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Base-Mediated Chemo- and Stereoselective Addition of 5-Aminoindole/Tryptamine and Histamines onto Alkynes

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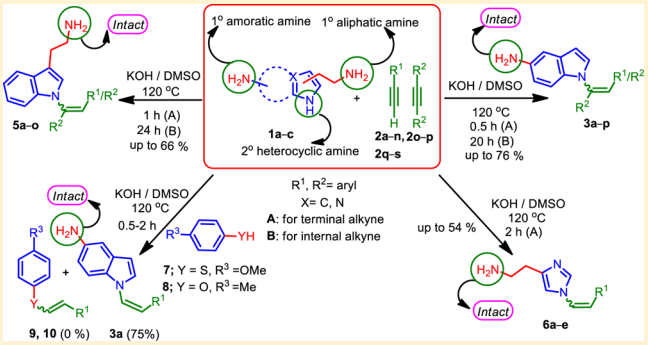
Supporting Information

ABSTRACT: Transition-metal-free chemo- and stereoselective addition of 5-aminoindole (**1a**), tryptamine (**1b**), and histamine (**1c**) to alkynes **2a−s** to synthesize the indolyl/imidazolyl enamines **3a−p**, **5a−o**, and **6a−e** using superbasic solutions of alkali-metal hydroxides in DMSO is described. The addition of N-heterocycles onto alkynes takes places chemoselectively without affecting the 1° amino groups (aromatic and aliphatic) of 5-aminoindole, tryptamine, and histamine. The stereochemistry of the products was found to be dependent upon reaction time; an increase in reaction time leads to the formation of a mixture of *E*/*Z* isomers and the thermodynamically stable *E* addition product. The chemoselective addition of N-heterocycle **1a** onto alkyne over thiophenol **7** and phenol **8** is supported by control experiments. Competitive experiments showed that 5-aminoindole was more reactive than tryptamine, and histamine was found to be the least reactive. The present methodology provides an efficient chemoselective method to synthesize a variety of (*Z*)-enamines of 5-aminoindole, tryptamine, and histamine without affecting the 1° amino group. The presence of the free amino group in enamines could be further used for synthetic elaboration, which proved to be highly advantageous for structural and biological activity assessments.



INTRODUCTION

Indole and its derivatives are widespread components of a variety of natural products and drug molecules.[1] Tryptamines and the other members of this class such as serotonin, melatonin, and histamine represent important examples, due to their potent neurological activities.[2,3] Other drugs belonging to the tryptan class such as sumatriptan, rizatriptan, and zolmitriptan (Figure 1) have proven to be significant advances in the acute treatment of migraine headaches.[4] Glennon and co-workers reported substituted tryptamines as efficient agents with high selectivity for the 5-HT_6 serotonin receptor.[5] Thus, due to the medicinal and pharmaceutical importance of indoles and tryptamines, functionalization of these heterocycles using cost-effective and easily accessible starting materials is an important area of current research.[6]

The stereo- and chemoselective synthesis of alkenes and biologically important compounds is an important protocol for the synthesis of natural products and industrially relevant compounds.[7] Very recently Feringa and co-workers found a significant improvement in antibacterial activity of the aza analogue of the quinolones by optical control of the stereochemistry of the product. The *Z* isomer of the aza-quinolone was found to be 4- and 8-fold active on *E. coli* (Gram-negative) and *M. luteus* (Gram-positive)[8] (Figure 2).

Several methodologies have been developed for the synthesis of functionalized tryptamines. For example, the substrates obtained by the Japp−Klingemann reaction are well-known for obtaining a diverse class of tryptamines.[9] In 1997, Dong and Busacca provided an easily accessible route for the synthesis of tryptamines and tryptophols by using sequential transition-metal-catalyzed reactions via a regioselective hydroformylation of functionalized anilines.[10] Beller and co-workers reported a titanium-catalyzed one -pot synthesis of tryptamines and their derivatives using chloroalkylalkynes and arylhydrazines.[11] Nicolau and co-workers have developed an elegant cascade approach for the synthesis of substituted tryptamines from anilines.[12]

The formation of N−C bonds by the addition of amines and N-heterocycles to alkenes and alkynes represents an attractive process for the synthesis of nitrogen heterocycles, enamines, substituted amines, imines, and natural products.[13] The inter- and intramolecular additions of primary amines to alkynes have been well recognized. A wide variety of catalysts such as titanium,[14] zirconium,[15] tantalum,[16a] rhodium,[16b] cesium,[17a] and K_3PO_4[17b] have been used for the addition of primary

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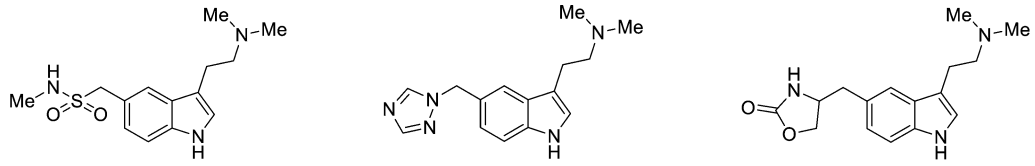
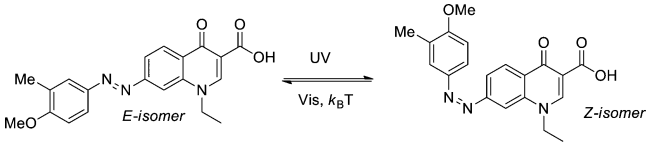


Figure 1. Common antimigraine drugs to tryptan family.



MIC (μg mL^{-1})	MIC (μg mL^{-1})
64 (*E. coli*)	16 (*E. coli*)
16 (*M. luteus*)	02 (*M. luteus*)

Figure 2. Antibacterial activity of *E* and *Z* isomers of aza-quinolone.

amines onto alkynes (Figure 3A). Yamamoto and Marks have explored the intramolecular catalytic hydroamination strategy

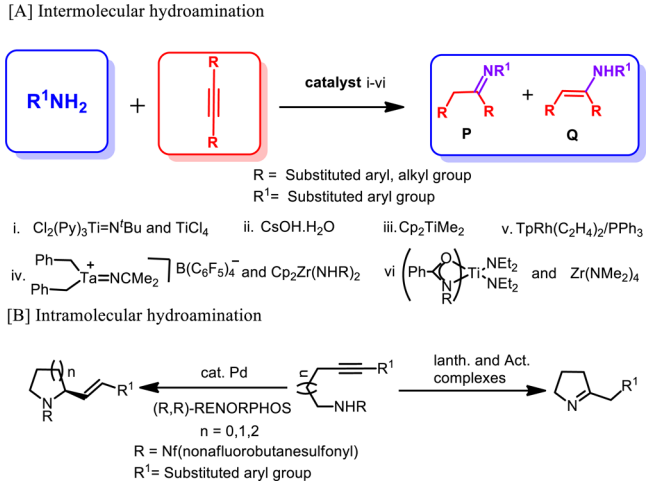


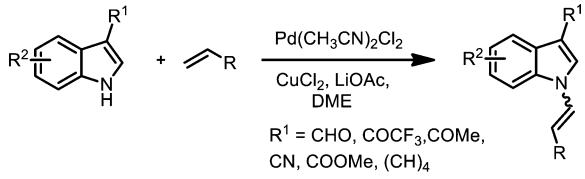
Figure 3. Selected examples of the hydroamination of alkynes using primary and secondary amines.

for the construction of pyrrolidine heterocycles (Figure 3B).[18] An elegant approach for the synthesis of indoles and pyrroles was reported by Knochel[19a,b] and Ackermann[19c−g] by using hydroamination chemistry. However, in contrast to the addition of primary and secondary amines, addition of N-heterocycles to alkynes has not been much explored.

In 1999 Knochel reported the first example of the addition of heterocyclic amines to alkynes[17] using CsOH·H_2O, and later Kondo[20a] reported the addition of pyrrole to diphenylacetylene using the phosphazene superbase P_4-*t*-Bu. Very recently Wu[20b] and co-workers reported the regio- and stereoselective N-alkenylation of indoles[20c] using a palladium catalyst (Scheme 1).

In 2009 we reported the copper-catalyzed tandem synthesis of indolo- and pyrrolo[2,1-*a*]isoquinolines via hydroamination followed by intramolecular C-2 arylation.[21] Our recent study

Scheme 1. N-Alkenylation of Indoles using a Palladium Catalyst



involved (i) base-mediated regio- and stereoselective intermolecular addition of alkynes to N-heterocycles[22a] and (ii) regioselective preferential nucleophilic addition of N-heterocycles to haloarylalkynes over N-arylation of aryl halides, confirming the mechanism proposed for the synthesis of indolo- and pyrrolo[2,1-*a*]isoquinolines.[22b] In a continuation of our ongoing work on the hydroamination of alkynes, herein we wish to report the chemo- and stereoselective addition of 5-aminoindole, tryptamine, and histamine without affecting the 1° amino group (Scheme 2). The presence of a free amino group in enamines could be further used for synthetic elaboration, which increases the synthetic utility of this developed procedure for structural and biological activity assessments.

RESULTS AND DISCUSSION

To identify the optimal reaction conditions for the reaction, we examined the reaction of 5-aminoindole (**1a**) with 3-ethynyltoluene (**2a**) using our previously optimized reaction conditions, i.e. 0.2 equiv of KOH in DMSO at 120 °C for 30 min,; the product (*Z*)-1-(3-methylstyryl)-1*H*-indol-5-amine (**3a**) was obtained in 45% yield (Table 1, entry 1).[22] The product **3a** was obtained in 74% yield upon increasing the loading of KOH from 0.2 to 0.5 equiv (entry 2); however, the use of 1.0 equiv of base gave no improvement in the yield of the product **3a** (entry 3). An increase in the reaction time from 0.5 to 1 h provided the product **3a** in 72% yield in a 40:60 stereoisomeric ratio (entry 4). However, a further increase in reaction time from 1 to 2 h provided the thermodynamically stable trans isomer in a 95:5 ratio in 70% yield (entry 5). When the reaction was carried out at 100 °C for 2 h, product **3a** was obtained in 43% yield in a 10:90 stereoisomeric ratio (entry 6). An increase in reaction temperature afforded the product **3a** in comparatively lower yield (entry 7). Other bases such as NaOH, CsOH·H_2O, and KO^{t}Bu afforded the product **3a** in 69, 62, and 60% yields respectively (entries 8−10); however, Et_3N was found to be ineffective (entry 11). When the reaction was carried out in the absence of base, the reactants remained almost unchanged during the course of the reaction (entry 12). Applying Ruimao conditions, no hydroamination product was observed (entries 13 and 14).[23,24] The use of zirconium, palladium, and copper catalysts reported in the literature for

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Scheme 2. Chemo- and Stereoselective Addition of 5-Aminoindole, Tryptamine, and Histamine to Alkynes

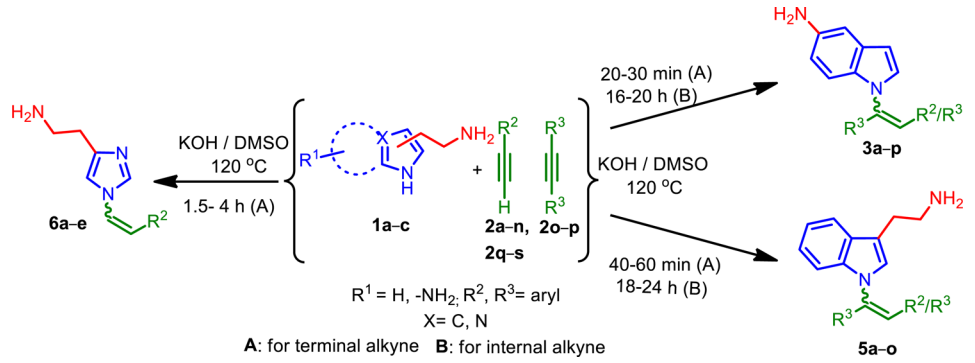
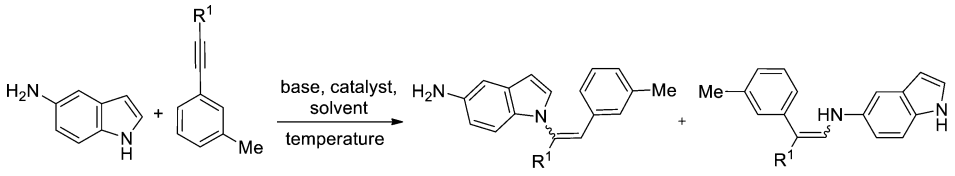


Table 1. Optimization of the Reaction Conditions[a]



entry	alkyne	base (amt (equiv))	catalyst	solvent	time (h)/T (°C)	yield (%)[b] of **3a**/**3p** (E:Z)[c]
1	**2a**	KOH (0.2)		DMSO	0.5/120	45 (0:100)[d]
2	**2a**	**KOH (0.5)**		**DMSO**	**0.5/120**	**74 (0:100)**[d]
3	**2a**	KOH (1.0)		DMSO	0.5/120	74 (00:100)[d]
4	**2a**	KOH (0.5)		DMSO	1.0/120	72 (40:60)[d]
5	**2a**	**KOH (0.5)**		**DMSO**	**2.0/120**	**70 (95:05)**[d]
6	**2a**	KOH (0.5)		DMSO	2.0/100	43 (10:90)[d]
7	**2a**	KOH (0.5)		DMSO	0.5/140	64 (00:100)[d]
8	**2a**	NaOH (0.5)		DMSO	0.5/120	69 (00:100)[d]
9	**2a**	$CsOH·H_2O$ (0.5)		DMSO	1.0/120	62 (00:100)[d]
10	**2a**	KO^{t}Bu (0.5)		DMSO	1.0/120	60 (20:80)[d]
11	**2a**	Et_3N (0.5)		DMSO	24/120	NR
12	**2a**			DMSO	6.0/120	NR
13[23]	**2a**		CuCl	toluene	24/100	NR
14[24]	**2a**		AgOTf	DMF	24/120	NR
15[15]	**2a**		Cp_2ZrCl_2	toluene	24/100	*e*
16[25]	**2a**		PA-Pd[f]	MeCN	4/80	*e*
17[26]	**2a**	K_2CO_3	Cu/Al-HT[g]	NMP	24/120	*e*
18[h]	**2a**		Cp_2ZrCl_2	toluene	1.0/100	*e*
19[h]	**2a**		PA-Pd[f]	MeCN	1.0/80	*e*
20[h]	**2a**	K_2CO_3	Cu/Al-HT[g]	NMP	1.0/120	*e*
21	**2p**	KOH (0.5)		DMSO	20/120	30 (00:100)[i]
22	**2p**	KOH (1.0)		DMSO	20/120	42 (00:100)[i]
23	**2p**	**KOH (2.0)**		**DMSO**	**20/120**	**62 (00:100)**[i]
24	**2p**	KOH (2.5)		DMSO	20/120	62 (00:100)[i]
25	**2p**	KOH (2.0)		toluene	20/120	NR

[a]Reactions were performed using N-heterocycle **1a** (1.0 mmol), alkyne **2a**/**2p** (1.0 mmol), and 1.5 mL of solvent. [b]Total yield of two isomers. [c]Stereoisomeric ratio. [d]Product **3a** is formed. [e]Inseparable complex mixtures. [f]PA denotes polymer assisted. [g]HT is the hydrotalcite of Cu/Al. [h]Using microware irradiation at 100 W. [i]Product **3p** is formed.

the hydroamination of primary amines failed to provide the hydroaminated product **3a**/**4a** (entries 15−17).[15,25,26] The reaction was also performed under microwave conditions using the above catalysts; however, we failed to obtain the hydroaminated product (entries 18−20). The reaction of the internal alkyne 1,2-di-*m*-tolylethyne (**2p**) with **1a** using 0.5 equiv of KOH at 120 °C for 20 h afforded the product **3p** in 30% yield (entry 21). An increase of KOH loading from 0.5 equiv to 1.0 and then to 2.0 equiv afforded the product **3p** in 42 and 62% yields, respectively, with Z stereoselectivity (entries 22 and 23). A further increase of the loading of base from 2.0 to 2.5 equiv gave no improvement in the yield of the product **3p** (entry 24). Toluene was found to be ineffective for the reaction (entry 25).

Chemoselective Addition of 5-Aminoindole to Alkynes. After optimizing the reaction conditions for the chemoselective addition of alkynes onto amines, we examined the scope and

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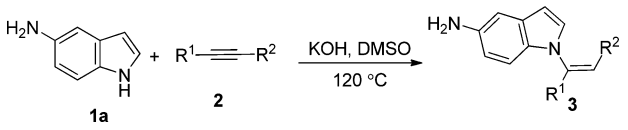
Table 2. Chemo- and Stereoselective Addition of 5-Aminoindole to Alkynes[a]



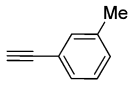
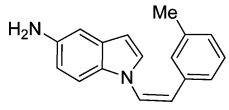
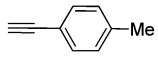
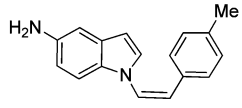
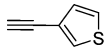
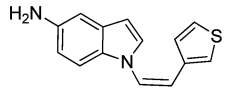
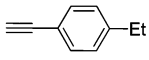
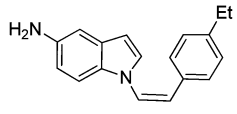
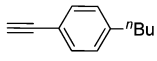
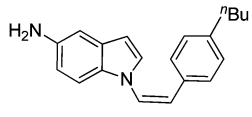
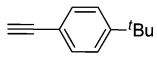
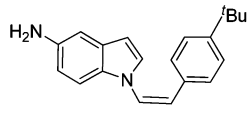
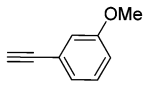
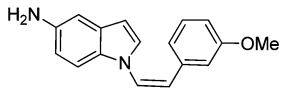
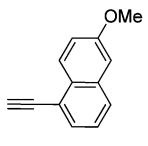
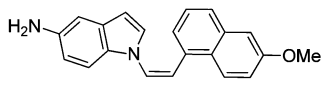
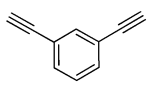
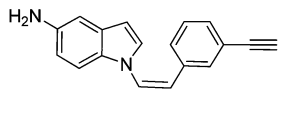
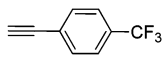
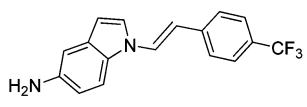
Entry	alkyne **2**		product **3**		yield (%)
1		**2a**		**3a**	74
2		**2b**		**3b**	76
3		**2c**		**3c**	74
4		**2d**		**3d**	75
5		**2e**		**3e**	72
6		**2f**		**3f**	75
7		**2g**		**3g**	76
8		**2h**		**3h**	62
9		**2i**		**3i**	46
10		**2j**		**3j**	72[b]

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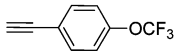
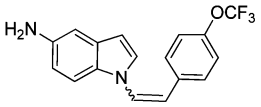
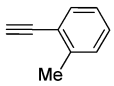
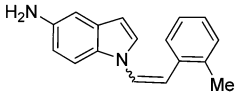
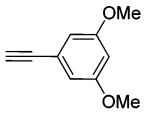
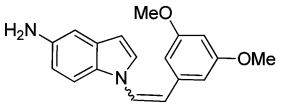
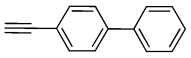
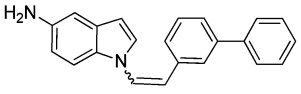
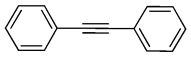
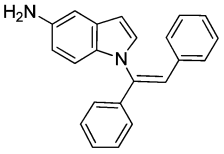
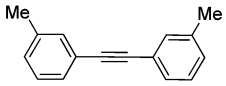
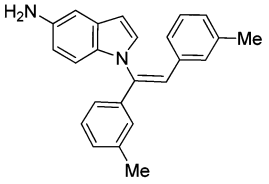
Table 2. continued

Entry	alkyne **2**		product **3**		yield (%)
11		**2k**		**3k** (*E*:*Z*::23:77)	69[c]
12		**2l**		**3l** (*E*:*Z*::25:75)	75[c]
13		**2m**		**3m** (*E*:*Z*::25:75)	70[c]
14		**2n**		**3n** (*E*:*Z*::1:1)	72[c]
15[b]		**2o**		**3o**	60[d]
16[b]		**2p**		**3p**	62[d]

[a]Reactions were performed using **1a** (1.0 mmol), alkyne **2** (1.0 mmol), and 0.5 equiv of KOH in 1.5 mL of DMSO at 120 °C for 0.5 h unless otherwise noted. [b]Reaction was run for 2.0 h. [c]Reaction was run for 1.0 h. [d]Reaction was carried out using 2.0 equiv of KOH for 20 h.

generality of the reaction by utilizing a variety of alkynes (Table 2, entries 1−16). Addition of 5-aminoindole (**1a**) on terminal alkynes **2a**−**n** provided the corresponding *Z*-addition products **3a**−**n** chemoselectively in good yields without affecting the 1° amino group (entries 1−14). The substituents attached on the alkynes have no significant effect on the yields of the products (entries 1−8). The reaction of 1,3-diethynylbenzene (**2i**) with **1a** provided the monohydroaminated product **3i** in 46% yield along with an inseparable complex mixture of other possible byproducts (entry 9). Reaction of alkyne **2j** with **1a** for 2 h provided the *E*-addition product **3j** in 72% yield (entry 10); however, reaction of alkynes **2k**−**n** with 5-aminoindole for 1 h provided mixtures of *E*/*Z* isomers **3k**−**n** in 69−75% yields (entries 11−14). Reactions of internal alkynes **2o**,**p** afforded the hydroaminated products **3o**,**p** in moderate yield using 2.0 equiv of KOH at 120 °C for 20 h (entries 15 and 16).

Chemo- and Stereoselective Addition of Tryptamine to Alkynes. The tryptamine skeleton is an important substructure occurring in both natural products and therapeutic agents having wide applications in pharmaceutical and medicinal chemistry.[2,3] Tryptamine-based drugs such as sumatriptan, rizatriptan, and zolmitriptan have attracted considerable attention due to their prominent biological activities. The success of the chemoselective addition of the 5-aminoindole onto alkynes encouraged us in the addition of tryptamine (bearing a 1° aliphatic amino group) to alkynes. Under the optimized reaction conditions (Table 1, entry 2), reaction of tryptamine (**1b**) with alkynes **2a**−**r** afforded the desired (*Z*)-styryl enamines **5a**−**l**,**n**,**o** chemoselectively in moderate to good yields (Table 3, entries 1−12, 14, and 15). It is interesting to note that no hydroamination was observed on the 1° amino group of the tryptamine. Dialkyne **2i** on reaction with **1b** provided the monohydroaminated product **5f** with *Z* stereoselectivity in 42% yield (entry 6). However, when the reaction of **1b** with dialkyne **2s** was allowed to run for 3 h, the product **5m** was obtained in 40% yield with *E* stereoselectivity (entry 13). Internal alkynes **2o**,**p** provided the *Z* isomers in 60 and 62% yields, respectively (entries 14 and 15).

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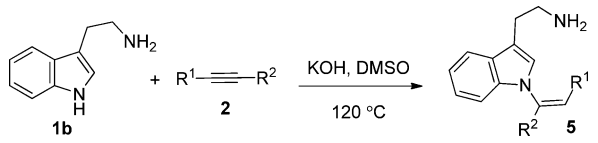
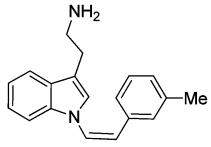
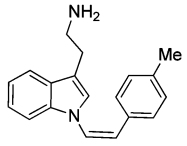
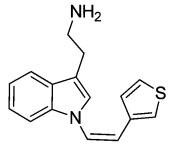
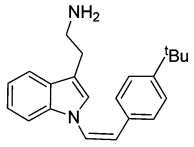
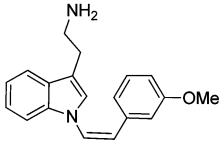
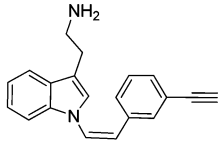
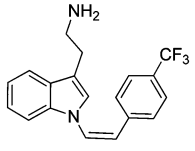
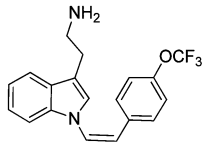
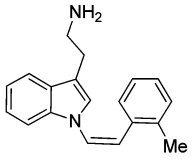
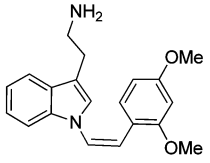
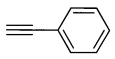
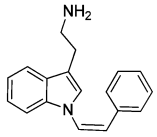
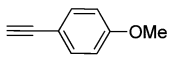
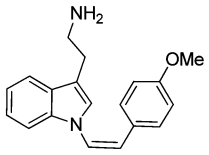
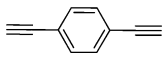
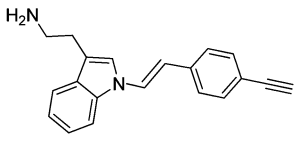
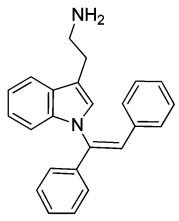
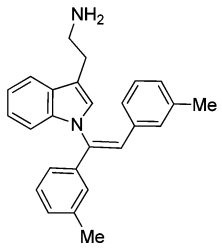
Table 3. Chemo- and Stereoselective Addition of Tryptamine to Alkynes[a]



entry	alkyne **2**	product **5**		yield (%)
1	**2a**		**5a**	64
2	**2b**		**5b**	65
3	**2c**		**5c**	65
4	**2f**		**5d**	63
5	**2g**		**5e**	62
6	**2i**		**5f**	42
7	**2j**		**5g**	60
8	**2k**		**5h**	59

dx.doi.org/10.1021/jo402352v | J. Org. Chem. 2014, 79, 172−186

Table 3. continued

entry	alkyne **2**	product **5**	yield (%)
9	**2l**	 **5i**	61
10	**2m**	 **5j**	58
11	 **2q**	 **5k**	60
12	 **2r**	 **5l**	66
13	 **2s**	 **5m**	40[b]
14	**2o**	 **5n**	60[c]
15	**2p**	 **5o**	62[c]

[a]The reactions were performed using amines **1** (1.0 mmol), alkynes **2** (1.0 mmol), and 0.5 equiv of KOH in 1.5 mL of DMSO at 120 °C for 1 h unless otherwise noted. [b]The reaction was run for 3 h. [c]The reaction was performed using 2.0 equiv of KOH for 24 h.

Chemo- and Stereoselective Addition of Histamine to Alkynes. Histamine and its derivatives play a very significant role in many immunological and natural processes.[27] The success of the chemoselective addition of 5-aminoindole **1a**

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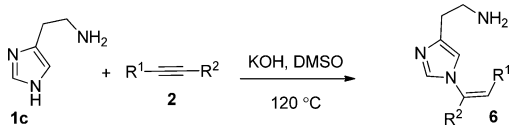
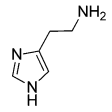
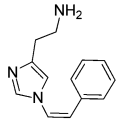
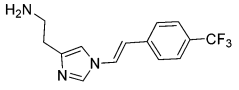
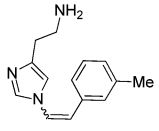
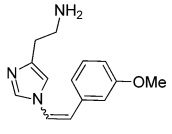
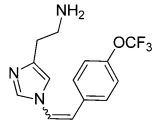
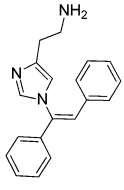
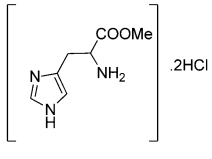
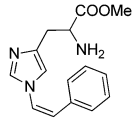
Table 4. Chemo- and Stereoselective Addition of Histamine to Alkynes[a]



entry	*N*-heterocycle **1**	alkyne **2**	product **6**	yield (%)
1	 **1c**	**2q**		**6a** 50
2	**1c**	**2j**		**6b** 52[b]
3	**1c**	**2a**		**6c** (*E*:*Z*::1:1) 54[c]
4	**1c**	**2g**		**6d** (*E*:*Z*::34:66) 50[c]
5	**1c**	**2k**		**6e** (*E*:*Z*::1:1) 51[c]
6[d]	**1c**	**2o**		**6f** -[d]
7[e]	 **1d**	**2q**		**6g** -

[a]The reactions were performed using N-heterocycle **1** (0.5 mmol), 1.0 mmol of the alkyne **2**, and 0.5 equiv of KOH in 1.5 mL of DMSO at 120 °C for 2 h. [b]Reaction was run for 4 h. [c]Reaction was run for 3 h. [d]Reaction was run for 24 h. [e]Triethylamine (2.0 equiv) was added.

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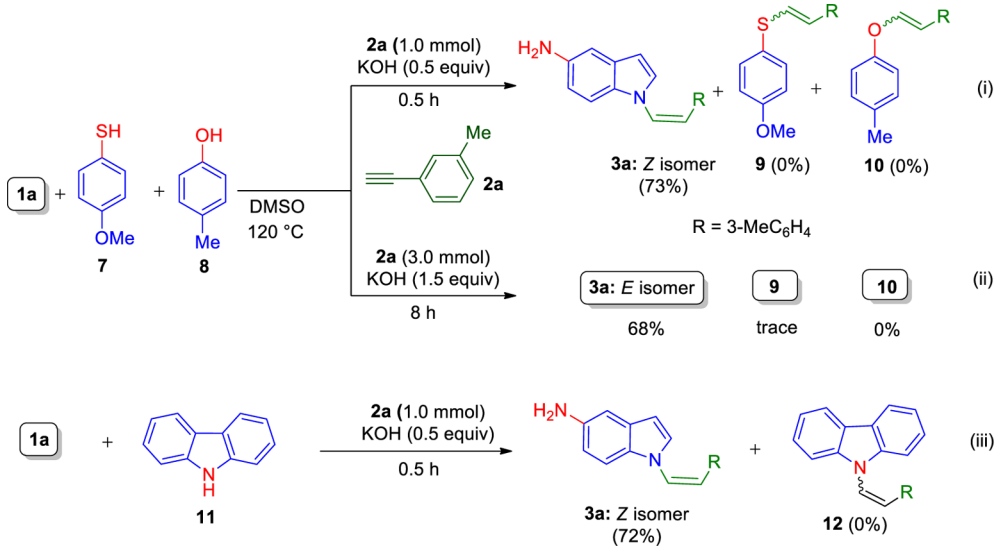
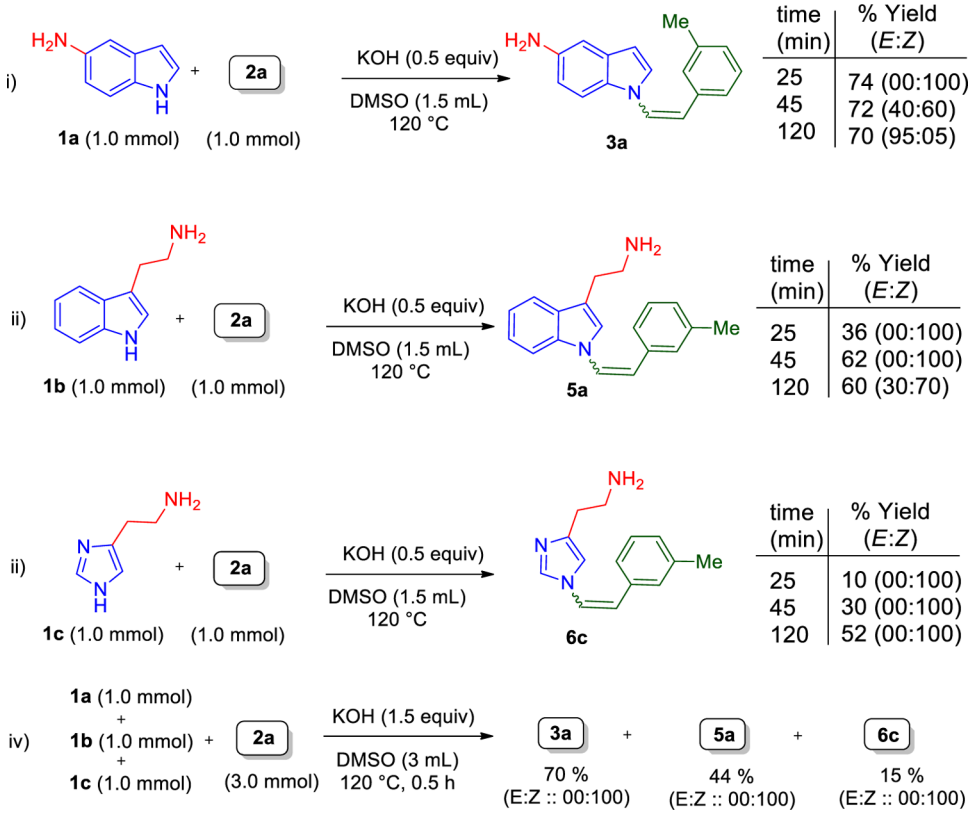
Scheme 3. Competitive Study: Hydroamination vs Thiolation and Hydroxylation



Scheme 4. Reactivity Behavior of 5-Aminoindole, Tryptamine, and Histamine with Alkynes



and, tryptamine **1b** onto various terminal and internal alkynes further encouraged us for the reaction of commercially available histamine **1c** onto alkynes (Table 4).

Reaction of histamine **1c** with alkyne **2q** provided the *Z*-addition product **6a** selectively in 50% yield after running the reaction for 2 h (Table 4, entry 1). However, to obtain the stereoselective *E*-addition product **6b**, it required 4 h to complete the reaction (entry 2). When the reaction was allowed to run for 3 h, a mixture of *E*/*Z* isomers was obtained (entries 3−5). However, addition of histamine onto internal alkyne **2o** failed to give the desired product **6f** (entry 6). Further reaction of histidine methyl ester hydrochloride **1d** with alkyne **2q** (using triethylamine for neutralization) under the optimized reaction conditions did not provide the desired product **6g** (entry 7).

Comparative Study: Hydroamination vs Thiolation and Hydroxylation. Base-catalyzed nuleophilic addition reactions of alkynes were first reported in 1957,[28] and later on the pioneering work of Trofimov et al. further demonstrated that a KOH−DMSO suspension played an important role in the activation of a variety of nucleophilic substrates.[29] In a recent report by his group,[30] they also explained that the

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addition of N-heterocyclic amines to alkynes is an exception to the *trans*-nucleophilic addition rule.[31] In our reaction system, we also observed that other nucleophiles such as phenols and thiols react with alkynes at a snail's pace in contrast to the case for N-heterocycles, to provide the corresponding addition products in the superbasic KOH−-DMSO suspension (Scheme 3).[32]

In order to observe the comparative studies between 5-aminoindole (**1a**), 4-methoxythiophenol (**7**), and 4-methylphenol (**8**) with alkyne **2a**, we carried out a control experiment (Scheme 3i). First we reacted **1a**, **7**, and **8** (1.0 mmol each) with 1.0 mmol of alkyne **2a** using 0.5 equiv of KOH in 1.5 mL of DMSO at 120 °C for 30 min. We observed that product **3a** was obtained in 73% yield; however, the formation of compounds **9** and **10** was not observed. In another set of reactions we carried out the reaction of **1a**, **7**, and 8 with 3.0 mmol of alkyne **2a** using 1.5 equiv of KOH at 120 °C for 8 h. It was noted that product **3a** (*E* isomer) was obtained in 68% yield along with a trace amount of thiolation product **9**, and no hydroxylation product **10** was observed (Scheme 3ii). The possible reason could be due to the low nucleophilicity of the thiophenol and phenol in comparison to that of indole.

Another control experiment was performed using 5-aminoindole and carbazole **11** as N-nucleophile. We carried out the reaction of **1a** (1.0 mmol) and **11** (1.0 mmol) with 1.0 mmol of alkyne **2a** using 0.5 equiv of KOH at 120 °C for 0.5 h. It was observed that product **3a** (*Z* isomer) was found in 72% yield; however, formation of product **12** was not observed. The possible reason for this could be the tricyclic structure of the carbazole, which alters its nucleophilicity (Scheme 3iii).

The nucleophilicity of the heterocyclic amine plays an important role in the product formation. The enamines **3a−p** synthesized from 5-aminoindole (**1a**) and alkynes **2a−p** were obtained in good yields and required less reaction time; however, products **5a−o** synthesized by using tryptamine **1b** were obtained in moderate yields and required longer reaction time in comparison to heterocycle **1a**. The products **6a−e** obtained by the reaction of histamine **1c** with alkynes **2a**,**g**,**j**,**k**,**o**,**q** were obtained in lower yields and required longer reaction times in comparison to the case for **1a**,**b** (compare the yields and reaction times of the products of Tables 1 and 2 vs Table 3).

To validate the reactivity behavior of 5-aminoindole, tryptamine, and histamine with alkynes, we performed four sets of reactions and monitored the formation of products at different time intervals (Scheme 4). In the first set of reactions we reacted **1a** with alkyne **2a** using 0.5 equiv of KOH and monitored the reaction products after 25, 45, and 120 min intervals. We observed that after 25 min product **3a** (only *Z* isomer) was obtained in 74% yield; however, after 45 min a 40:60 *E*:*Z* mixture was obtained in 72% yield and after 2 h the thermodynamically stable *E* isomer was observed in 70% yield (Scheme 4i). Similarly, in another set of reaction we performed the reaction of tryptamine **1b** with alkyne **2a** using reaction conditions similar to those used for the first set of reactions; we noticed that after 25 min product **5a** (only *Z* isomer) was formed in only 36% yield and after 45 min the stereoselective *Z*-addition product was obtained in 62% yield. Running the reaction for 2 h, we observed that mixture of *E* and *Z* isomers were obtained in a 30:70 sterioisomeric ratio (Scheme 4ii). The reaction of histamine **1c** with **2a** was found to be sluggish, as the hydroaminated product **6c** (only *Z* isomer) was obtained in only 10 and 30% yields after running the reaction for 25 and 45 min; however, after 2 h the *Z*-stereoselective product **6c** was obtained in 52% yield (Scheme 4iii). Finally, we performed a combined reaction using heterocycles **1a−c** with 3 equiv of alkyne **2b** for 0.5 h and found that *Z*-stereoselective products **3a** and **5a** were obtained in 70 and 44% yields, respectively; however, product **6c** was obtained in only 15% yield (Scheme 4iv).

These observations can be explained on the basis of the reactivity behavior of **1a−c** (Figure 4). In the case of **1a**, the

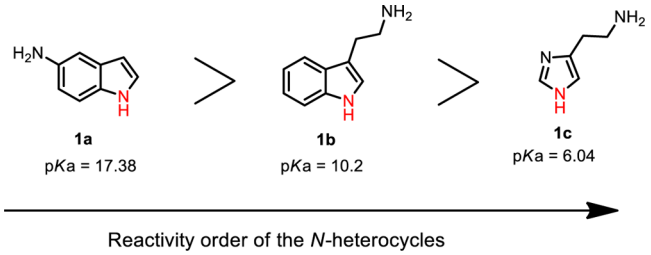

Figure 4. pK_a values and reactivity behavior of the N-heterocycles **1a−c**.

presence of the electron-rich indole ring system (+R effect of $-NH_2$) increases the reactivity of the N-heterocyclic amine, which facilitates the formation of the addition products, whereas in the case of histamine **1c**, the nucleophilicity of −NH decreases due to the −I effect of another nitrogen present in the ring. The pK_a values of 5-aminoindole (**1a**; 17.38), tryptamine (**1b**; 10.02), and histamine (**1c**; 6.04) also support the reactivity behavior of the N-heterocycles.[33]

CONCLUSION

In conclusion, we have demonstrated a general and efficient approach for the chemo- and stereoselective addition of 5-aminoindole, tryptamine, and histamine to a broad range of alkynes to synthesize a variety of indolyl/imidazolyl enamines. This developed chemistry involves base-mediated and transition-metal-free chemoselective addition of benchtop and inexpensive N-heterocycles to commercially available alkynes without affecting the 1° amino groups (aromatic and aliphatic) present in the substrates and provides a synthetically useful handle in the products for further elaboration. The stereochemistry of the products can be controlled by tuning the reaction time. Competition experiments demonstrated the chemoselective addition of 5-aminoindole onto alkyne over thiophenol and phenol. We observed that 5-aminoindole was more reactive than tryptamine, and histamine was found to be the least reactive, as validated by the control experiments. It is likely that the operational simplicity of the developed protocol will make it attractive for the synthesis of a variety of stereoselective enamines of biological importance. Further investigations of the scope of this attractive chemistry are underway and will be reported in due course.

EXPERIMENTAL SECTION

General Information and Method. All of the reactions were performed in an oven-dried Schlenk flask under an argon atmosphere. Column chromatography was performed using neutral and basic alumina. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates. Visualization of spots on TLC plates was accomplished with UV light (254 nm) and staining over an I_2 chamber. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, br s = broad singlet),

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coupling constants in hertz, and integration. High-resolution mass spectra were recorded with a q-TOF electrospray mass spectrometer, and Iinfrared spectra were recorded on a FT-IR spectrophotometer. All purchased chemicals were used as received. All melting points are uncorrected.

General Procedure for the Synthesis of Internal Alkyne 2p. The 1,2-diarylalkyne **2p** was prepared by the Sonogashira coupling reaction of the corresponding aryl iodide with terminal alkynes using the reported procedure and confirmed by comparison of its physical and spectral data (^{1}H NMR, ^{13}C NMR, and HRMS) with those reported in the literature.[34]

General Procedure for the Addition of *N*-Heterocycles to Alkynes. The compounds were synthesized as per the previously reported procedure.[22] To a solution of the N-heterocycle (1.0 mmol) in 1.5 mL of DMSO were added finely crushed KOH (0.5 equiv) and alkyne (1.0 mmol). The resulting mixture was heated at 120 °C. The progress of the reaction was monitored by TLC. After the complete consumption of alkynes, the reaction mixture was warmed to room temperature. The reaction mixture was diluted with water (8 mL) and extracted with ethyl acetate (5 mL × 3); further, the organic layer was washed with brine solution (5 mL × 3) and dried over Na_2SO_4. The crude reaction mixture was purified by column chromatography, using basic/neutral aluminum oxide.

Some data were recorded in $CDCl_3$, which does not show the $-NH_2$ proton; to confirm the $-NH_2$ proton, we have reported the IR data.

*(Z)-1-(3-Methylstyryl)-1H-indol-5-amine (**3a**).* The product was obtained as a brown semisolid (183.5 mg, 74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09−7.02 (m, 2H), 6.95−6.90 (m, 3H), 6.88 (d, J = 3.2 Hz, 1H), 6.82 (d, J = 1.8 Hz, 1H), 6.78 (d, J = 9.1 Hz, 1H), 6.60 (dd, J = 8.2 and 2.3 Hz, 1H), 6.22 (d, J = 3.2 Hz, 1H), 6.07 (d, J = 9.1 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 137.9, 135.0, 130.7, 129.4, 128.2, 128.1, 127.4, 125.6, 123.2, 118.2, 112.8, 110.6, 105.9, 102.9, 21.3; IR spectrum in film (ν_{max}, cm^{-1}) 3375, 2925, 1626, 1477, 772, 723, 696; HRMS (ESI) calcd for $C_{17}H_{16}N_2$ (M + H$^+$) 249.1391, found 249.1391.

*(Z)-1-(4-Methylstyryl)-1H-indol-5-amine (**3b**).* The product was obtained as a brown semisolid (188.4 mg, 76%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.07−7.00 (m, 5H), 6.96 (d, J = 9.1 Hz, 1H), 6.90 (d, J = 3.2 Hz, 1H), 6.70 (s,1H), 6.53 (d, J = 8.7 Hz, 1H), 6.24 (d, J = 3.2 Hz, 1H), 6.17 (d, J = 9.1 Hz, 1H), 4.63 (br s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 142.8, 136.6, 132.2, 129.0, 128.9, 128.2, 126.3, 123.3, 117.6, 112.3, 110.6, 103.7, 102.8, 20.8; IR spectrum in film (ν_{max}, cm^{-1}) 3394, 2922, 1653, 1477, 819, 726, 710; HRMS (ESI) calcd for $C_{17}H_{16}N_2$ (M + H$^+$) 249.1391, found 249.1391.

*(Z)-1-(2-(Thiophen-3-yl)vinyl)-1H-indol-5-amine (**3c**).* The product was obtained as a brown oil (177.6 mg, 74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07−7.03 (m, 3H), 6.96 (d, J = 2.9 Hz, 1H), 6.84 (d, J = 2.2 Hz, 1H), 6.73−6.68 (m, 2H), 6.59 (dd, J = 8.0 and 2.2 Hz, 1H), 6.30 (d, J = 2.9 Hz, 1H), 6.21 (d, J = 8.8 Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 135.6, 130.6, 129.5, 127.8, 127.6, 125.2, 124.3, 122.9, 115.5, 112.9, 110.8, 105.8, 102.8; IR spectrum in film (ν_{max}, cm^{-1}) 3403, 2921, 1646, 1476, 797, 757, 711; HRMS (ESI) calcd for $C_{14}H_{12}N_2S$ (M + H$^+$) 241.0799, found 241.0799.

*(Z)-1-(4-Ethylstyryl)-1H-indol-5-amine (**3d**).* The product was obtained as a brown semisolid (196.5 mg, 75% yield); ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.01−6.95 (m, 5H), 6.89 (d, J = 9.1 Hz, 1H), 6.83 (d, J = 3.2 Hz, 1H), 6.61 (d, J = 2.3 Hz, 1H), 6.45 (dd, J = 8.7 and 1.8 Hz, 1H), 6.17 (d, J = 2.7 Hz, 1H), 6.10 (d, J = 9.1 Hz, 1H), 4.56 (br s, 2H), 2.46 (q, J = 7.3 Hz, 2H), 1.05 (t, J = 7.7 Hz, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 143.4, 143.3, 133.0, 129.6, 129.4, 128.9, 128.3, 126.8, 123.8, 118.2, 112.8, 111.1, 104.2, 103.3, 28.4, 15.9; IR spectrum in film (ν_{max}, cm^{-1}): 3421, 2964, 1649, 1458, 799, 755, 716; HRMS (ESI) calcd for $C_{18}H_{18}N_2$ (M + H$^+$) 263.1548, found 263.1548.

*(Z)-1-(4-Butylstyryl)-1H-indol-5-amine (**3e**).* The product was obtained as a brown semisolid (208.8 mg, 72%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.07−7.02 (m, 5H), 6.97 (d, J = 9.5 Hz, 1H), 6.90 (d, J = 3.5 Hz, 1H), 6.68 (d, J = 2.2 Hz, 1H), 6.52 (dd, J = 8.7 and 2.7 Hz, 1H), 6.25 (d, J = 2.9 Hz, 1H), 6.18 (d, J = 8.8 Hz, 1H), 4.64 (br s, 2H), 2.52−2.48 (m, 2H), 1.53−1.46 (m, 2H), 1.32−1.21 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 142.7, 141.5, 132.4, 129.0, 128.9, 128.3, 126.4, 123.3, 117.8, 112.3, 110.6, 103.8, 102.8, 34.6, 32.9, 21.8, 13.8; IR spectrum in film (ν_{max}, cm^{-1}) 3394, 2923, 2854, 1655, 1460, 806, 766, 734; HRMS (ESI) calcd for $C_{20}H_{22}N_2$ (M + H$^+$) 291.1861, found 291.1861.

*(Z)-1-(4-tert-Butylstyryl)-1H-indol-5-amine (**3f**).* The product was obtained as a brown oil (217.5 mg, 75%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.22 (d, J = 8.7 Hz, 2H), 7.04 (t, J = 7.8 Hz, 3H), 6.93−6.89 (m, 2H), 6.65 (d, J = 1.8 Hz, 1H), 6.49 (dd, J = 8.7 and 2.3 Hz, 1H), 6.22 (d, J = 3.2 Hz, 1H), 6.14 (d, J = 9.1 Hz, 1H), 4.62 (br s, 2H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 149.9, 142.8, 132.2, 129.1, 129.0, 128.2, 126.4, 125.2, 123.4, 117.8, 112.4, 110.6, 103.9, 102.9, 34.4, 31.1; IR spectrum in film (ν_{max}, cm^{-1}) 3326, 2961, 1648, 1478, 800, 756, 717; HRMS (ESI) calcd for $C_{20}H_{22}N_2$ (M + H$^+$) 291.1861, found 291.1860.

*(Z)-1-(3-Methoxystyryl)-1H-indol-5-amine (**3g**).* The product was obtained as a brown semisolid (200.6 mg, 76%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.16 (t, J = 8.0 Hz, 1H), 7.07−7.01 (m, 2H), 6.91(d, J = 2.9 Hz, 1H), 6.77−6.71 (m, 2H), 6.67−6.64 (m, 2H), 6.51 (dd, J = 8.8 and 2.2 Hz, 1H), 6.25 (d, J = 2.9 Hz, 1H), 6.19 (d, J = 8.8 Hz, 1H), 4.64 (br s, 2H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 140.4, 136.4, 130.6, 129.4, 129.3, 127.4, 123.6, 121.3, 118.3, 113.6, 113.3, 112.8, 110.7, 105.8, 103.0, 55.0; IR spectrum in film (ν_{max}, cm^{-1}) 3357, 2958, 1648, 1479, 794, 756, 693; HRMS (ESI) calcd for $C_{17}H_{16}N_2O$ (M + H$^+$) 265.1341 found 265.1341.

*(Z)-1-(2-(6-Methoxynaphthalen-2-yl)vinyl)-1H-indol-5-amine (**3h**).* The product was obtained as a brown solid (194.6 mg, 62%): mp 125−130 °C; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.67 (t, J = 4.4 Hz, 2H), 7.61(d, J = 8.8 Hz, 1H), 7.23 (d, J = 2.2 Hz, 1H), 7.12−7.05 (m, 4H), 6.92 (d, J = 2.9 Hz, 1H), 6.70 (d, J = 2.2 Hz, 1H), 6.52 (dd, J = 8.8 and 2.2 Hz, 1H), 6.34 (d, J = 8.8 Hz, 1H), 6.25 (d, J = 2.9 Hz, 1H), 4.65 (br s, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 157.5, 142.9, 133.4, 130.4, 129.3, 129.1, 129.0, 128.3, 127.4, 126.59, 126.55, 126.4, 123.7, 118.9, 117.6, 112.3, 110.7, 105.9, 103.7, 102.9, 55.2; IR spectrum in film (ν_{max}, cm^{-1}) 3356, 2925, 1625, 1482, 758, 721, 669; HRMS (ESI) calcd for $C_{21}H_{18}N_2O$ (M + H$^+$) 315.1497, found 315.1496.

*(Z)-1-(3-Ethynylstyryl)-1H-indol-5-amine (**3i**).* The product was obtained as a brown oil (118.6 mg, 46%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 1H), 7.25 (d, J = 7.3 Hz, 1H), 7.12−7.06 (m, 3H), 6.84−6.82 (m, 3H), 6.60 (d, J = 8.8 Hz, 1H), 6.25−6.24 (m, 1H), 6.03 (dd, J = 9.5 and 3.7 Hz, 1H), 2.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 135.5, 132.3, 130.9, 130.6, 129.5, 128.9, 128.4, 127.2, 124.2, 122.2, 116.5, 112.9, 110.6, 105.9, 103.5, 83.3, 77.6; IR spectrum in film (ν_{max}, cm^{-1}) 3422, 3351, 2924, 1648, 1479, 798, 718, 692; HRMS (ESI) calcd for $C_{18}H_{14}N_2$ [M]$^+$ 258.1157, found 258.1157.

*(E)-1-(4-(Trifluoromethyl)styryl)-1H-indol-5-amine (**3j**).* The product was obtained as a brown oil (217.4 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 14.6 Hz, 1H), 7.51−7.49 (m, 2H), 7.42−7.40 (m, 2H), 7.32 (d, J = 2.9 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.83 (d, J = 2.2 Hz, 1H), 6.66 (dd, J = 8.8 and 2.2 Hz, 1H), 6.51 (d, J = 14.7 Hz, 1H), 6.43 (d, J = 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 140.1, 130.4, 130.3, 128.8, 128.3, 128.0, 125.7 (q, J = 4.7 Hz, 1C), 125.4, 124.0, 113.3, 110.8, 110.2, 106.2, 105.3; IR spectrum in film (ν_{max}, cm^{-1}) 3431, 2926, 1653, 1458, 850, 714, 609; HRMS (ESI) calcd for $C_{17}H_{13}F_3N_2$ [M]$^+$ 302.1031, found 302.1030.

*1-(4-(Trifluoromethoxy)styryl)-1H-indol-5-amine (**3k**).* The product was obtained as a brown oil (219.4 mg, 69%) as a mixture of *Z* and *E* isomers (77:23): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 [d, J = 14.6 Hz, 0.3H (for minor)], 7.35−7.31 [m, 1H (for major)], 7.27 [d, J = 6.5 Hz, 0.4 H (for minor)], 7.13−7.10 [m, 2.3H (major + minor)], 7.04 [d, J = 8.6 Hz, 1H (for major)], 6.99 [d, J = 8.2 Hz, 2H (for major)], 6.84−6.81 [m, 3.2H (major + minor)], 6.66 [dd, J = 8.6 and 2.2 Hz, 0.3H (for minor)], 6.60 [dd, J = 8.7 and 2.2 Hz, 1.0 H (for major)], 6.51 [d, J = 14.6 Hz, 0.3H (23% for minor regioisomer)], 6.42 [d, J = 3.2 Hz, 0.2 H (for minor)], 6.26 [d, J = 3.2 Hz, 1H (77% for major regioisomer)], 6.07 [d, J = 9.1 Hz, 1H (for major)]; ^{13}C NMR (100 MHz, $CDCl_3$), (major + minor) δ 148.0, 140.8, 140.6,

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135.2, 133.8, 130.5, 130.0, 129.6, 127.1, 126.6, 124.7, 124.2, 124.1, 121.4, 120.8, 116.9, 113.2, 113.0, 111.2, 110.7, 110.2, 106.2, 105.9, 104.8, 103.5; IR spectrum in film (ν_{max}, cm^{-1}) 3423, 2926, 1649, 1479, 849, 716, 671; HRMS (ESI) calcd for $C_{17}H_{13}F_3N_2O$ (M + H^+) 319.1058, found 319.1058.

*1-(2-Methylstyryl)-1H-indol-5-amine (**3l**).* The product was obtained as a brown semisolid (186.0 mg, 75%) as a mixture of *Z* and *E* isomers (75:25): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.77 [d, *J* = 2.9 Hz, 0.5H (for minor)], 7.74 [s, 0.2H (for minor)], 7.68 [d, *J* = 8.0 Hz, 0.3H (for minor)], 7.57 [d, *J* = 8.7 Hz, 0.4H (for minor)], 7.23−7.15 [m, 4.3H (major + minor)], 7.13−7.03 [m, 2H (major + minor)], 6.88 [d, *J* = 14.6 Hz, 0.4 H (for minor)], 6.75 [d, *J* = 1.4 Hz, 0.3H (for minor)], 6.67 [d, *J* = 2.2 Hz, 0.9H (for major)], 6.63 [dd, *J* = 8.8 and 2.2 Hz, 0.3H (for minor)], 6.59−6.56 [m, 2H (for major)], 6.42 [d, *J* = 3.6 Hz, 0.3H;(for minor)], 6.14 [d, *J* = 3.6 Hz, 0.9H (for major)], 6.10 [d, *J* = 9.5 Hz, 1H (for major)], 4.66 [br s, 2.7 H (major + minor)], 2.36 [s, 1H (25% for minor regioisomer)], 2.13 [s, 3H (75% for major regioisomer)]; ^{13}C NMR (100 MHz, $(CD_3)_2SO$), (major + minor) δ 143.0, 142.9, 135.9, 135.2, 135.18, 134.6, 130.2, 130.1, 129.8, 129.2, 128.9, 128.8, 128.6, 127.3, 126.3, 126.1, 125.9, 125.4, 125.1, 124.6, 124.4, 124.0, 112.8, 112.5, 112.4, 110.7, 110.3, 109.3, 104.2, 103.9, 103.7, 103.2, 19.8, 19.5; IR spectrum in film (ν_{max}, cm^{-1}) 3420, 3345, 2923, 2859, 1651, 1622, 1479, 1456, 755, 717, 619; HRMS (ESI) calcd for $C_{17}H_{16}N_2$ (M + H^+) 249.1391, found 249.1391.

*1-(3,5-Dimethoxystyryl)-1H-indol-5-amine (**3m**).* The product was obtained as brown oil (205.8 mg, 70%) as a mixture of *Z* and *E* isomers (75:25): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.93 [d, *J* = 14.6 Hz, 0.4H (for minor)], 7.65−7.62 [m, 0.8H (for major)], 7.05−6.94 [m, 3H (major + minor)], 6.74−6.67 [m, 2.5H (major + minor)], 6.60 [dd, *J* = 8.8 and 2.2 Hz, 0.3H (for minor)], 6.52 [dd, *J* = 8.0 and 1.4 Hz, 1H (for major)], 6.39 [d, *J* = 3.6 Hz, 0.3H (for minor)], 6.33−6.30 [m, 1.3H (major + minor)], 6.27−6.25 [m, 2.9H (major + minor)], 6.12 [d, *J* = 9.5 Hz, 1H;(for major)], 4.62 [br s, 2.3H (major + minor)], 3.74 [s, 2H (25% for minor regioisomer)], 3.55 [s, 6H (75% for major regioisomer)]; ^{13}C NMR (100 MHz, $(CD_3)_2SO$), (major + minor) δ 160.7, 160.2, 143.0, 142.8, 138.6, 136.9, 129.8, 129.1, 128.9, 126.5, 124.9, 124.2, 124.0, 117.5, 112.4, 112.3, 111.4, 111.0, 110.7, 106.3, 104.4, 103.9, 103.8, 103.6, 102.9, 99.5, 98.5, 55.2, 54.9; IR spectrum in film (ν_{max}, cm^{-1}) 3430, 3358, 2936, 2837,1651, 1622, 1480, 1456, 855, 829, 756, 689, 617; HRMS (ESI) calcd for $C_{18}H_{18}N_2O_2$ (M + H^+) 295.1446, found 295.1446.

*1-(2-([1,1′-Biphenyl]-4-yl)vinyl)-1H-indol-5-amine (**3n**).* The product was obtained as a brown solid (223.2 mg, 72%) as a mixture of *Z* and *E* isomers (1:1): mp 95−100 °C; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.96 (d, *J* = 14.6 Hz, 1.3H), 7.69 (d, *J* = 3.6 Hz, 1H), 7.65−7.59 (m, 10H), 7.53 (d, *J* = 8.0 Hz, 1.9H), 7.43−7.36 (m, 4.4H), 7.31−7.27 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 1.3H), 7.06 (d, *J* = 9.5 Hz, 1H), 7.02 (d, *J* = 10.2 Hz, 1H), 6.94 (d, *J* = 2.9 Hz, 1H), 6.79 (d, *J* = 15.3 Hz, 1H), 6.68−6.66 (m, 2H), 6.59 (dd, *J* = 8.0 and 2.2 Hz, 1H), 6.50 (dd, *J* = 7.3 and 0.7 Hz, 1H), 6.39 (d, *J* = 3.6 Hz, 1H), 6.26−6.20 (m, 2H), 4.66 (br s, 4H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 143.1, 143.0, 139.9, 139.5, 138.8, 137.7, 136.0, 134.4, 129.9, 129.2, 129.0, 127.6, 127.3, 126.9, 126.6, 126.5, 126.4, 126.1, 124.6, 124.1, 117.2, 112.6, 112.5, 110.9, 110.9, 110.8, 104.6, 104.0, 103.97, 103.2; IR spectrum in film (ν_{max}, cm^{-1}) 3406, 3327, 1648, 1478, 1458, 759, 723, 696; HRMS (ESI) calcd for $C_{22}H_{18}N_2$ (M + H^+) 311.1548, found 311.1549.

*(Z)-1-(1,2-Diphenylvinyl)-1H-indol-5-amine (**3o**).* The product was obtained as a brown oil (186.0 mg, 60%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.34−7.32 (m, 3H), 7.28 (s, 1H), 7.20−7.17 (m, 2H), 7.12−7.11 (m, 3H), 6.96 (d, *J* = 2.9 Hz, 1H), 6.82−6.80 (m, 2H), 6.76 (d, *J* = 2.2 Hz, 1H), 6.53 (d, *J* = 8.8 Hz, 1H), 6.42 (d, *J* = 3.6 Hz, 1H), 6.36 (dd, *J* = 8.8 and 2.2 Hz, 1H), 4.58 (br s, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 142.3, 138.2, 135.6, 134.7, 129.5, 128.8, 128.6, 128.4, 128.2, 127.9, 125.7, 124.8, 112.6, 111.2, 103.8, 102.6; IR spectrum in film (ν_{max}, cm^{-1}) 3423, 2927, 1626, 1458, 762, 695; HRMS (ESI) calcd for $C_{22}H_{18}N_2$ (M + H^+) 311.1548, found 311.1547.

*(Z)-1-(1,2-Di-m-tolylvinyl)-1H-indol-5-amine (**3p**).* The product was obtained as a brown oil (226.9 mg, 62%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.23−7.19 (m, 2H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.10 (s, 1H), 6.98−6.92 (m, 4H), 6.76 (d, *J* = 2.2 Hz, 1H), 6.69 (s, 1H), 6.53 (d, *J* = 8.7 Hz, 1H), 6.47 (d, *J* = 7.3 Hz, 1H), 6.42 (d, *J* = 2.9 Hz, 1H), 6.36 (dd, *J* = 8.8 and 2.2 Hz, 1H), 4.59 (br s, 2H), 2.25 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 142.2, 138.3, 137.8, 137.1, 135.5, 134.6, 129.8, 129.43, 129.41, 128.7, 128.6, 128.4, 128.1, 126.1, 125.3, 124.7, 123.0, 112.5, 111.1, 103.7, 102.3, 21.1, 21.0; IR spectrum in film (ν_{max}, cm^{-1}) 3429, 2922, 1626, 1478, 825, 763, 698; HRMS (ESI) calcd for $C_{24}H_{22}N_2$ (M + H^+) 339.1861, found 339.1860.

*(Z)-2-(1-(3-Methylstyryl)-1H-indol-3-yl)ethanamine (**5a**).* The product was obtained as a brown oil (176.6 mg, 64%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.55 (d, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 1H), 7.18−7.07 (m, 4H), 7.05−6.99 (m, 2H), 6.96−6.89 (m, 2H), 6.24 (d, *J* = 9.5 Hz, 1H), 3.25 [br s, 7H; 2H (for NH_2) + 5H (for moisture)], 2.73−2.69 (m, 4H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 136.3, 135.0, 129.3, 128.21, 128.18, 125.7, 124.9, 122.9, 122.6, 120.3, 118.9, 118.3, 114.8, 114.0, 110.1, 41.9, 29.7, 21.3; IR spectrum in film (ν_{max}, cm^{-1}) 3359, 2924, 1645, 1462, 798, 740, 696; HRMS (ESI) calcd for $C_{19}H_{20}N_2$ (M + H^+) 277.1704, found 277.1705.

*(Z)-2-(1-(4-Methylstyryl)-1H-indol-3-yl)ethanamine (**5b**).* The product was obtained as a yellow oil (179.4 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.3 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.07 (m, 4H), 6.88 (m, 2H), 6.20 (d, *J* = 8.8 Hz, 1H), 2.94 (t, *J* = 6.6 Hz, 2H), 2.81 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2, 136.2, 132.0, 128.9, 128.4, 128.0, 124.8, 122.4, 120.1, 118.8, 118.7, 114.8, 110.0, 41.9, 29.1, 21.1; IR spectrum in film (ν_{max}, cm^{-1}) 3360, 2921, 1651, 1462, 822, 742, 711; HRMS (ESI) calcd for $C_{19}H_{20}N_2$ (M + H^+) 277.1704, found 277.1705.

*(Z)-2-(1-(2-(Thiophen-3-yl)vinyl)-1H-indol-3-yl)ethanamine (**5c**).* The product was obtained as a brown oil (174.2 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1H), 7.24−7.22 (m, 1H), 7.17−7.13 (m, 1H), 7.10−7.04 (m, 3H), 6.86 (s, 1H), 6.75 (d , *J* = 8.7 Hz, 1H), 6.67 (d , *J* = 5.8 Hz, 1H), 6.23 (d, *J* = 8.8 Hz, 1H), 2.91 (t , *J* = 7.3 Hz, 2H), 2.79 (t , *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.4, 135.6, 128.2, 127.7, 125.3, 125.0, 124.3, 122.65, 122.56, 120.2, 119.0, 115.3, 114.9, 114.0, 110.3, 42.0, 28.9; IR spectrum in film (ν_{max}, cm^{-1}) 3414, 2925, 1648, 1462, 798, 744, 645; HRMS (ESI) calcd for $C_{16}H_{16}N_2S$ (M + H^+) 269.1112, found 269.1111.

*(Z)-2-(1-(4-tert-Butylstyryl)-1H-indol-3-yl)ethanamine (**5d**).* The product was obtained as an orange oil (200.3 mg, 63%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.52 (d, *J* = 7.8 Hz, 1H), 7.32 (d , *J* = 7.8 Hz, 1H), 7.21 (d , *J* = 8.7 Hz, 2H), 7.13−7.05 (m, 2H), 7.02−7.00 (m, 3H), 6.87 (s, 1H), 6.25 (d , *J* = 9.1 Hz, 1H), 3.29 [br s, 10H, 2H (for NH_2) and 8H (for moisture)], 2.71−2.67 (m, 4H), 2.49 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 150.0, 135.7, 132.0, 128.2, 127.9, 125.1, 124.4, 123.1, 122.3, 120.0, 118.9, 118.8, 115.0, 110.4, 41.7, 34.3, 31.0, 28.2; IR spectrum in film (ν_{max}, cm^{-1}) 3425, 2961, 1649, 1462 832, 744; HRMS (ESI) calcd for $C_{22}H_{26}N_2$ (M + H^+) 319.2174, found 319.2173.

*(Z)-2-(1-(3-Methoxystyryl)-1H-indol-3-yl)ethanamine (**5e**).* The product was obtained as a brown oil (181.0 mg, 62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.18−7.14 (m, 2H), 6.94 (d , *J* = 10.3 Hz, 1H), 6.87 (s, 1H), 6.79 (d, *J* = 7.3 Hz, 1H), 6.78−6.75 (m, 1H), 6.71 (s, 1H), 6.20 (d , *J* = 9.5 Hz, 1H), 3.65 (s, 3H), 2.92 (t, *J* = 6.6 Hz, 2H), 2.79 (t, *J* = 6.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 136.4, 129.3, 128.2, 124.9, 123.2, 122.5, 121.3, 120.3, 119.0, 118.2, 115.0, 114.0, 113.1, 110.2, 55.1, 41.0, 29.2; IR spectrum in KBr (ν_{max}, cm^{-1}) 3432, 2926, 1630, 1466, 740, 615; HRMS (ESI) calcd for $C_{19}H_{20}N_2O$ (M + H^+) 293.1654, found 293.1654.

*(Z)-2-(1-(3-Ethynylstyryl)-1H-indol-3-yl)ethanamine (**5f**).* The product was obtained as a brown oil (120.1 mg, 42%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.56 (d, *J* = 7.3 Hz, 1H), 7.36−7.30 (m, 3H), 7.24 (t, *J* = 8.0 Hz, 2H), 7.17−7.14 (m, 2H), 6.94 (d, *J* = 9.5 Hz, 1H), 6.79 (s, 1H), 6.13 (d, *J* = 9.5 Hz, 1H), 3.02 (s, 1H), 2.95 (t, *J* = 5.8 Hz, 2H), 2.81 (t, *J* = 5.8 Hz, 2H), 2.52 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.3, 132.2, 131.0, 129.0, 128.4, 124.7, 123.8, 122.8, 122.2, 120.6, 119.1, 116.8, 115.0, 114.0, 110.1, 83.2, 77.5, 41.6, 28.3; IR spectrum in film (ν_{max}, cm^{-1}) 3291, 2923, 2852, 1651, 1461, 801, 744, 692; HRMS (ESI) calcd for $C_{20}H_{18}N_2$ (M + H^+) 287.1548, found 287.1548.

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(Z)-2-(1-(4-(Trifluoromethyl)styryl)-1H-indol-3-yl)ethanamine ***(5g)***. The product was obtained as a brown solid (198.0 mg, 60%): mp 85−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.25−7.15 (m, 4H), 7.10 (t, J = 7.3 Hz, 1H), 6.94 (d, J = 9.5 Hz, 1H), 6.73 (s, 1H), 6.13 (d, J = 8.7 Hz, 1H), 2.91 (t, J = 7.3 Hz, 2H), 2.81 (t, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 136.2, 128.8, 128.2, 125.3, 125.2 (q, J = 3.8 Hz, 1C), 124.9, 124.6, 123.0, 120.8, 119.1, 116.8, 115.0, 110.3, 41.4, 27.4; IR spectrum in film (ν_{max}, cm^{-1}) 3364, 2925, 2854, 1652, 1462, 800, 744, 668; HRMS (ESI) calcd for $C_{19}H_{17}F_3N_2$ (M + H$^+$) 331.1422, found 331.1422.

(Z)-2-(1-(4-(Trifluoromethoxy)styryl)-1H-indol-3-yl)ethanamine ***(5h)***. The product was obtained as a yellow oil (204.1 mg, 59%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.55 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.24 (s, 3H), 7.19−7.16 (m, 2H), 7.13−7.07 (m, 2H), 6.85 (s, 1H), 6.31 (d, J = 9.5 Hz, 1H), 3.16 [br s, 9H; 2H (for NH_2) + 7H (for moisture)], 2.71−2.66 (m, 4H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 147.2, 135.6, 134.5, 130.2, 128.0, 124.5, 124.1, 122.5, 121.3, 120.9, 120.2, 119.0, 118.8, 116.4, 115.9, 110.5, 42.0, 28.8; IR spectrum in film (ν_{max}, cm^{-1}) 3404, 2924, 1648, 1461, 814, 744, 670; HRMS (ESI) calcd for $C_{19}H_{17}F_3N_2O$ (M + H$^+$) 347.1371, found 347.1371.

(Z)-2-(1-(2-Methylstyryl)-1H-indol-3-yl)ethanamine ***(5i)***. The product was obtained as a yellow oil (168.3 mg, 61%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.39 (dd, J = 8.0 and 2.9 Hz, 2H), 7.16 (d, J = 9.5 Hz, 1H), 7.11−7.03 (m, 3H), 6.99−6.90 (m, 3H), 6.46 (s, 1H), 6.08 (d, J = 9.5 Hz, 1H), 2.71 (br s, 2H), 2.50−2.45 (m, 4H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 136.2, 134.8, 130.0, 128.8, 127.9, 127.4, 125.6, 124.2, 123.1, 122.4, 120.2, 118.8, 115.0, 114.3, 109.6, 41.7, 28.9, 19.8; IR spectrum in film (ν_{max}, cm^{-1}) 3418, 2924, 1652, 1462, 743; HRMS (ESI) calcd for $C_{19}H_{20}N_2$ (M + H$^+$) 277.1704, found 277.1704.

(Z)-2-(1-(2,4-Dimethoxystyryl)-1H-indol-3-yl)ethanamine ***(5j)***. The product was obtained as a brown oil (186.7 mg, 58%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.26 (s, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.11 (t , J = 7.3 Hz, 1H), 7.07−7.03 (m, 1H), 6.93 (s, 1H), 6.32 (t, J = 2.2 Hz, 1H), 6.25 (d, J = 2.2 Hz, 2H), 6.19 (d, J = 9.5 Hz, 1H), 3.52 (s, 6H), 2.90 (br s, 2H), 2.68 (m, 4H), ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 160.2, 136.6, 135.7, 127.9, 124.3, 123.8, 122.3, 120.1, 118.9, 118.3, 115.4, 110.5, 109.4, 106.3, 101.8, 99.7, 54.9, 42.1, 28.8; IR spectrum in film (ν_{max}, cm^{-1}) 3368, 2935, 1648, 744, 688; HRMS (ESI) calcd for $C_{20}H_{22}N_2O_2$ (M + H$^+$) 323.1759, found 323.1761.

(Z)-2-(1-Styryl-1H-indol-3-yl)ethanamine ***(5k)***. The product was obtained as an orange oil (157.2 mg, 60%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.49 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.17−7.08 (m, 7H), 6.84 (d , J = 8.7 Hz, 1H), 6.74 (s, 1H), 6.15 (d, J = 8.7 Hz, 1H), 2.85 (t, J = 6.6 Hz, 2H), 2.73 (t , J = 6.6 Hz, 2H), 2.21 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 136.3, 135.1, 128.6, 128.3, 128.1, 127.5, 124.9, 123.1, 122.6, 120.4, 119.0, 118.6, 114.7, 114.0, 110.2, 41.7, 28.5; IR spectrum in film (ν_{max}, cm^{-1}) 3370, 2924, 1651, 1462, 744, 694; HRMS (ESI) calcd for $C_{18}H_{18}N_2$ (M + H$^+$) 263.1548, found 263.1548.

(Z)-2-(1-(4-Methoxystyryl)-1H-indol-3-yl)ethanamine ***(5l)***. The product was obtained as a brown oil (192.7 mg, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.17−7.13 (m, 2H), 7.07 (t, J = 7.3 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 6.80 (s, 1H), 6.74 (d , J = 9.5 Hz, 1H), 6.67 (d, J = 8.8 Hz, 2H), 6.12 (d, J = 8.8 Hz, 1H), 3.69 (s, 3H), 2.90 (t, J = 5.8 Hz, 2H), 2.78 (t , J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 139.2, 136.3, 130.0, 128.0, 127.3, 125.0, 122.6, 121.8, 120.2, 119.5, 118.9, 114.3, 114.0, 113.7, 110.3, 55.2, 41.8, 28.4; IR spectrum in film (ν_{max}, cm^{-1}) 3386, 2921, 1640, 1460, 833, 743; HRMS (ESI) calcd for $C_{19}H_{20}N_2O$ (M + H$^+$) 293.1654, found 293.1654.

(E)-2-(1-(4-Ethynylstyryl)-1H-indol-3-yl)ethanamine ***(5m)***. The product was obtained as a brown oil (114.1 mg, 40%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 14.7 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.30−7.18 (m, 4H), 7.12−7.07 (m, 2H), 6.50 (d, J = 14.7 Hz, 1H), 3.05 (s, 1H), 3.01 (t, J = 4.4 Hz, 2H), 2.86 (t, J = 5.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 132.6, 132.0, 128.9, 128.6, 125.3, 124.0, 123.2, 121.2, 120.8, 119.4, 117.3, 117.2, 111.9, 110.2, 109.6, 83.7, 77.6, 41.8, 28.9; IR spectrum in film (ν_{max}, cm^{-1}) 3368, 3280, 2924, 2853, 1648, 1460, 804, 739, 617; HRMS (ESI) calcd for $C_{20}H_{18}N_2$ (M + H$^+$) 287.1548, found 287.1548.

(Z)-2-(1-(1,2-Diphenylvinyl)-1H-indol-3-yl)ethanamine ***(5n)***. The product was obtained as a brown oil (202.8 mg, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 1H), 7.24−7.15 (m, 6H), 7.04−6.98 (m,3H), 6.96−6.92 (m, 2H), 6.79 (d, J = 8.0 Hz, 1H), 6.70−6.68 (m, 3H), 2.92 (t, J = 6.6 Hz, 2H), 2.83 (t, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 136.3, 135.8, 134.8, 128.8, 128.6, 128.4, 128.2, 127.7, 126.4, 126.2, 124.4, 122.2, 119.8, 118.8, 114.8, 112.0, 42.0, 29.0; IR spectrum in film (ν_{max}, cm^{-1}) 3369, 2926, 1626, 1459, 743, 695, 668; HRMS (ESI) calcd for $C_{24}H_{22}N_2$ (M + H$^+$) 339.1861, found 339.1861.

(Z)-2-(1-(1,2-Di-m-tolylvinyl)-1H-indol-3-yl)ethanamine ***(5o)***. The product was obtained as a yellow oil (226.9 mg, 62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.3 Hz, 1H), 7.15−7.09 (m, 1H), 7.06−6.99 (m, 3H), 6.96−6.92 (m, 2H), 6.89−6.79 (m, 4H), 6.70 (s, 1H), 6.52 (s, 1H), 6.38 (d, J = 7.3 Hz, 1H), 2.93 (t, J = 6.4 Hz, 2H), 2.85 (t, J = 5.9 Hz, 2H), 2.23 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.4, 137.8, 136.4, 136.1, 134.9, 129.8, 129.7, 128.7, 128.6, 128.5, 128.2, 126.9, 126.6, 125.6, 124.6, 123.6, 122.4, 119.8, 118.9, 114.6, 112.1, 42.2, 29.0, 21.6, 21.4; IR spectrum in film (ν_{max}, cm^{-1}) 3369, 2924, 2854, 1628, 1458, 768, 698, 668; HRMS (ESI) calcd for $C_{26}H_{26}N_2$ (M + H$^+$) 367.2174, found 367.2173.

(Z)-2-(1-Styryl-1H-imidazol-4-yl)ethanamine ***(6a)***. The product was obtained as a yellow-brown oil (106.5 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 2H), 7.23 (t, J = 1.8 Hz, 1H), 7.21 (t, J = 1.8 Hz, 1H), 7.06 (dd, J = 7.8 and 1.8 Hz, 2H), 6.62 (d, J = 9.1 Hz, 1H), 6.55 (s, 1H), 6.23 (d, J = 9.6 Hz, 1H), 2.87 (t, J = 6.4 Hz, 2H), 2.57 (t, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 136.6, 133.8, 128.8, 128.7, 128.5, 128.2, 127.2, 126.0, 122.4, 115.3, 41.6, 32.1; IR spectrum in film (ν_{max}, cm^{-1}) 3363, 2925, 1656, 1494, 753, 698, 628; HRMS (ESI) calcd for $C_{13}H_{15}N_3$ [M]$^+$ 213.1266, found 213.1266.

(E)-2-(1-(4-(Trifluoromethyl)styryl)-1H-imidazol-4-yl)ethanamine ***(6b)***. The product was obtained as a brown oil (146.1 mg, 52%): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.31 (s, 1H), 7.97−7.91 (m, 1H), 7.70−7.65 (m, 4H), 7.48 (s, 1H), 7.01 (d, J = 14.6 Hz, 1H), 2.99 (br s, 2H), 2.79 (t, J = 6.4 Hz, 2H), 2.57 (t, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 142.3, 140.2, 137.5, 127.9, 127.5, 127.4, 126.8, 126.6, 126.1 (q, J = 4.7 Hz, 1C), 123.5, 114.8, 113.0, 41.9, 32.5; IR spectrum in film (ν_{max}, cm^{-1}) 3420, 2254, 1661, 824, 763; HRMS (ESI) calcd for $C_{14}H_{14}F_3N_3$ [M]$^+$ 281.1140, found 281.1140.

2-(1-(3-Methylstyryl)-1H-imidazol-4-yl)ethanamine ***(6c)***. The product was obtained as a yellow -brown oil (122.5 mg, 54%) as a mixture of Z and E isomers (1:1): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.50 (s, 1H), 7.29 (s, 1H), 7.18 (t, J = 7.3 Hz, 1H), 7.13−7.09 (m, 2H), 7.07 (t, J = 5.1 Hz, 2H), 6.91−6.88 (m, 3H), 6.81−6.75 (m, 3H), 6.67−6.59 (m, 2H), 6.32 (d, J = 9.5 Hz, 1H), 3.25 [br s, 10H; 2H (NH_2 for Z isomer) + 2H (NH_2 for E isomer) + 6H (for moisture)], 2.78 (t, J = 7.3 Hz, 2H), 2.73 (t, J = 7.3 Hz, 2H), 2.58−2.52 (m, 4H), 2.22 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$), (major + minor) δ 140.2, 139.4, 138.8, 137.8, 136.7, 135.8, 134.0, 133.4, 129.2, 129.0, 128.6, 128.5, 128.3, 126.4, 125.4, 125.1, 123.2, 123.0, 122.7, 121.9, 121.3, 115.5, 115.0, 40.1, 31.5, 27.1, 20.9; IR spectrum in film (ν_{max}, cm^{-1}) 3364, 2924, 1642, 1466, 760, 697; HRMS (ESI) calcd $C_{14}H_{17}N_3$ [M]$^+$ 227.1422, found 227.1421.

2-(1-(3-Methoxystyryl)-1H-imidazol-4-yl)ethanamine ***(6d)***. The product was obtained as a brown oil (121.5 mg, 50%) as a mixture of Z and E isomers (66:34): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.46 [s, 0.9H (for major)], 7.28 [s, 0.6H (for minor)], 7.20−7.11 [m, 1.4H (major + minor)], 6.88 [d, J = 7.5 Hz, 1H (for major)], 6.81−6.77 [m, 2.7H (major + minor)], 6.70 [s, 0.7H (for minor)]; 6.66 [d, J = 5.1 Hz, 0.9H (for major)], 6.61−6.58 [m, 1.4H (major + minor)], 6.49 [d, J = 10.2 Hz, 0.6H (for minor)], 6.30 [d, J = 10.2 Hz, 1.6H (for minor)], 3.61 [s, 3H (66% for major regioisomer)], 3.54 [s, 1.6H (34% for minor regioisomer)], 2.97 [br s, 3H, (major + minor)], 2.68−2.65 [m, 3H (major + minor)], 2.45−2.42 [m, 2H (major + minor)]; ^{13}C NMR (100 MHz, $(CD_3)_2SO$), (major + minor) δ 159.23, 159.19, 140.5, 136.6, 135.8, 135.4, 134.7, 129.7, 129.4, 128.3,

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126.4, 123.4, 123.4, 122.3, 121.3, 120.9, 120.8, 114.8, 114.3, 113.8, 113.4, 113.0, 54.9, 54.8, 40.4, 40.1, 31.7, 28.0 ; IR spectrum in film (ν_{max}, cm^{-1}) 3414, 1652, 765, 695, 632; HRMS (ESI) calcd for $C_{14}H_{17}N_3O$ $[M]^+$ 243.1372, found 243.1372.

*2-(1-(4-(Trifluoromethoxy)styryl)-1H-imidazol-4-yl)ethanamine (**6e**).* The product was obtained as a brown oil (151.4 mg, 51%) as a mixture of *Z* and *E* isomers (1:1): ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.80−7.72 (m, 1.3H), 7.51 (d, J = 8.7 Hz, 2H), 7.44 (s, 1H), 7.37 (s, 1H), 7.28−7.22 (m, 4H), 7.16−7.14 (m, 2H), 6.96−6.87 (m, 3H), 6.63−6.60 (m, 1H), 6.31(d, J = 9.6 Hz, 1H), 3.03 (br s, 4H), 2.72 (t, J = 6.4 Hz, 2H), 2.65−2.62 (m, 4H), 2.48 (t, J = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 147.7, 147.2, 140.7, 136.7, 136.6, 135.0, 133.5, 130.3, 130.1, 127.5, 124.9, 124.1, 123.0, 121.4, 121.1, 119.6, 114.6, 114.4, 112.6, 41.4, 41.2, 32.0, 31.7; IR spectrum in film (ν_{max}, cm^{-1}) 3412, 2918, 2850, 1658, 1506, 953, 808, 754, 670, 626; HRMS (ESI) calcd for $C_{14}H_{14}F_3N_3O$ $[M]^+$ 297.1089, found 297.1090.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving ^{1}H and ^{13}C NMR and HRMS spectra for selected compounds. 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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