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Counter Ion Effect in Au/Ag-Catalyzed Chemoselective 6-*endo-dig* N- and O-Cyclizations of Enyne–Urea System: Diversity-Oriented Synthesis of Annulated Indoles

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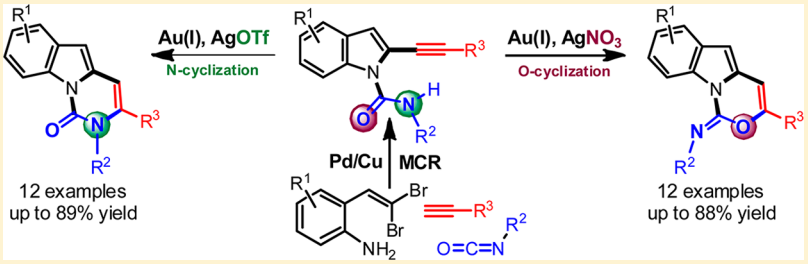
Supporting Information



ABSTRACT: A two-step protocol for the diversity-oriented synthesis of annulated indoles following MCR-post MCR modification concept is described. The reaction initially proceeds through the annulation of 2-(2,2-dibromovinyl)aniline, an isocyanate, and a terminal alkyne in a three-component tandem format via Cu/Pd-catalyzed cross coupling to afford *N*-1 and *C*-2 functionalized indole. In the subsequent step, the enyne–urea derivative undergoes chemo- and regioselective 6-*endo* cyclization to afford *O*-cyclized product in the presence of Au(I)/$AgNO_3$ and *N*-cyclized product in the presence of Au(I)/AgOTf under a post-MCR modification step. A mechanistic investigation following a recent pioneering work on the silver effect in gold catalysis (Shi, X. et al. *J. Am. Chem. Soc.* **2012**, *134*, 9012) explains the role of counterion on Au/Ag-catalyzed regiodivergent pathways.

INTRODUCTION

In recent years, transition-metal-catalyzed consecutive multicomponent reaction (MCR)-post MCR modification[1] concept has become a powerful approach for the diversity-oriented synthesis[2,3] (DOS) of druglike polyheterocyclic chemprobes. Strategically, the concept is executed by synthesizing MCR product having bifunctionalized handles followed by another ring formation utilizing those handles under post MCR modification.[4] However, chemoselective activation of MCR products comprising multiple nucleophilic/electrophilic sites in either of the handles, remains a challenging task.[5] Therefore, the development of complementary set of conditions is required that would lead to the desired chemoselective transformations from a common starting material.

In continuation of our reports[6] for the synthesis of the indole-based polyheterocycles,[7] we planned for a sequenced MCR-post MCR modification approach that involves the formation of an indole derived enyne–urea synthon (**4**) using a three-component (3C) strategy and subsequent chemoselective cyclization of the enyne–urea derivative under the post MCR modification step (Figure 1). Although there are several reports[8] describing intramolecular nucleophilic attack via either *O* or *N* onto alkynes, reports for chemoselective cyclization using both the nucleophiles are scarce.[9] During the course of our manuscript preparation, van Eycken et al.[10] reported

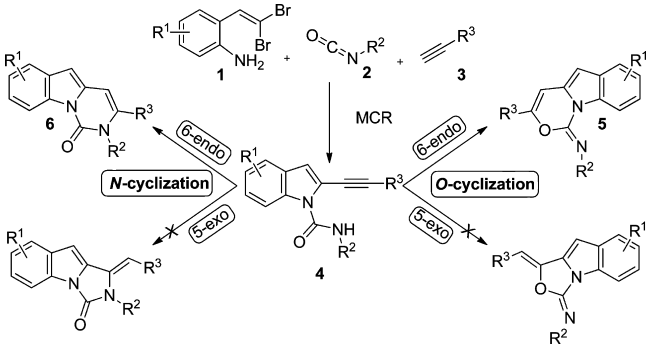


Figure 1. MCR-post MCR modification concept leading to regio-and chemo-selective *O*- and *N*-cyclized products **5** and **6** from synthon **4**.

chemoselective 5-*exo-dig* cycloisomerization of propargylic urea to provide *O*- and *N*-cyclized derivatives. Herein, we report a Cu/Pd-catalyzed multicomponent synthesis of bifunctionalized indole synthons and their chemo- and regioselective 6-*endo-dig* cyclization to cyclic imidate (**5**) and pyrimido[1,6-*a*]indolone (**6**) derivatives using orthogonal set of catalysts; while the

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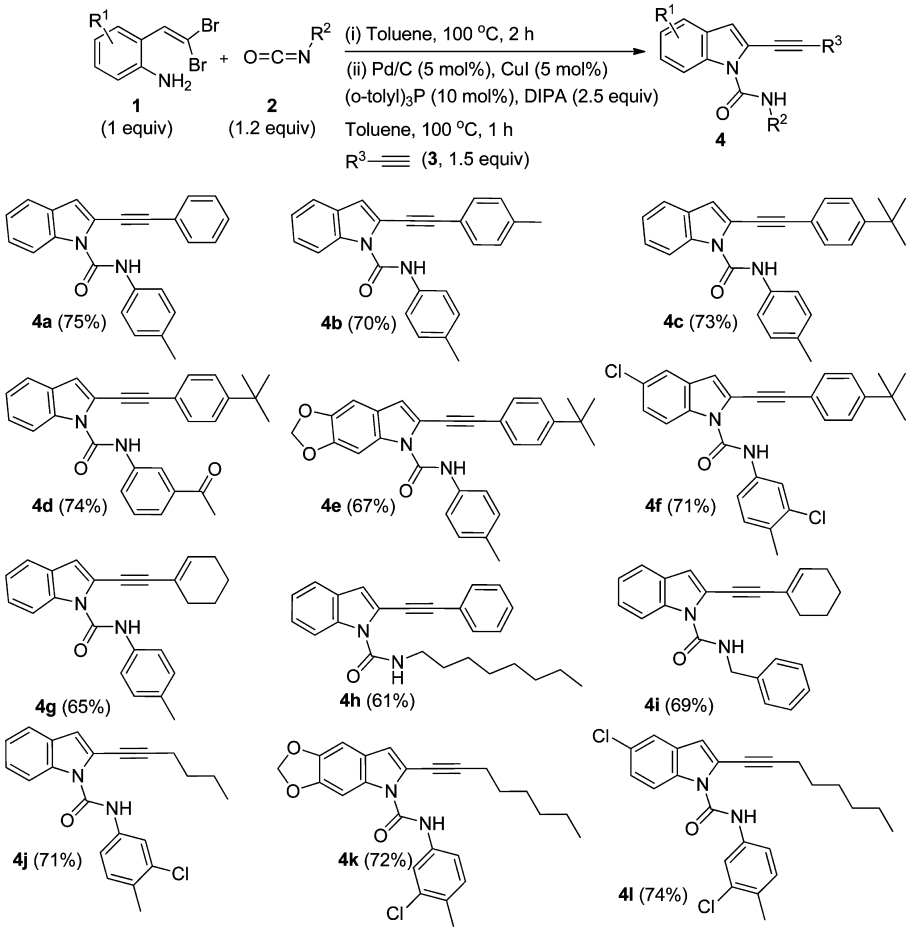
Scheme 1. Three-Component Sequential Synthesis of Synthon 4a–l in One Pot



former is useful synthetic building block and important pharmacophore,[11] the latter is known to have importance in medicinal chemistry as 5-HT_3 receptor antagonist,[12] topoisomerase II inhibitor[13] and fluorescent material.[14]

RESULTS AND DISCUSSION

Our initial attempt to derivatize 2-alkynylindole with the substituted isocyanate to produce indole derivative **4** was unsuccessful. Therefore, a MCR approach was undertaken using 2-(2,2-dibromovinyl)aniline (**1a**), an isocyanate (**2a**), and a terminal alkyne (**3a**) following a modified procedure described earlier by Lautens et al.[15] Although the domino fashion did not furnish the desired bifunctionalized indole **4a**, heating **1a** and **2a** at 100 °C in toluene followed by the addition of **3a** in the presence of 10% Pd–C/CuI, PPh_3, and DIPA (diisopropylamine) furnished the desired **4a**, albeit in a moderate (51%) yield. Extensive screening of reaction parameters[16] such as varying catalyst, ligand, base, and solvent led to an optimal reaction condition (10% Pd–C/CuI, (2-$CH_3C_6H_4)_3P$, DIPA, toluene, 100 °C) to produce **4a** in 75% isolated yield. The optimized reaction condition allowed annulation of a wide range of *gem*-dibromovinylanilines **1**, aryl/alkyl isocyanate derivatives **2**, and terminal aryl/alkyl alkynes **3**, giving diverse bifunctionalized indole derivatives **4b–l** in good yields (61–75%, Scheme 1).

Given the outstanding performance of gold and silver catalysts[17,18] as π-acids, we examined several gold and silver salts to promote the cycloisomerization using **4a** as model substrate (Table 1). While Au(I), Au(III), AgOTf completely failed, $AgNO_3$ in toluene at reflux temperature furnished **5a** in moderate yield (Table 1, entries 1–8). Interestingly, while **4a** could lead to four possible regiomers (Figure 1) via either 5-*exo* or 6-*endo-dig* pathways,[19] the process furnished *O*-cyclized product **5a** exclusively. DCE was relatively better than toluene as a solvent (Table 1, entry 9). Various catalytic combinations[20] were then employed to improve the yield (Table 1, entries 10–13). To our delight, $AuClPPh_3/AgNO_3$ (catalyst set A) exclusively afforded 6-*endo-dig*-*O*-cyclized **5a** in 87% yield at rt in DCE within 4 h (Table 1, entry 11). Aiming to promote the chemoselective *N*-cyclization, several other Ag salts in combination with Au(I) and Au(III) salts were also screened (Table 1, entries 14–18). Pleasingly, $AuClPPh_3$/AgOTf (catalyst set B) in DCE at rt within 5 min provided 6-*endo-dig*-*N*-cyclized product **6a** in 85% yield (entry 16) with no detectable **5a** or 5-*exo* product. Thus, a novel reaction pathway is obtained on switching the catalyst from $AgNO_3$ to AgOTf, although Shi et al.[21] demonstrated the presence of Tf_2N^- as a coordinating anion with Au catalyst promoted few reactions which could not be possible by using TfO^- and Au catalyst. However, it promoted only N-cyclization (entry 19) in our system, albeit at a relative slower rate (3.5 h) with lesser yield (78%).

We next studied the scope of this reaction. Subjecting substrates **4b–l** under the optimized conditions using catalyst set A, *O*-cyclized derivatives (**5b–l**) were isolated in 81–88% yields (Table 2). The reaction was tolerated by both aromatic

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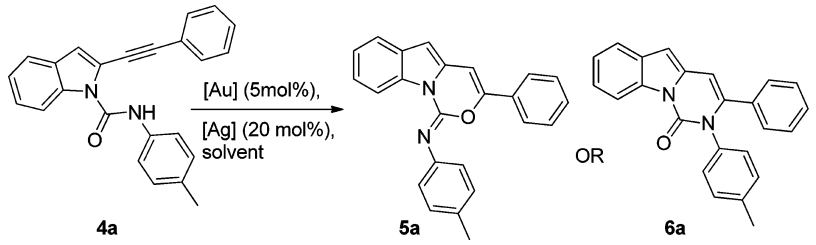
Table 1. Optimization of the Reaction Conditions[a] for the Synthesis of *O*- and *N*-Cyclized Products 5a and 6a



entry	catalyst	co-catalyst	solvent	time	yield[b] (%) **5a**/**6a**
1	$AuCl_3$		toluene	24 h	
2	$AuClPPh_3$		toluene	24 h	
3	$AuClPPh_3$		toluene, reflux	24 h	
4	$AuClPPh_3$		DCE	16 h	
5	$AuClPPh_3$		DCE, reflux	16 h	
6	AgOTf		toluene, reflux	24 h	
7	AgOTf		DCE, reflux	16 h	
8	$AgNO_3$		toluene, reflux	24 h	56[c]/0
9	$AgNO_3$		DCE, reflux	16 h	60/0
10	$AuCl_3$	$AgNO_3$	DCE	16 h	
11	**$AuClPPh_3$**	**$AgNO_3$**	**DCE**	**4 h**	**87/0**
12	$AuClPPh_3$	$AgNO_3$	THF	16 h	42[d]/0
13	$AuClPPh_3$	$AgNO_3$	DMF	16 h	32/0
14	$AuClPPh_3$	AgI	DCE	24 h	
15	$AuClPPh_3$	AgCl	DCE	24 h	
16	$AuClPPh_3$	AgBr	DCE	24 h	
17	**$AuClPPh_3$**	**AgOTf**	**DCE**	**5 min**	**0/85**
18	$AuCl_3$	AgOTf	DCE	30 min	5/74
19	$AuClPPh_3$	$AgNTf_2$	DCE	3.5 h	0/78

[a]Reaction conditions: **4a** (0.2 mmol), [Au] catalyst (5 mol %), [Ag] catalyst (20 mol %), solvent (2 mL), under N_2. [b]Isolated yield. [c]14% **4a** was recovered. [d]**4a** was recovered in 34% yield.

and aliphatic substituents present on either handles (**5b–l**). Electron-withdrawing or -donating substituents on either of the aryl rings (R^1, R^2, and R^3) had also no adverse effect on the yield and chemoselectivity (**5a–l**). On the contrary, using catalyst set B, the *N*-cyclized derivatives (**6b–i**) were isolated in 79–89% yields. Unfortunately, substrates with R^3 as aliphatic substituents furnished cyclized products with very good overall yield in a nonchemoselective fashion. A tentative reason for the loss of chemoselectivity might be due to the positive inductive effect of the aliphatic group. The positive inductive effect reduces the electrophilicity of the cationic gold intermediate. This in turn makes the complex less prone to nucleophilic attack thereby opening up the probability of the attack by both the *O*- and *N*-nucleophiles. However, none of our substrate led to the formation of 5-*exo*-*dig* cyclized product probably to avoid the ring strain.[22] The structures were confirmed unambiguously by X-ray crystallographic analysis of **5e** and **6e**.[23]

A mechanistic study following the recent report of Shi et al[21] regarding the "silver effect in gold catalysis" was conducted to explain the phenomenon for such an excellent chemoselectivity. We envisaged that the nature of counterion and/or Ag catalyst might be playing a significant role in controlling the *O*/*N* cyclization. Therefore, we performed several control experiments with **4a** adding a variety of Ag and K salts as a source for counterions to catalyst set B (Table 3). Although lowering the concentration of the catalyst set B did not affect the chemoselectivity, it took 1 h for the completion (entry 1). $AgNO_3$ with the catalyst set B promoted the *O*-cyclization, but in a low yield (entry 2). KNO_3 (20 mol %) with the catalyst set B made the reaction sluggish and furnished **5a** in 43% yield, indicating a possibility of counteranion controlled *O*-cyclization (entry 3). Addition of KI (20 mol %) with the catalyst set B resulted only traces of **6a** with no detectable **5a**, thereby ruling out the involvement of K^+, and the result emphasized the exclusive role of nitrate anion in promoting *O*-cyclization (entry 4).

However, to gain further insight, **4a** was treated with $[Ph_3PAu]^+TfO^-$ (preformed Ag free Au-salt derived from the catalyst set B following Shi et al[21] protocol). The reaction was slow and nonchemoselective (entry 5), thereby indicating the necessity of a counterion and/or influence of Ag-catalyst for the chemoselective transformation. This is further evident from the fact that neither AgCl nor KI with $[Ph_3PAu]^+TfO^-$ was able to catalyze the said transformation (entries 6 and 7). The addition of KNO_3 to $[Ph_3PAu]^+TfO^-$ again made the reaction sluggish but facilitated the formation of **5a** in 41% yield (entry 8). Addition of $AgNO_3$ to $[Ph_3PAu]^+TfO^-$ favored the exclusive formation of **5a** in 92% yield (entry 9). As anticipated, AgOTf with $[Ph_3PAu]^+TfO^-$ furnished *N*-cyclized product **6a** in quantitative yield (entry 10). It is thus apparent that while using catalyst set A, the NO_3^- (counterion) together with Au complex played a major role in controlling the exclusive formation of the *O*-cyclized product, the use of catalyst set B (Type II gold catalyzed reaction[21]) involving a cationic gold complex in association with AgOTf favored the chemoselective *N*-cyclization.

On the basis of these findings, a plausible mechanism is proposed (Figure 2). In the case of catalyst set B, the intermediate $[Ph_3P–Au]^+TfO^-$, generated in situ, in the presence of AgOTf activates the alkyne to form the soft

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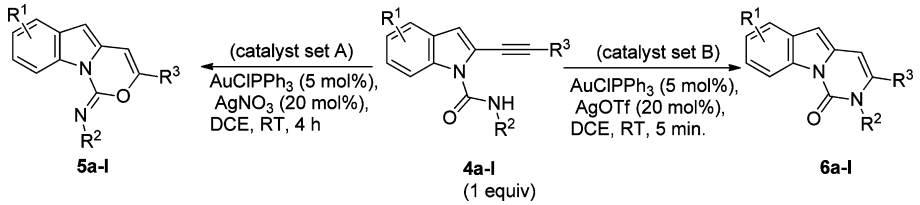
Table 2. Scope for Chemoselective *O*- and *N*-Cyclization in 4a–l



catalyst set A (*O*-cyclization)[a]	substrate	catalyst set B (*N*-cyclization)[a]
5a (87%) R^2 = 4-(Me)Ph	**4a**	**6a** (85%) R^2 = 4-(Me)Ph
5b (87%) R^2, R^3 = 4-(Me)Ph	**4b**	**6b** (80%) R^2, R^3 = 4-(Me)Ph
5c (84%) R^2 = 4-(Me)Ph, R^3 = 4-(*t*Bu)Ph	**4c**	**6c** (86%) R^2 = 4-(Me)Ph, R^3 = 4-(*t*Bu)Ph
5d (81%) R^2 = 3-(Ac)Ph, R^3 = 4-(*t*Bu)Ph	**4d**	**6d** (89%) R^2 = 3-(Ac)Ph, R^3 = 4-(*t*Bu)Ph
5e (87%) R^2 = 4-(Me)Ph, R^3 = 4-(*t*Bu)Ph	**4e**	**6e** (84%) R^2 = 4-(Me)Ph, R^3 = 4-(*t*Bu)Ph
5f (85%) R^2 = 3-(Cl)-4-(Me)Ph, R^3 = 4-(*t*Bu)Ph	**4f**	**6f** (85%) R^2 = 3-(Cl)-4-(Me)Ph, R^3 = 4-(*t*Bu)Ph
5g (88%) R^2 = 4-(Me)Ph, R^3 = 1-cyclohexenyl	**4g**	**6g** (80%) R^2 = 4-(Me)Ph, R^3 = 1-cyclohexenyl
5h (84%)	**4h**	**6h** (79%)
5i (82%) R^3 = 1-cyclohexenyl	**4i**	**6i** (85%) R^3 = 1-cyclohexenyl
5j (86%) R^2 = 3-(Cl)-4-(Me)Ph	**4j**	**6j** (33%)[b] R^2 = 3-(Cl)-4-(Me)Ph
5k (83%) R^2 = 3-(Cl)-4-(Me)Ph	**4k**	**6k** (36%)[b] R^2 = 3-(Cl)-4-(Me)Ph
5l (82%) R^2 = 3-(Cl)-4-(Me)Ph	**4l**	**6l** (35%)[b] R^2 = 3-(Cl)-4-(Me)Ph

[a]Yield of the isolated product. [b]Compounds **5j**, **5k**, and **5l** were isolated in 39%, 44%, and 42% isolated yield, respectively, along with the desired product after 8 h of stirring.

electrophilic intermediate **I**. Next, the nitrogen of the urea, being less electronegative than oxygen, favorably attacks as a relatively softer nucleophile onto the electron-deficient alkyne to afford *N*-cyclized product **6**, a phenomenon that could be well explained following HSAB theory.[24] In contrast, *O*-cyclization promoted by type III Au catalyst,[21] may involve activation of the alkyne by Au catalyst along with coordination of Ag with the oxygen[25] of the urea to furnish the intermediate

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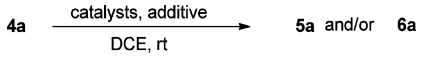
Table 3. Investigation of the Reaction Mechanism[a]



entry	catalysts (mol %)[b]	additive[b] (20 mol %)	time (h)	4a:5a:6a[c]
1	$AuClPPh_3$ (1) + AgOTf (4)		1	0:0:100
2	$AuClPPh_3$ (1) + AgOTf (4)	$AgNO_3$	1	0:10:90
3	$AuClPPh_3$ (1) + AgOTf (4)	KNO_3	24	40:43:17
4	$AuClPPh_3$ (1) + AgOTf (4)	KI	24	97:0:3
5	$[Ph_3P–Au]^+TfO^-$ (5)		24	3:62:35
6	$[Ph_3P–Au]^+TfO^-$ (5)	AgCl	24	81:14:5
7	$[Ph_3P–Au]^+TfO^-$ (5)	KI	24	93:5:2
8	$[Ph_3P–Au]^+TfO^-$ (5)	KNO_3	24	49:41:10
9	$[Ph_3P–Au]^+TfO^-$ (5)	$AgNO_3$	1	0:92:8
10	$[Ph_3P–Au]^+TfO^-$ (5)	AgOTf	1	0:0:100

[a]See the Supporting Information. [b]For reaction conditions, see the Supporting Information. [c]Relative ratio of **4a**, **5a**, and **6a** was based on the ^1H NMR spectra of the crude reaction mixture.

IV which upon cyclization and protodeauration delivers the *O*-cyclized product **5**.

CONCLUSION

In summary, we have developed a two-step protocol using Pd/Cu and Au/Ag catalytic combinations for the rapid and efficient access of highly functionalized indole based tricyclic heteroaromatics following MCR-post MCR modification concept. Furthermore, we implemented chemoselective cycloisomerization processes using orthogonal set of catalysts leading to the generation of an array of *N*-[1,3]oxazino[3,4-*a*]indol-1-ylideneamine and pyrimido[1,6-a]indolone derivatives from a common intermediate. Our mechanistic investigation reveal the significance of selecting the correct counterion for the gold-catalyzed reactions as it can play an important role in identifying new regio-divergence pathway and in turn lead to diversity oriented synthesis.

EXPERIMENTAL SECTION

I. General Information and Methods. All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with 200, 300, and 400 MHz spectrometers for ^1H NMR and 50, 75, and 100 MHz for ^{13}C NMR. Chemical shifts δ are given in ppm relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$/DMSO-d_6 for ^1H and ^{13}C NMR. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). High-resolution mass spectra were taken with a mass spectrometer. Column chromatography was performed using silica gel (100–200 mesh) as the stationary phase. All reactions were monitored by thin-layer chromatography (TLC). The purity and characterization of these compounds were further established using HR/EI Mass spectroscopy. Melting points were measured on a capillary melting point apparatus and are uncorrected.

General Procedure for the Preparation of 2-(2,2-Dibromovinyl)-aniline Derivatives ***1a–c.*** To a stirred solution of 2-nitro benzaldehyde derivatives (1.0 equiv) and tetrabromomethane (1.5 equiv) in dichlomethane (4.5 mL/mmol of 2-nitro benzaldehyde derivatives) at 0 °C was added triphenylphosphine (3.0 equiv) slowly in small lots so that the internal temperature remained at 1–5 °C. After addition, the mixture was stirred for another 0.5 h at 0 °C before being warmed to rt and stirred for another 1 h. The reaction mixture was filtered through a short plug of silica gel (60–120 mesh size), and the silica gel was washed with copious amount of dichlomethane until no product was found. Solvent was removed under vacuum to give a solid mixture of desired product and tripheny phosphine oxide. To the mixture was added absolute ethanol (3.0 mL/mmol of 2-nitro benzaldehyde derivatives) under nitrogen followed by the addition of iron powder (3.0 equiv) and ammonium chloride (3.0 equiv). The resulting suspension was heated to 90 °C under nitrogen for 1 h. The mixture was cooled to rt, and most of the solvent was removed under vacuum. The residue was dissolved in EtOAc and passed through Celite bed and the bed was washed with EtOAc. To the filtrate was added saturated potassium carbonate solution, and the resulted mixture was extracted with EtOAc. The combined organic layer was washed with brine and dried over anhydrous sodium sulfate. Solvent was removed under vacuum. The crude product was purified by silica gel flash chromatography and concentration of the appropriate fractions in vacuo afforded the desired compounds **1a–c**.

*2-(2,2-Dibromovinyl)aniline (**1a**):* brown liquid; yield 72% (1.320 g); FT-IR (neat) 3105, 3037, 1624, 1490, 1217 cm^{-1}; ^1H NMR (300

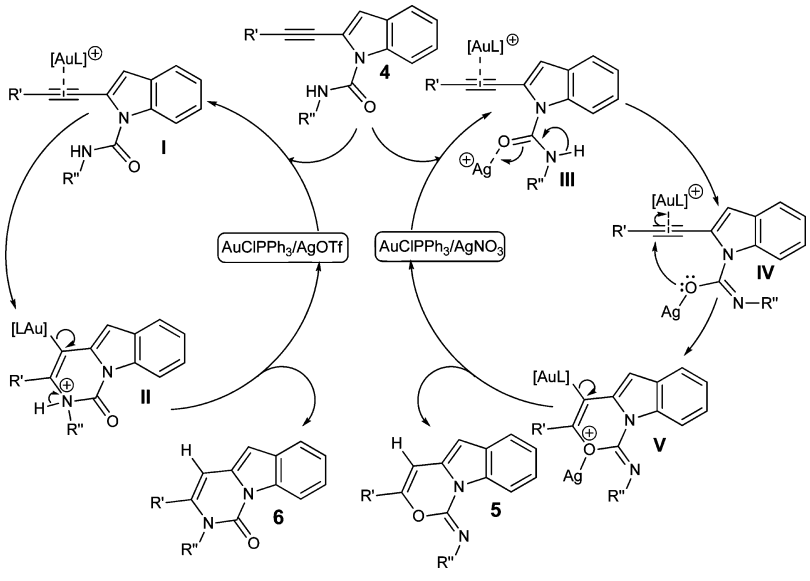


Figure 2. Plausible mechanism for the chemoselectivity.

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MHz, $CDCl_3$) δ 7.38−7.34 (m, 2H), 7.21−7.18 (m, 1H), 6.86−6.81 (m, 1H), 6.75−6.72 (m, 1H), 3.73 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.6, 134.1, 129.8, 129.3, 121.8, 118.5, 115.9, 92.8 ppm; HRMS (ESI) calcd for $C_8H_8Br_2N$ [M + H] 275.9023, found 275.9005.

*6-(2,2-Dibromovinyl)-1,3-benzodioxol-5-amine (**1b**):* brown solid; yield 75% (1.235 g); mp 96−97 °C; FT-IR (KBr) 3114, 1613, 1480, 1377, 1174 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (s, 1H), 6.88 (s, 1H), 6.27 (s, 1H), 5.88 (s, 2H), 3.38 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 140.4, 139.2, 133.5, 113.8, 108.2, 101.0, 97.9, 91.4 ppm; HRMS (ESI) calcd for $C_9H_8Br_2NO_2$ [M + H] 319.8922, found 319.8904.

*4-Chloro-2-(2,2-dibromovinyl)aniline (**1c**):* brown liquid; yield 73% (1.227 g); FT-IR (neat) 2920, 1631, 1479, 1376 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.44 (s, 1H), 7.25 (d, J = 2.2 Hz, 1H), 7.07 (dd, J = 7.2, 2.2 Hz, 1H), 6.66 (d, J = 8.7 Hz, 1H), 5.44 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 132.9, 129.6, 128.8, 123.1, 123.0, 117.1, 94.3 ppm; HRMS (ESI) calcd for $C_8H_7Br_2ClN$ [M + H] 309.8634, found 309.8624.

II. General Procedure for the Preparation of N-and 2-Substituted 1*H*-Indole-1-carboxamide Derivatives 4a−l. To a stirred solution of 2-(2,2-dibromovinyl)aniline derivatives **1a−c** (1.0 equiv) in toluene (15 mL/mmol of **1a−c**) under N_2 was added isocyanate derivatives **2a−e** (1.2 equiv), and the resulted reaction mixture was heated at 100 °C for 2 h. DIPA (2.5 equiv), tri-*o*-tolylphosphine (10 mol %) and Pd/C (5 mol %) were added to the reaction mixture under N_2 and heated to 100 °C for 5 min. It was followed by the addition of alkyne derivatives **3a−f** (1.5 equiv) and CuI (5 mol %) ,and the reaction mixture was stirred at 100 °C for 1 h. The reaction mixture was filtered through a short Celite bed, and the bed was washed with EtOAc. The filtrate was washed with water and brine. The organic layer was dried over anhydrous sodium sulfate using EtOAc/hexane as eluent, and solvent was removed under vacuum. The crude product was purified by silica gel column chromatography, and concentration of the appropriate fractions in vacuo afforded the desired compounds **4a−l**.

*N-(4-Methylphenyl)-2-(2-phenylethynyl)-1H-indole-1-carboxamide (**4a**):* pale yellow solid; yield 75% (0.285 g); mp 140−142 °C; FT-IR (KBr) 3301, 3057, 2254, 1679, 1606, 1447, 1319 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.58−7.52 (m, 3H), 7.46 (d, J = 8.4 Hz, 2H), 7.42−7.37 (m, 4H), 7.29−7.24 (m, 1H), 7.16 (d, J = 8.4 Hz, 2H), 7.08 (s, 1H), 2.34 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 137.5, 134.8, 134.4, 131.7, 129.9, 129.7, 128.9, 128.2, 126.2, 123.3, 121.4, 120.8, 120.2, 117.4, 116.6, 116.4, 98.7, 81.2, 20.9 ppm; HRMS (ESI) calcd for $C_{24}H_{19}N_2O$ [M + H] 351.1497, found 351.1498.

*N-(4-Methylphenyl)-2-[2-(4-methylphenyl)ethynyl]-1H-indole-1-carboxamide (**4b**):* white solid; yield 70% (0.276 g); mp 155−156 °C; FT-IR (KBr) 3299, 2976, 1679, 1521, 1321 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.44 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.47−7.36 (m, 5H), 7.28−7.15 (m, 5H), 7.05 (s, 1H), 2.40 (s, 3H), 2.34 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.4, 140.2, 137.4, 134.9, 134.3, 131.6, 129.8, 129.6, 128.2, 126.0, 123.2, 120.8, 120.2, 118.2, 117.6, 116.4, 116.3, 99.0, 80.5, 21.8, 21.0 ppm; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ [M + H] 365.1654, found 365.1653.

*2-[2-(4-tert-Butylphenyl)ethynyl]-N-(4-methylphenyl)-1H-indole-1-carboxamide (**4c**):* white solid; yield 73% (0.321 g); mp 158−159 °C; FT-IR (KBr) 3384, 2956, 1711, 1602, 1530, 1306 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.45 (d, J = 8.2 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.48−7.36 (m, 7H), 7.26 (s, 1H), 7.17 (d, J = 7.6 Hz, 2H), 7.06 (s, 1H), 2.35 (s, 3H), 1.34 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.2, 149.5, 137.4, 134.9, 134.3, 131.5, 129.8, 128.2, 126.0, 125.9, 123.2, 120.8, 120.3, 118.3, 117.6, 116.4, 99.1, 80.6, 35.1, 31.2, 21.0 ppm; HRMS (ESI) calcd for $C_{28}H_{27}N_2O$ [M + H] 407.2123, found 407.2122.

*N-(3-Acetylphenyl)- 2-[2-(4-tert-butylphenyl)ethynyl]-1H-indole-1-carboxamide (**4d**):* white solid; yield 74% (0.348 g); mp 158−159 °C; FT-IR (KBr) 3358, 2963, 1687, 1606, 1544, 1312 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.45 (d, J = 8.2 Hz, 1H), 8.02 (s, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.59−7.38 (m, 7H), 7.30−7.26 (m, 1H), 7.08 (s, 1H), 2.48 (s, 3H), 1.34 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.4, 153.5, 149.3, 138.0, 137.9, 137.2, 131.5, 129.6, 128.1, 126.1, 125.9, 124.3, 124.0, 123.4, 120.8, 119.7, 117.9, 117.3, 116.7, 116.3, 99.2, 80.3, 35.0, 31.1, 26.5 ppm; HRMS (ESI) calcd for $C_{29}H_{27}N_2O_2$ [M + H] 435.2073, found 435.2063.

*N-(4-Methylphenyl)-6-[2-(4-tert-butylphenyl)ethynyl]-5H-[1,3]-dioxolo[4,5-f]indole-5-carboxamide (**4e**):* White solid; yield 67% (0.282 g); mp 189−190 °C; FT-IR (KBr) 3379, 2957, 2195, 1705, 1598, 1534, 1322, 1243 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.99 (s, 1H), 7.46−7.38 (m, 6H), 7.15 (d, J = 8.1 Hz, 2H), 6.92 (s, 1H), 6.89 (s, 1H), 5.99 (s, 2H), 2.34 (s, 3H), 1.34 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.9, 149.5, 147.9, 145.1, 134.9. 134.3, 132.8, 131.3, 129.8, 125.9, 122.3, 120.3, 118.5, 116.5, 116.0, 101.4, 98.7, 97.8, 80.8, 35.1, 31.2, 21.0 ppm; HRMS (ESI) calcd for $C_{29}H_{27}N_2O_3$ [M + H] 451.2022 found 451.2014.

*5-chloro-N-(3-chloro-4-methylphenyl)-2-[2-(4-tert-butylphenyl)-ethynyl]-1H-indole-1-carboxamide (**4f**):* white solid; yield 71% (0.324 g); mp 149−151 °C; FT-IR (KBr) 3305, 2960, 2138, 1688, 1598, 1527, 1314, 1197 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.37 (d, J = 8.9 Hz, 1H), 7.62 (d, J = 1.7 Hz, 1H), 7.52−7.42 (m, 5H), 7.34−7.31 (m, 2H), 7.18 (d, J = 8.2 Hz, 1H), 6.98 (s, 1H), 2.35 (s, 3H), 1.35 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 148.9, 136.0, 135.6, 134.8, 132.3, 131.5, 131.3, 129.2, 129.0, 126.2, 126.0, 120.6, 120.1, 118.7, 118.2, 117.7, 117.4, 115.5, 99.9, 80.0, 35.2, 31.2, 19.6 ppm; HRMS (ESI) calcd for $C_{28}H_{25}Cl_2N_2O$ [M + H] 475.1344, found 475.1341.

*2-(2-Cyclohex-1-en-1-ylethynyl)-N-(4-methylphenyl)-1H-indole-1-carboxamide (**4g**):* white solid; yield 65% (0.249 g); mp 152−153 °C; FT-IR (KBr) 3312, 2927, 2157, 1679, 1606, 1543, 1317, 1234 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.43 (d, J = 8.4 Hz, 1H), 7.54−7.46 (m, 3H), 7.38−7.33 (m, 1H), 7.25−7.18 (m, 3H), 6.94 (s, 1H), 6.34 (s, 1H), 2.35 (s, 3H), 2.23−2.21 (m, 4H), 1.68−1.66 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 138.3, 137.3, 134.9, 134.3, 129.8, 128.2, 125.8, 123.2, 120.6, 120.4, 119.7, 117.8, 116.5, 115.9, 100.7, 78.6, 28.9, 26.0, 22.2, 21.4, 21.0 ppm; HRMS (ESI) calcd for $C_{24}H_{23}N_2O$ [M + H] 355.1810, found 355.1803.

*N-Octyl-2-(2-phenylethynyl)-1H-indole-1-carboxamide (**4h**):* white solid; yield 61% (0.246 g); mp 108−109 °C; FT-IR (KBr) 3432, 2925, 1670, 1640, 1532, 1447, 1316 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, J = 8.5 Hz, 1H), 7.55−7.53 (m, 3H), 7.42−7.34 (m, 4H), 7.26−7.21 (m, 1H), 7.09 (s, 1H), 7.02 (s, 1H), 3.50 (t, J = 6.9 Hz, 2H), 1.68−1.60 (m, 2H), 1.42−1.32 (m, 2H), 1.26−1.23 (m, 8H), 0.86 (t, J = 6.6 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.1, 137.4, 131.6, 129.6, 128.8, 127.9, 125.9, 122.9, 121.7, 120.6, 117.3, 116.3, 116.2, 97.7, 81.4, 41.2, 31.9, 29.7, 29.4, 29.2, 27.2, 22.7, 14.2 ppm; HRMS (ESI) calcd for $C_{25}H_{29}N_2O$ [M + H] 373.2280, found 373.2272.

*N-Benzyl-2-(2- cyclohex-1-en-1-ylethynyl)-1H-indole-1-carboxamide (**4i**):* white solid; yield 69% (0.265 g); mp 138−140 °C; FT-IR (KBr) 3357, 3019, 2930, 1675, 1529, 1325 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, J = 8.4 Hz, 1H), 7.55 (s, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 7.2 Hz, 2H), 7.38−7.29 (m, 4H), 7.24−7.19 (m, 1H), 6.87 (s, 1H), 5.87−5.85 (m, 1H), 4.66 (d, J = 5.2 Hz, 2H), 2.04−2.02 (m, 2H), 1.91−1.90 (m, 2H), 1.59−1.52 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 137.7, 137.6, 137.3, 128.9, 128.3, 128.1, 127.8, 125.7, 122.9, 120.5, 119.4, 117.9, 116.5, 115.7, 100.0, 78.8, 45.2, 28.3, 25.9, 22.1, 21.3 ppm; HRMS (ESI) calcd for $C_{24}H_{23}N_2O$ [M + H] 355.1810, found 355.1804.

*N-(3-Chloro-4-methylphenyl)-2-hex-1-ynyl-1H-indole-1-carboxamide (**4j**):* white solid; yield 71% (0.281 g); mp 98−99 °C; FT-IR (KBr) 3308, 2934, 1680, 1598, 1533, 1310, 1205 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.41 (d, J = 8.3 Hz, 1H), 7.64 (s, 1H), 7.51 (d, J = 7.7 Hz, 1H), 7.38−7.34 (m, 2H), 7.25−7.21 (m, 2H), 6.91 (s, 1H), 2.60 (t, J = 7.0 Hz, 2H), 2.37 (s, 3H), 1.70−1.60 (m, 2H), 1.52−1.42 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.4, 136.9, 136.3, 134.8, 132.2, 131.3, 128.1, 125.8, 123.3, 120.7, 120.6, 118.4, 117.7, 116.4, 116.1, 101.0, 73.1, 30.5, 22.3, 19.6, 13.6 ppm; HRMS (ESI) calcd for $C_{22}H_{22}ClN_2O$ [M + H] 365.1421, found 365.1416.

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*N-(3-Chloro-4-methylphenyl)-6-oct-1-ynyl-5H-[1,3]dioxolo[4,5-f]indole-5-carboxamide (**4k**):* white solid; yield 72% (0.294 g); mp 104−105 °C; FT-IR (KBr) 3341, 2934, 2869, 2130, 1697, 1604, 1540, 1304 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.96 (s, 1H), 7.61 (s, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.26−7.20 (m, 1H), 6.85 (s, 1H), 6.77 (s, 1H), 5.98 (s, 2H), 2.57 (t, J = 7.0 Hz, 2H), 2.36 (s, 3H), 1.69−1.59 (m, 2H), 1.43 (s, 2H), 1.28−1.27 (m, 4H), 0.87 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 147.5, 144.9, 136.2, 134.7, 132.1, 132.0, 131.1, 122.0, 120.6, 118.3, 116.1, 116.0, 101.2, 100.5, 98.6, 97.8, 73.1, 31.3, 28.8, 28.5, 22.5, 19.9, 19.4, 14.0 ppm; HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_3$ [M + H] 437.1632, found 437.1633.

*5-Chloro-N-(3-chloro-4-methylphenyl)-2-oct-1-ynyl-1H-indole-1-carboxamide (**4l**):* white solid; yield 74% (0.305 g); mp 106−107 °C; FT-IR (KBr) 3300, 2931, 2862, 2225, 1683, 1593, 1534, 1387, 1206 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.35 (d, J = 9.0 Hz, 1H), 7.61 (s, 1H), 7.47 (d, J = 1.4 Hz, 1H), 7.34−7.21 (m, 3H), 6.83 (s, 1H), 2.58 (t, J = 7.0 Hz, 2H), 2.37 (s, 3H), 1.71−1.61 (m, 2H), 1.44 (s, 2H), 1.29−1.27 (m, 4H), 0.88 (m, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.1, 136.0, 135.2, 134.9, 132.4, 131.3, 129.2, 128.9, 125.9, 120.8, 119.9, 119.0, 118.4, 117.5, 115.0, 101.9, 72.7, 31.4, 28.9, 28.4, 22.6, 20.0, 19.6, 14.1 ppm; HRMS (ESI) calcd for $C_{24}H_{25}Cl_2N_2O$ [M + H] 427.1344, found 427.1338.

III. General Procedure for the Preparation of Oxazino[3,4-*a*]indol-1-ylidenes 5a−l. To a stirred solution of the desired indole-1-carboxamide **4a−l** (1.0 equiv) in 1,2-dichloroethane under N_2 (8 mL/mmol of **4**) was added $AuClPPh_3$ (5 mol %) and $AgNO_3$ (20 mol %). The reaction mixture was stirred at rt. After completion, the solvent was removed under vacuum. The crude product was purified by silica gel column chromatography using EtoAc/hexane as eluent and concentration of the appropriate fractions in vacuo afforded the desired compounds **5a−l**.

*(Z)-4-Methyl-N-(3-phenyl[1,3]oxazino[3,4-a]indol-1-ylidene)-aniline (**5a**):* white solid; yield 87% (0.087 g); mp 180−181 °C; FT-IR (KBr) 3057, 1680, 1606, 1447, 1400, 1346 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.82 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 7.4 Hz, 3H), 7.38−7.30 (m, 5H), 7.24−7.22 (m, 4H), 6.84 (s, 1H), 6.60 (s, 1H), 2.40 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.3, 142.4, 137.9, 133.8, 132.9, 131.9, 131.3, 130.8, 129.6, 129.4, 128.8, 124.5, 123.8, 123.6, 123.1, 120.0, 116.5, 101.1, 94.4, 21.1 ppm; HRMS (ESI) calcd for $C_{24}H_{19}N_2O$ [M + H] 351.1497 found 351.1497.

*(Z)-4-Methyl-N-[3-(4-methylphenyl)[1,3]oxazino[3,4-a]indol-1-ylidene]aniline (**5b**):* white solid; yield 87% (0.087 g); mp 213-214 °C; FT-IR (KBr) 3023, 2917, 1688, 1403, 1245 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.1 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.39−7.29 (m, 2H), 7.25−7.16 (m, 6H), 6.78 (s, 1H), 6.57 (s, 1H), 2.39 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.7, 142.6, 139.9, 138.2, 133.9, 133.0, 132.2, 130.9, 129.6, 129.5, 128.6, 124.6, 123.8, 123.6, 123.2, 120.0, 116.6, 100.8, 93.7, 21.5, 21.1 ppm; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ [M + H] 365.1654, found 365.1652.

*(Z)-4-Methyl- N-[3-(4-tert-butylphenyl)[1,3]oxazino[3,4-a]indol-1-ylidene]aniline (**5c**):* white solid; yield 84% (0.084 g); mp 183−185 °C; FT-IR (KBr) 2959, 1672, 1407, 1078 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.82 (d, J = 7.7 Hz, 1H), 7.61 (d, J = 7.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.42−7.30 (m, 4H), 7.26−7.23 (m, 4H), 6.82 (s, 1H), 6.59 (s, 1H), 2.41 (s, 3H), 1.33 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.0, 148.5, 142.4, 138.1, 133.8, 132.9, 132.1, 130.8, 129.4, 128.5, 125.8, 124.3, 123.7, 123.5, 123.1, 119.9, 116.5, 100.8, 93.7, 34.9, 31.2, 21.1 ppm; HRMS (ESI) calcd for $C_{28}H_{27}N_2O$ [M + H] 407.2123, found 407.2127.

*(Z)-1-[3-[3-(4-tert-butylphenyl)[1,3]oxazino[3,4-a]indol-1-ylidene]amino]phenyl[ethan-1-one (**5d**):* white solid; yield 81% (0.081 g); mp 183−184 °C; FT-IR (KBr) 2963, 1677, 1584, 1400, 1353, 1270 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, J = 7.7 Hz, 1H), 7.90 (s, 1H), 7.78 (s, 1H), 7.62 (d, J = 7.2 Hz, 1H), 7.49−7.47 (m, 4H), 7.38−7.31 (m, 4H), 6.83 (s, 1H), 6.61 (s, 1H), 2.64 (s, 3H), 1.31 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 153.4, 148.6, 145.9, 139.2, 138.1, 133.8, 132.0, 131.0, 129.1, 128.3, 128.2, 125.9, 124.4, 124.0, 123.9, 123.5, 123.4, 120.2, 116.5, 101.3, 94.1, 34.9, 31.3, 26.9 ppm; HRMS (ESI) calcd for $C_{29}H_{27}N_2O_2$ [M + H] 435.2073, found 435.2069.

*(Z)-4-Methyl-N-[8-(4-tert-butylphenyl)[1,3]dioxolo[4,5-f][1,3]-oxazino[3,4-a]indol-6-ylidene]aniline (**5e**):* white solid; yield 87% (0.087 g); mp 245−246 °C; FT-IR (KBr) 2957, 1693, 1459, 1307, 1212 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.24−7.21 (m, 4H), 6.97 (s, 1H), 6.74 (s, 1H), 6.45 (s, 1H), 6.00 (s, 2H), 2.40 (s, 3H), 1.32 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.7, 147.5, 145.7, 145.3, 142.4, 138.2, 132.9, 131.2, 129.5, 128.8, 128.7, 125.9, 125.4, 124.2, 123.3, 101.3, 100.9, 98.7, 98.2, 93.9, 34.9, 31.3, 21.2 ppm; HRMS (ESI) calcd for $C_{29}H_{27}N_2O_3$ [M + H] 451.2022, found 451.2021.

*(Z)-N-[3-(4-tert-Butylphenyl)-7-chloro[1,3]oxazino[3,4-a]indol-1-ylidene]-3-chloro-4-methylaniline (**5f**):* white solid; yield 85% (0.085 g); mp 142−143 °C; FT-IR (KBr) 2956, 1676, 1403, 1273 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (d, J = 8.8 Hz, 1H), 7.55−7.53 (m, 3H), 7.43−7.37 (m, 3H), 7.31−7.24 (m, 2H), 7.12 (d, J = 8.0 Hz, 1H), 6.79 (s, 1H), 6.51 (s, 1H), 2.42 (s, 3H), 1.33 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.6, 150.0, 149.2, 143.7, 138.4, 134.3, 133.2, 132.1, 131.2, 130.9, 129.5, 128.0, 126.0, 124.5, 124.1, 123.9, 121.9, 119.5, 117.5, 100.2, 93.6, 34.9, 31.3, 19.7 ppm; HRMS (ESI) calcd for $C_{28}H_{25}Cl_2N_2O$ [M + H] 475.1344, found 475.1333.

*(Z)-N-(3-Cyclohex-1-en-1-yl[1,3]oxazino[3,4-a]indol-1-ylidene)-4-methylaniline (**5g**):* white solid; yield 88% (0.088 g); mp 166−168 °C; FT-IR (KBr) 2928, 1671, 1448, 1364 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 7.9 Hz, 1H), 7.57 (d, J = 7.0 Hz, 1H), 7.35−7.29 (m, 2H), 7.17 (s, 4H), 6.49 (s, 1H), 6.33 (s, 1H), 6.24 (s, 1H), 2.37 (s, 3H), 2.21−2.16 (m, 4H), 1.72−1.71 (m, 2H), 1.62−1.60 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.4, 142.6, 138.2, 133.9, 132.8, 132.4, 130.9, 129.4, 129.0, 127.8, 123.6, 123.4, 123.2, 119.9, 116.5, 100.5, 92.9, 25.8, 23.9, 22.3, 21.9, 21.1 ppm; HRMS (ESI) calcd for $C_{24}H_{23}N_2O$ [M + H] 355.1810, found 355.1812.

*(Z)-N-Octyl-N-(3-phenyl[1,3]oxazino[3,4-a]indol-1-ylidene)amine (**5h**):* white solid; yield 84% (0.084 g); mp 72−74 °C; FT-IR (KBr) 2923, 2852, 1639, 1493, 1449, 1351, 1219 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.71 (d, J = 8.1 Hz, 1H), 7.80−7.77 (m, 2H), 7.58 (d, J = 7.5 Hz, 1H), 7.49−7.38 (m, 3H), 7.36−7.25 (m, 2H), 6.78 (s, 1H), 6.53 (s, 1H), 3.72 (t, J = 6.9 Hz, 2H), 1.84−1.74 (m, 2H), 1.60−1.50 (m, 2H), 1.41−1.31(m, 8H), 0.91−0.89 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 139.0, 133.8, 132.1, 130.5, 122.9, 122.8, 119.7, 116.1, 98.0, 95.2, 45.6, 32.4, 32.1, 31.4, 29.7, 29.5, 28.8, 27.7, 22.9, 22.2, 14.3, 13.9 ppm; HRMS (ESI) calcd for $C_{25}H_{29}N_2O$ [M + H] 373.2280, found 373.2277.

*(Z)-N-Benzyl-N-(3-cyclohex-1-en-1-yl[1,3]oxazino[3,4-a]indol-1-ylidene)amine (**5i**):* white solid; yield 82% (0.082 g); mp 125−127 °C; FT-IR (KBr) 3020, 2932, 1690, 1637, 1448, 1348, 1215 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (d, J = 8.0 Hz, 1H), 7.56−7.53 (m, 3H), 7.40−7.33 (m, 2H), 7.31−7.23 (m, 3H), 6.64 (s, 1H), 6.45 (s, 1H), 6.23 (s, 1H), 4.88 (s, 2H), 2.28−2.26 (m, 4H), 1.79−1.76 (m, 2H), 1.68−1.65 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 141.5, 139.7, 134.1, 132.4, 130.7, 128.5, 128.4, 128.3, 127.6, 126.6, 123.6, 123.2, 119.9, 116.4, 100.1, 93.0, 49.5, 25.9, 24.2, 22.5, 22.1 ppm; HRMS (ESI) calcd for $C_{24}H_{23}N_2O$ [M + H] 355.1810, found 355.1800.

*(Z)-N-(3-Butyl[1,3]oxazino[3,4-a]indol-1-ylidene)-3-chloro-4-methylaniline (**5j**):* white solid; yield 86% (0.086 g); mp 87−88 °C; FT-IR (KBr) 2949, 1688, 1400 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.74 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 6.7 Hz, 1H), 7.36−7.25 (m, 3H), 7.19 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.42 (s, 1H), 6.15 (s, 1H), 2.42−2.38 (m, 5H), 1.41−1.26 (m, 4H), 0.94 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.0, 144.1, 139.4, 134.1, 133.5, 131.8, 130.8, 130.7, 124.0, 123.7, 123.5, 121.9, 119.9, 116.6, 99.3, 96.1, 32.2, 28.6, 22.1, 19.6, 13.9 ppm; HRMS (ESI) calcd for $C_{22}H_{22}ClN_2O$ [M + H] 365.1421, found 365.1410.

*(Z)-N-(8-Hexyl[1,3]dioxolo[4,5-f][1,3]oxazino[3,4-a]indol-6-ylidene)-3-chloro-4-methylaniline (**5k**):* white solid; yield 83% (0.083 g); mp 96−97 °C; FT-IR (KBr) 2924, 1678, 1465, 1403, 1302 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.26 (s, 1H), 7.17 (d, J = 8.0 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.95 (s, 1H), 6.30 (s, 1H), 6.09 (s, 1H), 5.99 (s, 2H), 2.40 (s, 3H), 2.37 (s, 2H), 1.59−1.56 (m, 2H),

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1.30 (s, 6H), 0.88 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 145.4, 145.3, 144.1, 139.5, 134.2, 130.9, 130.8, 130.7, 128.4, 125.2, 124.1, 122.1, 101.3, 99.4, 98.7, 98.3, 96.2, 32.4, 31.6, 28.7, 26.6, 22.6, 19.6, 14.2 ppm; HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_3$ [M + H] 437.1632, found 437.1630.

*(Z)-3-Chloro-N-(7-chloro-3-hexyl[1,3]oxazino[3,4-a]indol-1-ylidene)-4-methylaniline (**5l**):* white solid; yield 82% (0.082 g); mp 115−117 °C; FT-IR (KBr) 2934, 1674, 1595, 1399, 1154 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (d, J = 8.8 Hz, 1H), 7.54 (s, 1H), 7.28−7.18 (m, 3H), 7.02 (d, J = 8.0 Hz, 1H), 6.35 (s, 1H), 6.13 (s, 1H), 2.42−2.38 (m, 5H), 1.60−1.56 (m, 2H), 1.30 (s, 6H), 0.89 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 143.7, 138.9, 134.2, 133.1, 131.9, 131.8, 131.0, 130.9, 129.3, 123.9, 123.6, 121.9, 119.4, 117.5, 98.5, 95.8, 32.5, 31.6, 28.7, 26.5, 22.6, 19.6, 14.2 ppm; HRMS (ESI) calcd for $C_{24}H_{25}Cl_2N_2O$ [M + H] 427.1344, found 427.1339.

IV. General Procedure for the Preparation of Pyrimido[1,6-*a*]indol-1(2*H*)-ones 6a−l. To a stirred solution of the desired indole-1-carboxamide **4** (1.0 equiv) in 1,2-dichloroethane under N_2 (8 mL/mmol of **4**) were added $AuClPPh_3$ (5 mol %) and AgOTf (20 mol %). The reaction mixture was stirred at rt. After completion of the reaction, the solvent was removed under vacuum. The crude product was purified by silica gel column chromatography using EtoAc/hexane as eluent, and concentration of the appropriate fractions in vacuo afforded the desired compounds (**6**).

*2-(4-Methylphenyl)-3-phenylpyrimido[1,6-a]indol-1(2H)-one (**6a**):* white solid; yield 85% (0.085 g); mp 200−201 °C (lit.[14a] mp 199−200 °C); FT-IR (KBr) 3022, 2995, 1692, 1512, 1366, 1281 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (d, J = 7.2 Hz, 1H), 7.66 (d, J = 7.3 Hz, 1H), 7.39−7.30 (m, 2H), 7.19 (s, 5H), 7.04 (s, 4H), 6.59 (s, 1H), 6.53 (s, 1H), 2.28 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 140.7, 137.8, 135.6, 135.4, 134.4, 133.6, 130.9, 129.5, 129.4, 129.0, 128.3, 128.1, 124.0, 122.9, 119.8, 116.4, 101.2, 98.6, 21.2 ppm; HRMS (ESI) calcd for $C_{24}H_{19}N_2O$ [M + H] 351.1497, found 351.1497.

*2,3-Bis(4-methylphenyl)pyrimido[1,6-a]indol-1(2H)-one (**6b**):* white solid; yield 80% (0.080g); mp 220−222 °C; FT-IR (KBr) 3023, 2930, 1703, 1620, 1385 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, J = 7.4 Hz, 1H), 7.64 (d, J = 6.9 Hz, 1H), 7.38−7.29 (m, 2H), 7.08−6.97 (m, 8H), 6.57 (s, 1H), 6.50 (s, 1H), 2.29 (s, 3H), 2.27 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 140.8, 138.2, 137.8, 135.6, 134.5, 133.6, 132.5, 131.0, 129.5, 129.4, 128.9, 128.8, 124.0, 122.8, 119.7, 116.4, 100.9, 98.4, 21.3, 21.2 ppm; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ [M + H] 365.1654, found 365.1652.

*3-(4-tert-Butylphenyl)-2-(4-methylphenyl)pyrimido[1,6-a]indol-1(2H)-one (**6c**):* white solid; yield 86% (0.086 g); mp 206−207 °C; FT-IR (KBr) 3025, 2959, 1705, 1631, 1508, 1364, 1270 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.4 Hz, 1H), 7.41−7.32 (m, 2H), 7.21 (d, J = 8.1 Hz, 2H), 7.13−7.11 (m, 6H), 6.60 (s, 1H), 6.55 (s, 1H), 2.32 (s, 3H), 1.27 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.4, 149.3, 140.8, 137.7, 135.6, 134.6, 133.6, 132.4, 131.0, 129.4, 129.3, 128.7, 124.9, 124.0, 122.8, 119.7, 116.4, 101.0, 98.4, 34.7, 31.3, 21.2 ppm; HRMS (ESI) calcd for $C_{28}H_{27}N_2O$ [M + H] 407.2123, found 407.2123.

*2-(3-Acetylphenyl)-3-(4-tert-butylphenyl)pyrimido[1,6-a]indol-1(2H)-one (**6d**):* white solid; yield 89% (0.089 g); mp 203−204 °C; FT-IR (KBr) 2963, 1691, 1378, 1279 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (d, J = 7.4 Hz, 1H), 7.82 (d, J = 7.3 Hz, 1H), 7.74 (s, 1H), 7.67 (d, J = 6.8 Hz, 1H), 7.47−7.34 (m, 4H), 7.18 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 6.63 (s, 1H), 6.58 (s, 1H), 2.48 (s, 3H), 1.22 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.0, 151.8, 148.9, 140.2, 138.8, 137.6, 134.3, 134.2, 133.6, 132.0, 131.0, 129.8, 129.0, 128.8, 127.5, 125.2, 124.2, 123.1, 119.9, 116.3, 101.5, 99.1, 34.7, 31.2, 26.7 ppm; HRMS (ESI) calcd for $C_{29}H_{27}N_2O_2$ [M + H] 435.2073, found 435.2070.

*8-(4-tert-Butylphenyl)-7-(4-methylphenyl)[1,3]dioxolo[4,5-f]-pyrimido[1,6-a]indol-6(7H)-one (**6e**):* white solid; yield 84% (0.084 g); mp 175−176 °C; FT-IR (KBr) 2944, 2891, 1691, 1458, 1396, 1313 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.2 (s, 1H), 7.17 (d, J = 8.3 Hz, 2H), 7.09−7.07 (m, 6H), 7.01 (s, 1H), 6.47 (s, 2H), 6.00 (s, 2H), 2.29 (s, 3H), 1.24 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 149.1, 145.6, 145.0, 139.3, 137.7, 135.7, 133.7, 132.5, 129.4, 129.3, 128.7, 128.3, 125.6, 124.9, 101.2, 101.1, 98.5, 98.3, 97.8, 34.7, 31.3, 31.2 ppm; HRMS (ESI) calcd for $C_{29}H_{27}N_2O_3$ [M + H] 451.2022, found 451.2024.

*7-Chloro-2-(3-chloro-4-methylphenyl)-3-(4-tert-butylphenyl)-pyrimido[1,6-a]indol-1(2H)-one (**6f**):* white solid; yield 85% (0.085 g); mp 168−169 °C; FT-IR (KBr) 2956, 1689, 1382, 1284 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 1.4 Hz, 1H), 7.29−7.21 (m, 4H), 7.14−7.07 (m, 3H), 6.97 (d, J = 8.0 Hz, 2H), 6.52 (s, 1H), 2.31 (s, 3H), 1.26 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.0, 148.7, 141.2, 136.6, 136.2, 135.5, 134.3, 132.2, 131.9, 131.8, 130.8, 130.2, 129.8, 128.7, 127.9, 125.2, 123.1, 119.3, 117.3, 101.0, 98.1, 34.8, 31.3, 19.9 ppm; HRMS (ESI) calcd for $C_{28}H_{25}Cl_2N_2O$ [M + H] 475.1344, found 475.1328.

*3-Cyclohex-1-en-1-yl-2-(4-methylphenyl)pyrimido[1,6-a]indol-1(2H)-one (**6g**):* white solid; yield 80% (0.080 g); mp 132−133 °C; FT-IR (KBr) 2932, 1692, 1635, 1369 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.35−7.18 (m, 6H), 6.50 (s, 1H), 6.35 (s, 1H), 5.94 (s, 1H), 2.40 (s, 3H), 2.02−2.01 (m, 2H), 1.66 (s, 2H), 1.41−1.38 (m, 2H), 1.29−1.26 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 143.9, 138.1, 135.4, 134.9, 134.4, 133.5, 131.2, 131.0, 129.4, 129.3, 123.9, 122.5, 119.6, 116.3, 98.7, 97.7, 28.5, 25.4, 22.3, 21.6, 21.3 ppm; HRMS (ESI) calcd for $C_{24}H_{23}N_2O$ [M + H] 355.1810, found 355.1810.

*2-Octyl-3-phenylpyrimido[1,6-a]indol-1(2H)-one (**6h**):* colorless liquid; yield 79% (0.079 g); FT-IR (neat) 2958, 2928, 1638, 1449, 1406, 1360, 1220 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73−8.69 (m, 1H), 7.65−7.62 (m, 1H), 7.48−7.45 (m, 3H), 7.43−7.39 (m, 2H), 7.36−7.33 (m, 2H), 6.49 (s, 1H), 6.32 (s, 1H), 3.86 (t, J = 5.9 Hz, 2H), 1.59−1.50 (m, 2H), 1.25−1.09 (m, 10H), 0.84 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 140.6, 135.4, 134.4, 133.3, 130.9, 129.2, 129.1, 128.7, 123.9, 122.5, 119.7, 116.4, 101.1, 97.4, 45.7, 31.8, 31.7, 29.1, 29.0, 26.6, 22.7, 14.2 ppm; HRMS (ESI) calcd for $C_{25}H_{29}N_2O$ [M + H] 373.2280, found 373.2276.

*2-Benzyl-3-cyclohex-1-en-1-ylpyrimido[1,6-a]indol-1(2H)-one (**6i**):* white solid; yield 85% (0.085 g); mp 103−104 °C; FT-IR (KBr) 3432, 3020, 2932, 1683, 1635, 1446, 1355, 1216 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.36−7.21 (m, 5H), 7.18 (d, J = 7.1 Hz, 2H), 6.45 (s, 1H), 6.24 (s, 1H), 5.79 (s, 1H), 5.16 (s, 2H), 2.09−2.04 (m, 4H), 1.68−1.62 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 143.3, 138.3, 134.9, 133.4, 133.2, 131.4, 130.9, 128.7, 127.4, 126.9, 123.9, 122.4, 119.6, 116.5, 99.1, 97.3, 48.6, 29.9, 25.4, 22.6, 21.8 ppm; HRMS (ESI) calcd for $C_{24}H_{23}N_2O$ [M + H] 355.1810, found 355.1776.

*3-Butyl-2-(3-chloro-4-methylphenyl)pyrimido[1,6-a]indol-1(2H)-one (**6j**):* white solid; yield 33% (0.033 g); mp 119−120 °C; FT-IR (KBr) 3065, 2972, 1685, 1598, 1396 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (d, J = 7.9 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.40−7.26 (m, 4H), 7.15 (d, J = 8.0 Hz, 1H), 6.47 (s, 1H), 6.33 (s, 1H), 2.46 (s, 3H), 2.18 (t, J = 7.5 Hz, 2H), 1.52−1.41 (m, 2H), 1.28−1.25 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.1, 140.4, 137.4, 136.0, 135.1, 134.6, 133.4, 131.6, 130.9, 130.1, 127.9, 124.0, 122.5, 119.6, 116.2, 97.6, 97.2, 32.6, 29.9, 22.2, 20.0, 13.9 ppm; HRMS (ESI) calcd for $C_{22}H_{22}ClN_2O$ [M + H] 365.1421, found 365.1421.

*7-(3-Chloro-4-methylphenyl)-8-hexyl[1,3]dioxolo[4,5-f]pyrimido-[1,6-a]indol-6(7H)-one (**6k**):* white solid; yield 36% (0.036 g); mp 125−126 °C; FT-IR (KBr) 2929, 1697, 1461, 1327 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.39−7.33 (m, 2H), 7.14 (d, J = 7.7 Hz, 1H), 6.99 (s, 1H), 6.36 (s, 1H), 6.27 (s, 1H), 5.99 (s, 2H), 2.46 (s, 3H), 2.15 (t, J = 7.4 Hz, 2H), 1.45−1.43 (m, 2H), 1.24−1.19 (m, 6H), 0.84 (t, J = 6.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9, 145.6, 144.8, 138.9, 137.3, 136.1, 135.1, 133.8, 131.6, 130.2, 127.9, 127.8, 125.6, 101.1, 98.3, 97.8, 97.7, 97.4, 32.9, 31.5, 28.8, 27.8, 22.5, 20.0, 14.1 ppm; HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_3$ [M + H] 437.1632, found 437.1631.

*7-Chloro-2-(3-chloro-4-methylphenyl)-3-hexylpyrimido[1,6-a]-indol-1(2H)-one (**6l**):* white solid; yield 35% (0.035 g); mp 151−152 °C; FT-IR (KBr) 3435, 1644, 1494, 1435, 1396, 1288 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, J = 8.8 Hz, 1H), 7.58 (d, J = 1.4 Hz,

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1H), 7.39 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 1.5 Hz, 1H), 7.26−7.21 (m, 1H), 7.14 (d, J = 8.0 Hz, 1H), 6.40 (s, 1H), 6.32 (s, 1H), 2.46 (s, 3H), 2.16 (s, 2H), 1.52−1.45 (m, 2H), 1.25−1.20 (m, 6H), 0.85 (t, J = 5.9 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9, 141.4, 137.6, 135.8, 135.7, 135.2, 132.2, 131.7, 130.0, 129.7, 127.7, 122.6, 119.1, 117.1, 97.4, 96.5, 32.9, 31.5, 28.8, 27.7, 22.5, 20.1, 14.1 ppm; HRMS (ESI) calcd for $C_{24}H_{25}Cl_2N_2O$ [M + H] 427.1344, found 427.1339.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra and information regarding the X-ray crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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