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1-(2′-Anilinyl)prop-2-yn-1-ol Rearrangement for Oxindole Synthesis

Prasath Kothandaraman, Bing Qin Koh, Taweetham Limpanuparb, Hajime Hirao,* and Philip Wai Hong Chan*[a]

Abstract: A synthetic method that relies on NIS (*N*-iodosuccinimide)-mediated cycloisomerization reactions of 1-(2′-anilinyl)prop-2-yn-1-ols to *gem*-3-(diiodomethyl)indolin-2-ones and 2-(iodomethylene)indolin-3-ones has been developed. The reactions were shown to be chemoselective, with secondary and tertiary alcoholic substrates exclusively giving the 3- and 2-oxindole products, respectively. In the case of the latter, the transformation features an unprecedented double 1,2-OH and 1,2-alkyl migration relay. Density functional theory (DFT) calculations based on proposed iodoaminocyclization species provide insight into this unique divergence in product selectivity.

Keywords: alcohols · cyclization · domino reactions · *N*-iodosuccinimide · oxindoles

Introduction

Oxindoles are common structural motifs found in a myriad of pharmaceutically interesting compounds and bioactive natural products (Figure 1).[1–7] The nitrogen heterocycle is also an invaluable chemical probe in biomimetic studies and a versatile building block in organic synthesis. For this reason, the development of methods to construct this member of the indole family in an efficient manner with control of product substitution patterns, from low-cost and readily accessible substrates, continues to be actively pursued.[1,8]

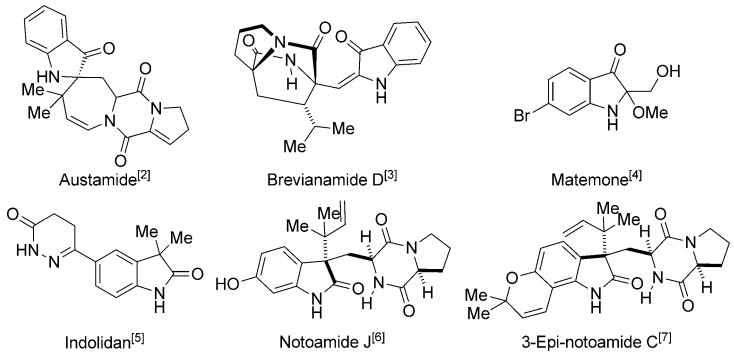
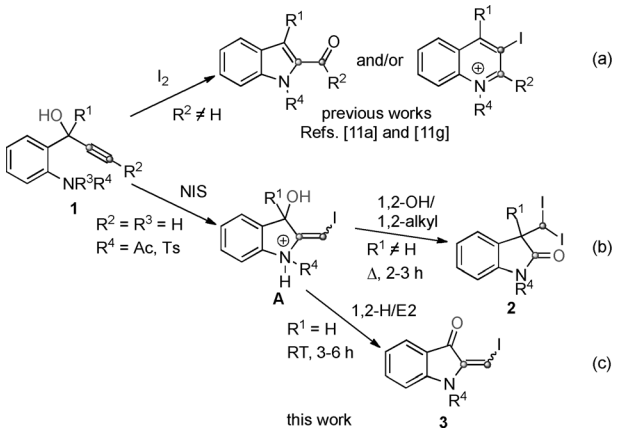


Figure 1. Examples of bioactive natural products.

One approach for nitrogen ring synthesis that has come under increasing attention over the years is the iodoaminocyclization of alkenes, alkynes, and allenes with an amine nucleophile and iodide source under Lewis or Brønsted acid or base catalysis.[9–11] This has included a handful of synthetic strategies to form a variety of N-heterocycles from readily available unsaturated alcohols.[11,12] A recent notable example is the synthesis of 2-acyl-1*H*-indoles and 3-iodoquinolines that relied on the cycloisomerization of propargylic alcohols **1** with molecular iodine (Scheme 1 a).[11a,g] In contrast, there are no studies that explore the potential iodoaminocyclization chemistry of this class of compounds that contain a terminal alkyne moiety. This is surprising in view of recent work by our group that shows gold(I)-catalyzed cy-



Scheme 1. Iodoaminocyclization reactivities of 1-(2′-anilinyl)prop-2-yn-1-ols **1**.

[a] Dr. P. Kothandaraman, B. Q. Koh, Dr. T. Limpanuparb, Prof. Dr. H. Hirao, Prof. Dr. P. W. H. Chan
Division of Chemistry and Biological Chemistry
School of Physical and Mathematical Sciences
Nanyang Technological University
Singapore 637371 (Singapore)
Fax: (+65) 6791-1961
E-mail: waihong@ntu.edu.sg

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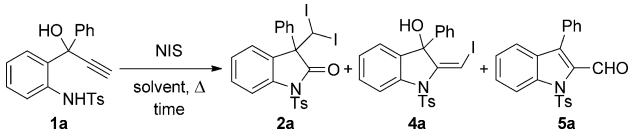
cloisomerization of such substrates to have the propensity to undergo 1,3-allylic alcohol isomerization (1,3-AAI) upon addition of the nitrogen nucleophile to the alkyne moiety.[13d,f] We therefore anticipated that a new cascade process in these compounds might ensue if the initial cyclization step, which involves the addition of the nitrogen nucleophile to the alkyne moiety, was triggered by an electrophilic iodide source instead of the metal catalyst. In doing so, and as part of an ongoing program examining the utility of alcohol pro-electrophiles in heterocyclic synthesis,[13] we discovered that when $R^1 \neq H$, the resultant putative iodoaminocyclization species **A** generated in situ by NIS was susceptible to a 1,2-hydroxyl shift (Scheme 1b).[14] This was followed by a 1,2-alkyl migration and oxidation of the alcohol moiety to give the *gem*-3-(diiodomethyl)indolin-2-one ring system. On the other hand, in substrates where $R^1 = H$, we found that a 1,2-hydride shift and oxidation of the secondary carbinol carbon center occurred to give 2-(iodomethylene)indolin-3-one derivatives (Scheme 1c). To our knowledge, the construction of 2- and 3-oxindoles in this manner by the iodoaminocyclization of a propargylic substrate with NIS is not known. Moreover, the reaction leading to 2-oxindoles represents an exceedingly rare example of both a 1,2-OH shift and a double migration involving two functional groups mediated by NIS.[14,15] The role of NIS in this context is notable as it extends the synthetic utility of this reagent beyond that of cycloiodinations, functional group deprotections/protections, iodinations, oxidations, and semipinacol rearrangements. Herein, we disclose the details of this chemistry, which offers an expedient and chemoselective approach to these two new and potentially useful classes of oxindole compounds in good to excellent yields. A density functional theory (DFT) calculation study on the origin of the divergence in product selectivity is also presented.

Results and Discussion

The 1-(2′-anilinyl)prop-2-yn-1-ols studied in this work were prepared from the reaction of the corresponding 2-tosylaminophenyl ketone with ethynylmagnesium bromide following literature procedures.[16] By choosing **1a** as the model substrate, we began our investigations by examining its transformations with NIS to establish the optimal reaction conditions (Table 1). This initially revealed that the treatment of **1a** with 2 equiv of NIS in $MeNO_2$ at room temperature for 18 h gave **2a** and **4a** in 17 and 68% yield, respectively (Table 1, entry 1). The structure of the 2-oxindole was determined on the basis of ^{1}H NMR spectroscopic analysis and X-ray crystallography (Figure 2).[17] By repeating the reaction at reflux for 3 h, the suppression of **4a** was found to give **2a** as the sole adduct in 86% yield (Table 1, entry 2). A further increase of 10% in the product yield and a shorter reaction time of 1 h for complete substrate consumption was achieved by increasing the amount of NIS from 2 to 3 equiv (Table 1, entry 3). In contrast, repeating this reaction in non-distilled $MeNO_2$ was found to give a markedly lower yield of **2a** (22%), as well as **5a** in 61% yield (Table 1, entry 4).[13d] Likewise, an inspection of entries 5–7 in Table 1 shows that changing the solvent from $MeNO_2$ to MeCN, 1,2-dichloroethane, or 1,4-dioxane gave lower product yields of 47–82%. Replacing $MeNO_2$ with DMSO as the solvent was found to lead to a mixture of side products that could not be identified by ^{1}H NMR analysis of the crude mixture (Table 1, entry 8). Similarly, the analogous reaction mediated by molecular iodine, which is shown to promote the intramolecular cyclization of substituted 2-alkynylanilines to 2-acyl-1*H*-indoles and 3-iodoquinolines, in place of NIS was found to be ineffective (Table 1, entry 9).[11a,g] On the basis of the above results, the reaction of **1a** with 3 equiv of NIS

Table 1. Optimization of the reaction conditions.[a]



Entry	NIS [equiv]	Solvent	Time [h]	Yield [%][b]		
				2a	**4a**	**5a**
1[c]	2	$MeNO_2$	18	17	68	–
2	2	$MeNO_2$	3	86	–	–
3	3	$MeNO_2$	1	96	–	–
4[d]	3	$MeNO_2$	24	22	–	61
5	3	MeCN	3	82	–	–
6	3	$(CH_2Cl)_2$	18	53	–	–
7	3	1,4-dioxane	18	47	–	–
8	3	DMSO	18	–[e]	–	–
9	–[f]	$MeNO_2$	5	–[e]	–	–

[a] Unless otherwise stated, all reactions were performed in distilled solvent with 0.06 mmol of **1a** and heated at reflux. [b] Yield of isolated product. [c] Reaction performed at room temperature. [d] Reaction performed with non-distilled $MeNO_2$. [e] Mixture of byproducts obtained that could not be identified by ^{1}H NMR analysis or mass spectrometry. [f] Reaction performed with 3 equiv of I_2.

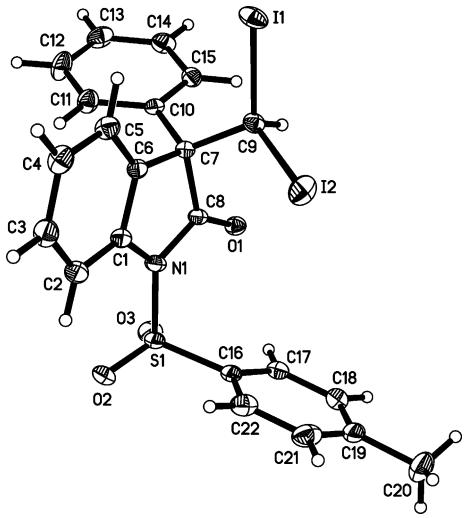


Figure 2. ORTEP drawing of **2a** with thermal ellipsoids at 50% probability levels.[17]

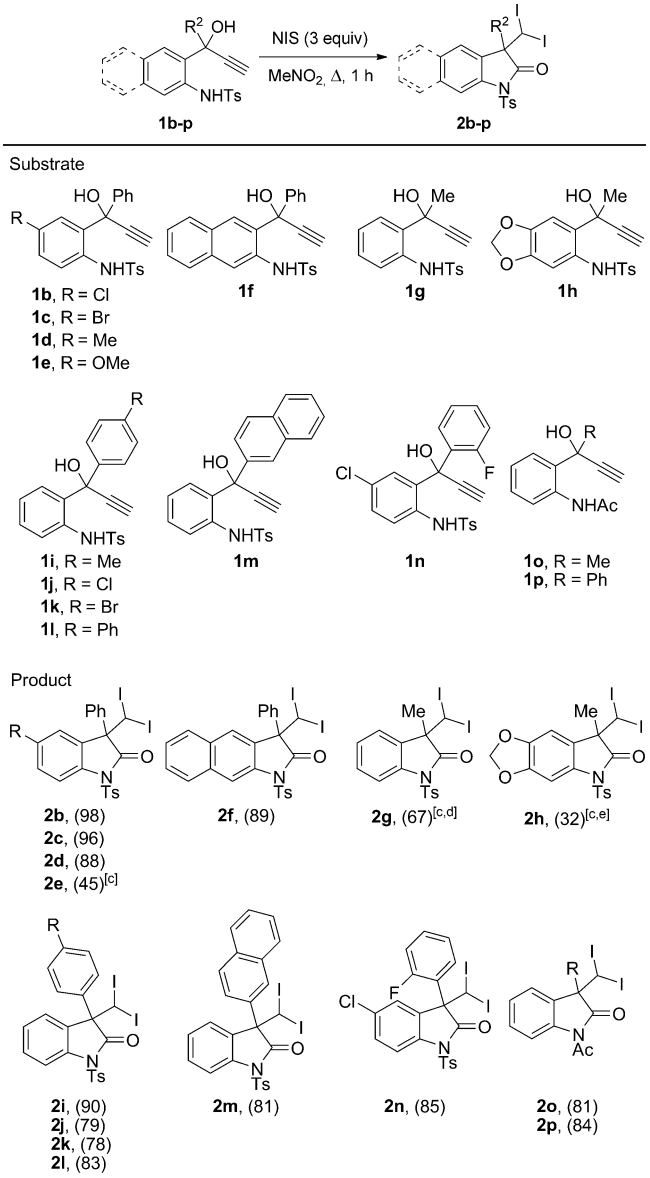
in $MeNO_2$ at reflux for 1 h provided the optimum conditions.

To define the scope of the present reaction, we next turned our attention to the reactions of a series of tertiary 1-(2′-anilinyl)prop-2-yn-1-ols and the results are summarized in Table 2. These experiments showed that with 3 equiv of NIS, the conditions were found to be broad and a variety of *gem*-3-(diiodomethyl)indolin-2-ones **2** could be furnished in 32–98% yield from the corresponding substrates **1b–p** (Table 2). Tertiary alcohols with a pendant electron-withdrawing (**1b** and **1c**) or electron-donating (**1d**) group, or a benzo-fused ring (**1f**) on the aniline ring, were found to be tolerated under the reaction conditions and provided the corresponding products **2b–d** and **2f** in excellent yields of up to 98%. Similarly, reactions of substrates containing a Me, naphthyl, or aryl group with an electron-donating or electron-withdrawing substituent at the *ortho* or *para* position on the carbinol carbon center, as in **1g** and **1i–n**, were found to proceed well, providing **2g** and **2i–n** in 67–90% yield. The presence of an Ac instead of a tosyl (Ts) protecting group on the nitrogen center was found to have no influence on the course of the reaction, and **2o** and **2p** were formed in 81 and 84% yield, respectively. Under the standard conditions, the reaction of starting alcohols with a pendant *p*-OMe (**1e**) or benzo[*d*][1,3]dioxole (**1h**) substituent on the aniline moiety were the only examples found to give the corresponding products **2e** and **2h** in lower yields of 45 and 32%, respectively.

With the reaction conditions for forming the 2-oxindole established, we next investigated the applicability of this new method for the synthesis of 2-(iodomethylene)indolin-3-one derivatives. As shown in Scheme 1c, we reasoned that a change in the mode of reactivity should be accomplished by switching from a tertiary to a secondary alcohol substrate. With this in mind, we first tested the reaction of **1q** with 3 equiv of NIS in $MeNO_2$ at room temperature for 3 h (Table 3). This experiment gave **3a** in 87% yield and as an inseparable mixture of *E*/*Z* isomers in a ratio of 5:1. The structure of the 3-oxindole adduct was determined on the basis of ^{1}H NMR spectroscopic measurements and X-ray crystallographic analysis (Figure 3).[17] A similar outcome was observed on applying these conditions to other secondary alcohols **1r–v**. In these reactions, the corresponding 2-(iodomethylene)indolin-3-one products **3b–f** were formed in yields of 66–92% as inseparable mixture of *E*/*Z* stereoisomers in ratios of up to 4:1. Additionally, no other side products were detected based on ^{1}H NMR analysis of the crude mixtures.

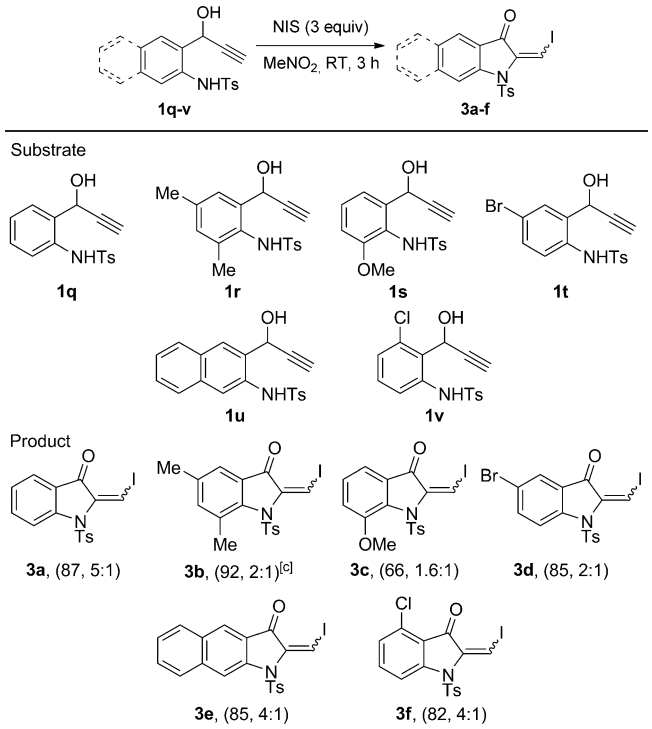
A plausible mechanism for the present NIS-mediated cycloisomerization reactions is outlined in Scheme 2. This could involve addition of NIS to the alkyne moiety of **1**. As a result, this triggers nucleophilic attack by the pendant tosylamido group in a 5-*exo*-dig manner to produce the cationic nitrogen ring species **A**. Deprotonation of this newly formed adduct would then give the vinyl iodide intermediate **4**, which can react with a further equivalent of NIS to give the *gem*-diiodo species **B**. This is the active species (when R≠H) that undergoes the double migration process involving a 1,2-shift of the OH group to the iminium cation carbon center to give indolin-2-ol adduct **C** (Scheme 2, route 1). This is followed by oxidative 1,2-migration of the CHI_2 moiety from the C2 to C3 position in **C**. Subsequent deprotonation of the resultant oxonium species **D** would then deliver **2**. In the case where R=H in the substrate, it is thought that 1,2-hydride migration from the carbinol to the iminium carbon center, followed by oxidation of the hydrox-

Table 2. NIS-mediated rearrangement of **1b–p**.[a]



[a] Unless otherwise stated, all reactions were performed with **1** (68 μmol) and NIS (0.21 mmol) in distilled $MeNO_2$ and heated at reflux for 1–1.5 h; refer to the Supporting Information for individual reaction times. [b] Values in parentheses represent yield of isolated product [%]. [c] Reaction performed with 0.272 mmol of NIS. [d] Reaction performed for 3.5 h. [e] Reaction performed for 18 h.

Table 3. NIS-mediated rearrangement of **1q–v**.[a]



[a] All reactions were performed with **1** (68 μmol) and NIS (0.21 mmol) in distilled $MeNO_2$ at room temperature for 3 h. [b] Values in parentheses represent yield of isolated product [%] and ratio of the *E*/*Z* isomers, respectively. [c] Reaction performed for 6 h.

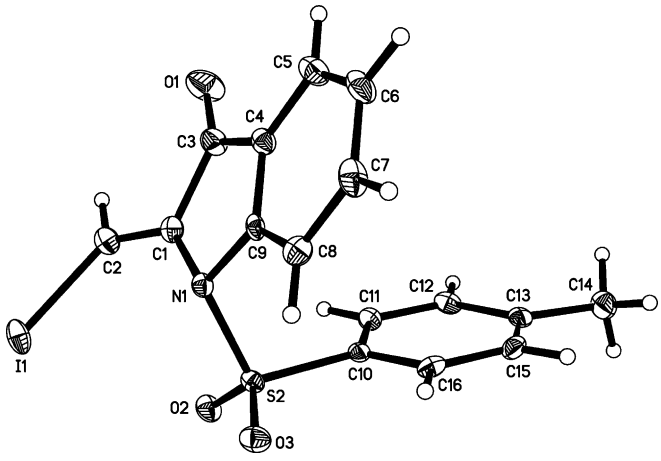
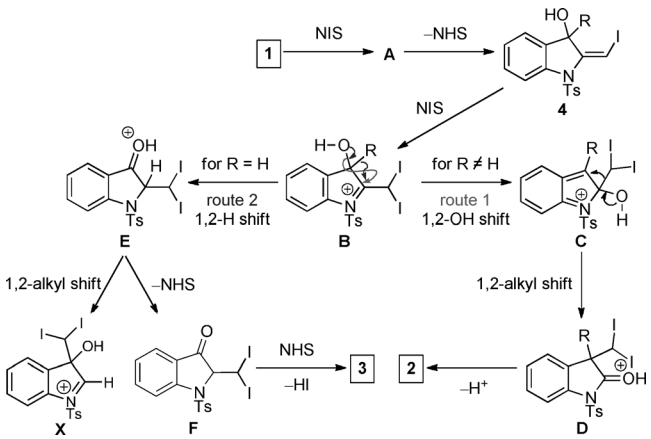


Figure 3. ORTEP drawing of **3a** with thermal ellipsoids at 50% probability levels.[17]

yl moiety in **B**, occurs preferentially to give the oxonium species **E** (Scheme 2, route 2). Deprotonation of this cationic ring adduct would then give the indolin-3-one intermediate **F**, which eliminates HI to provide **3**. Although fortuitous, the formation of **4a** from the cyclization of **1a** at room temperature under the conditions described in Table 1, entry 1 argues in favor of the mechanism proposed in Scheme 2.



Scheme 2. Proposed mechanism for NIS-mediated reactions of **1**.

This argument was further supported by the observation that when a solution of **4a** in $MeNO_2$ was subjected to 2 equiv of NIS and heated at reflux for 1 h, the expected 2-oxindole **2a** was obtained as the sole product in 86% yield. The formation of the aldehyde side product **5a** could be due to competitive nucleophilic substitution of **4** by H_2O that is present in non-distilled $MeNO_2$. Indeed, our findings showing **2a** and **5a** could be obtained in 17 and 66% yield on treating **4a** with 2 equiv of NIS in non-distilled $MeNO_2$ heated at reflux for 24 h would suggest this to be the case.

Next, to support the mechanistic premise put forward in Scheme 2 for the divergence in product selectivity, we performed DFT calculations at the B3LYP/[SDD(I),6-31G*-(others)] level, taking into account the solvent effect of $MeNO_2$ by the integral equation formalism variant of the polarizable continuum model (IEFPCM) method (Figure 4).[18–21] The reported energy values include zero-point energy corrections as obtained from frequency calculations at the same level. UCSF Chimera was used for drawing the molecules.[22] We examined routes 1 and 2 shown in Scheme 2 (from intermediate **B**) with R being Ph or H. Route 1 was found to be more favorable than route 2 when R = Ph (Figure 4a), which is consistent with the proposed mechanism in Scheme 2. This path begins with 1,2-migration of the hydroxyl group via an epoxide-like transition state, and the energy barrier of 19.1 kcal mol^{-1} for this migration is readily surpassed. The OH migration is followed by a 1,2-shift of the CHI_2 group, which also has a low energy barrier (15.9 kcal mol^{-1}), to give intermediate **D**. These results suggest that the reaction with R = Ph is likely to follow these two steps and the final product **2** is generated upon deprotonation of **D**. In contrast, when R = H, a 1,2-hydride shift was found to be more favorable than the 1,2-OH migration in the initial step (Figure 4b). The energy barrier for the hydride shift was rather low (16.8 kcal mol^{-1}), supporting the hypothesis that the reaction with R = H follows route 2. However, a subsequent step involving a 1,2-shift of the CHI_2 group, as shown in Scheme 2, route 2, was found to require an energy barrier of 38.0 kcal mol^{-1}. This unusually high activation energy disfavors the mechanism shown in Scheme 2,

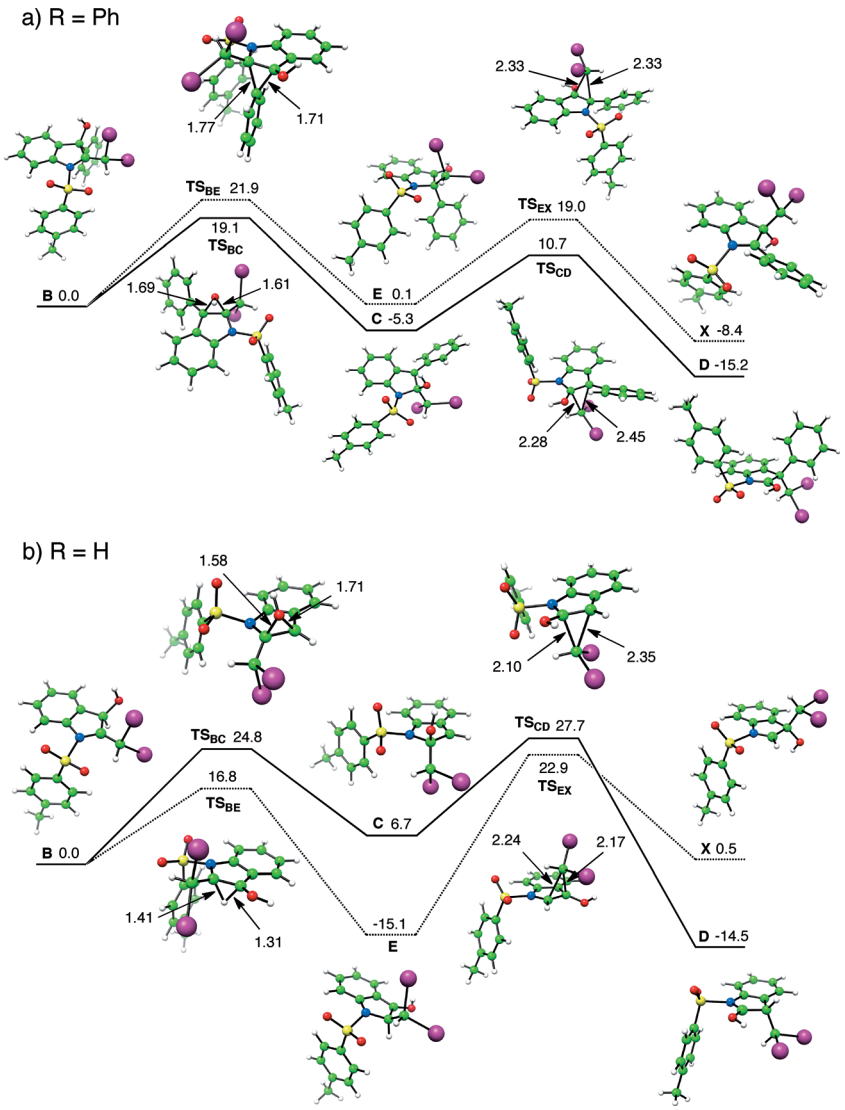


Figure 4. Energy profiles (in kcal mol^{-1}) for the reactions with a) R = Ph and b) R = H (solid and dotted lines indicate routes 1 and 2, respectively) and bond distances given in Å.

route 2 in which **X** is generated after **E**; indeed, the formation of a product derived from **X** was not observed in the experiment.

In an attempt to find a likely pathway from **E** toward the experimentally obtained **3**, we examined the possibility of an E2 reaction, assuming that NHS acts as a base which can abstract a proton from **F** (Figure 5). Two distinct conformers of a complex between **F** and NHS (**F′**$_E$ and **F′**$_Z$), which differ in the conformation of the CHI_2 group, led to different products, **3′**$_E$ and **3′**$_Z$, respectively. These products are similar to the experimentally obtained **3**. As shown in Figure 5, the energy barrier for the E2 reaction that yields the *E* product is 24.9 kcal mol^{-1}, which is much lower than that of the second step involving 1,2-shift of CHI_2 (38.0 kcal mol^{-1}, Figure 4). Moreover, the calculated preference for formation of the *E* product by the E2 mechanism is consistent with the experimentally observed *E*/*Z* ratios of up to 5:1 in the product. Therefore, our DFT calculations suggest that the E2 mechanism operates in the second half of the reaction when R = H. When $MeNO_2$ was used instead of NHS as a base for the reaction, the relative energies of **TS**$_{e2,E}$ and **TS**$_{e2,Z}$ were 35.3 and 38.5 kcal mol^{-1}, respectively. Thus, it is more likely that the E2 reaction is triggered by NHS rather than by $MeNO_2$.

Conclusion

In summary, we have developed an NIS-mediated strategy for the construction of highly functionalized 2-(iodomethylene)indolin-3-ones and *gem*-3-(diiodomethyl)indolin-2-ones from secondary and tertiary 1-(2′-anilinyl)prop-2-yn-1-ols, respectively. Our studies suggest that complete control over product selectivity is possible by exploiting the differing functional group migratory aptitude of the alcohol moiety in these secondary and tertiary substrates. In the case of the tertiary alcohols, which lead to 2-oxindole products, the nitrogen-ring-forming process also provided a unique example of a double migratory cascade reaction involving a 1,2-OH migration followed by a 1,2-alkyl shift. Efforts to explore the scope and synthetic applications of the present reactions are currently underway and will be reported in due course.

Experimental Section

General procedure for NIS-mediated reactions of 1a–1p: A solution of **1** (0.07 mmol) in nitromethane (1.5 mL) was added dropwise to a solution of NIS (45 mg, 0.20 mmol) in nitromethane (1 mL) at room temperature under a nitrogen atmosphere. The resulting mixture was stirred and heated at reflux, and monitored for completion by TLC analysis. On completion of the reaction, the mixture was cooled to room temperature, quenched with saturated aqueous $Na_2S_2O_3$·$5H_2O$ solution (5 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 19:1) gave the product **2**.

General procedure for NIS-mediated reactions of 1q–1v: A solution of **1** (0.07 mmol) in nitromethane (1.5 mL) was added dropwise to a solution

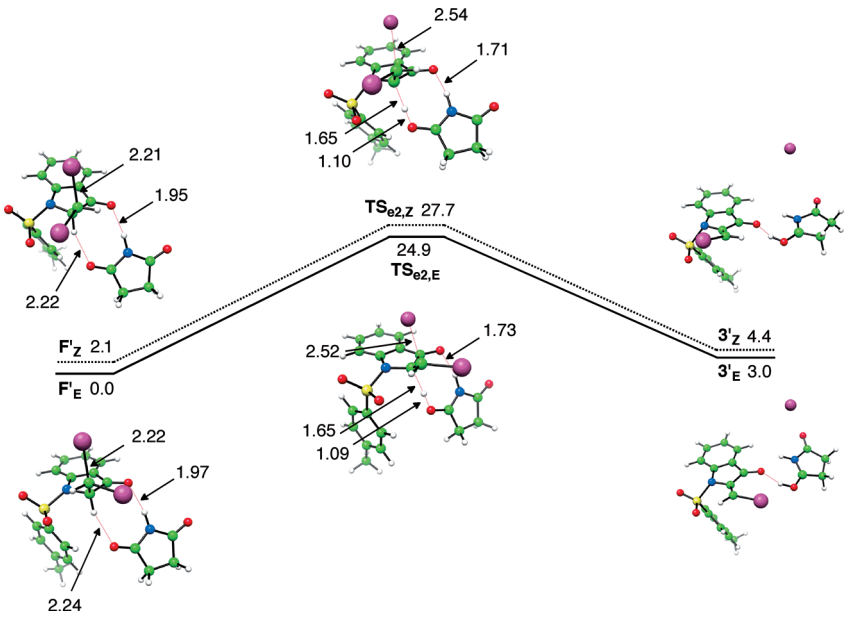


Figure 5. Energy profiles (in kcal mol^{-1}) for the E2 mechanism in route 2 with bond distances given in Å.

of NIS (45 mg, 0.20 mmol) in nitromethane (1 mL) at room temperature under a nitrogen atmosphere. The resulting mixture was stirred at room temperature and monitored for completion by TLC analysis. On completion of the reaction, the mixture was quenched with saturated aqueous $Na_2S_2O_3{\cdot}5H_2O$ solution (5 mL) and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 19:1) gave the product **3**.

3-(Diiodomethyl)-3-phenyl-1-tosylindolin-2-one (2a): White solid; m.p. 186–188 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.07 (2H, t, J = 7.9 Hz), 7.96 (2H, d, J = 8.4 Hz), 7.58 (1H, td, J = 1.2, 8.1 Hz), 7.43 (1H, td, J = 0.9, 7.5 Hz), 7.38–7.24 (7H, m), 5.75 (1H, s), 2.37 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.4, 145.9, 139.9, 136.8, 134.5, 130.6, 129.6, 129.1, 129.0, 128.4, 128.2, 127.2, 125.4, 124.7, 114.1, 62.1, 21.7, −21.8 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1751, 1597, 1462, 1381, 1176, 1087, 952 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{18}NO_3SI_2$: 629.9097 (M^++H); found: 629.9095.

5-Chloro-3-(diiodomethyl)-3-phenyl-1-tosylindolin-2-one (2b): Yellow solid; m.p. 160–162 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.06 (2H, d, J = 9.3 Hz), 7.93 (2H, d, J = 8.4 Hz), 7.56 (1H, dd, J = 2.1, 8.7 Hz), 7.37–7.25 (7H, m), 5.70 (1H, s), 2.38 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.3, 146.1, 138.4, 136.3, 134.2, 130.7, 130.3, 129.9, 129,7, 129.3, 129.2, 128.4, 127.0, 125.5, 115.3, 62.2, 21.8, 1.0, −23.3 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1751, 1597, 1463, 1382, 1307, 1178, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{17}ClNO_3SI_2$: 663.8707 (M^++H); found: 663.8716.

5-Bromo-3-(diiodomethyl)-3-phenyl-1-tosylindolin-2-one (2c): White solid; m.p. 163–165 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.20 (1H, d, J = 2.1 Hz), 8.00 (1H, d, J = 9.0 Hz), 7.93 (2H, d, J = 8.4 Hz), 7.71 (1H, dd, J = 2.1, 8.7 Hz), 7.37–7.24 (7H, m), 5.70 (1H, s), 2.38 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 171.8, 146.2, 138.9, 136.3, 134.2, 133.6, 130.3, 129.7, 129,3, 129.2, 128.4, 128.3, 127.0, 117.7, 115.6, 62.1, 21.8, 1.0, −23.3 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3439, 1753, 1597, 1492, 1382, 1305, 1176, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{17}NBrO_3SI_2$: 707.8202 (M^++H); found: 707.8237.

3-(Diiodomethyl)-5-methyl-3-phenyl-1-tosylindolin-2-one (2d): White solid; m.p. 194–196 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.03 (1H, s), 7.96 (3H, t, J = 4.2 Hz), 7.45–7.20 (8H, m), 5.74 (1H, s), 2.54 (3H, s), 2.37 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.7, 145.8, 141.1, 136.9, 134.6, 129.6, 129.0, 128.4, 127.2, 125.4, 125.2, 125.1, 114.7, 62.0, 22.3, 21.7, 1.0, −21.2 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3417, 1751, 1614, 1597, 1448, 1381, 1165, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{20}NO_3SI_2$: 643.9253 (M^++H); found: 643.9254.

3-(Diiodomethyl)-5-methoxy-3-phenyl-1-tosylindolin-2-one (2e): Yellow solid; m.p. 188–190 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.02 (1H, d, J = 9.0 Hz), 7.93 (2H, d, J = 8.4 Hz), 7.65 (1H, d, J = 2.7 Hz), 7.37–7.23 (7H, m), 7.10 (1H, dd, J = 2.7, 9.0 Hz), 5.75 (1H, s), 3.91 (3H, s), 2.36 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.4, 156.7, 145.7, 136.8, 133.1, 129.6, 129.5, 129.0, 128.4, 127.2, 115.2, 114.9, 111.8, 62.3, 55.8, 21.7, −22.3 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 2962, 1749, 1681, 1597, 1492, 1373, 1159, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{20}NO_4SI_2$: 659.9203 (M^++H); found: 659.9200.

3-(Diiodomethyl)-3-phenyl-1-tosyl-1*H*-benzo[*f*]indol-2(3*H*)-one (2f): White solid; m.p. 217–219 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.56 (1H, s), 8.50 (1H, s), 8.01 (2H, d, J = 8.4 Hz), 7.96 (2H, s) 7.63 (1H, t, J = 6.9), 7.56 (1H, t, J = 6.9), 7.38–7.23 (7H, m), 5.85 (1H, s), 2.36 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.2, 146.0, 136.9, 136.8, 134.4, 134.3, 130.3, 129.6, 129.0, 128.7, 128.5, 128.4, 128.1, 127.7, 127.3, 126.0, 125.2, 111.0, 61.8, 21.7, −21.2 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1749, 1635, 1597, 1492, 1448, 1381, 1172, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{26}H_{20}NO_3SI_2$: 679.9253 (M^++H); found: 679.9258.

3-(Diiodomethyl)-3-methyl-1-tosylindolin-2-one (2g): White solid; m.p. 186–188 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.03 (1H, d, J = 8.7 Hz), 8.00 (2H, d, J = 8.4 Hz), 7.78 (1H, d, J = 7.4 Hz), 7.48 (1H, td, J = 1.0, 7.1 Hz), 7.29 (2H, d, J = 8.4 Hz), 7.25 (1H, d, J = 0.9 Hz), 5.24 (1H, s), 2.39 (3H, s), 1.47 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 173.3, 145.4, 138.9, 130.2, 130.0, 129.7, 128.5, 124.3, 123.1, 113.8, 53.9, 26.3, 21.7, −23.5 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3444, 1745, 1602, 1462, 1379, 1300, 1176, 1085 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{17}H_{16}NO_3SI_2$: 567.8940 (M^++H); found: 567.8941.

7-(Diiodomethyl)-7-methyl-5-tosyl-5*H*-[1,3]dioxolo[4,5-*f*]indol-6(7*H*)-one (2h): Colorless gum; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.97 (2H, d, J = 8.1 Hz), 7.64 (1H, s), 7.29 (2H, d, J = 8.4 Hz), 7.26 (1H, s), 6.05 (2H, s), 5.20 (1H, s), 2.39 (3H, s), 1.42 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.5, 148.9, 145.9, 144.7, 134.7, 133.0, 129.7, 128.5, 122.5, 103.7, 101.8, 97.2, 54.1, 29.7, 26.2, 21.7, 1.0, 0.0, −22.4 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 2962, 1749, 1681, 1492, 1373, 1190, 1176, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{16}NO_5SI_2$: 611.8839 (M^++H); found: 611.8834.

3-(Diiodomethyl)-3-(*p*-tolyl)-1-tosylindolin-2-one (2i): Yellow solid; m.p. 195–197 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.08 (2H, t, J = 8.7 Hz), 7.95 (2H, d, J = 8.1 Hz), 7.57 (1H, td, J = 1.2, 8.0 Hz), 7.39 (1H, td, J = 0.7, 7.6 Hz), 7.24 (2H, d, J = 6.6 Hz), 7.16 (2H, d, J = 8.4 Hz), 7.08 (2H, d, J = 8.1 Hz), 5.73 (1H, s), 2.36 (3H, s), 2.29 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.5, 145.8, 139.8, 139.2, 134.6, 133.9, 130.5, 129.7, 129.6, 128.4, 127.1, 125.4, 124.6, 114.1, 61.9, 21.7, 21.2, −21.2 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3412, 1751, 1602, 1460, 1381, 1192, 1176, 1087 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{20}NO_3SI_2$: 643.9253 (M^++H); found: 643.9250.

3-(4-Chlorophenyl)-3-(diiodomethyl)-1-tosylindolin-2-one (2j): White solid; m.p. 200–202 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.09 (1H, d, J = 7.2 Hz), 8.06 (1H, d, J = 7.4), 7.93 (2H, d, J = 8.1 Hz), 7.60 (1H, td, J = 1.2, 8.0 Hz), 7.41 (1H, td, J = 0.8, 7.5 Hz), 7.28–7.21 (6H, m), 5.69 (1H, s), 2.38 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.2, 146.0, 139.9, 135.3, 135.2, 134.4, 130.8, 129.6, 129.2, 128.6, 128.4, 127.9, 125.2, 124.8, 114.3, 61.7, 21.7, −22.9 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3433, 1749, 1600, 1490, 1462, 1382, 1176, 1089 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{17}NO_3SCII_2$: 663.8707 (M^++H); found: 663.8714.

3-(4-Bromophenyl)-3-(diiodomethyl)-1-tosylindolin-2-one (2k): Yellow solid; m.p. 180–182 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.11 (1H, d, J = 8.1 Hz), 8.06 (1H, d, J = 7.2), 7.93 (2H, d, J = 8.4 Hz), 7.60 (1H, td, J = 1.2, 8.0 Hz), 7.36–7.32 (3H, m), 7.25 (2H, d, J = 7.8 Hz), 7.16 (2H, d, J = 8.7 Hz), 5.69 (1H, s), 2.38 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.4, 146.0, 139.9, 135.8, 134.4, 132.2, 130.8, 129.6, 128.9, 128.4, 127.8, 125.2, 124.8, 123.5, 114.3, 61.8, 21.7, −23.1 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3676, 1751, 1598, 1487, 1460, 1382, 1176, 1087 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{17}NO_3SBrI_2$: 707.8202 (M^++H); found: 707.8200.

3-([1,1′-Biphenyl]-4-yl)-3-(diiodomethyl)-1-tosylindolin-2-one (2l): White solid; m.p. 184–186 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.13 (2H, d, J = 8.4 Hz), 7.96 (2H, d, J = 8.1), 7.63–7.50 (5H, m), 7.43 (3H, t, J = 7.4 Hz), 7.35 (3H, d, J = 8.4 Hz), 7.25 (2H, d, J = 7.8 Hz), 5.79 (1H, s), 2.35 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.4, 145.9, 141.4, 140.0, 139.9, 135.7, 134.5, 130.6, 129.6, 128.9, 128.4, 128.3, 127.8, 127.7, 127.6, 127.0, 125.4, 124.7, 114.2, 62.0, 21.7, −21.9 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1749, 1600, 1517, 1462, 1382, 1192, 1178, 1089 cm^{-1}; HRMS (ESI): m/z calcd for $C_{28}H_{22}NO_3SI_2$: 705.9410 (M^++H); found: 705.9415.

3-(Diiodomethyl)-3-(naphthalen-2-yl)-1-tosylindolin-2-one (2m): Yellow solid; m.p. 231–233 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.16 (2H, t, J = 7.1 Hz), 7.92 (2H, d, J = 8.4), 7.80 (2H, d, J = 8.4 Hz), 7.70–7.60 (2H, m), 7.55–7.44 (5H, m), 7.17 (2H, d, J = 8.1 Hz), 5.90 (1H, s), 2.28 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.4, 145.9, 139.9, 134.4, 134.2, 133.1, 132.9, 130.7, 129.6, 129.1, 128.5, 128.4, 128.3, 127.6, 127.5, 127.1, 126.6, 125.5, 124.8, 123.6, 114.3, 62.4, 21.6, −22.3 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1751, 1600, 1521, 1460, 1382, 1178, 1089 cm^{-1}; HRMS (ESI): m/z calcd for $C_{26}H_{20}NO_3SI_2$: 679.9253 (M^++H); found: 679.9259.

5-Chloro-3-(diiodomethyl)-3-(2-fluorophenyl)-1-tosylindolin-2-one (2n): Yellow gum; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.03 (1H, d, J = 9.0 Hz), 8.00 (2H, d, J = 8.4), 7.80 (1H, s), 7.51 (1H, dd, J = 2.0, 8.9 Hz), 7.40–7.34 (1H, m), 7.31 (2H, d, J = 8.4 Hz), 7.13–7.06 (1H, m), 7.01 (1H, t, J = 7.7 Hz), 6.84 (1H, t, J = 7.7 Hz), 6.20 (1H, s), 2.40 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.7, 146.2, 134.3, 131.3, 131.2, 130.7, 130.4, 129.9, 129.8, 128.6, 124.8, 117.7, 117.4, 115.0, 21.8, 1.0 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3676, 1757, 1597, 1463, 1382, 1190, 1178, 1087 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{16}NO_3SClFI_2$: 681.8613 (M^++H); found: 681.8619.

1-Acetyl-3-(diiodomethyl)-3-methylindolin-2-one (2o): Yellow solid; m.p. 114–116 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.27 (1H, d, J = 8.24 Hz), 7.77 (1H, d, J = 7.6 Hz), 7.43 (1H, t, J = 8.54 Hz), 7.28 (1H, t, J = 7.6 Hz), 5.39 (1H, s), 2.69 (3H, s), 1.55 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.6, 170.4, 139.6, 130.1, 129.8, 125.2, 122.5, 116.7, 54.2, 26.7, 25.9, −22.2 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3076, 1751, 1604, 1477, 1463, 1371, 1168, 1089 cm^{-1}; HRMS (ESI): m/z calcd for $C_{12}H_{12}NO_2I_2$: 455.8958 (M^++H); found: 455.8966.

1-Acetyl-3-(diiodomethyl)-3-phenylindolin-2-one (2p): Yellow solid; m.p. 157–161 °C; ^{1}H NMR (CDCl3, 400 MHz): δ = 8.39 (1H, d, J = 8.24 Hz), 8.11 (1H, d, J = 7.64 Hz), 7.55 (1H, t, J = 7.86 Hz), 7.42 (1H, t, J = 7.62 Hz), 7.32–7.38 (5H, m) 5.96 (1H, s), 2.62 ppm (3H, s); ^{13}C NMR (CDCl3, 100 MHz): δ = 174.9, 170.4, 140.7, 137.3, 130.3, 129.0, 128.2, 127.3, 125.0, 124.8, 117.0, 62.6, 26.7, −21.3 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1751, 1716, 1604, 1494, 1477, 1371, 1186, 1089 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{14}NO_2I_2$: 517.9114 (M^++H); found: 517.9122.

2-(Iodomethylene)-1-tosylindolin-3-one (3a): Yellow solid; *E/Z* (4.6:1); m.p. 143–145 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.27 (1H, s, major), 8.13 (1H, d, J = 9.0 Hz, major), 8.07 (1H, s, minor), 8.00 (1H, d, J = 8.1 Hz, minor), 7.74–7.67 (2H, m), 7.55 (2H, d, J = 7.5 Hz, minor), 7.49 (2H, d, J = 8.4 Hz), 7.30–7.24 (2H, m), 7.17 (2H, d, J = 8.4 Hz, major), 7.06 (2H, d, J = 8.1 Hz, minor), 2.34 (3H, s, major), 2.30 ppm (3H, s, minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 183.3, 146.8, 145.7, 136.9, 135.1, 133.2, 129.9, 129.5, 127.8, 127.2, 127.0, 125.6, 125.1, 124.9, 117.0, 21.6 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3446, 1707, 1606, 1458, 1363, 1199, 1174, 1083 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{13}INO_3S$: 425.9661 (M^++H); found: 425.9668.

2-(Iodomethylene)-5,7-dimethyl-1-tosylindolin-3-one (3b): Yellow solid; *E/Z* (2:1); m.p. 168–170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (1H, s, major), 7.88 (1H, s, minor), 7.41 (1H, s, major), 7.39 (1H, s, minor), 7.22 (1H, s, major), 7.14–7.06 (4H, m), 2.68 (3H, s, minor), 2.65 (3H, s, major), 2.37 (6H, s, minor), 2.34 ppm (6H, s, major); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 184.8, 182.7, 149.1, 148.4, 145.5, 145.4, 145.3, 140.5, 140.0, 139.4, 137.9, 137.5, 133.7, 132.7, 130.6, 129.9, 129.8, 129.5, 129.3, 129.2, 128.9, 128.6, 122.3, 122.0, 87.7, 82.0, 21.7, 21.0, 20.9, 19.6, 18.9 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1716, 1618, 1587, 1481, 1371, 1170, 1141, 1087 cm^{-1}; HRMS (ESI): m/z calcd for $C_{18}H_{17}NO_3SI$: 453.9974 (M^++H); found: 453.9976.

2-(Iodomethylene)-7-methoxy-1-tosylindolin-3-one (3c): Yellow gum; *E/Z* (1.6:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.02 (1H, s, minor), 7.93 (1H, s, major), 7.57 (2H, d, J = 8.2, minor), 7.31–7.14 (11H, m), 3.97 (3H, s, minor), 3.90 (3H, s, major), 2.38 (3H, s, major), 2.36 ppm (3H, s, minor); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 182.4, 152.2, 151.8, 148.0, 145.1, 144.9, 140.4, 138.4, 133.4, 132.4, 130.3, 129.5, 129.2, 128.5, 128.3, 128.2, 128.1, 120.6, 120.1, 116.7, 116.4, 85.9, 81.8, 56.7, 56.4, 21.7 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1716, 1620, 1597, 1496, 1438, 1375, 1170, 1087 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{15}NO_4SI$: 455.9767 (M^++H); found: 455.9771.

5-Bromo-2-(iodomethylene)-1-tosylindolin-3-one (3d): Yellow gum; *E/Z* (2:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.34 (1H, s, minor), 8.13 (1H, s, major), 8.03 (1H, d, J = 8.0 Hz, minor), 7.90 (1H, d, J = 8.7 Hz, major), 7.81–7.77 (2H, m), 7.67 (1H, s), 7.48 (2H, d, J = 8.3 Hz), 7.29 (2H, d, J = 8.2 Hz), 7.20 (2H, d, J = 8.2 Hz), 7.11 (2H, d, J = 8.1 Hz), 2.36 (3H, s, minor), 2.33 ppm (3H, s, major); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 180.6, 149.4, 146.2, 146.0, 145.7, 139.5, 139.0, 132.8, 131.3, 130.1, 129.8, 127.8, 127.7, 127.6, 127.5, 127.2, 126.6, 122.6, 120.6, 119.1, 118.7, 87.3, 78.6, 21.7 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 2926, 1716, 1597, 1458, 1355, 1305, 1172, 1089 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{12}NO_3SI_{81}Br$: 505.8746 ($M^+$+H); found: 505.8753.

2-(Iodomethylene)-1-tosyl-1*H*-benzo[*f*]indol-3(2*H*)-one (3e): Brown gum; *E/Z* (4:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.46 (1H, s, major), 8.35 (1H, s, minor), 8.29 (1H, s, major), 8.21 (1H, s, major), 8.12 (1H, s, minor), 8.08 (1H, s, minor), 7.99–7.88 (3H, m), 7.68–7.64 (1H, m), 7.55–7.49 (3H, m), 7.28 (1H, d, J = 8.3 Hz, minor), 7.13 (2H, d, J = 8.2 Hz, major), 6.98 (2H, d, J = 8.2 Hz, minor), 2.31 (3H, s, major), 2.24 ppm (3H, s, minor); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 183.8, 182.3, 147.1, 145.6, 145.2, 143.7, 140.5, 138.1, 137.4, 135.4, 133.3, 132.0, 131.4, 130.6, 130.4, 130.0, 129.9, 129.5, 128.8, 127.8, 127.2, 127.0, 126.9, 126.6, 126.5, 124.4, 124.2, 118.7, 113.9, 85.5, 75.3, 21.6, 21.5 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 3676, 1716, 1629, 1419, 1373, 1174, 1116, 1018 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{15}NO_3SI$: 475.9817 (M^++H); found: 475.9814.

4-Chloro-2-(iodomethylene)-1-tosylindolin-3-one (3f): Yellow gum; *E/Z* (4:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.35 (1H, s, minor), 8.09 (1H, s, major), 7.92 (1H, d, J = 8.2 Hz, major), 7.61–7.56 (1H, m), 7.49 (2H, d, J = 8.4 Hz, minor), 7.31 (2H, d, J = 8.3 Hz, major), 7.21 (1H, dd, J = 4.0, 8.0 Hz, minor), 7.11 (2H, d, J = 8.1 Hz, major), 2.37 (3H, s, minor), 2.33 ppm (3H, s, major); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 179.4, 151.9, 146.0, 145.8, 136.7, 136.2, 133.1, 131.5, 130.1, 129.7, 128.4, 127.8, 127.2, 127.1, 122.7, 119.3, 115.2, 86.7, 21.6 ppm; IR (NaCl, neat): $\tilde{\nu}$ = 1708, 1598, 1589, 1467, 1429, 1373, 1172, 1087 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{12}NO_3SClI$: 459.9271 (M^++H); found: 459.9269.

(*E*)-2-(Iodomethylene)-3-phenyl-1-tosylindolin-3-ol (4a):[13d] Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.91 (1H, d, J = 8.3 Hz), 7.58 (2H, d, J = 8.2 Hz), 7.31 (2H, d, J = 8.2 Hz), 7.24 (2H, d, J = 8.1 Hz), 7.12 (3H m), 7.01 (3H, m), 6.95 (1H, d, J = 7.5 Hz), 2.65 (1H, s), 2.41 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.0, 145.3, 142.3, 139.7, 135.1, 133.6, 130.2, 129.8, 128.2, 127.6, 127.3, 126.0, 125.6, 125.3, 116.6, 82.9, 65.9, 21.7 ppm; MS (ESI): m/z (%): 504 [M+H]$^+$.

3-Phenyl-1-tosyl-1*H*-indole-2-carbaldehyde (5a):[13d] Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.22 (1H, s), 8.30 (1H, d, J = 8.5 Hz), 7.83 (2H, d, J = 8.3 Hz), 7.58–7.52 (2H, m), 7.45 (5H, m), 7.26 (1H, m), 7.24 (2H, d, J = 6.5 Hz), 2.36 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 182.4, 145.3, 138.2, 135.8, 135.2, 132.5, 130.5, 130.4, 129.7, 129.3, 129.2, 129.0, 128.4, 127.2, 124.6, 122.6, 115.7, 21.7 ppm; MS (ESI): m/z (%): 376 [M+H]$^+$.

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