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Ag-Catalyzed Intramolecular Sequential Vicinal Diamination of Alkynes with Isocyanates: Synthesis of Fused Indole-Cyclic Urea Derivatives

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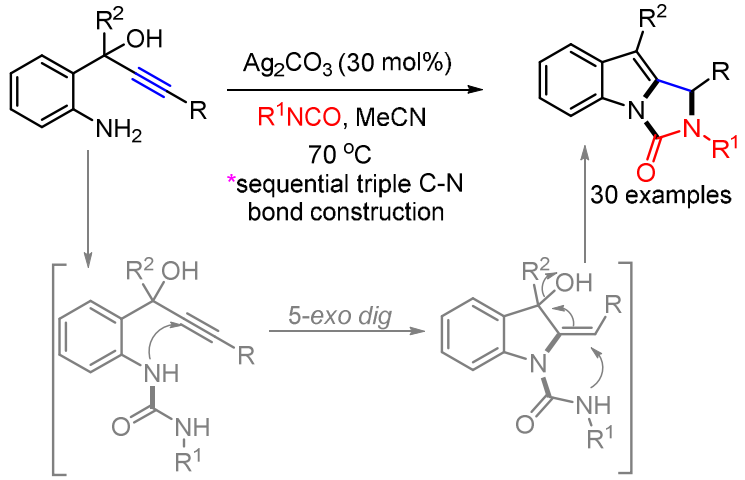
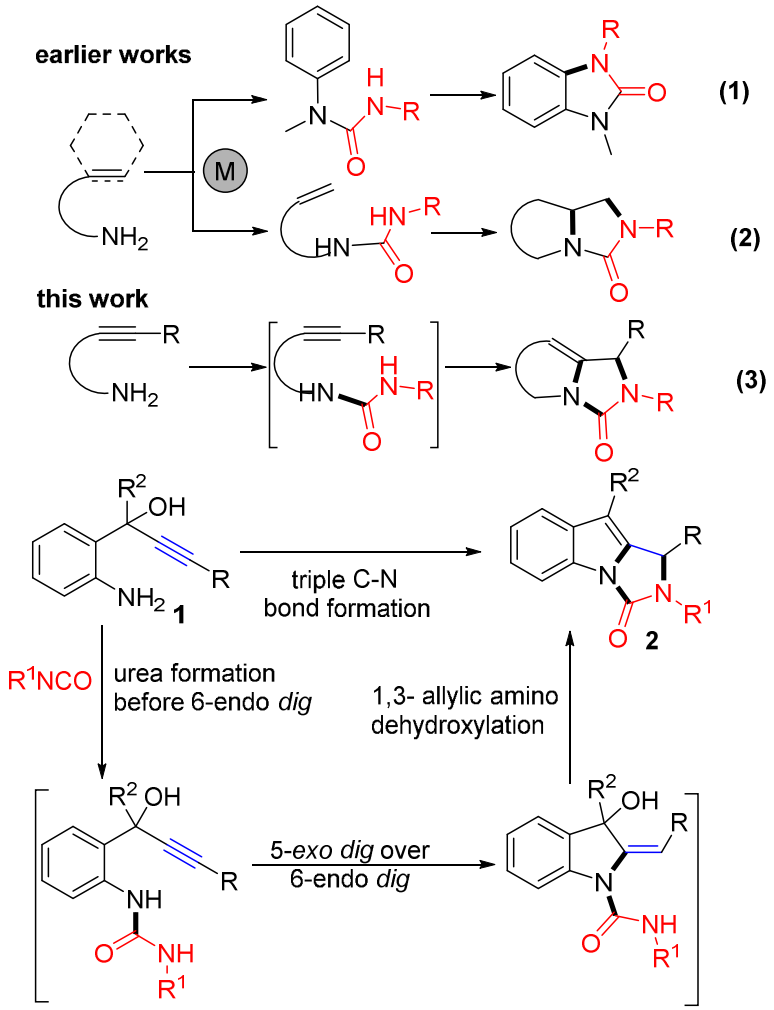


ABSTRACT: A formal intramolecular vicinal 1,2-diamination of alkynes is achieved for the synthesis of indole-cyclic urea fused derivatives through double cyclization process from readily available aminophenyl propargyl alcohols. This sequential triple C-N bond construction event was possible using isocyanate as urea precursor and Ag(I) catalyst as alkyne activating agent.Control experiments reveal that the cyclization followed by 1,3-allylic amino dehydroxylation is preceded by urea formation.

INTRODUCTION

Difunctionalization of alkynes[1-3] is a swift strategy for the rapid construction of a variety of multifunctional frameworks, mainly olefin bearing scaffolds. In this line, intermolecular 1,2-diamination of alkynes[2] was well developed as an outstanding strategy for various important N-heterocycles like imidazoles,[2d] imidazopyridines,[2e] quinoxalines,[2f-h] 3-amidoindoles,[2i] triazoles (click reaction), cyclic urea derivatives, etc. whereas, intramolecular vicinal diamination, which would deliver multicyclic N-heterocycles, is less explored perhaps due to geometric constraints. Nonetheless, few groups (Muñiz *et al.,* Zhu *et al.,* Jin *et al.*, and Du*et al*.,)[3] successfully achieved this diamination of alkynes through internal double nucleophilic addition via Pd and/or Cu catalysis. These studies mainly provided the indole based acenes. On the other hand, the cyclic urea frameworks are privileged structural motifs and are found in a wide range of biologically active and chemically significant molecules.[4-5] Therefore, decorations around cyclic ureas have recently attracted much attention of organic chemists. Chemler *et al*., Muñiz *et al*., Fu *et al*., Youn *et al*., and others[6] reported the intramolecular cyclization of ureas on to tethered olefins or arenes respectively for the synthesis of aryl/cycloalkyl fused urea derivatives (Scheme 1, eqs 1-2). As part of our ongoing program aiming at the discovery of the novel reactivities of alkyne,[7] we herein disclose a complimentary approach featuring intramolecular sequential vicinal diamination for the assembly of imidazo[1,5-a]indol-3-one skeletons (Scheme 1, eq 3). Noteworthy, our process represents the first example of the one-pot urea formation followed by cyclization onto the triple bond for the synthesis of the indole-fused cyclic urea derivatives.

Scheme 1. Synthesis of cyclic ureas.

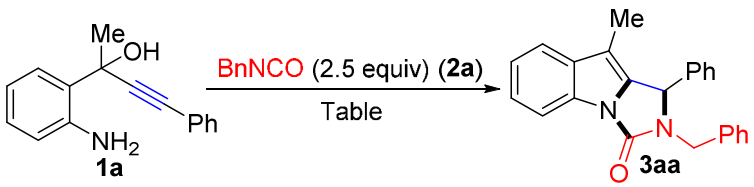


These indole fused cyclic urea motifs were found to be potent CNS depressant agents, analgesics, 5-HT3 receptor antagonists, antifungals, antihypertensive agents and TNF-α (Tumor Necrosis Factor-α) antagonists.[5] The synthesis of these derivatives is thus at a high demand. It was earlier achieved through hydroamination and annulation process with Pd, Cu, Au metal catalysis which required harsh reaction conditions and multiple steps.[8] Herein we are disclosing a mild process for these privileged scaffolds through Ag- catalyzed sequential vicinal diamination of alkynes via bis cyclization form readily available starting materials.

RESULTS AND DISCUSSION

We began our optimization studies using 2-amino phenyl propargylic alcohol **1a** and benzyl isocyanate **2a** as test substrates (Table-1). Initially we used $PdCl_2$ as catalyst and Na_2CO_3 as base in CH_3CN at room temperature (entry 1) no desired product **3aa** was detected. Upon heating the reaction contents to 70 ^oC, pleasingly, the product was obtained but in 10% yield (entry 2). Changing the catalyst to $Pd(OAc)_2$, $Cu(OAc)_2$ or CuI (entries 3-5) did not bring any change in the yield of the desired product (20-40%) but rather led to the formation of corresponding quinoline derivative via 6-*endo dig* cyclization. Next we switched to Ag_2CO_3 as catalyst where the yield was dramatically improved up to 60% (entry 6). We reasoned that this silver catalyst gave enough room for urea formation on amino group of **1a** before it underwent 6-*endo dig* cyclization.

Table 1. Optimization studies.[a]



entry	catalyst	base	solvent	temp (^oC)	yield(%)[b]
1	$PdCl_2$	Na_2CO_3	CH_3CN	RT	N.R
2	$PdCl_2$	Na_2CO_3	CH_3CN	70	10
3	$Pd(OAc)_2$	Na_2CO_3	CH_3CN	70	20
4	$Cu(OAc)_2$	Na_2CO_3	CH_3CN	70	25
5	CuI	Na_2CO_3	CH_3CN	70	40
6	Ag_2CO_3	Na_2CO_3	CH_3CN	70	60
7	**Ag_2CO_3**	--	**CH_3CN**	**70**	**82**
8	AgOAc	--	CH_3CN	70	35
9	Ag_2O	--	CH_3CN	70	20
10	AgOTf	--	CH_3CN	70	15
11	--	--	CH_3CN	70	N.R
12	Ag_2CO_3	--	DMSO	70	20
13	Ag_2CO_3	--	1,4-dioxane	70	30
14	Ag_2CO_3	--	DCE	70	55
15	Ag_2CO_3	--	toluene	70	25
16	Ag_2CO_3	--	THF	70	18
17	Ag_2CO_3	--	DMF	70	N.R

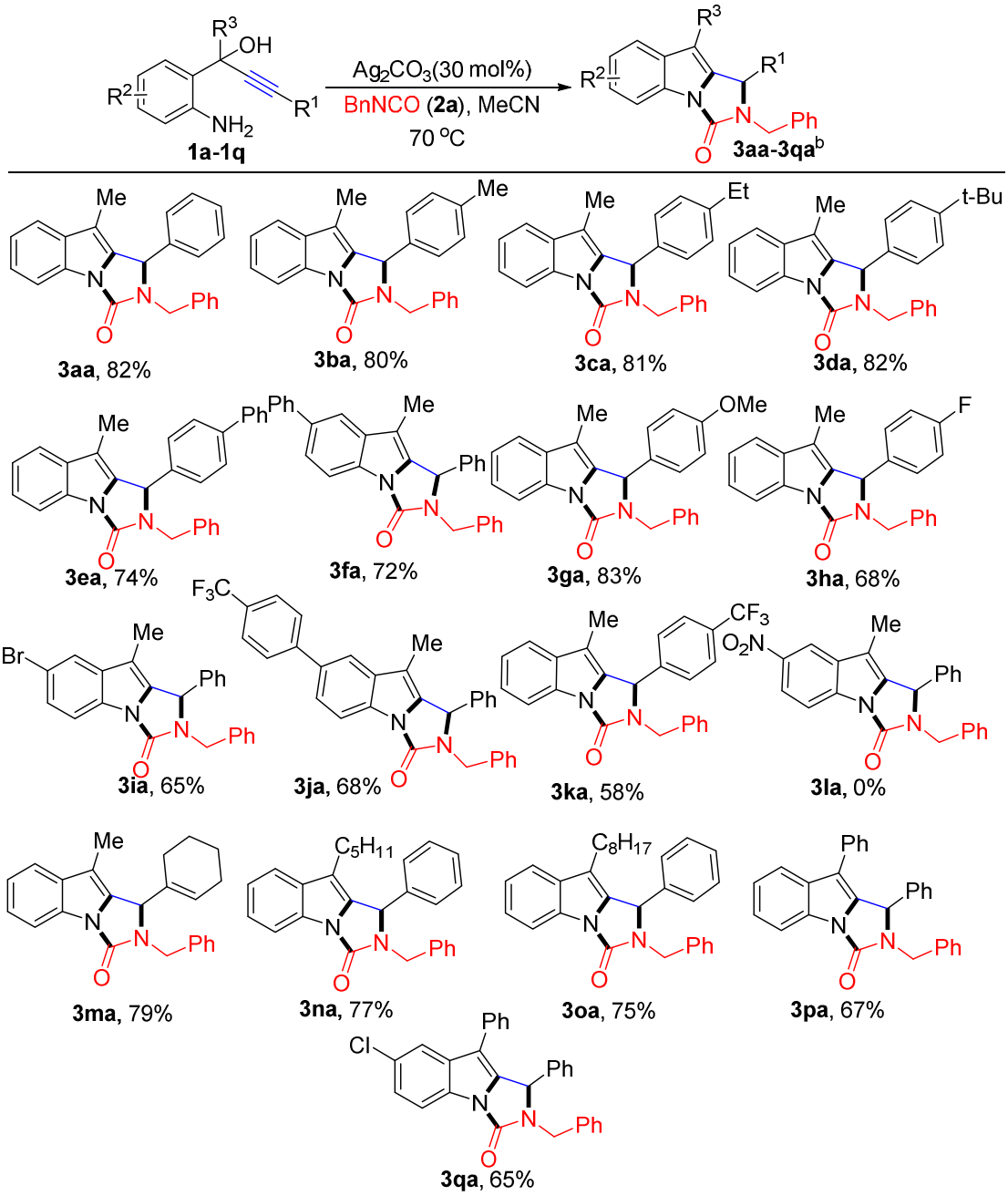
[a]Reaction conditions: **1a** (0.5 mmol), BnNCO (1.25 mmol), base (1 mmol), catalyst (0.15 mmol) in solvent (2.5 mL) at 70 ^oC under air. [b]Isolated yield.

Delightedly, in the absence of the base, the yield was enhanced up to 82% (entry 7). Other Ag salts were not as productive as Ag_2CO_3 (entries 8-10). No desired product was detected in the absence of the metal catalyst (entry 11). MeCN was found to be best solvent over all the tested solvents (entries 12-17).

With the optimized conditions in hand, we next assessed the generality of this double cyclization. We first studied the reaction scope of 2-amino phenyl propargylic alcohols. As is apparent from Table 2, the reaction accommodated substrates with distinct electron properties. Initially, variation of substitution on alkyne terminus of amino propargylic alcohols was studied. Substrates with alkylated phenyl substitution on the alkyne terminal (**1b-d**) led to the desired urea products (**3ba-3da**) with good to excellent yields (80-82%). Similarly, substrates with phenyl substitution either on the phenyl group on alkyne terminus or on core aryl group (**1e-f)** underwent the reaction smoothly to afford the final products **3ea** and **3fa** in 74% and 72% yields respectively. The electronic effect on the phenyl substituted substrates has a perceptible influence on the outcome. Thus the electron-rich methoxy bearing counterpart (**1g**) gave the corresponding adduct **3ga** with high yield (83%) whereas the halo (F and Br) phenyl substrates (**1h-i**) showed slightly decreased activity and thus led to the products with moderate yields (68-65%).

Likewise, electronically slightly deficient CF_3 analogues (**1j-k**) were transformed to the desired adducts **3ja-ka** in moderate yields (62-58%) whereas strongly electron deficient NO_2 tethered substrate **1l** was found to be totally unreactive in this transformation. Here the intramolecular 6-*endo dig* cyclization was found to be faster (to yield quinoline byproduct)

Table 2.Scope of 2-Amino propargylic alcohols.[a]

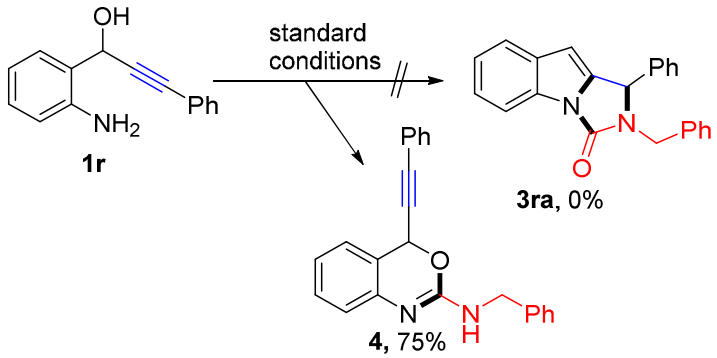


[a]Reaction conditions: 1a (0.5 mmol), BnNCO (1.25 mmol), catalyst (0.15 mmol) in MeCN (2.5 mL) at 70 °C under air. [b]Isolated yield

over probable intermolecular urea formation with isocyanate. Proceeding further, the reaction of the cyclohexenyne **1m** under standard conditions smoothly led to the desired cyclohexenyl substituted indole fused cyclic urea product **3ma** in 79% yield. Finally, we aimed to

synthesize the products with varied substitution at C3 of indole substructure. Thus the substrates **1n-q** having the R^3 substitution other than methyl group (n-pentyl, n-octyl and phenyl) was efficiently converted to the final products in 77−65% yields. However, the alkyl substitution at the alkyne terminus was found to be ineffective for this conversion. In continuation, we aimed to synthesize 3-unsubstituted derivative **3ra** from secondary propargyl alcohol **1r**. Surprisingly, the reaction under standard conditions led to oxy cyclicoxazine amine derivative **4** in 75% yield probably through urea formation followed by benzylic/propargyl hydroxyl elimination and urea cyclization (Scheme 2).

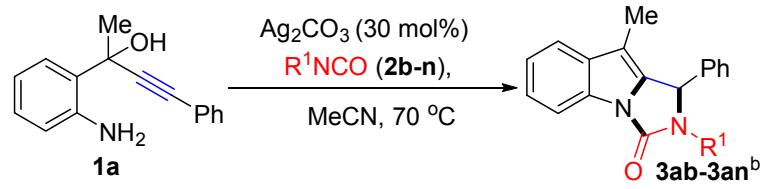
Scheme 2. Benzo-[d][1,3]oxazin-2-amine transformation from 1r.

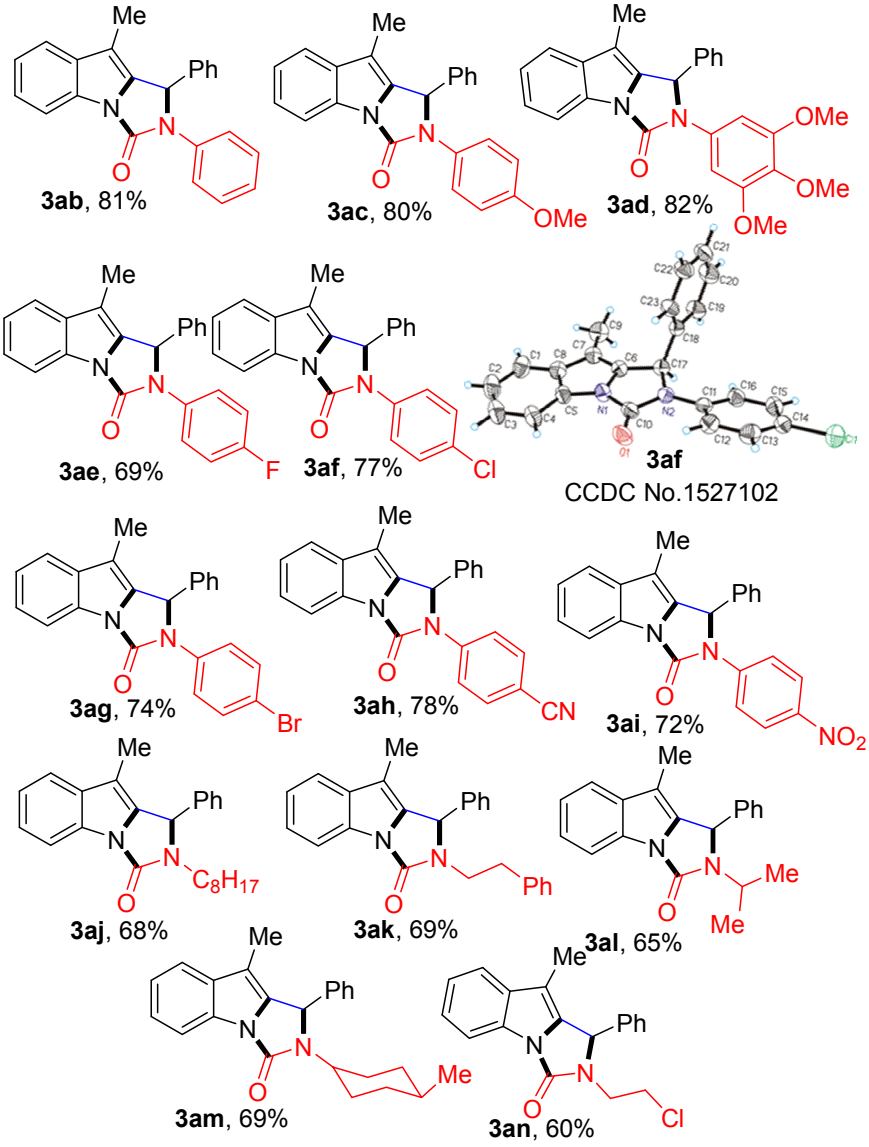


We reason that the trajectory required for the desired cyclization, i.e. 5-*exo dig* cyclization, is developed only in tertiary propargyl alcohols perhaps due to Thorpe Ingold effect. In case of **1r**, no intended 5-exo dig cyclization occurred because of the wide angle between the reaction centres which might have led to the slow elimination of the benzylic/propargylic group followed by cyclization of urea oxygen on the resultant benzylic/proaprgylic carbocation.

Moving further, the scope of the double cyclization for indole-urea derivatives was further investigated with respect to isocyanates (Table 3). A wide range of arylisocyanates including alkyl and aryl groups with varied substitution were thus employed in the reaction. Initially,

Table 3. Scope of Isocyantes.[a]





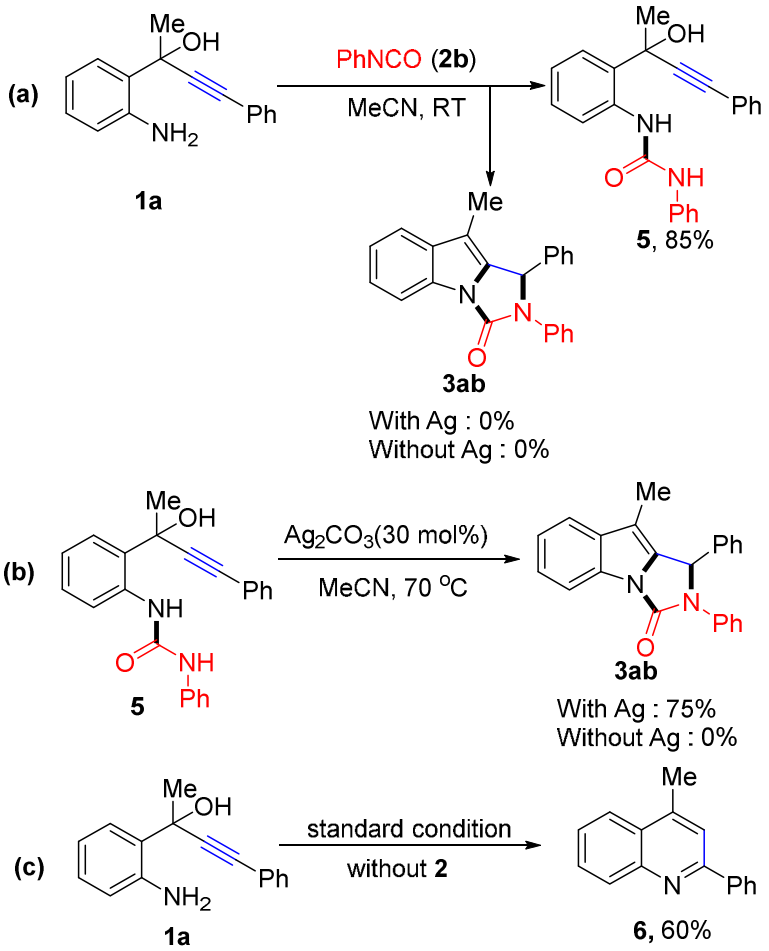
[a]Reaction conditions: **1a** (0.5 mmol), **2** (1.25 mmol), catalyst (0.15 mmol) in solvent (2.5 mL) at 70 °C under air. [b]Isolated yield

the electronically neutral and rich substrates (with single to multiple alkoxy groups) **2b-d** were tested under standard reaction conditions which all pleasingly afforded the desired products (**3ab-ad**) in excellent yields (80−82%).

The halo groups (F, Cl, and Br) as in case of **2e-f** survived well in the reaction to deliver the corresponding adducts **3ae-af** in 77-69% yields. The electron deficient CN and NO_2 tethered aryl isocyanates **2h-i** was well tolerated under standard conditions to produce the expected adducts in 69-78% yields. The structure of **3af** was unambiguously confirmed by X-ray crystallography. Further expanding the scope of the reaction, we aimed to synthesize the products with alkyl substitution on nitrogen. Thus the aliphatic isocyanates **2j-m**, irrespective of linear, branched or cyclic substitution, were cleanly transformed to the anticipated adducts **3aj**-**3am** in 69-65% yields. Pleasingly, sensitive chloroethyl group of **2n** survived successfully through the optimized conditions and afforded **3an** in 60% yield.

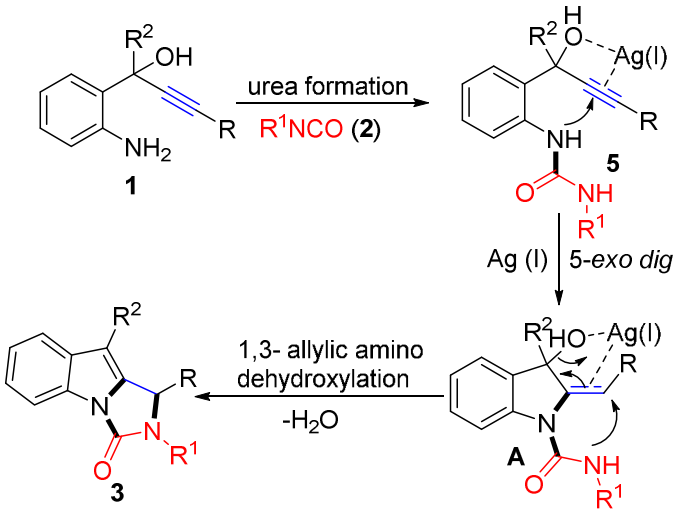
To probe the mechanism, we conducted some control experiments as shown in Scheme 3. When we conducted a reaction at room temperature in the absence of the catalyst Ag_2CO_3, urea derivative **5** was formed as a sole product. Heating the reaction contents to 70 ^oC, however, did not lead to the desired product. This urea derivative **5** under the standard conditions cleanly converted to the final double cyclized product, suggesting that the catalyst free intermolecular urea formation is the initiating step. Surprisingly, under absence of isocyanate from the optimized conditions, **1a** led to 6-*endo dig* cyclization to form quinoline derivative demonstrating that the urea formation prior to the cyclization turned the atmosphere towards 5-*exo dig* cyclization.

Scheme 3. Control experiments.



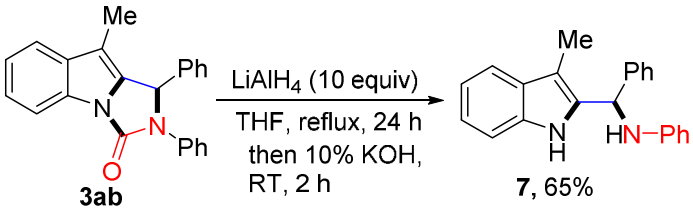
On the basis of these observations and previous reports,[9] a plausible reaction mechanism was proposed as shown in Scheme 4. Initially 2-amino phenyl propargylic alcohol **1** was reacted with isocyanate **2** to give urea intermediate **5** which on Ag-catalyzed 5-*exo dig* cyclization led to the intermediate **A**. 1,3-aminative dehydroxylation of **A**, driven by aromatization, revealed the end cyclic urea adduct.

Scheme 4. Proposed reaction mechanism.



To expand the use of this protocol, we embarked on to derivatize these adducts. We first attempted to reduce and disengage the cyclic urea to get indoloimidazolidine and indolyl methyl amine (Scheme 5) respectively. Thus we treated **3ab** with 10 equivalents of $LiAlH_4$ in refluxing THF.[10] Surprisingly, this directly produced the demethylative adduct **7** in 65% yield. This 2-(aminomethyl)-indole scaffolds represents the key structures that exist in several indole alkaloids as well as biologically active synthetic compounds.[11] Efforts (by varying temperature of the reaction and equivalents of $LiAlH_4$) on controlled reduction of **3ab** towards indoloimidazolidine were not successful.

Scheme 5.Reductive cleavage of cyclic urea of 3ab.



CONCLUSIONS

In summary, we have demonstrated a general and straightforward approach for the synthesis of indole fused cyclic urea derivatives from readily available 2-amino phenyl propargylic alcohols. This one-pot triple C-N bond construction event was possible using isocyanate as urea surrogate and Ag(I) catalyst as alkyne activating agent. The proposed reaction mechanism proceeds likely via urea formation followed by unprecedented sequential vicinal diamination of alkyne through double cyclization. This new and simple one-pot protocol features high functional group tolerance along with excellent productivity which makes it an easy access to the synthesis of highly privileged motifs.

EXPERIMENTAL SECTION

General Information

All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 400 or 500 MHz spectrometer for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$ for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using QTof mass spectrometer. Column chromatography was performed with silica gel (100–200 mesh) as the stationary phase. All reactions were monitored by using TLC. The characterization of compounds was further established by using HRMS.

Starting Materials **1** Were Prepared in One Step Following the Literature Procedures. [12,7d]

General Procedure A for the Synthesis of 1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-ones (3aa-3qa) from (1a-1q) taking Synthesis of 3aa as an example:

To a stirred solution of **1a** (120 mg, 0.5 mmol, 1 eq) in 2.5 mL of CH_3CN was added N-benzyl isocyanate (**2a**) (166 mg, 1.25 mmol, 2.5 eq) and Ag_2CO_3 (41 mg, 0.15 mmol, 0.3 eq) at room temperature. The reaction mixture was stirred at 70 ^oC until complete conversion of starting material (12h for **3aa-3da**, 10h for **3ea-3fa**, 14h for **3ga-3ka**, 16h for **3ma-3qa** 18h for **3ab-3nd**, 20h for **3ae-3ai** 22h for **3aj-3an**). The reaction mixture was diluted with EtOAc and filtered through short celit pad. The filtrate was diluted with water and extracted with EtOAc. Combined extracts were washed with brine (10 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the crude material was purified on silica gel using 10% EtOAc/hexane to get **3aa** (146 mg, 82%) as off white solid.

2-Benzyl-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3aa):mp 111-1113 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.9 Hz, 1H), 7.41-7.36 (m, 3H), 7.36-7.29 (m, 4H), 7.27-7.19 (m, 5H), 5.33 (s, 1H), 5.15 (d, J = 15.1 Hz, 1H), 3.74 (d, J = 15.1 Hz, 1H), 1.89 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 136.4, 135.7, 134.6, 133.9, 130.4, 129.1, 129.0, 128.8, 128.4, 128.1, 127.8, 123.3, 122.1, 118.9,112.6, 107.3, 58.4, 44.5, 7.8; DEPT90 (100 MHz, $CDCl_3$) δ 129.1, 129.0, 128.8, 128.4, 128.1, 127.8, 123.3, 122.1, 118.9, 112.6, 58.4; DEPT135 (100 MHz, $CDCl_3$) δ 129.1, 129.0, 128.8, 128.4, 128.1, 127.8, 123.3, 122.1, 118.9, 112.6, 58.4, 44.5 (-ve), 7.8; IR (KBr) v 3400, 2403, 1567, 1385, 1030, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{21}N_2O$ $[M + H]^+$ 353.1654, found 353.1664.

2-Benzyl-9-methyl-1-(*p*-tolyl)-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ba): 3ba (0.147 g) was obtained from **1b** (0.126 g, 0.5 mmol) following general procedure **A**. Yield 80%; white solid, mp 141-143 ^oC; R_f = 0.50 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.37-7.28 (m, 4H), 7.27-7.22 (m, 3H), 7.19 (d, J = 7.9 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 5.30 (s, 1H), 5.14 (d, J = 15.2 Hz, 1H), 3.73 (d, J = 15.2 Hz, 1H), 2.38 (s, 3H), 1.89 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 152.0,138.9, 136.5, 134.7,133.9, 132.5, 130.4, 129.8, 128.8, 128.4, 128.0, 127.8, 123.2, 122.0, 118.9, 112.5, 107.12, 58.2, 44.4, 21.2, 7.9; IR (KBr) v 3686, 3401, 1727, 1478, 1456, 1310, 929, 627 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{23}N_2O[M + H]^+$ 367.1810, found 367.1815.

2-Benzyl-1-(4-ethylphenyl)-9-methyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ca): **3ca** (0.154 g) was obtained from **1c** (0.133 g, 0.5 mmol) following general procedure **A**. Yield 81%; off white solid, mp 118-120 ^oC; R_f = 0.50 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.37-7.30 (m, 4H), 7.29-7.20 (m, 5H), 7.13 (d, J = 7.9 Hz, 2H), 5.33 (s, 1H), 5.15 (d, J = 15.2 Hz, 1H), 3.77 (d, J = 15.2 Hz, 1H), 2.70 (q, J = 7.5 Hz, 3H), 1.92 (d, J = 1.4 Hz, 3H), 1.28 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 145.2, 136.5, 134.8, 133.9, 132.7, 130.4, 128.8, 128.5, 128.4, 128.0, 127.7, 123.2, 122.0, 118.9, 112.5, 107.1, 58.2, 44.4, 28.5, 15.3, 7.9; IR (KBr) v 3401, 2400, 1567, 1385, 1029, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$ 381.1967, found 381.1970.

2-Benzyl-1-(4-(*tert*-butyl)phenyl)-9-methyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3da): **3da** (0.168 g) was obtained from **1d** (0.147 g, 0.5 mmol) following general procedure **A**. Yield 82%; off white solid, mp 117-119 ^oC; R_f= 0.40 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.40-7.36 (m, 4H), 7.28-7.18 (m, 3H), 7.12 (d, J = 7.2 Hz, 2H), 5.32 (s, 1H), 5.12 (d, J = 15.2 Hz, 1H), 3.79 (d, J = 15.2 Hz, 1H), 1.90 (d, J = 1.4 Hz, 3H), 1.33 (s,9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 152.0, 136.6, 134.7, 134.0, 132.4, 130.4, 128.7, 128.4, 127.7, 125.9, 123.2, 122.0, 118.9, 112.5, 107.1, 58.2, 44.5, 34.7, 31.7, 7.9; IR (KBr) v 3426, 2401, 1309, 1021, 625 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{28}H_{29}N_2O$ $[M + H]^+$ 409.2280, found 409.2285.

1-([1,1'-Biphenyl]-4-yl)-2-benzyl-9-methyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ea): 3ea (0.158 g) was obtained from **1e** (0.157 g, 0.5 mmol) following general procedure A. Yield 74%; pale brown solid, mp 189-191 ^{o}C; R_f = 0.45 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 1H), 7.66-7.58 (m, 4H), 7.53-7.42 (m, 3H), 7.40-7.29 (m, 5H), 7.28-7.26 (m, 5H), 5.38 (s, 1H), 5.17 (d, J = 15.2 Hz, 1H), 3.81 (d, J = 15.2 Hz, 1H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 141.9, 140.2, 136.4, 134.6, 134.5, 134.0, 130.4, 128.9, 128.5, 128.5, 127.8, 127.7, 127.1, 123.4, 122.2, 119.0, 112.6, 107.45, 58.2, 44.6, 8.0; IR (KBr) v3401, 3019, 2400, 1601, 1524, 1383, 1023, 929, 627 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{30}H_{25}N_2O$ $[M + H]^+$429.1967, found 429.1972.

2-Benzyl-9-methyl-1,7-diphenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3fa): 3fa (0.154 g) was obtained from **1f** (0.157 g, 0.5 mmol) following general procedure **A**. Yield 72%; off white solid, mp 140-142 ^{o}C; R_f = 0.55 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 1H), 7.69-7.62 (m, 3H), 7.59 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.48-7.44 (m, 2H), 7.42-7.37 (m, 2H), 7.37-7.30 (m, 4H), 7.26-7.20 (m, 4H), 5.35 (s, 1H), 5.16 (d, J = 15.2 Hz, 1H), 3.75 (d, J = 15.2 Hz, 1H), 1.92 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 142.1, 136.4, 135.9, 135.7, 135.3, 134.6, 129.9, 129.2, 128.9, 128.8, 128.5, 128.2, 128.0, 127.5, 126.8, 123.1, 117.7, 112.8, 107.7, 58.6, 44.7, 8.0; IR (KBr) v3401, 3019, 2400, 1730, 1603, 1026, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{30}H_{24}N_2O$ $[M + H]^+$429.1967, found 429.1976.

2-Benzyl-1-(4-methoxyphenyl)-9-methyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ga): 3ga (0.159 g) was obtained from **1g**(0.134 g, 0.5 mmol) following general procedure **A**. Yield 83%; white solid, mp 130-132 ^{o}C; R_f = 0.45 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.38-7.28 (m, 4H), 7.26-7.20 (m, 3H), 7.11 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 5.29 (s, 1H), 5.12 (d, J = 15.1 Hz, 1H), 3.82 (s, 3H), 3.72 (d, J = 15.1 Hz, 1H), 1.88 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 160.1, 151.9, 136.5, 134.8, 134.0, 130.4, 129.4, 128.8, 128.4, 127.8, 127.4, 123.2, 122.1, 118.9, 114.4, 112.6, 107.1, 57.9, 55.3, 44.4, 7.9; IR (KBr) ν 3403, 2401, 1387, 1030, 928, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{23}N_2O_2$ $[M + H]^+$ 383.1760, found 383.1751.

2-Benzyl-1-(4-fluorophenyl)-9-methyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ha): 3ha (0.126 g) was obtained from **1h** (0.128 g, 0.5 mmol) following general procedure **A**. Yield 68%; pale yellow gum; R_f = 0.50 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.37-7.29 (m, 4H), 7.29-7.20 (m, 3H), 7.20-7.15 (m, 2H), 7.11-7.03 (m, 2H), 5.32 (s, 1H), 5.13 (d, J = 15.2 Hz, 1H), 3.74 (d, J = 15.2 Hz, 1H), 1.89 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (d, J = 248.8 Hz), 151.9, 136.2, 134.1 (d, J = 40.5 Hz), 131.5 (d, J = 3.2 Hz), 130.4, 129.8 (d, J = 8.4 Hz), 128.8, 128.3, 127.9, 123.5, 122.2, 119.0, 116.2, 116.0, 112.6, 107.4, 57.7, 44.6, 7.9; IR (neat) ν 3429, 2400, 1606, 1415, 1021, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{20}FN_2O$ $[M + H]^+$ 371.1560, found 371.1568.

2-Benzyl-7-bromo-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ia): 3ia (0.141 g) was obtained from **1i** (0.158 g, 0.5 mmol) following general procedure **A**. Yield 65%; yellow solid, mp 148-150 ^{o}C; R_f = 0.35 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.6 Hz, 1H), 7.62-7.56 (m, 1H), 7.43-7.38 (m, 4H), 7.37-7.30 (m, 4H), 7.25-7.17 (m, 4H), 5.33 (s, 1H), 5.13 (d, J = 15.2 Hz, 1H), 3.73 (d, J = 15.2 Hz, 1H), 1.84 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 136.2, 135.9, 135.7, 135.3, 129.3, 129.0, 128.9, 128.5, 128.1, 128.0, 126.2, 121.9, 115.5, 113.9, 106.8, 58.6, 44.7 7.8; IR (KBr) ν3401, 3019, 2399, 1522, 1384, 1023, 627 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{20}BrN_2O$ $[M + H]^+$431.0759, found 431.0750.

2-Benzyl-9-methyl-1-phenyl-7-(4-(trifluoromethyl)phenyl)-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ja): 3ja (0.169 g) was obtained from **1j** (0.190 g, 0.5 mmol) following

general procedure **A**. Yield 68%; light yellow solid, mp 152-154 ^{o}C; R_f = 0.45 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.4 Hz, 1H), 7.77-7.73 (m, 2H), 7.72-7.59 (m, 3H), 7.58 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.42-7.38 (m, 3H), 7.37-7.31 (m, 3H), 7.27-7.19 (m, 4H), 5.36 (d, J = 0.9 Hz, 1H), 5.16 (d, J = 15.1 Hz, 1H), 3.76 (d, J = 15.1 Hz, 1H), 1.92 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.9, 140.0, 15.9, 133.7 (d, J = 26.9 Hz), 131.3 (d, J = 32.8 Hz), 130.4, 129.3, 128.9, 128.7, 128.4, 128.3, 128.2, 128.0, 127.8, 126.1, 126.1, 125.1, 123.7, 122.3, 119.7, 119.1, 112.6, 107.7, 57.9, 44.8, 7.9; IR (KBr) v 3401, 2400, 1385, 929, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{31}H_{24}F_3N_2O$ $[M + H]^+$ 497.1841, found 497.1834.

2-Benzyl-9-methyl-1-(4-(trifluoromethyl)phenyl)-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ka): 3ka (0.123 g) was obtained from **1k** (0.153 g, 0.5 mmol) following general procedure **A**. Yield 58%; light brown solid; mp 138-140 ^{o}C; R_f = 0.55 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.38-7.31 (m, 6H), 7.36-7.26 (m, 1H), 7.23-7.19 (m, 2H), 5.38 (d, J = 1.0 Hz, 1H), 5.16 (d, J = 15.2 Hz, 1H), 3.65 (d, J = 15.2 Hz, 1H), 1.88 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 145.5, 136.2, 135.5 (d, J = 13.7 Hz), 134.4 (d, J = 37.7 Hz), 130.2, 129.2, 128.8, 128.6, 128.4, 128.1, 127.9, 127.6, 125.6, 125.6, 125.5, 122.9, 117.8, 112.9, 107.6, 58.5, 44.6, 7.9; IR (KBr) v 3402, 2401, 1730, 1416, 1325, 1020, 928, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{20}F_3N_2O$ $[M + H]^+$ 421.1528, found 421.1524.

2-Benzyl-1-(cyclohex-1-en-1-yl)-9-methyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ma):3ma (0.142 g) was obtained from **1m** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 79%; off white solid, mp 132-134 ^{o}C; R_f = 0.55 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.34-7.31 (m, 4H), 7.31-7.26 (m, 2H), 7.26-7.21 (m, 1H), 5.98-5.91 (m, 1H), 4.96

(d, J = 15.0 Hz, 1H), 4.84 (s, 1H), 4.08 (d, J = 15.0 Hz, 1H), 2.18-2.12 (m, 2H), 2.12 (d, J = 1.4 Hz, 3H), 1.66-1.58 (m, 2H), 1.56-1.42 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 136.9, 133.9, 132.7, 132.4, 130.5, 130.4, 128.6, 128.5, 127.6, 123.0, 121.9, 118.7, 112.4, 107.0, 61.9, 44.7, 25.4, 22.5, 22.3, 22.1, 7.7; IR (KBr) v 3684, 3020, 2926, 2401, 1725, 1455, 1076, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{25}N_2O$ $[M + H]^+$ 357.1967 found 357.1973.

2-Benzyl-9-pentyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3na): 3na (0.157 g) was obtained from **1n** (0.147 g, 0.5 mmol) following general procedure **A**. Yield 77%; off white solid, mp 123-125 ^{o}C; R_f = 0.40 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.39-7.29 (m, 7H), 7.26-7.21 (m, 3H), 7.21-7.17 (m, 2H), 5.30 (m, 1H), 5.14 (d, J = 15.2 Hz, 1H), 3.73 (d, J = 15.2 Hz, 1H), 2.40-2.24 (m, 2H), 1.34-1.25 (m, 1H), 1.20-1.04 (m, 3H), 1.02-0.93 (m, 2H), 0.71 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 136.3, 136.2, 134.5, 133.3, 130.4, 129.1, 128.8, 128.4, 128.1, 127.8, 123.2, 122.0, 119.3, 112.6, 112.5, 58.7, 44.5, 31.5, 29.0, 23.6, 22.2, 13.9; IR (KBr) v3401, 3019, 2399, 1522, 1216, 1070, 928, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{28}H_{29}N_2O$ $[M + H]^+$ 409.2280, found 409.2268.

2-Benzyl-9-octyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3oa): 3oa (0.169 g) was obtained from **1o** (0.168 g, 0.5 mmol) following general procedure **A**. Yield 75%; pale yellow gum; R_f = 0.40 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.39-7.36 (m, 3H), 7.35-7.29 (m, 4H), 7.26-7.21 (m, 3H), 7.21-7.17 (m, 2H), 5.30 (m, 1H), 5.15 (d, J = 15.2 Hz, 1H), 3.73 (d, J = 15.2 Hz, 1H), 2.40-2.24 (m, 2H), 1.33-1.19 (m, 3H), 1.19-0.96 (m, 9H), 0.85 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 136.4, 136.2, 134.5, 133.4, 130.4, 129.1, 128.8, 128.4, 128.1, 127.8, 123.2, 122.0, 119.3, 112.6, 112.5, 58.7, 44.6, 31.8, 29.3, 29.3, 29.2, 29.1, 23.6, 22.6, 14.0; IR (neat) v 3401, 3019, 2400, 1650, 1385, 1069, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{31}H_{35}N_2O$ $[M + H]^+$ 451.2749, found 451.2732.

2-Benzyl-1,9-diphenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3pa): 3pa (0.140 g) was obtained from **1p** (0.150 g, 0.5 mmol) following general procedure **A**. Yield 67%; light yellow solid, mp 153-155 ^{o}C; R_f = 0.50 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.46-7.34 (m, 4H), 7.34-7.28 (m, 4H), 7.27-7.10 (m, 9H), 5.44 (s, 1H), 5.18 (d, J = 15.2 Hz, 1H), 3.72 (d, J = 15.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 136.4, 136.3, 135.1, 132.6, 132.0, 130.9, 129.3, 129.2, 129.0, 128.6, 128.5, 128.4, 128.0, 126.8, 124.0, 123.0, 120.3, 113.9, 113.0, 59.3, 44.7; IR (KBr) v 3401, 3019, 2400, 1380, 1023, 929, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{29}H_{23}N_2O$ $[M + H]^+$415.1810, found 415.1813.

2-Benzyl-7-chloro-1,9-diphenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3qa): 3qa (0.147 g) was obtained from **1q** (0.167 g, 0.5 mmol) following general procedure **A**. Yield 65%; light brown solid, mp 143-145 ^{o}C; R_f = 0.40 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 1.4 Hz, 1H), 7.39-7.29 (m, 7H), 7.25-7.12 (m, 7H), 7.09-7.00 (m, 2H), 5.42 (s, 1H), 5.15 (d, J = 15.2 Hz, 1H), 3.71 (d, J = 15.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 136.2, 136.0, 136.0, 133.1, 131.8, 129.4, 129.2, 129.0, 128.8, 128.6, 128.5, 128.4, 128.4, 128.1, 127.9, 127.1, 124.2, 120.0, 113.8, 113.5, 59.3, 44.7; IR (KBr) v 3401, 3019, 2399, 1522, 1384, 1023, 627 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{29}H_{22}ClN_2O[M + H]^+$449.1421, found 449.1411.

N-Benzyl-4-(phenylethynyl)-4*H*-benzo[*d*][1,3]oxazin-2-amine (4): 4 (0.128 g) was obtained from **1r** (0.112 g, 0.5 mmol) following general procedure **A**. Yield 75%; light yellow solid, mp 105-107 ^{o}C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (bs, 1H), 7.60 (d, J = 8.2 Hz, 1H), 7.52-7.49 (m, 3H), 7.46-7.41 (m, 1H), 7.40-7.31 (m, 7H), 7.30-7.26 (m, 2H), 6.18 (s, 1H), 4.66-4.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 151.8, 137.6, 134.1, 132.1, 129.5, 129.4, 128.7, 128.4, 127.6, 127.6, 125.8, 125.4, 125.4, 124.4, 122.7, 121.0, 90.5, 81.0, 69.3, 44.8; DEPT-135 (100 MHz, $CDCl_3$) δ

132.1, 129.5, 129.4, 128.7, 128.4, 127.6, 127.6, 125.8, 124.4, 122.7, 69.3, 44.8 (-ve); IR (KBr) *v* 3400, 3019, 2401, 1651, 1385, 1069, 929, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{19}N_2O$ $[M + H]^+$ 339.1497, found 339.1490.

9-Methyl-1,2-diphenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ab): 3ab (0.138 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 81%; white solid, mp 156-158 ^oC; R_f = 0.40 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.0 Hz, 1H), 7.52-7.48 (m, 3H), 7.38-7.27 (m, 9H), 7.12-7.07 (m, 1H), 6.14 (d, J = 1.3 Hz, 1H), 2.00 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 137.2, 136.4, 134.2, 133.3, 130.4, 129.1, 128.9, 128.7, 127.3, 124.9, 123.5, 122.5, 122.0, 119.0, 112.8, 107.3, 60.9, 7.9; IR (KBr) *v* 3401, 2400, 1567, 1384, 1066, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{19}N_2O$ $[M + H]^+$ 339.1497, found 339.1499.

2-(4-Methoxyphenyl)-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ac): 3ac (0.147 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 80%; light brown solid, mp 140-142 ^oC; R_f = 0.45 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.9 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.38-7.34 (m, 1H), 7.33-7.25 (m, 8H), 6.82 (d, J = 8.8 Hz, 2H), 6.02 (m, 1H), 3.75 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 150.9, 136.6, 134.2, 133.7, 130.6, 130.0, 129.1, 128.9, 127.7, 125.1, 123.6, 122.5, 119.1, 114.4, 112.9, 107.4, 61.9, 55.5, 8.0; IR (KBr) *v* 3402, 3021, 2927, 2401, 1733, 1022, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{21}N_2O_2$ $[M + H]^+$369.1603, found 369.1600.

9-Methyl-1-phenyl-2-(3,4,5-trimethoxyphenyl)-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ad): 3ad (0.176 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 82%; white solid, mp 169-171 ^oC; R_f = 0.35 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.7

Hz, 1H), 7.35-7.31 (m, 5H), 7.30-7.26 (m, 1H), 6.70 (m, 2H), 6.03 (d, J = 1.3 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 6H), 1.98 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 150.6, 136.7, 135.4, 133.2, 133.1, 130.4, 129.1, 128.9, 127.4, 123.6, 122.6, 119.1, 112.7, 107.4, 100.3, 61.7, 60.8, 56.0, 7.9; IR (KBr) v 3401, 2400, 1514, 1384, 1022, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{25}N_2O_4$ $[M + H]^+$ 429.1814, found 429.1807.

2-(4-Fluorophenyl)-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ae): **3ae** (0.123 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A.** Yield 69%; pale yellow solid; mp 130-132 ^{o}C; R_f = 0.55 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.43-7.37 (m, 2H), 7.36-7.26 (m, 7H), 7.03-6.94 (m, 2H), 6.07 (s, 1H), 1.99 (d, J = 1.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (d, J = 245.3 Hz), 150.6, 136.4, 134.3, 133.3, 133.2 (d, J = 2.7 Hz), 130.5, 129.2, 129.0, 127.5, 124.5 (d, J = 8.1 Hz), 123.7, 122.7, 119.2, 115.9 (d, J = 23.0 Hz), 112.9, 107.6, 61.5, 8.0; IR (KBr) v3401, 3019, 2400, 1513, 1024, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{18}FN_2O$ $[M + H]^+$357.1403, found 357.1404.

2-(4-Chlorophenyl)-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3af): **3af** (0.144 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 77%; light brown solid, mp 189-191 ^{o}C; R_f = 0.50 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 1H), 7.51-7.41 (m, 3H), 7.38-7.28 (m, 6H), 7.28-7.21 (m, 3H), 6.07 (d, J = 0.9 Hz, 1H), 1.98 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 136.1, 136.0, 134.3, 133.0, 130.5, 130.1, 129.3, 129.1, 129.1, 129.0, 127.3, 123.8, 122.9, 122.8, 119.2, 112.9, 107.7, 60.9, 7.9; IR (KBr) v 3430, 2406, 1506, 1415, 1028, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{18}ClN_2O$ $[M + H]^+$ 373.1108, found 373.1112.

2-(4-Bromophenyl)-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ag): **3ag** (0.154 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**.

Yield 74%; off white solid, mp 219-221 °C; R_f = 0.55 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.9 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.42-7.37 (m, 4H), 7.36-7.26 (m, 1H), 6.08 (d, J = 1.0 Hz, 1H), 1.99 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 136.5, 136.1, 134.3, 133.0, 132.0, 130.5, 129.3, 129.0, 127.3, 123.8, 123.1, 122.8, 119.2, 117.8, 112.9, 107.7, 60.8, 7.9; IR (KBr) ν 3401, 2400, 1650, 1509, 1385, 1083, 909, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{18}BrN_2O$ $[M + H]^+$ 417.0603, found 417.0608.

4-(9-Methyl-3-oxo-1-phenyl-1*H*-imidazo[1,5-*a*]indol-2(3*H*)-yl)benzonitrile (3ah): 3ah (0.142 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 78%; pale yellow solid, mp 213-215 °C; R_f = 0.40 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H),7.93-7.89 (m, 1H), 7.81-7.74 (m, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.40-7.25 (m, 9H), 6.09 (d, J = 1.4 Hz, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 138.4, 135.6, 134.3, 132.4, 130.3, 129.8, 129.4, 129.2, 127.7, 127.0, 124.9, 123.9, 123.9, 123.0, 119.2, 118.3, 113.1, 112.9, 108.1, 60.5, 7.8; IR (KBr) ν 3401, 2400, 1738, 1579, 1215, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{18}N_3O$ $[M + H]^+$ 364.1450, found 364.1458.

9-Methyl-2-(4-nitrophenyl)-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ai): 3ai (0.139 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 72%; yellow solid, mp 205-207 °C; R_f = 0.45 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 9.0 Hz, 2H), 8.07 (d, J = 7.7 Hz, 1H), 7.80 (d, J = 9.0 Hz, 2H), 7.48 (d, J = 7.7 Hz, 1H), 7.41-7.28 (m, 7H), 6.22 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 143.5, 143.2, 135.6, 134.4, 132.0, 130.3, 129.5, 129.2, 126.7, 124.7, 124.0, 123.2, 119.5, 119.3, 112.9, 108.2, 60.6, 7.8; IR (KBr) ν 3401, 2400, 1335, 1065, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{18}N_3O_3$ $[M + H]^+$ 384.1348, found 384.1342.

9-Methyl-2-octyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3aj): 3aj (0.127 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 68% colourless oil; R_f = 0.60 (SiO_2, 5% EtOAc/hexanes);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-7.99 (m, 1H), 7.49-7.45 (m, 1H), 7.40-7.35 (m, 3H), 7.34-7.21 (m, 4H), 5.53 (s, 1H), 3.74-3.59 (m, 1H), 2.96-2.81 (m, 1H), 1.94 (d, J = 2.4 Hz, 3H), 1.32-1.19 (m, 12H), 0.89-0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 136.2, 134.8, 133.9, 130.4, 129.1, 129.0, 127.9, 123.2, 122.0, 118.9, 112.5, 106.9, 59.5, 41.1, 31.8, 29.2, 29.1, 27.9, 26.7, 22.6, 14.1, 7.9; IR (neat) v 3401, 3019, 2399, 1522, 1216, 928, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{30}N_2O$ [M + H]$^+$375.2436, found 375.2435.

9-Methyl-2-phenethyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3ak): 3ak (0.126 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 69%; yellow solid, mp 139-141 ^{o}C; R_f = 0.65 (SiO_2, 10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.40-7.36 (m, 3H), 7.35-7.23 (m, 5H), 7.20-7.14 (m, 4H), 5.27 (d, J = 1.1 Hz, 1H), 4.00-3.89 (m, 1H), 3.19-3.08 (m, 1H), 3.02-2.93 (m, 1H), 2.85-2.74 (m, 1H), 1.90 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 138.6, 135.9, 134.7, 133.9, 130.5, 129.1, 128.8, 128.6, 128.0, 126.6, 123.2, 122.0, 118.9, 112.5, 107.0, 60.0, 42.6, 34.6, 7.9; IR (KBr) v 3402, 2400, 1646, 1568, 1217, 771, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{23}N_2O$ [M + H]$^+$ 367.1810, found 367.1806.

2-Isopropyl-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3al): 3al (0.99 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 65%; light yellow solid, mp 129-131 ^{o}C; R_f = 0.60 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.37-7.28 (m, 6H), 7.25-7.20 (m, 1H), 5.56 (s, 1H), 4.14-4.05 (m, 1H), 1.88 (d, J = 1.2 Hz, 3H), 1.35 (d, J = 6.8 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 138.0, 135.2, 133.9, 130.2, 128.9, 128.8, 127.8, 123.1, 121.9, 118.8, 112.5, 106.5, 58.7, 46.2, 21.2, 20.3, 7.7; IR

(KBr) *v* 3401, 2400, 1455, 1215, 929, 669 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{21}N_2O$ [M + H]$^+$ 305.1654, found 305.1657.

9-Methyl-2-((1r,4r)-4-methylcyclohexyl)-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3am): 3am (0.124 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 69%; yellow solid, mp 149-151 ^oC; R_f = 0.60 (SiO_2, 10% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.36-7.27 (m, 6H), 7.25-7.19 (m, 1H), 5.57 (s, 1H), 3.75-3.62 (m, 1H), 1.87 (d, J = 1.2 Hz, 3H), 1.81-1.70 (m, 2H), 1.67-1.53 (m, 3H), 1.29-1.16 (m, 2H), 1.03-0.89 (m, 2H), 0.83 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 138.2, 135.3, 133.9, 130.21, 128.8, 128.7, 127.8, 123.1, 121.9, 118.8, 112.5, 106.4, 58.7, 54.1, 34.4, 31.7, 31.2, 30.3, 22.0, 7.7; IR (KBr) *v* 3401, 2400, 1384, 1023, 929, 669, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{27}N_2O$ [M + H]$^+$ 359.2123, found 359.2125.

2-(2-Chloroethyl)-9-methyl-1-phenyl-1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one (3an): 3an (0.97 g) was obtained from **1a** (0.120 g, 0.5 mmol) following general procedure **A**. Yield 60%; light yellow solid, mp 129-131 ^oC; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.43-7.37 (m, 3H), 7.36-7.26 (m, 4H), 5.77 (s, 1H), 4.03-3.93 (m, 1H), 3.79-3.69 (m, 1H), 3.59-3.51 (m, 1H), 3.31-3.21 (m, 1H), 1.95 (d, J = 1.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 135.7, 134.4, 134.0, 130.3, 129.3, 129.2, 128.0, 123.4, 122.2, 119.0, 112.5, 107.4, 60.7, 42.9, 42.9, 42.1, 7.9; IR (neat) *v* 3686, 3019, 2400, 1413, 1023, 929, 627 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{18}ClN_2O$ [M + H]$^+$ 325.1108, found 325.1113.

Control experiments

Scheme-A: To a stirred solution of **1a** (237 mg, 1 mmol, 1 eq) in 2.5 mL of CH_3CN was added Phenyl isocyanate (332 mg, 2.5 mmol, 2.5 eq) at room temperature. The reaction

mixture was stirred at RT. until complete conversion of starting material (1h). The reaction mixture was diluted with water and extracted with EtOAc (2x10 ml). Combined extracts were washed with brine (10 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the crude material was purified on silica gel using 30% EtOAc/hexane to get **5** (305 mg, 85 %) as off white solid.

1-(2-(2-Hydroxy-4-phenylbut-3-yn-2-yl)phenyl)-3-phenylurea (5): mp 233-235 ^oC R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (bs, 1H), 7.93 (d, J = 7.1 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.41 (d, J = 6.8 Hz, 2H), 7.35-7.30 (m, 4H), 7.25-7.20 (m, 3H), 7.12-7.02 (m, 3H), 6.82 (bs, 1H), 3.13 (bs, 1H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 137.9, 136.7, 132.8, 131.7, 129.1, 128.9, 128.7, 128.3, 126.4, 124.2, 123.5, 123.5, 123.3, 121.6, 120.3, 91.0, 85.9, 71.2, 30.2; IR (KBr) ν 3400, 3019, 1650, 1385, 1069, 669 cm^{-1} HRMS (ESI-TOF) calcd for $C_{23}H_{19}N_2O$ $[M^+ - H_2O]^+$ 339.1497, found 339.1487.

Scheme-B: To a stirred solution of **5** (179 mg, 0.5 mmol, 1 eq) in 2.5 mL of CH_3CN was added Ag_2CO_3 (42 mg, 0.15 mmol, 0.3 eq) at room temperature. The reaction mixture was stirred at 70 ^oC, until complete conversion of starting material (12 h). The reaction mixture was diluted with water and extracted with EtOAc (2x10 ml). Combined extracts were washed with brine (10 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the crude material was purified on silica gel using 30% EtOAc/hexane to get **3ab** (127 mg, 75 %) as off white solid.

Scheme-C: Starting material **1a** was subjected to the general procedure **A** in absence of Isocyanate.

The product **6** was compared with reported data.[12]

Reductive cleavage of cyclic urea

The 1,2-dihydro-3H-imidazo[1,5-a]indol-3-one **3ab** (170 mg, 0.5 mmol, 1 equiv) in THF (10 mL) was added to a suspension of $LiAlH_4$ (189 mg, 5 mmol, 10 equiv) in THF (10 mL). The mixture was refluxed for 24 h until TLC showed no more starting material. On completion, the reaction mixture was carefully hydrolysed with aqueous KOH (0.65 mL, 10% solution) and water (0.8 mL). After complete addition stirring was continued for 2 h. After filtration the filtrate was diluted with water and extracted with ethyl acetate (20 mL). Combined extracts were washed with brine (10 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the crude material was purified on silica gel using 10% EtOAc/hexane to get **7** (103 mg, 65%) as off white solid.

N-((3-Methyl-1*H*-indol-2-yl)(phenyl)methyl)aniline (7): mp 164-166 ^oC R_f = 0.50 (SiO_2, 20% EtOAc/Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (bs, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.42-7.31 (m, 5H), 7.29-7.26 (m, 1H), 7.19-7.11 (m, 4H), 6.82-6.75 (m, 1H), 6.62 (d, J = 7.7 Hz, 2H), 5.74 (d, J = 1.0 Hz, 1H), 4.18 (bs, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 141.2, 135.0, 134.6, 129.7, 129.3, 129.0, 127.9, 127.3, 121.6, 119.2, 118.6, 118.4, 113.7, 110.9, 107.4, 56.5, 8.4; IR (KBr) ν 3400, 3019, 2320, 1385, 1069, 669 cm^{-1} HRMS (ESI-TOF) calcd for $C_{22}H_{21}N_2$ $[M + H]^+$ 313.1705, found 313.1710.

ASSOCIATED CONTENT

Spectroscopic data of all the products is available in Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

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