.4; IR (ATR) 3238, 3056, 2989, 1587, 1435 cm^{-1}; HRMS (FAB) calcd for $C_{15}H_{14}NO$ 224.1075 ($[M+H]^+$), found 224.1066.

*4.1.2. 2-(Pyridin-2-yl)-4-p-tolylbut-3-yn-2-ol (**26**).* Pale yellow solid, mp: 80.3–81.1 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J=4.5 Hz, 1H), 7.76 (td, J=1.5, 8.0 Hz, 1H), 7.68 (d, J=8.0 Hz, 1H), 7.33 (d, J=8.0 Hz, 2H), 7.26 (dd, J=1.0, 7.0 Hz, 1H), 7.09 (d, J=7.5 Hz, 2H), 5.58 (s, 1H), 2.33 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 147.5, 138.6, 137.5, 131.8, 129.1, 120.3, 119.7, 91.6, 84.0, 76.9, 69.1, 32.5, 21.6; IR (ATR) 3093, 3030, 3000, 2977, 1591, 1509, 1468, 1431 cm^{-1}; HRMS (FAB) calcd for $C_{16}H_{16}NO$ 238.1232 ($[M+H]^+$), found 238.1234.

*4.1.3. 2-(Pyridin-2-yl)-4-(thiophen-3-yl)but-3-yn-2-ol (**27**).* Pale brown solid, mp: 102.7–103.7 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J=4.5 Hz, 1H), 7.77 (td, J=1.0, 8.0 Hz, 1H), 7.67 (d, J=8.0 Hz, 1H), 7.44 (dd, J=1.0, 3.0 Hz, 1H), 7.27 (dd, J=5.0, 7.0 Hz, 1H), 7.23 (dd, J=3.0, 5.0 Hz, 1H), 7.10 (d, J=5.0 Hz, 1H), 5.61 (s, 1H), 1.86 (s, 3H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 162.1, 147.5, 137.6, 131.9, 128.5, 128.3, 122.9, 122.8, 120.2, 92.4, 83.9, 69.1, 32.4; IR (ATR) 3167, 3097, 2989, 2933, 1587, 1360 cm^{-1}; HRMS (FAB) calcd for $C_{13}H_{12}NOS$ 230.0640 ($[M+H]^+$), found 230.0644.

*4.1.4. 4,4-Dimethyl-1-phenyl-1-(pyridin-2-yl)pent-2-yn-1-ol (**28**).* White solid, mp: 116.0–116.9 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, J=5.0 Hz, 1H), 7.67–7.59 (m, 3H), 7.43 (d, J=8.0 Hz, 1H), 7.33–7.28 (m, 2H), 7.25–7.21 (m, 1H), 7.19 (dd, J=5.0, 7.5 Hz, 1H), 6.46 (s, 1H), 1.30 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 146.9, 145.1, 137.5, 128.3, 127.7, 126.4, 122.7, 121.7, 95.7, 80.8, 73.2, 31.0, 27.8; IR (ATR) 3193, 3059, 2966, 2862, 2240, 1587, 1446 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{20}NO$ 266.1545 ($[M+H]^+$), found 266.1552.

*4.1.5. 2-(Pyridin-2-yl)oct-3-yn-2-ol (**29**).* Pink liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J=5.0 Hz, 1H), 7.74 (dt, J=1.5, 7.5 Hz, 1H), 7.61 (d, J=8.0 Hz, 1H), 7.22 (dd, J=5.0, 7.5 Hz, 1H), 5.39 (s, 1H), 2.23 (t, J=7.0 Hz, 2H), 1.75 (s, 3H), 1.54–1.46 (m, 2H), 1.44–1.34 (m, 2H), 0.90 (t, J=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.7, 147.4, 137.3, 122.7, 120.1, 84.7, 83.4, 68.8, 32.8, 30.8, 22.1, 18.6, 13.7; IR (ATR) 3380, 2929, 2862, 2247, 1591, 1431, 1379 cm^{-1}; HRMS (FAB) calcd for $C_{13}H_{18}NO$ 204.1388 ($[M+H]^+$), found 204.1386.

*4.1.6. 3-Cyclohexenyl-1-phenyl-1-(pyridin-2-yl)prop-2-yn-1-ol (**30**).* Pale brown solid, mp: 85.5–87.7 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J=5.0 Hz, 1H), 7.67–7.61 (m, 3H), 7.42 (d, J=8.0 Hz, 1H), 7.34–7.29 (m, 2H), 7.27–7.23 (m, 1H), 7.22–7.18 (m, 1H), 6.49 (s, 1H), 6.22–6.17 (m, 1H), 2.23–2.15 (m, 2H), 2.13–2.06 (m, 2H), 1.68–1.54 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 147.0, 144.7, 137.5, 135.9, 128.3, 127.9, 126.6, 122.8, 121.8, 120.3, 88.6, 88.4, 73.7, 29.2, 25.8, 22.4, 21.6; IR (ATR) 3372, 3059, 2918, 2210, 1591, 1427, 1353 cm^{-1}; HRMS (FAB) calcd for $C_{20}H_{20}NO$ 290.1545 ($[M+H]^+$), found 290.1553.

*4.1.7. 1-Phenyl-1-(pyridin-2-yl)-3-(pyridin-3-yl)prop-2-yn-1-ol (**31**).* Pale yellow solid, mp: 101.2–102.9 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, J=1.5 Hz, 1H), 8.56 (d, J=5.0 Hz, 1H), 8.53 (dd, J=1.5, 5.0 Hz, 1H), 7.78 (dt, J=1.5, 8.0 Hz, 1H), 7.73–7.63 (m, 3H), 7.48 (d, J=8.0 Hz, 1H), 7.33–7.28 (m, 2H), 7.28–7.22 (m, 1H), 7.28–7.23 (m, 2H), 6.72 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 152.6, 149.1, 147.2, 143.8, 138.9, 137.8, 128.6, 128.2, 126.5, 123.2, 123.1, 121.8, 119.8, 94.7, 83.2, 73.8; IR (ATR) 3123, 3085, 3048, 2787, 1584, 1565, 1409 cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{15}N_2O$ 287.1184 ($[M+H]^+$), found 287.1191.

*4.1.8. 3-Phenyl-1,1-di(pyridin-2-yl)prop-2-yn-1-ol (**32**).* Dark orange solid, mp: 89.9–91.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J=4.0 Hz, 2H), 7.94 (d, J=8.0 Hz, 2H), 7.74–7.67 (m, 2H), 7.54–7.45 (m, 2H), 7.32–7.24 (m, 3H), 7.23–7.16 (m, 2H), 6.81 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 148.1, 137.2, 132.0, 128.6, 128.2, 123.0, 122.6, 121.5, 91.2, 85.6, 74.3; IR (ATR) 3346, 3078, 2921, 2225, 1569, 1427 cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{15}N_2O$ 287.1184 ($[M+H]^+$), found 287.1180.

*4.1.9. 1-(4-Methoxyphenyl)-3-phenyl-1-(pyridin-2-yl)prop-2-yn-1-ol (**33**).* Brown oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.84 (d, J=4.5 Hz, 1H), 7.69 (t, J=7.5 Hz, 1H), 7.61 (d, J=7.5 Hz, 2H), 7.54–7.48 (m, 2H), 7.46 (d, J=8.0 Hz, 1H), 7.37–7.27 (m, 3H), 7.25 (d, J=6.5 Hz, 1H), 6.87 (d, J=8.5 Hz, 2H), 6.55 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 158.5, 147.0, 137.7, 136.6, 132.0, 128.7, 128.4, 127.9, 122.9, 122.7, 121.9, 113.8, 91.3, 86,6, 73.4, 55.4; IR (ATR) 3320, 3052, 2929, 2836, 2221, 1587, 1505, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{18}NO_2$ 316.1338 ($[M+H]^+$), found 316.1330.

*4.1.10. 1,1-Di(pyridin-2-yl)hept-2-yn-1-ol (**34**).* Brown solid, mp: 60.9–62.8 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J=4.5 Hz, 2H), 7.91 (d, J=8.0 Hz, 2H), 7.69 (t, J=8.0 Hz, 2H), 7.18 (t, J=6.0 Hz, 2H), 6.58 (s, 1H), 2.32 (t, J=7.5 Hz, 2H), 1.59–1.50 (m, 2H), 1.45–1.35 (m, 2H), 0.89 (t, J=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 148.1, 137.1, 122.8, 121.4, 86.9, 82.3, 74.0, 30.8, 22.2, 18.9, 13.7; IR (ATR) 3417, 3044, 2955, 2869, 1584, 1461, 1427 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{19}N_2O$ 267.1497 ($[M+H]^+$), found 267.1495.

*4.1.11. 3-Cyclohexenyl-1-(4-methoxyphenyl)-1-(pyridin-2-yl)prop-2-yn-1-ol (**35**).* Brown gum; ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 (d, J=5.0 Hz, 1H), 7.64 (td, J=2.0, 8.0 Hz, 1H), 7.54 (d, J=8.5 Hz, 2H), 7.39 (d, J=8.0 Hz, 1H), 7.20 (dd, J=5.0, 7.5 Hz, 1H), 6.84 (d, J=9.0 Hz, 2H), 6.42 (br s, 1H), 6.21–6.15 (m, 1H), 3.78 (s, 3H), 2.22–2.14 (m, 2H), 2.13–2.05 (m, 2H), 1.68–1.53 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 159.3, 146.9, 137.5, 137.0, 135.8, 127.9, 122.7, 121.8, 120.3, 113.7, 88.6, 88.5, 73.3, 55.4, 29.2, 25.8, 22.4, 21.6; IR (ATR) 3316, 3056, 2929, 2858, 1587, 1505, 1431 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{22}NO_2$ 320.1651 ($[M+H]^+$), found 320.1645.

*4.1.12. 1-(4-Methoxyphenyl)-1-(pyridin-2-yl)-3-(thiophen-3-yl) prop-2-yn-1-ol (**36**).* Pale brown solid, mp: 109.5–111.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J=5.0 Hz, 1H), 7.67 (td, J=1.0, 8.0 Hz, 1H), 7.59 (d, J=9.0 Hz, 2H), 7.50 (d, J=3.0 Hz, 1H), 7.44 (d, J=8.0 Hz, 1H), 7.28–7.21 (m, 2H), 7.16 (d, J=5.0 Hz, 1H), 6.87 (d, J=8.5 Hz, 2H), 6.54 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 159.4, 147.0, 137.6, 136.5, 130.1, 129.4, 1247.9, 125.4, 122.9, 121.9, 121.7, 113.8, 90.9, 81.8, 73.4, 55.4; IR (ATR) 3287, 3085, 2992, 2962, 2929, 2221, 1569, 1505, 1248 cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{16}NO_2S$ 322.0902 ($[M+H]^+$), found 322.0904.

*4.1.13. 2-(4-Methylpyridin-2-yl)-4-phenylbut-3-yn-2-ol (**37**).* Pale brown solid, mp: 91.8–94.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, J=5.0 Hz, 1H), 7.47 (s, 1H), 7.46–7.42 (m, 2H), 7.32–7.27 (m, 3H), 7.09 (d, J=5.0 Hz, 1H), 5.68 (s, 1H), 2.42 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 149.0, 147.2, 132.0, 128.5, 128.3, 124.1, 122.9, 120.9, 92.6, 83.7, 68.9, 32.4, 21.4; IR (ATR) 3097, 2992, 2929, 2784, 1669 cm^{-1}; HRMS (FAB) calcd for $C_{16}H_{16}NO$ 238.1232 ($[M+H]^+$), found 238.1247.

*4.1.14. 2-(Pyridin-2-yl)but-3-yn-2-ol (**95**).* Ethynylmagnesium bromide solution (0.5 M in THF) was used for the synthesis of **95** and **96**. Pale pink solid, mp: 88.9–89.8 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J=4.5 Hz, 1H), 7.77 (td, J=1.5, 8.0 Hz, 1H), 7.62 (d, J=8.0 Hz, 1H), 7.27 (dd, J=6.0, 6.5 Hz, 1H), 5.49 (s, 1H), 2.55 (s, 1H), 1.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 147.6, 137.6, 123.0, 120.2, 87.2, 72.0, 68.5, 32 0; IR (ATR) 3223, 3089, 2985, 2754, 2109, 1617, 1431 cm^{-1}; HRMS (FAB) calcd for $C_9H_{10}NO$ 148.0762 ($[M+H]^+$), found 148.0765.

*4.1.15. 1-Phenyl-1-(pyridin-2-yl)prop-2-yn-1-ol (**96**).* Pale yellow solid, mp: 66.0–66.7 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J=5.5 Hz, 1H), 7.69–7.62 (m, 3H), 7.41 (d, J=8.5 Hz, 1H), 7.36–7.31 (m, 2H), 7.28–7.26 (m, 1H), 7.23 (dd, J=5.0, 7,5 Hz, 1H), 6.50 (s, 1H), 2.80 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 147.1, 143.6, 137.7, 128.5., 128.2, 126.4, 123.1, 121.7, 85.8, 74.9, 73.2; IR (ATR) 3305, 3261, 3052, 3022, 1591, 1427, 1364 cm^{-1}; HRMS (FAB) calcd for $C_{14}H_{12}NO$ 210.0919 ($[M+H]^+$), found 210.0921.

4.2. General procedure for the synthesis of poly-substituted indolizinones

A mixture of tertiary propargylic alcohol **5** (0.13 mmol), (hetero) aryl halide (1.5 equiv), $Pd(PPh_3)_4$ (5 mol %), and K_2CO_3 (2.5 equiv) in CH_3CN (1 mL) was heated at 90 °C for 13 h. The reaction mixture was concentrated under reduced pressure to give the crude residue, which was diluted with ethyl acetate and washed with water. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a crude mixture, which was purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to afford the indolizinone **7**.

For spectral data of **13**–**25** and **38**–**56**, see the Supplementary data of Ref. 10. For spectral data of **82**, see the Supplementary data of Ref. 9.

*4.2.1. 2-(4-Nitrophenyl)-3-phenyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**57**).* Orange solid, mp: 163.0–163.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, J=5.0 Hz, 1H), 7.95 (d, J=9.0 Hz, 2H), 7.68 (td, J=2.0, 8.0 Hz, 1H), 7.65–7.40 (m, 6H), 7.32 (d, J=9.5 Hz, 2H), 7.19 (dd, J=5.0, 7.5 Hz, 1H), 6.62–6-53 (m, 2H), 6.18 (dd, J=5.5, 9.0 Hz, 1H), 5.39 (dd, J=5.5, 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 171.9, 158.1, 149.4, 145.1, 138.9, 137.1, 131.3, 129.7, 128.7, 128.6, 128.3, 124.3, 124.2, 123.2, 123.1, 122.2, 120.7, 109.9, 108.5, 73.5; IR (ATR) 3044, 2918, 1673, 1535, 1323 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{18}N_3O_3$ 408.1348 ([M+H]$^+$), found 408.1359.

*4.2.2. 2-(4-Acetylphenyl)-3-phenyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**58**).* Red gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J=5.0 Hz, 1H), 7.70 (d, J=8.0 Hz, 2H), 7.66 (dd, J=1.5, 7.5 Hz, 1H), 7.57 (d, J=8.0 Hz, 2H), 7.54 (br s, 4H), 7.25 (d, J=8.5 Hz, 2H), 7.18 (dd, J=5.0, 7.0 Hz, 1H), 6.58 (d, J=7.5 Hz, 1H), 6.54 (d, J=9.0 Hz, 1H), 6.16 (dd, J=5.5, 9.0 Hz, 1H), 5.39–5.32 (m, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 196.9, 171.3, 158.4, 149.4, 137.0, 136.6, 134.2, 131.0, 129.5, 128.93, 128.90, 128.2, 128.0, 124.4, 124.1, 123.0, 122.1, 120.5, 109.5, 109.2, 73.3, 26.5; IR (ATR) 3048, 2918, 2851, 1669, 1263 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{21}N_2O_2$ 405.1603 ([M+H]$^+$), found 405.1594.

*4.2.3. 2-(4-Chlorophenyl)-3-phenyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**59**).* Orange solid, mp: 152.3–154.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J=5.0 Hz, 1H), 7.66 (td, J=2.0, 8.0 Hz, 1H), 7.56 (d, J=8.0 Hz, 1H), 7,52 (br s, 5H), 7,17 (dd, J=5.0, 7.5 Hz, 1H), 7.07 (s, 4H), 6.56 (d, J=7.5 Hz, 1H), 6.51 (d, J=9.0 Hz, 1H), 6.14 (dd, J=5.5, 9.0 Hz, 1H), 5.35–5.28 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 170.4, 158.7, 149.4, 137.0, 131.6, 130.8, 129.8, 129.5, 129.4, 129.0, 128.1, 124.5, 124.2, 122.9, 121.9, 120.5, 109.6, 108.7, 73.1; IR (ATR) 3052, 2921, 2851, 1673, 1535, 1327 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{18}ClN_2O$ 397.1108 ([M+H]$^+$), found 397.1099.

*4.2.4. Methyl 4-(1-oxo-3-phenyl-8a-(pyridin-2-yl)-1,8a-dihydroindolizin-2-yl)benzoate (**60**).* Orange solid, mp: 141.8–145.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J=5.0 Hz, 1H), 7.77 (d, J=9.0 Hz, 2H), 7.67 (td, J=1.5, 7.5 Hz, 1H), 7.57 (d, J=8.0 Hz, 1H), 7.53 (br s, 5H), 7.22 (d, J=8.5 Hz, 2H), 7.18 (dd, J=4.5, 7.0 Hz, 1H), 6.58 (d, J=7.5 Hz, 1H), 6.53 (d, J=9.0 Hz, 1H), 6.16 (dd, J=9.0, 5.5 Hz, 1H), 6.34 (dd, J=5.5, 7.0 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 171.2, 167.2, 158.6, 149.5, 137.0, 136.3, 131.0, 129.5, 129.2, 129.02, 128.99, 128.2, 127.1, 124.5, 124.2, 123.0, 122.2, 120.6, 109.7, 109.1, 73.3, 52.0; IR (ATR) 3048, 2996, 2944, 1714, 1673, 1602, 1539, 1416, 1271 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{21}N_2O_3$ 421.1552 ([M+H]$^+$), found 421.1532.

*4.2.5. Methyl 3-(1-oxo-3-phenyl-8a-(pyridin-2-yl)-1,8a-dihydroindolizin-2-yl)benzoate (**61**).* Red gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, J=4.0 Hz, 1H), 7.80 (t, J=1.5 Hz, 1H), 7,73 (dt, J=1.5, 8.0 Hz, 1H), 7.67 (td, J=2.0, 8.0 Hz, 1H), 7.58 (d, J=8.0 Hz, 1H), 7.52 (br s, 5H), 7.36 (dt, J=1.0, 8.0 Hz, 1H), 7.22–715 (m, 2H), 6.58 (d, J=8.5 Hz, 1H), 6.53 (d, J=9.5 Hz, 1H), 6.16 (dd, J=5.5, 9.0 Hz, 1H), 5.37–5.29 (m, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 170.8, 167.2, 158.7, 149.5, 137.0, 133.0, 131.4, 130.8, 129.9, 129.8, 129.4, 129.01, 128.99, 128.2, 127.1, 124.6, 124.2, 122.9, 122.0, 120.5, 109.8, 108.8, 73.1, 52.0; IR (ATR) 3048, 2948, 1718, 1673, 1535, 1423, 1241 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{21}N_2O_3$ 421.1552 ([M+H]$^+$), found 421.1567.

*4.2.6. 3-Phenyl-8a-(pyridin-2-yl)-2-(thiophen-2-yl)indolizin-1(8aH)-one (**62**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, J=4.5 Hz, 1H), 7.66 (td, J=6.5, 8.0 Hz, 1H), 7.60 (br s, 5H), 7.55 (d, J=8.0 Hz, 1H), 7.16 (dd, J=5.0, 7.0 Hz, 1H), 7.00–6.96 (m, 2H), 6.80 (t, J=4.5 Hz, 1H), 6.51 (d, J=9.0 Hz, 1H), 6.38 (d, J=7.0 Hz, 1H), 6.14 (dd, J=5.5, 9.5 Hz, 1H), 5.34–5.27 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 168.2, 158.5, 149.5, 137.0, 132.5, 130.9, 129.5, 129.01, 128.97, 126.4, 124.4, 124.3, 124.0, 123.1, 122.9, 121.9, 120.5, 108.8, 106.4, 72.7; IR (ATR) 3048, 2921, 2851, 1669, 1423 cm^{-1}; HRMS (FAB) calcd for $C_{23}H_{17}N_2OS$ 369.1062 ([M+H]$^+$), found 369.1064.

*4.2.7. 2,3-Diphenyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**63**).* Red gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, J=4.5 Hz, 1H), 7.66 (dt, J=2.0, 8.0 Hz, 1H), 7.57 (d, J=8.0 Hz, 1H), 7.56–7.45 (m, 5H), 7.17 (dd, J=5.0, 7.5 Hz, 1H), 7.15–7.09 (m, 4H), 7.08–7.02 (m, 1H), 6.57 (d, J=7.5 Hz, 1H), 6.51 (d, J=9.0 Hz, 1H), 6.14 (dd, J=5.5, 9.0 Hz, 1H), 5.30 (dd, J=5.5, 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 170.3, 158.9, 149.5, 136.9, 130.9, 130.7, 129.6, 129.3, 129.2, 128.8, 127.9, 126.0, 124.7, 124.1, 122.9, 122.0, 120.4, 110.8, 108.3, 73.0; IR (ATR) 3048, 2921, 2851, 1669, 1535, 1423, 1364, 1323 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{19}N_2O$ 363.1497 ([M+H]$^+$), found 363.1512.

*4.2.8. 2-(4-Methoxyphenyl)-3-phenyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**64**).* Orange solid, mp: 127.3–132.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, J=5.0 Hz, 1H), 7.65 (td, J=2.0, 8.0 Hz, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.55–7.45 (m, 5H), 7.16 (dd, J=5.0, 7.5 Hz, 1H), 7.06 (d, J=9.0 Hz, 2H), 6.67 (d, J=9.0 Hz, 2H), 6.55 (d, J=7.5 Hz, 1H), 6.49 (d, J=9.5 Hz, 1H), 6.14 (dd, J=5.5, 9.0 Hz, 1H), 5.32–5.24 (m, 1H), 3.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 169.5, 159.0, 158.0, 149.5, 136.9, 130.6, 129.9, 129.5, 129.3, 129.2, 124.7, 124.1, 123.1, 122.8, 121.8, 120.3, 113.5, 110.6, 108.0, 72.8, 55.3; IR (ATR) 3044, 3003, 2929, 2832, 1669, 1539, 1509, 1423, 1364, 1323, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{26}H_{21}N_2O_2$ 393.1603 ([M+H]$^+$), found 393.1583.

*4.2.9. 2-(4-Acetylphenyl)-8a-(4-methoxyphenyl)-3-phenylindolizin-1(8aH)-one (**65**).* Orange gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J=8.5 Hz, 2H), 7.58–7.50 (m, 3H), 7.49 (d, J=9.0 Hz, 2H), 7.47–7.41 (m, 2H), 7.24 (d, J=8.5 Hz, 2H), 6.90 (d, J=9.0 Hz, 2H), 6.51 (d, J=7.5 Hz, 1H), 6.41 (d, J=9.5 Hz, 1H), 6.08 (dd, J=7.0, 9.5 Hz, 1H), 5.40 (dd, J=5.5, 7.5 Hz, 1H), 3.77 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 197.8, 170.5, 159.9, 136.4, 134.4, 132.3, 131.1, 129.6, 128.9, 128.8, 128.3, 128.0, 125.7, 123.9, 123.4, 123.0, 114.3, 110.2, 109.5, 71.1, 55.4, 26.6; IR (ATR) 3052, 2925, 1669, 1416, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{29}H_{24}NO_3$ 434.1756 ([M+H]$^+$), found 434.1748.

*4.2.10. 4-(8a-(4-Methoxyphenyl)-1-oxo-3-phenyl-1,8a-dihydroindolizin-2-yl)benzonitrile (**66**).* Orange gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61–7.51 (m, 3H), 7.50–7.39 (m, 4H), 7.37 (d, J=8.5 Hz, 2H), 7.25 (d, J=8.5 Hz, 2H), 6.90 (d, J=9.0 Hz, 2H), 6.50 (d, J=7.5 Hz, 1H), 6.46 (d, J=9.0 Hz, 1H), 6.08 (dd, J=5.5, 9.5 Hz, 1H), 5.45–5.37 (m, 1H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.4, 170.8, 159.6, 136.4, 132.1, 131.6, 131.3, 129.7, 128.6, 125.7, 123.7, 123.5, 123.0, 119.3, 114.3, 110.6, 108.8, 108.6, 71.2, 55.4; IR (ATR) 3048, 2951, 2929, 2221, 1677, 1535, 1248, 1178 cm^{-1}; HRMS (FAB) calcd for $C_{28}H_{21}N_2O_2$ 417.1603 ([M+H]$^+$), found 417.1613.

*4.2.11. 8a-(4-Methoxyphenyl)-3-phenyl-2-(pyrazin-2-yl)indolizin-1(8aH)-one (**67**).* Red gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 (d, J=1.0 Hz, 1H), 8.22–8.17 (m, 2H), 7.57–7.41 (m, 7H), 6.90 (d. J=9.0 Hz, 2H), 6.51 (d, J=7.0 Hz, 1H), 6.47 (d, J=9.5 Hz, 1H), 6.11 (dd, J=5.5, 9.0 Hz, 1H), 5.47–5-42 (m, 1H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 173.1, 159.7, 147.8, 144.7, 143.6, 141.2, 131.8, 130.8, 129.1, 128.7, 125.9, 124.0, 123.8, 123.1, 114.4, 111.3, 107.7, 71.6, 55.5; IR (ATR) 3048, 2921, 2851, 1673, 1494, 1405, 1248 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{20}N_3O_2$ 394.1556 ([M+H]$^+$), found 394.1551.

*4.2.12. 2,8a-Bis(4-methoxyphenyl)-3-phenylindolizin-1(8aH)-one (**68**).* Orange gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.48 (m, 5H),

7.48–7.43 (m, 2H), 7.07 (d, *J*=9.0 Hz, 2H), 6.90 (d, *J*=9.0 Hz, 2H), 6.70 (d, *J*=9.0 Hz, 2H), 6.49 (d, *J*=8.0 Hz, 1H), 6.36 (d, *J*=9.5 Hz, 1H), 6.07 (dd, *J*=5.5, 9.5 Hz, 1H), 5.33 (dd, *J*=5.5, 7.0 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.6, 168.7, 159.5, 158.0, 133.0, 130.6, 130.0, 129.5, 129.3, 129.0, 125.9, 124.3, 123.1, 123.0, 122.9, 114.2, 113.6, 110.6, 108.8, 70.6, 55.4, 55.3; IR (ATR) 3048, 2996, 2832, 1673, 1543, 1505, 1241 cm^{-1}; HRMS (FAB) calcd for $C_{28}H_{24}NO_3$ 422.1756 ([M+H]$^+$), found 422.1770.

*4.2.13. 2-(3-Methoxyphenyl)-8a-(4-methoxyphenyl)-3-phenylindolizin-1(8aH)-one (**69**).* Orange gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.43 (m, 7H), 7.02 (t, *J*=8.0 Hz, 1H), 6.89 (d, *J*=9.0 Hz, 2H), 6.72 (d, *J*=8.0 Hz, 2H), 6.63 (d, *J*=8.5 Hz, 1H), 6.48 (d, *J*=7.0 Hz, 1H), 6.37 (d, *J*=9.5 Hz, 1H), 6.07 (dd, *J*=5.5, 9.0 Hz, 1H), 5.38–5.30 (m, 1H), 3.78 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 169.7, 159.5, 159.2, 132.8, 132.1, 130.7, 129.5, 129.4, 129.0, 128.9, 125.9, 124.2, 123.2, 123.1, 121.3, 114.3, 113.5, 112.8, 110.5, 109.4, 70.8, 55.5, 55.1; IR (ATR) 3056, 2921, 2851, 1673, 1599, 1502, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{28}H_{24}NO_3$ 422.1756 ([M+H]$^+$), found 422.1760.

*4.2.14. 4-(3-Butyl-1-oxo-8a-(pyridin-2-yl)-1,8a-dihydroindolizin-2-yl)benzonitrile (**70**).* Yellow solid, mp: 120.5–124.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, *J*=5.0 Hz, 1H), 7.64 (dd, *J*=1.5, 8.0 Hz, 1H), 7.61 (d, *J*=8.5 Hz, 2H), 7.47 (d, *J*=8.5 Hz, 2H), 7.42 (d, *J*=8.0 Hz, 1H), 7.15 (dd, *J*=5.0, 7.5 Hz, 1H), 6.75 (d, *J*=7.0 Hz, 1H), 6.50 (d, *J*=9.5 Hz, 1H), 6.17 (dd, *J*=5.5, 9.0 Hz, 1H), 5.56–5.51 (m, 1H), 2.90–2.75 (m, 2H), 1.90–1.75 (m, 2H), 1.58–1.46 (m, 2H), 0.99 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.3, 173.9, 158.0, 149.3, 137.0, 136.9, 132.0, 129.0, 124.0, 123.1, 123.0, 122.9, 120.5, 119.3, 110.4, 109.3, 108.8, 72.6, 29.9, 25.6, 22.9, 13.7; IR (ATR) 3044, 2951, 2925, 2862, 2217, 1666, 1524, 1423 cm^{-1}; HRMS (FAB) calcd for $C_{24}H_{22}N_3O$ 368.1763 ([M+H]$^+$), found 368.1744.

*4.2.15. 2-(4-Acetylphenyl)-3-butyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**71**).* Yellow solid, mp: 108.2–109.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J*=5.0 Hz, 1H), 7.93 (d, *J*=8.5 Hz, 2H), 7.63 (dt, *J*=2.0, 8.0 Hz, 1H), 7.46 (d, *J*=8.5 Hz, 2H), 7.42 (d, *J*=8.2 Hz, 1H), 7.14 (dd, *J*=5.0, 7.5 Hz, 1H), 6.76 (d, *J*=7.0 Hz, 1H), 6.51 (d, *J*=9.5 Hz, 1H), 6.16 (dd, *J*=5.0, 9.0 Hz, 1H), 5.54–5.48 (m, 1H), 2.95–2.75 (m, 2H), 2.58 (s, 3H), 1.95–1.75 (m, 2H), 1.60–1.45 (m, 2H), 0.98 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 196.6, 173.7, 158.3, 149.3, 137.0, 136.8, 134.8, 128.6, 128.4, 123.9, 123.2, 123.1, 122.8, 120.3, 110.0, 109.5, 72.5, 30.0, 26.6, 25.7, 22.9, 13.8; IR (ATR) 3044, 2955, 2925, 2862, 1669, 1423, 1267 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{25}N_2O_2$ 385,1916 ([M+H]$^+$), found 385.1906.

*4.2.16. 3-Butyl-2-(4-chlorophenyl)-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**72**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J*=5.0 Hz, 1H), 7.62 (dt, *J*=2.0, 8.0 Hz, 1H), 7.42 (d, *J*=8.0 Hz, 1H), 7.30 (d, *J*=8.5 Hz, 2H), 7.25 (d, *J*=8.5 Hz, 2H), 7.14 (dd, *J*=4.5, 7.0 Hz, 1H), 6.72 (d, *J*=7.0 Hz, 1H), 6.48 (d, *J*=9.0 Hz, 1H), 6.1 (dd, *J*=5.0, 8.0 Hz, 1H), 5.50–5.44 (m, 1H), 2.87–2.70 (m, 2H), 1.86–1.72 (m, 2H), 1.55–1.43 (m, 2H), 0.97 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 173.2, 158.5, 149.3, 136.8, 132.3, 130.3, 130.0, 128.6, 124.0, 123.3, 122.9, 122.8, 130.3, 109.6, 109.5, 72.4, 30.0, 25.6, 22.9, 13.8; IR (ATR) 3048, 2955, 2929, 2869, 1669, 1532, 1423 cm^{-1}; HRMS (FAB) calcd for $C_{23}H_{22}ClN_2O$ 377.1421 ([M+H]$^+$), found 377.1406.

*4.2.17. 3-Butyl-8a-(pyridin-2-yl)-2-(thiophen-2-yl)indolizin-1(8aH)-one (**73**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, *J*=5.0 Hz, 1H), 7.61 (dt, *J*=2.0, 8.0 Hz, 1H), 7.46 (d, *J*=8.0 Hz, 1H), 7.29 (d, *J*=3.5 Hz, 1H), 7.19 (d, *J*=5.0 Hz, 1H), 7.13 (dd, *J*=5.0, 7.5 Hz, 1H), 7.02 (dd, *J*=3.5, 5.0 Hz, 1H), 6.74 (d, *J*=7.5 Hz, 1H), 6.49 (d, *J*=8.0 Hz, 1H), 6.14 (dd, *J*=5.5, 9.5 Hz, 1H), 5.48 (dd, *J*=5.5, 7.0 Hz, 1H), 3.09–2.88 (m, 2H), 1.93–1.77 (m, 2H), 1.66–1.54 (m, 2H), 1.04 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.7, 171.9, 158.4, 149.3, 136.8, 132.7, 127.0, 124.3, 124.0, 123.3, 123.2, 123.1, 122.8, 120.4, 109.9, 105.0, 72.3, 29.6, 26.1, 23.1, 13.9; IR (ATR) 3048, 2955, 2925, 2869, 1669, 1539, 1423 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{21}N_2OS$ 349.1375 ([M+H]$^+$), found 349.1359.

*4.2.18. Methyl 4-(3-cyclohexenyl-8a-(4-methoxyphenyl)-1-oxo-1,8a-dihydroindolizin-2-yl)benzoate (**74**).* Yellow solid, mp: 143.2–146.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J*=8.5 Hz, 2H), 7.62 (d, *J*=8.5 Hz, 2H), 7.36 (d, *J*=9.0 Hz, 2H), 6.85 (d, *J*=9.0 Hz, 2H), 6.70 (d, *J*=7.0 Hz, 1H), 6.35 (d, *J*=9.0 Hz, 1H), 6.20 (br s, 1H), 6.06 (dd, *J*=5.5, 9.5 Hz, 1H), 5.45 (dd, *J*=5.5, 7.0 Hz, 1H), 3.88 (s, 3H), 3.75 (s, 3H), 2.32–2.24 (m, 2H), 2.18–2.10 (m, 2H), 1.81–1.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 172.7, 167.3, 159.5, 136.9, 133.9, 132.4, 129.3, 128.5, 127.3, 127.2, 125.7, 123.7, 123.4, 123.1, 114.2, 109.9, 107.6, 70.6, 55.4, 52.1, 27.1, 25.4, 22.3, 21.5; IR (ATR) 3048, 2921, 2832, 1707, 1599, 1532, 1502, 1420, 1252 cm^{-1}; HRMS (FAB) calcd for $C_{29}H_{28}NO_4$ 454.2018 ([M+H]$^+$), found 454.2020.

*4.2.19. 8a-(4-Methoxyphenyl)-2-phenyl-3-(thiophen-3-yl)indolizin-1(8aH)-one (**75**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.50–7.43 (m, 3H), 7.23–7.07 (m, 6H), 6.88 (d, *J*=8.5 Hz, 2H), 6.65 (d, *J*=7.0 Hz, 1H), 6.34 (d, *J*=9.5 Hz, 1H), 6.07 (dd, *J*=5.5, 9.0 Hz, 1H), 5.42–5.33 (m, 1H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.1, 164.5, 159.5, 132.8, 130.9, 129.2, 128.9, 128.3, 128.0, 127.7, 127.4, 126.4, 125.9, 124.4, 123.13, 123.07, 114.2, 111.0, 109.3, 70.9, 55.4; IR (ATR) 3100, 2921, 1677, 1505, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{20}NO_2S$ 398.1215 ([M+H]$^+$), found 398.1227.

*4.2.20. 2-(4-Acetylphenyl)-8a-(4-methoxyphenyl)-3-(thiophen-3-yl) indolizin-1(8aH)-one (**76**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J*=8.0 Hz, 2H), 7.57–7.54 (m, 1H), 7.54–7.50 (m, 1H), 7.45 (d, *J*=8.5 Hz, 2H), 7.26 (d, *J*=8.5 Hz, 2H), 7.14 (d, *J*=5.0 Hz, 1H), 6.88 (d, *J*=9.0 Hz, 2H), 6.65 (d, *J*=7.5 Hz, 1H), 6.39 (d, *J*=9.5 Hz, 1H), 6.08 (dd, *J*=5.5, 9.0 Hz, 1H), 5.45–5.39 (m, 1H), 3.76 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 197.8, 165.4, 159.6, 136.5, 134.6, 132.3, 128.8, 128.44, 128.38, 128.1, 128.0, 127.5, 125.8, 124.1, 123.5, 123.0, 114.3, 110.2, 109.7, 71.2, 55.4, 26.6; IR (ATR) 3085, 2921, 2854, 1669, 1595, 1546, 1505, 1427, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{22}NO_3S$ 440.1320 ([M+H]$^+$), found 440.1313.

*4.2.21. 4-(8a-(4-Methoxyphenyl)-1-oxo-3-(thiophen-3-yl)-1,8a-dihydroindolizin-2-yl)benzonitrile (**77**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.53 (m, 2H), 7.45–7.39 (m, 4H), 7.26 (d, *J*=8.5 Hz, 2H), 7.13 (dd, *J*=1.5, 4.0 Hz, 1H), 6.88 (d, *J*=9.0 Hz, 2H), 6.64 (d, *J*=7.5 Hz, 1H), 6.40 (d, *J*=9.5 Hz, 1H), 6.09 (dd, *J*=5.5, 9.0 Hz, 1H), 5.44 (dd, *J*=5.5, 7.0 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.2, 165.7, 159.7, 136.4, 132.0, 131.7, 128.7, 128.5, 128.41, 128.37, 127.3, 125.8, 123.9, 123.6, 123.0, 119.3, 114.3, 110.7, 109.1, 108.9, 71.4, 55.4; IR (ATR) 3130, 2951, 2221, 1673, 1505, 1431, 1319, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{26}H_{19}N_2O_2S$ 423.1167 ([M+H]$^+$), found 423.1176.

*4.2.22. 2-(4-Chlorophenyl)-8a-(4-methoxyphenyl)-3-(thiophen-3-yl)indolizin-1(8aH)-one (**78**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dd, *J*=1.5, 3.0 Hz, 1H), 7.50 (dd, *J*=2.5, 5.0 Hz, 1H), 7.44 (d, *J*=9.0 Hz, 2H), 7.15–7.10 (m, 3H), 7.10–7.05 (d, *J*=8.5 Hz, 2H), 6.88 (d, *J*=9.0 Hz, 2H), 6.63 (d, *J*=7.0 Hz, 1H), 6.36 (d, *J*=9.5 Hz, 1H), 6.07 (dd, *J*=5.5, 9.5 Hz, 1H), 5.39 (dd, *J*=5.5, 7.5 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 164.7, 159.6, 132.5, 132.0, 130.0, 129.4, 128.9, 128.3, 128.2, 127.8, 127.6, 125.9, 124.3, 123.3, 123.1, 114.3, 109.73, 109.69, 71.0, 55.4; IR (ATR) 3078, 2921, 2851, 1669,

1505, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{19}ClNO_2S$ 432.0825 ($[M+H]^+$), found 432.0837.

*4.2.23. Methyl 3-(8a-(4-methoxyphenyl)-1-oxo-3-(thiophen-3-yl)-1,8a-dihydroindolizin-2-yl)benzoate (**79**).* Brown gum; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81–7-76 (m, 2H), 7.55–7.53 (m, 1H), 7.50 (dd, *J*=3.0, 5.0 Hz, 1H), 7.46 (d, *J*=9.0 Hz, 2H), 7.39 (d, *J*=8.0 Hz, 1H), 7.28–7.21 (m, 1H), 7.12 (dd, *J*=1.0, 5.0 Hz, 1H), 6.88 (d, *J*=9.0 Hz, 2H), 6.65 (d, *J*=7.5 Hz, 1H), 6.38 (d, *J*=9.0 Hz, 1H), 6.08 (dd, *J*=5.5, 9.0 Hz, 1H), 5.44–5.36 (m, 1H), 3.82 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 167.1, 165.1, 159.5, 133.2, 132.5, 131.4, 130.0, 129.9, 128.8, 128.3, 128.1, 127.9, 127.5, 127.4, 125.9, 124.2, 123.3, 123.1, 114.3, 109.84, 109.76, 71.0, 55.4, 52.1; IR (ATR) 3108, 2921, 1714, 1673, 1505, 1420, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{22}NO_4S$ 456.1270 ($[M+H]^+$), found 456.1266.

*4.2.24. 2-(4-Acetylphenyl)-7,8a-dimethyl-3-phenylindolizin-1(8aH)-one (**80**).* Dark yellow solid, mp: 102.8–105.5 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J*=8.5 Hz, 2H), 7.55–7.44 (m, 3H), 7.35 (d, *J*=6.5 Hz, 2H), 7.24 (d, *J*=8.5 Hz, 2H), 6.34 (d, *J*=7.5 Hz, 1H), 5.74 (s, 1H), 5.27 (dd, *J*=1.0, 7.5 Hz, 1H), 2.52 (s, 3H), 1.80 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 197.8, 168.6, 137.0, 134.2, 130.9, 130.8, 129.5, 129.1, 128.8, 128.3, 128.1, 122.3, 119.3, 113.3, 109.3, 68.4, 26.6, 25.7, 20.7; IR (ATR) 2918, 2851, 2240, 1666, 1595, 1539, 1341, 1263 cm^{-1}; HRMS (FAB) calcd for $C_{24}H_{22}NO_2$ 356.1651 ($[M+H]^+$), found 356.1642.

*4.2.25. Methyl 4-(7,8a-dimethyl-1-oxo-3-phenyl-1,8a-dihydroindolizin-2-yl)benzoate (**81**).* Orange gum; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J*=8.5 Hz, 2H), 7.55–7.43 (m, 3H), 7.34 (d, *J*=6.0 Hz, 2H), 7.21 (d, *J*=8.5 Hz, 2H), 6.33 (d, *J*=7.5 Hz, 1H), 5.74 (br s, 1H), 5.26 (dd, *J*=1.5, 7.5 Hz, 1H), 3.85 (s, 3H), 1.80 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 168.5, 167.3, 136.7, 130.9, 130.8, 129.4, 129.3, 129.1, 128.8, 128.2, 127.1, 122.3, 119.3, 113.2, 109.5, 68.4, 52.0, 25.7, 20.7; IR (ATR) 2921, 2851, 1714, 1673, 1602, 1580, 1431, 1271 m^{-1}; HRMS (FAB) calcd for $C_{24}H_{22}NO_3$ 372.1600 ($[M+H]^+$), found 372.1612.

*4.2.26. 4-(8a-Methyl-1-oxo-3-phenyl-1,8a-dihydroindolizin-2-yl) benzaldehyde (**83**).* Yellow solid, mp: 147.7–152.1 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.65 (d, *J*=8.5 Hz, 2H), 7.58–7.45 (m, 3H), 7.36 (d, *J*=5.5 Hz, 2H), 7.32 (d, *J*=9.0 Hz, 2H), 6.38 (d, *J*=8.0 Hz, 1H), 6.06 (d, *J*=9.5 Hz, 1H), 5.99 (dd, *J*=5.5, 9.0 Hz, 1H), 5.42 (dd, *J*=5.5, 7.0 Hz, 1H), 1.53 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 192.0, 168.9, 138.4, 133.7, 131.0, 129.6, 129.5, 128.9, 128.72, 128.68, 124.4, 122.8, 122.4, 109.8, 108.8, 68.2, 25.7; IR (ATR) 3052, 2921, 2851, 1688, 1666, 1595, 1539 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{18}NO_2$ 328.1338 ($[M+H]^+$), found 328.1327.

*4.2.27. 8a-Methyl-3-phenyl-2-(thiophen-3-yl)indolizin-1(8aH)-one (**84**).* Yellow gum; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57–7.49 (m, 3H), 7.45–7.36 (m, 3H), 7.06 (dd, *J*=3.0, 5.0 Hz, 1H), 6.67 (dd, *J*=1.0, 5.0 Hz, 1H), 6.23 (d, *J*=7.0 Hz, 1H), 6.00 (d, *J*=9.0 Hz, 1H), 5.95 (dd, *J*=5.0, 9.0 Hz, 1H), 5.34 (dd, *J*=5.0, 7.5 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 166.5, 131.0, 130.6, 129.7, 129.4, 128.7, 126.7, 124.2, 123.8, 123.1, 122.5, 121.2, 108.6, 106.3, 67.4, 25.5; IR (ATR) 3160, 3115, 2921, 2851, 1666, 1543, 1420, 1315 cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{16}NOS$ 306.0953 ($[M+H]^+$), found 306.0971.

4.3. General procedure for the O-allylation of 12, 31, 32, and 36 with diallyl carbonate

A mixture of propargylic alcohol (0.22 mmol), diallyl carbonate (10 equiv), $Pd(OAc)_2$ (5 mol %), xantphos (5 mol %) in THF (2 mL) was heated at 80 °C for 3 h. The reaction mixture was concentrated under reduced pressure and purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to give *O*-allylated tertiary propargylic alcohol.

*4.3.1. 2-(2-(Allyloxy)-4-phenylbut-3-yn-2-yl)pyridine (**86**).* Yellow gum; ^1H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J*=4.5 Hz, 1H), 7.78 (d, *J*=8.0 Hz, 1H), 7.72 (td, *J*=1.5, 7.5 Hz, 1H), 7.55–7.48 (m, 2H), 7.36–7.30 (m, 3H), 7.23 (dd, *J*=5.0, 7.0 Hz, 1H), 6.07–5.94 (m, 1H), 5.32 (d, *J*=17.0 Hz, 1H), 5.16 (d, *J*=10.5 Hz, 1H), 4.28 (dd, *J*=5.5, 12.0 Hz, 1H), 3.93 (dd, *J*=5.5, 12.0 Hz, 1H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 149.4, 136.7, 135.1, 132.0, 128.5, 128.3, 122.8, 122.7, 120.7, 116.7, 89.5, 87.2, 77.3, 66.6, 30.1; IR (ATR) 3056, 2985, 2929, 2858, 2228, 1584, 1431 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{18}NO$ 264.1388 ($[M+H]^+$), found 264.1380.

*4.3.2. 2,5′-(3-(Allyloxy)-3-phenylprop-1-yne-1,3-diyl)dipyridine (**87**).* Brown solid, mp: 77.9–79.6 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.26 (dd, *J*=1.5, 10.0 Hz, 2H), 7.87–7.80 (m, 2H), 7.74–7.65 (m, 3H), 7.36 (t, *J*=7.5 Hz, 2H), 7.29 (d, *J*=7.5 Hz, 1H), 7.28–7.23 (m, 1H), 7.16 (dd, *J*=5.0, 7.5 Hz, 1H), 6.15–6.00 (m, 1H), 5.40 (d, *J*=12.5 Hz, 1H), 5.21 (d, *J*=10.5 Hz, 1H), 4.28 (dd, *J*=5.0, 14.0 Hz, 1H), 4.02 (dd, *J*=5.0, 12.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 152.7, 149.4, 149.1, 141.7, 139.0, 136.9, 134.7, 128.5, 128.2, 127.1, 123.0, 122.7, 120.2, 119.8, 116.5, 91.9, 85.9, 82.0, 66.4; IR (ATR) 3089, 2854, 1580, 1431 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{19}N_2O$ 327.1497 ($[M+H]^+$), found 327.1498.

*4.3.3. 2,2′-(1-(Allyloxy)-3-phenylprop-2-yne-1,1-diyl)dipyridine (**89**).* Pale brown solid, mp: 95.5–98.2 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.5 Hz, 2H), 8.01 (d, *J*=8.0 Hz, 2H), 7.74 (td, *J*=1.5, 7.5 Hz, 2H), 7.59–7.52 (m, 2H), 7.35–7.29 (m, 3H), 7.17 (dd, *J*=5.0, 7.5 Hz, 2H), 6.12–6.00 (m, 1H), 5.37 (dd, *J*=1.5, 17.0 Hz, 1H), 5.19 (dd, *J*=1.0, 10.0 Hz, 1H), 4.21 (d, *J*=5.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 149.4, 136.7, 134.8, 132.1, 128.7, 128.3, 122.7, 122.6, 121.6, 116.7, 89.3, 88.1, 82.7, 66.7; IR (ATR) 3089, 2959, 1580, 1427 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{19}N_2O$ 327.1497 ($[M+H]^+$), found 327.1488.

*4.3.4. 2-(1-(Allyloxy)-1-(4-methoxyphenyl)-3-(thiophen-3-yl)prop-2-ynyl)pyridine (**91**).* Brown gum; ^1H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.0 Hz, 1H), 7.84 (d, *J*=8.0 Hz, 1H), 7.69 (t, *J*=7.5 Hz, 1H), 7.60 (d, *J*=9.0 Hz, 2H), 7.53 (s, 1H), 7.28–7.24 (m, 1H), 7.19 (d, *J*=5.0 Hz, 1H), 7.13 (dd, *J*=5.0, 7.5 Hz, 1H), 6.86 (d, *J*=9.0 Hz, 2H), 6.10–5.98 (m, 1H), 5.37 (d, *J*=17.5 Hz, 1H), 5.18 (d, *J*=10.5 Hz, 1H), 4.27 (dd, *J*=5.5, 12.5 Hz, 1H), 4.02 (dd, *J*=5.5, 12.5 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 159.4, 149.4, 136.8, 135.1, 134.2, 130.2, 129.5, 128.6, 125.3, 122.4, 121.7, 120.2, 116.3, 113.7, 88.1, 84.4, 81.7, 66.2, 55.6; IR (ATR) 3067, 2907, 2854, 2221, 1584, 1505, 1461, 1431, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{20}NO_2S$ 362.1215 ($[M+H]^+$), found 362.1228.

4.4. General procedure for the synthesis of *C*2-allylated indolizinones

A mixture of propargylic alcohol (0.22 mmol), diallyl carbonate (10 equiv), $Pd(PPh_3)_4$ (5 mol %), and K_2CO_3 (2.5 equiv) in THF (2 mL) was heated at 80 °C for 18 h. The reaction mixture was concentrated under reduced pressure to give the crude residue, which was diluted with ethyl acetate and washed with water. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a crude mixture, which was purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to give the *C*2-allylated indolizinone.

*4.4.1. 2-Allyl-8a-methyl-3-phenylindolizin-1(8aH)-one (**85**).* Brown gum; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54–7.46 (m, 3H), 7.44–7.36 (m,

2H), 6.25 (d, *J*=7.0 Hz, 1H), 5.91–5.87 (m, 2H), 5.84–5.74 (m, 1H), 5.27 (ddd, *J*=1.5, 5.0, 8.5 Hz, 1H), 4.92 (dd, *J*=1.5, 10.0 Hz, 1H), 4.89 (dd, *J*=2.0, 17.0 Hz, 1H), 2.83 (dd, *J*=6.0, 14.5 Hz, 2H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 168.5, 136.2, 130.4, 129.1, 129.0, 128.5, 123.6, 123.0, 122.4, 114.8, 108.0, 107.5, 66.9, 26.0, 25.2; IR (ATR) 3063, 2854, 1673, 1241 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{18}NO$ 264.1388 ([M+H]$^+$), found 264.1361.

*4.4.2. 2-Allyl-8a-phenyl-3-(pyridin-3-yl)indolizin-1(8aH)-one (**88**).* Red gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 2H), 7.85 (d, *J*=8.0 Hz, 1H), 7.54–7.47 (m, 3H), 7.36 (t, *J*=7.5 Hz, 2H), 7.32–7.27 (m, 1H), 6.36 (d, *J*=7.5 Hz, 1H), 6.29 (d, *J*=9.0 Hz, 1H), 5.79–5.66 (m, 1H), 5.33 (dd, *J*=5.5, 7.0 Hz, 1H), 4.89 (d, *J*=10.0 Hz, 1H), 4.81 (d, *J*=17.0 Hz, 1H), 2.88–2.75 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 166.7, 151.8, 149.8, 140.4, 136.2, 135.7, 128.9, 128.1, 125.3, 124.5, 124.1, 123.8, 123.2, 122.4, 115.4, 109.8, 109.2, 70.7, 25.6; IR (ATR) 3056, 2918, 1681, 1599, 1543, 1409 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{19}N_2O$ 327.1497 ([M+H]$^+$), found 327.1475.

*4.4.3. 2-Allyl-3-phenyl-8a-(pyridin-2-yl)indolizin-1(8aH)-one (**90**).* Brown solid, mp: 102.6–106.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J*=4.5 Hz, 1H), 7.66 (t, *J*=8.0 Hz, 1H), 7.62–7.46 (m, 6H), 7.17 (dd, *J*=5.0, 7.0 Hz, 1H), 6.47 (d, *J*=8.0 Hz, 1H), 6.38 (d, *J*=9.5 Hz, 1H), 6.11 (dd, *J*=5.5, 9.0 Hz, 1H), 5.81–5.69 (m, 1H), 5.24 (t, *J*=6.0 Hz, 1H), 4.88 (s, 1H), 4.86 (d, *J*=6.0 Hz, 1H), 2.88–2.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 171.1, 159.3, 149.5, 136.8, 136.0, 130.6, 129.1, 129.0, 128.7, 125.0, 124.1, 122.7, 121.2, 120.5, 115.0, 108.8, 107.5, 72.4, 26.1; IR (ATR) 3044, 2910, 1658, 1427 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{19}N_2O$ 327.1497 ([M+H]$^+$), found 327.1476.

*4.4.4. 2-Allyl-8a-(4-methoxyphenyl)-3-(thiophen-3-yl)indolizin-1(8aH)-one (**92**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (dd, *J*=1.0, 3.0 Hz, 1H), 7.54 (dd, *J*=3.0, 5.0 Hz, 1H), 7.41 (d, *J*=9.0 Hz, 2H), 7.32 (dd, *J*=1.0, 5.0 Hz, 1H), 6.87 (d, *J*=9.0 Hz, 2H), 6.58 (d, *J*=7.0 Hz, 1H), 6.25 (d, *J*=9.5 Hz, 1H), 6.02 (dd, *J*=5.5, 9.0 Hz, 1H), 5.87–5.75 (m, 1H), 5.31 (dd, *J*=5.5, 7.0 Hz, 1H), 4.94 (dd, *J*=2.0, 10.0 Hz, 1H), 4.89 (dd, *J*=1.5, 12.0 Hz, 1H), 3.78 (s, 3H), 2.94–2.80 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 165.3, 159.3, 136.3, 132.9, 129.2, 128.0, 127.3, 125.9, 124.8, 123.1, 122.3, 115.0, 114.1, 108.5, 108.4, 70.2, 55.4, 26.2; IR (ATR) 3074, 3000, 2929, 1669, 1576, 1505, 1420, 1245 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{20}NO_2S$ 362.1215 ([M+H]$^+$), found 362.1227.

4.5. General procedure for the Sonogashira coupling of 95 or 96 with aryl iodide

A mixture of **95** or **96** (0.14 mmol), aryl iodide (1.3 equiv), copper(I) iodide (0.1 equiv), and bis(triphenylphosphine)palladium(II) dichloride (0.1 equiv) in Et_3N (2 mL) was stirred at temperature as indicated in Table 7. After the reaction was complete, the reaction mixture was concentrated under reduced pressure and purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to give tertiary propargylic alcohols.

*4.5.1. 4-(4-Nitrophenyl)-2-(pyridin-2-yl)but-3-yn-2-ol (**97**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J*=4.5 Hz, 1H), 8.16 (d, *J*=8.0 Hz, 2H), 7.81 (td, J=1.5, 7.5 Hz, 1H), 7.65 (d, *J*=8.0 Hz, 1H), 7.58 (d, *J*=9.0 Hz, 2H), 7.32 (dd, *J*=5.0, 7.50 Hz, 1H), 5.76 (s, 1H), 1.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 147.7, 147.3, 137.8, 132.7, 129.7, 123.6, 123.3, 120.1, 97.8, 81.9, 69.0, 31.9; IR (ATR) 3283, 3074, 2925, 2851, 2236, 1591, 1513, 1338 cm^{-1}; HRMS (FAB) calcd for $C_{15}H_{13}N_2O_3$ 269.0926 ([M+H]$^+$), found 269.0926.

*4.5.2. 4-(3-Hydroxy-3-(pyridin-2-yl)but-1-ynyl)benzonitrile (**98**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J*=5.0 Hz, 1H), 7.80 (td, *J*=1.5, 8.0 Hz, 1H), 7.64 (d, *J*=7.5 Hz, 1H), 7.58 (d, *J*=7.5 Hz, 2H), 7.51 (d, *J*=8.0 Hz, 2H), 7.31 (dd, *J*=5.0, 6.5 Hz, 1H), 5.72 (s, 1H), 1.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 147.7, 137.8, 132.4, 132.0, 127.7, 123.2, 120.1, 118.5, 111.9, 96.9, 82.1, 68.9, 31.9; IR (ATR) 3387, 3056, 2929, 2854, 2221, 1587, 1502, 1431, 1364 cm^{-1}; HRMS (FAB) calcd for $C_{16}H_{13}N_2O$ 249.1028 ([M+H]$^+$), found 249.1031.

*4.5.3. 4-(4-Chlorophenyl)-2-(pyridin-2-yl)but-3-yn-2-ol (**99**).* Brown solid, mp: 67.7–69.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J*=5.0 Hz, 1H), 7.78 (td, *J*=2.0, 8.0 Hz, 1H), 7.66 (d, *J*=8.0 Hz, 1H), 7.36 (d, *J*=7.5 Hz, 2H), 7.31–7.23 (m, 3H), 5.64 (s, 1H), 1.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 147.6, 137.6, 134.6, 133.2, 128.7, 123.0, 121.3, 130.2, 93.4, 82.7, 69.0, 32.2; IR (ATR) 3216, 2925, 2851, 1587, 1487, 1468 cm^{-1}; HRMS (FAB) calcd for $C_{15}H_{13}ClNO$ 258.0686 ([M+H]$^+$), found 258.0682.

*4.5.4. 1-(4-(3-Hydroxy-3-(pyridin-2-yl)but-1-ynyl)phenyl)ethanone (**100**).* Brown gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.5 Hz, 1H), 7.88 (d, *J*=7.5 Hz, 2H), 7.80 (td, *J*=1.5, 8.0 Hz, 1H), 7.67 (d, *J*=10.0 Hz, 1H), 7.52 (d, *J*=7.5 Hz, 2H), 7.30 (dd, *J*=5.0, 7.5 Hz, 1H), 5.70 (s, 1H), 2.59 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 161.6, 147.6, 137.7, 136.5, 132.0, 128.2, 127.7, 123.1, 120.2, 95.7, 83.0, 69.0, 32.1, 26.7; IR (ATR) 3365, 2921, 2851, 1677, 1599, 1356, 1260 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{16}NO_2$ 266.1181 ([M+H]$^+$), found 266.1187.

*4.5.5. 1,3-Diphenyl-1-(pyridin-2-yl)prop-2-yn-1-ol (**101**).* Orange gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J*=4.5 Hz, 1H), 7.73–7.69 (m, 2H), 7.68 (dd, *J*=1.5, 7.5 Hz, 1H), 7.53–7.47 (m, 3H), 7.38–7.27 (m, 6H), 7.26–7.23 (m, 1H), 6.62 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ161.3, 147.1, 144.3, 137.7, 132.0, 128.7, 128.5, 128.4, 128.1, 126.6, 123.0, 122.7, 121.9, 91.2, 86.7, 73.8; IR (ATR) 3298, 3056, 2921, 2851, 2225, 1681, 1587, 1446, 1431, 1379 cm^{-1}; HRMS (FAB) calcd for $C_{20}H_{16}NO$ 286.1232 ([M+H]$^+$), found 286.1222.

*4.5.6. 3-(4-Chlorophenyl)-1-phenyl-1-(pyridin-2-yl)prop-2-yn-1-ol (**102**).* Orange solid, mp: 85.2–88.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J*=5.0 Hz, 1H), 7.72–7.65 (m, 3H), 7.46 (d, *J*=8.0 Hz, 1H), 7.43 (d, *J*=8.5 Hz, 2H), 7.38–7.33 (m, 2H), 7.31–7.23 (m, 4H), 6.63 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 147.1, 144.1, 137.7, 134.8, 133.2, 128.8, 128.5, 128.2, 126.5, 123.1, 121.9, 121.1, 92.1, 85.5, 73.7; IR (ATR) 3272, 3082, 3056, 2921, 2225, 1591, 1487, 1431, 1394 cm^{-1}; HRMS (FAB) calcd for $C_{20}H_{15}ClNO$ 320.0842 ([M+H]$^+$), found 320.0840.

*4.5.7. Methyl 4-(3-hydroxy-3-phenyl-3-(pyridin-2-yl)prop-1-ynyl) benzoate (**103**).* Pale brown solid, mp: 103.2–106.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.5 Hz, 1H), 7.99 (d, *J*=8.5 Hz, 2H), 7.73–7.67 (m, 3H), 7.57 (d, *J*=8.5 Hz, 2H), 7.47 (d, *J*=8.0 Hz, 1H), 7.39–7.34 (m, 2H), 7.32–7.24 (m, 2H), 6.66 (s, 1H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 160.9, 147.2, 143.9, 137.8, 131.9, 130.0, 129.6, 128.5, 128.2, 127.3, 126.5, 123.2, 121.9, 94.1, 85.8, 73.8, 52.4; IR (ATR) 3261, 2921, 2851, 1722, 1591, 1435, 1401, 1271 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{18}NO_3$ 344.1287 ([M+H]$^+$), found 344.1279.

*4.5.8. 4-(3-Hydroxy-3-phenyl-3-(pyridin-2-yl)prop-1-ynyl)benzonitrile (**104**).* Pale brown solid, mp: 108.0–111.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J*=5.0 Hz, 1H), 7.70 (td, *J*=1.5, 7.5 Hz, 1H), 7.78–7.65 (m, 2H), 7.63–7.56 (m, 4H), 7.44 (d, *J*=8.0 Hz, 1H), 7.39–7.34 (m, 2H), 7.33–7.29 (m, 1H), 7.28 (dd, *J*=5.0, 7.5 Hz, 1H), 6.67 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 147.2, 143.6, 137.8, 132.5, 132.1, 128.6, 128.6, 127.5, 126.5, 123.3, 121.8, 118.5, 112.2, 95.6, 84.8, 73.7; IR (ATR) 3272, 2921, 2851, 2225, 1587, 1431,

1394 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{15}N_2O$ 311.1184 ($[M+H]^+$), found 311.1182.

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Supplementary data

Copies of ^1H and ^{13}C NMR spectra of **12**, **26**–**37**, **57**–**81**, **83**–**92**, and **95**–**104**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2012.04.091.

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