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Intramolecular Gold-Catalyzed and NaH-Supported Cyclization Reactions of *N*-Propargyl Indole Derivatives with Pyrazole and Pyrrole Rings: Synthesis of Pyrazolodiazepinoindole, Pyrazolopyrazinoindole, and Pyrrolopyrazinoindole

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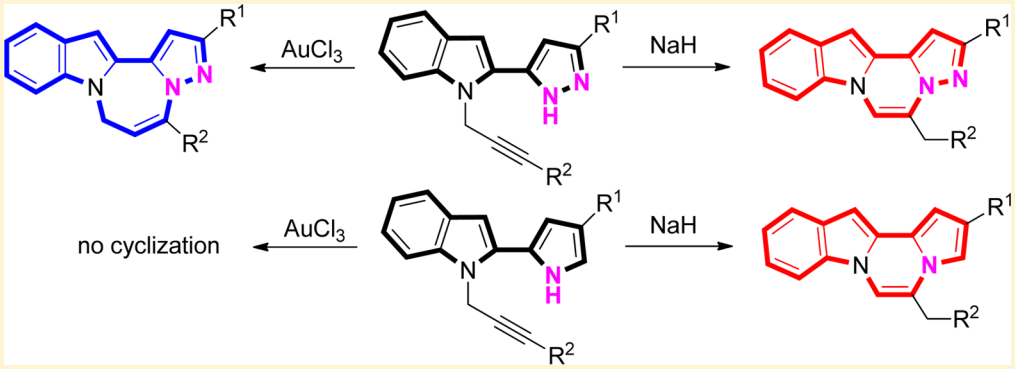
Supporting Information



ABSTRACT: Gold-catalyzed and NaH-supported intramolecular cyclization of *N*-propargyl indole derivatives with pyrazole and pyrrole units attached to indole is described. An efficient route to the synthesis of pyrazolodiazepinoindole, pyrazolopyrazinoindole, and pyrrolopyrazinoindole has been established. First, *N*-propargyl 2-(1*H*-pyrazol-5-yl)-1*H*-indole and 2-(1*H*-pyrrol-2-yl)-1*H*-indole were synthesized. Introduction of various substituents into the alkyne functionality was accomplished by Sonogashira cross-coupling reaction. Gold-catalyzed cyclization of pyrazoles having a terminal alkyne afforded the 6-*exo*-dig cyclization product. However, exclusive formation of 7-*endo*-dig cyclization products was observed with internal alkynes. On the other hand, cyclization with NaH only resulted in the formation of 6-*exo*-dig cyclization products regardless of the substitution of the alkyne functionality. Allenic intermediates were postulated for this outcome.

INTRODUCTION

Heterocycles are the most important structural classes of chemical compounds,[1] and they are particularly well represented among agrochemicals, natural products, and pharmaceuticals. It is estimated that more than 70% of all pharmaceutical products possess heterocyclic structural subunits.[2] Indole (**1**), a bicyclic aromatic heterocycle containing a nitrogen atom, exists in many natural products and pharmaceuticals.[2,3] Furthermore, the indole nucleus is also a common moiety in material science.[4] Therefore, the search for an efficient synthesis of the indole ring system is of great interest. Most of the indole derivatives can also be obtained by functionalizing simple indoles.[5] Indole derivative pyrazino[1,2-*a*]indole (**2**) or analogues have been found in a variety of complex compounds displaying interesting biological activities. Substituted derivatives of **2** were identified as a novel potent antiproliferative agent against the human chronic myelogenous leukemia K562 cell line,[6] and some isomers showed potent antibacterial activity.[7]

On the other hand, pyrazolo[1,5-*a*]pyrazine (**3**) and pyrrolo[1,2-*a*]pyrazine (**4**) derivatives have been shown as potent and selective Vasopressin$_{1b}$ receptor antagonists.[8] Furthermore, it was shown that attachment of substituents to the core structure allowed generation of compounds with high inhibitory potency. Some derivatives of pyrazolo[1,5-*a*]pyrazine are Janus kinase (JAK) inhibitors and are useful in the treatment of diseases.[9] These inhibitors have therapeutic application in the treatment of cancer and inflammatory diseases. Moreover, pyrrolo[1,2-*a*]pyrazine derivatives are potent and selective noncompetitive mGluR5 antagonists.[10] We recently described the synthesis of pyrazolopyrrolopyrazine derivatives.[11] The key feature of this methodology was the synthesis of *N*-propargyl pyrrole derivatives substituted at the C-2 position with a pyrazole unit. Gold-catalyzed cyclization of pyrazoles or cyclization with NaH resulted in the formation

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pyrazolopyrrolopyrazine and pyrazolopyrrolodiazepine derivatives. As an extension of this work, we describe full studies directed toward the synthesis of indole-fused pyrazolo[1,5-*a*]pyrazine (**5**), pyrrolo[1,2-*a*]pyrazine (**6**), and pyrazolodiazepine (**7**) starting from *N*-propargyl indole derivatives (Figure 1).

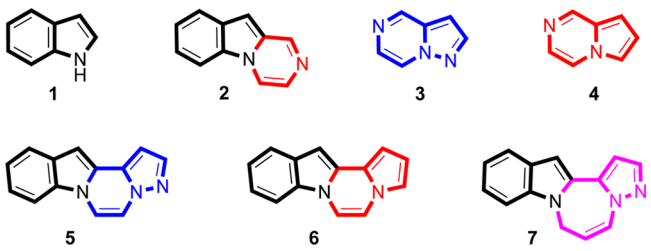
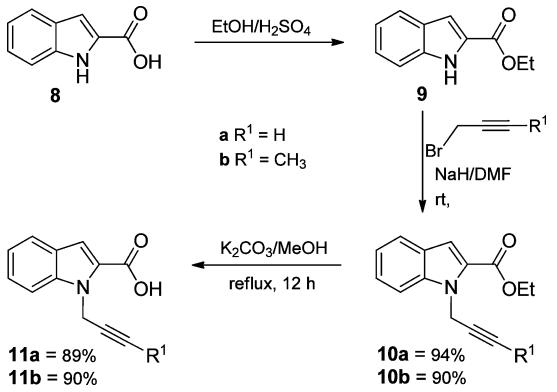


Figure 1. Structures **1**–**7**.

RESULTS AND DISCUSSION

In planning our synthetic approach to the target indole-fused heterocycles **5** and **7**, we first explored the reactivity of *N*-propargyl-indole carboxylic acid **11a,b** for the synthesis of *α,β*-alkynyl ketones **13a,b**. The preparation of *N*-propargyl carboxylic acids **11a,b** was performed from commercially available carboxylic acid **8**, according to the four-step route illustrated in Scheme 1. Acid **8** was treated with H_2SO_4 in

Scheme 1. Synthesis of *N*-Propargyl Carboxylic Acids 11a,b

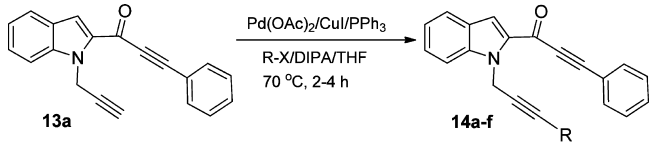


ethanol. The resulting ethyl 1*H*-indole-2-carboxylate (**9**)[12] was then reacted with NaH in the presence of propargyl bromide[13] or 1-bromobut-2-yne to give ethylindole-2-carboxylates **10a,b**, which were then hydrolyzed with K_2CO_3 to the corresponding acids **11a,b**.[14]

For the synthesis of *α,β*-alkynyl ketones **13a,b** from *N*-propargyl carboxylic acids **11**, prior activation of carboxylic groups was necessary. This was accomplished by treatment of **11a,b** with thionyl chloride in the presence of triethylamine in THF at room temperature. The resulting acid chlorides **12a,b** were then condensed in situ with trimethylsilylphenyl acetylene[15] to furnish the corresponding alkynyl product **13a,b** as shown in Scheme 2.

The next step was the synthesis of a library of dialkynyl ketones **14a**–**f** with various substituents. The Sonogashira cross-coupling reaction[16] of aryl halides with terminal alkynes is an effective approach to the synthesis of functionalized alkynes. For the Sonogashira coupling reaction we used a palladium catalyst and a copper(I) cocatalyst, in which the palladium has the function of promoting the cross-coupling of an aryl fragment in the presence of triphenylphosphine and diisopropylamine (DIPA) as the base. Several halo-substituted aromatic compounds were smoothly coupled with alkyne derivatives **13a** to give dialkynes **14a**–**f** substituted at the terminal alkyne carbon atom in high yields (Scheme 3).

Scheme 3. Synthesis of *N*-Substituted *α,β*-Alkynyl Ketones 14a–f



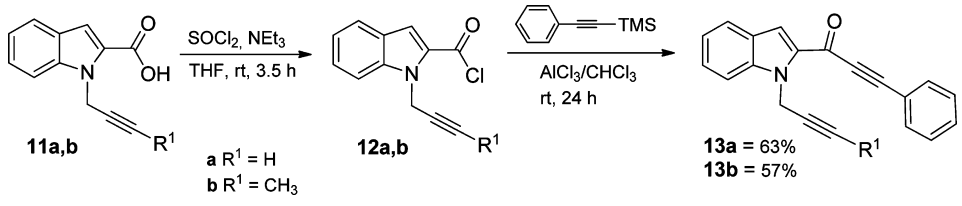
	R—X	R	Yield (%)
a =	Ph-I	Ph	79
b =	*p*-Br-C_6H_4-CH_3	*p*-C_6H_4-CH_3	80
c =	*p*-I-C_6H_4-OCH_3	*p*-C_6H_4-OCH_3	78
d =	*m*-I-C_6H_4-NO_2	*m*-C_6H_4-NO_2	86
e =	*p*-I-C_6H_4-F	*p*-C_6H_4-F	83
f =	2-Py-Br	2-Py	85

After the successful generation of substituted dialkynes **14a**–**f**, the next step was the synthesis of pyrazole derivatives **15a**–**h**. Knorr pyrazole synthesis[17] involving the condensation of 1,3-dicarbonyl compounds with hydrazine in one step has attracted great interest in synthetic organic chemistry. Our strategy toward the synthesis of pyrazoles is outlined in Scheme 4. It involves the intermolecular reaction of *α,β*-alkynyl compounds **13a,b** and **14a**–**g** with hydrazine monohydrate under a N_2 atmosphere to afford the desired pyrazoles **15a**–**h** in good yields.

Interestingly, we found that compound **14f** having a pyridine group attached to the acetylene unit directly gave heterocyclization product **16f** upon reaction with hydrazine (Scheme 5). We assume that pyrazole **15f**, formed as an intermediate, underwent a further cyclization reaction because of the increased reactivity of alkyne functionality due to the electron deficiency of the pyridine ring.

As the next step, we started to investigate the feasibility of the intended synthetic approach to the target skeletons **5** and **7** using gold-catalyzed reactions. For cyclization, gold salts and

Scheme 2. Two-Step Synthesis of Substituted *N*-Propargyl *α,β*-Alkynyl Ketones 13a,b



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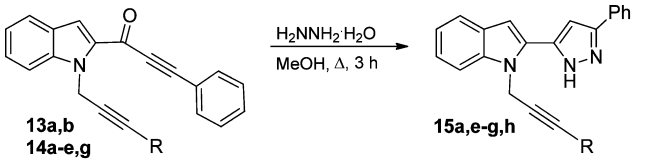
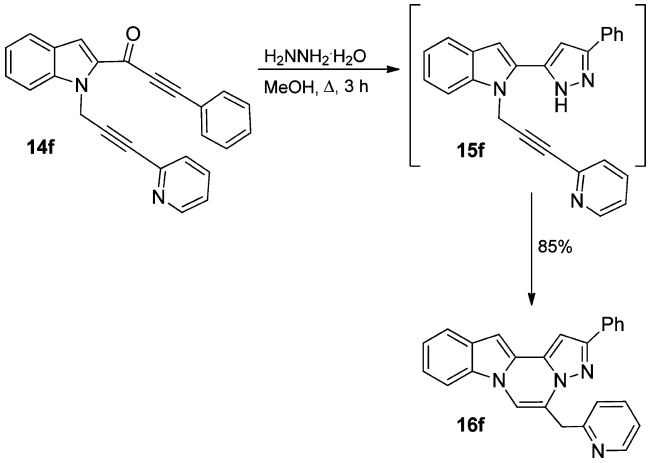
Scheme 4. Preparation of 3,5-Disubstituted Pyrazoles 15a−h



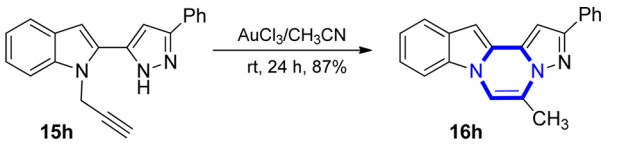
	R	Yield (%)
a =	Ph	94
b =	*p*-C_6H_4-CH_3	92
c =	*p*-C_6H_4-OCH_3	90
d =	*m*-C_6H_4-NO_2	92
e =	*p*-C_6H_4-F	88
g =	CH_3	92
h =	H	92

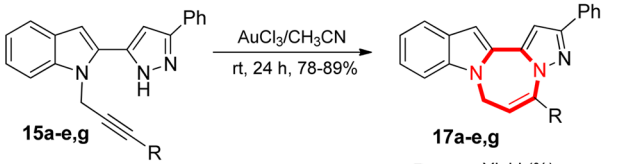
Scheme 5. Reaction of 14f with Hydrazine



complexes have emerged as the most powerful catalysts for electrophilic activation followed by reaction with nucleophiles.[18,19] The catalyst, $AuCl_3$, was used for the intramolecular cyclization reaction of **15a−e,g,h**. The reaction of **15h** having a terminal alkyne with $AuCl_3$ at room temperature afforded the cyclization product **16h** (Scheme 6). The reaction proceeds via

Scheme 6. Intramolecular Cyclization of Pyrazoles 15a−e,g,h with $AuCl_3$





	R	Yield (%)
a =	Ph	83
b =	*p*-C_6H_4-CH_3	80
c =	*p*-C_6H_4-OCH_3	80
d =	*m*-C_6H_4-NO_2	83
e =	*p*-C_6H_4-F	78
g =	CH_3	89

electrophilic activation of the triple bond followed by 6-*exo*-dig heterocyclization and H-shift leading to the pyrazolopyrazinoindole **16h**. However, exclusive formation of 7-*endo*-dig cyclization products **17a−e** and **17g** having a pyrazolodiazepinoindole skeleton was observed by the reaction of internal alkynes **15a−e** and **15g** with $AuCl_3$ under the same reaction conditions (Scheme 6).

The structures of those cyclization products **17a−e,g** were determined using NMR spectra recorded in $CDCl_3$. The exact location of the methylene group in **17a** was determined from 2D NMR (COSY, HSQC, and HMBC) spectra. The methylene protons resonating at 4.85 ppm as a doublet showed strong correlation with the quaternary carbon atoms resonating at 145.8, 135.9, and 129.1 as well as with the olefinic carbon (=CH) at 113.8 ppm. In addition, the methylene carbon resonating at 39.1 ppm correlates only with the =CH proton appearing at 6.15 ppm as a triplet. All this information clearly shows that the methylene group is located between the indole nitrogen atom and the double bond (Figure 2).

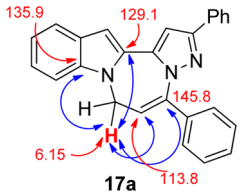


Figure 2. Correlations of the methylene group in **17a**.

The electronic structure of the substituents attached to the triple bond is responsible for the 6-*exo*-dig and 7-*endo*-dig cyclization process. To understand this chemoselectivity, we performed some calculations. Geometry optimization and frequency calculations of complexes **15h** and **15a** with $AuCl_3$ were performed using the B3LYP hybrid level with the 6-31G(d,p) and LANL2DZ (Au) basis set. Natural bond orbital analysis was performed at the same level of theory (Figure 3).

In the case of the complex of **15h** + $AuCl_3$, the distance between the terminal alkyne carbon atom and the gold atom is shorter (2.307 Å) than the distance between the internal alkyne carbon atom and the gold atom, indicating that the positive charge is localized on the internal alkyne carbon atom (Figure 3). Therefore, the pyrazole nitrogen atom attacks exclusively the carbon atom positively charged, forming 6-*exo*-dig cyclization product **16h**. On the other hand, if the terminal alkyne carbon is substituted by a phenyl group, in the complex the gold atom has a stronger interaction with the C-2 carbon atom (Au−C distance 2.162 Å) and the positive charge is concentrated on C-1 because of the better stabilization of the positive charge by the aromatic ring and methyl group in the case of **15a**. Therefore, the alkyne carbon atoms, substituted by phenyl or methyl groups, are exclusively attacked at the C-1 carbon atom, giving rise to the formation of 7-*endo*-dig cyclization products **17a−e** and **17g**.

After successful cyclization reaction of **15a−e** and **15g** having internal alkyne functionality with $AuCl_3$, we only obtained 7-*endo*-dig cyclization products **17a−e** and **17g**; we then turned our attention to the exclusive formation of 6-*exo*-dig products **16a−e** and **16h**. For this purpose, pyrazole derivatives **15a−e,h** were reacted with NaH in *N,N*-dimethylforamide (DMF) at room temperature. To our delight, in all cases 6-*exo*-dig cyclization products **16a−e,h** were exclusively formed (Scheme

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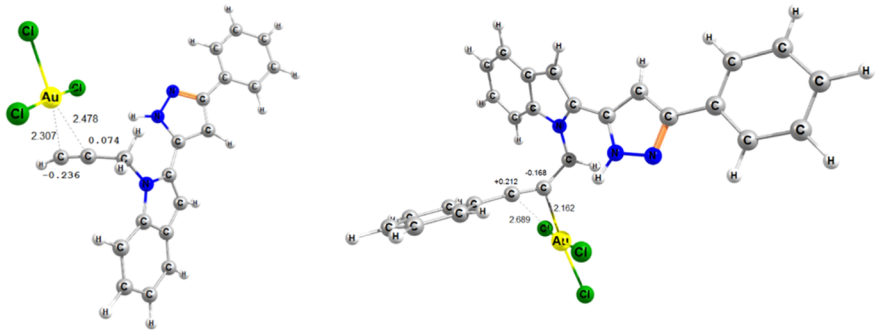
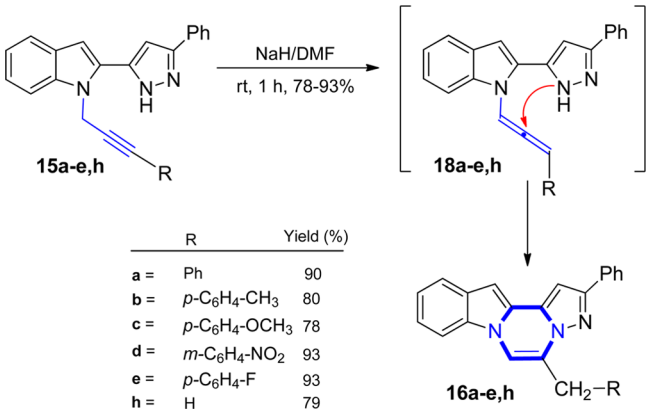


15h + $AuCl_3$ **15a** + $AuCl_3$

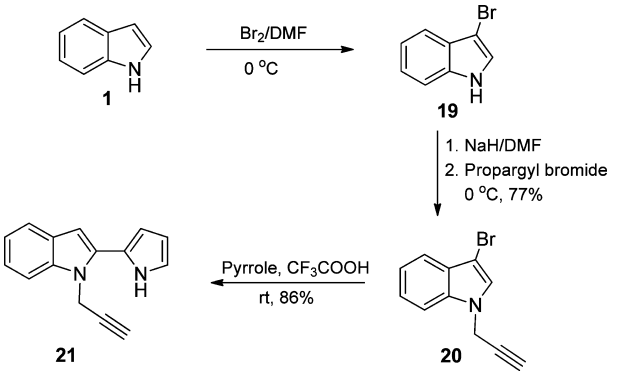
Figure 3. Geometry optimized structures of **15h** + $AuCl_3$ and **15a** + $AuCl_3$ complexes; NBO charges and distances in Å.

Scheme 7. NaH-Supported Intramolecular Cyclization of Pyrazoles 15a−e,h



	R	Yield (%)
a =	Ph	90
b =	*p*-C_6H_4-CH_3	80
c =	*p*-C_6H_4-OCH_3	78
d =	*m*-C_6H_4-NO_2	93
e =	*p*-C_6H_4-F	93
h =	H	79

Scheme 8. Synthesis of Propargylated Pyrroloindole Derivative 21



7). On the basis of information gathered so far, we favor the mechanism outlined in Scheme 7 as the most likely.[20] The alkyne functionality first undergoes NaH-catalyzed isomerization to generate the corresponding allenes **18a−e,h**. Recently, we showed that 1-(prop-2-yn-1-yl)-1*H*-pyrrole-2-carbaldehyde was isomerized to the corresponding allene in the presence of NaH in DMF at 0 °C in a yield of 94%.[20] Under the reaction conditions we were not able to isolate the allenic intermediate. Since the central carbon atom in the allene moiety is the most electropositive carbon, a nitrogen atom of the pyrazole ring exclusively attacks the central carbon atom, forming 6-*exo*-dig cyclization products **16a−e,h**.

After regiospecific alkyne-cyclization reactions with pyrazole rings, we were interested in the synthesis of pyrrolopyrazinoindole skeleton **6** where the pyrazole unit in **5** is replaced by a pyrrole unit. For the synthesis of the starting material **21** suitable for a ring-closure reaction, indole (**1**) was selectively brominated at the C-3 carbon atom to protect this position. Bromoindole **19**[21] was reacted with propargyl bromide in the presence of NaH to give **20**. Reaction of propargylated bromoindole **20** with pyrrole in dichloromethane in the presence of trifluoracetic acid led to the formation of the desired product **21** (Scheme 8).

Again, the Sonogashira cross-coupling reaction was used for derivatization of the terminal alkyne functionality in **21**. Three halo-substituted aromatic compounds were coupled smoothly with the terminal alkyne to give **22a−c** in high yields (Scheme 9).

As the next step, with the optimal conditions in hand, we embarked on the gold-catalyzed cyclization reaction of **21** and **22a−c**. Unfortunately, we were not able to observe any trace of 6-*exo*-dig or 7-*endo*-dig cyclization products using AuCl and $AuCl_3$. We assume that the nucleophilicity of the pyrrole ring is less than that of the pyrazole ring. Therefore, again we turned our attention to NaH-supported cyclizations. Analogously, the reaction of **21** and **22a−c** with NaH in DMF at room temperature exclusively gave 6-*exo*-dig heterocyclization products **23a−d** in high yields. As there was no trace of 7-*endo*-dig cyclization products observed, we propose that the cascade process relies on the interception of allene intermediates followed by a H-shift as described above (see Scheme 7).

■ CONCLUSION

In short, the reported gold-catalyzed as well as NaH-supported cyclizations provide a versatile approach to the synthesis of new heterocycles with new skeletons such as pyrazolodiazepinoindole, pyrazolopyrazinoindole, and pyrrolopyrazinoindole (**5−7**). Those compounds can be very attractive for further synthetic as well as medicinal applications. Furthermore, this methodology will allow us to introduce various substituents into all positions of the target compounds.

■ EXPERIMENTAL SECTION

General Methods. All reagents were used as purchased from commercial suppliers without further purification. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a 400 MHz instrument, and chemical shifts are reported in parts per million (ppm) downfield from TMS, using $CDCl_3$ as the internal standard. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C NMR)

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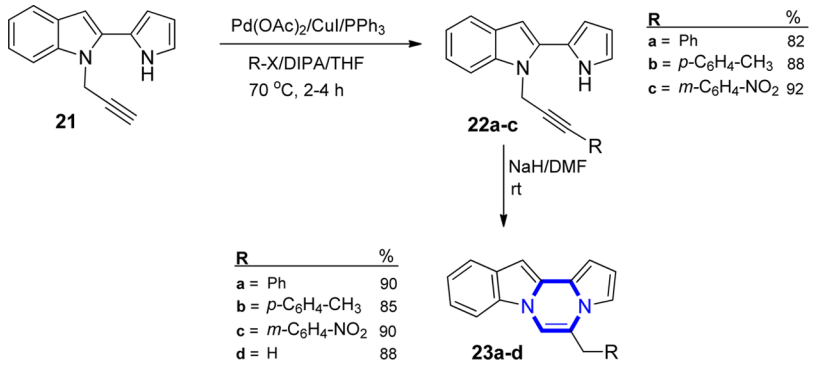
Scheme 9. NaH-Supported Intramolecular Cyclization of Pyrroles 21 and 22a−c



spectra were recorded on a 100 MHz instrument. Column chromatography was performed on silica gel (60-mesh). TLC was carried out on 0.2 mm silica gel 60 F_{254} analytical aluminum plates. High resolution mass spectra were recorded by an LC-MS TOF electrospray ionization technique. Infrared (IR) spectra were recorded in the range of 4000−600 cm^{-1} via ATR diamond. Melting points (uncorrected) were measured using a melting point apparatus.

*Ethyl-1H-indole-2-carboxylate (**9**).*[12] To a stirred solution of 1*H*-indole-2-carboxylic acid (**8**) (3.0 g, 18.61 mmol) in dry ethanol (50 mL) sulfuric acid (1 mL) was added as a catalyst. Then, the solution was heated at reflux temperature for 24 h. After complete consumption of starting material monitored by TLC, water (50 mL) was added; the resulting mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic phase was washed with brine and water and dried over $MgSO_4$. Then, the solvent was evaporated under vacuum to give ethyl-1*H*-indole-2-carboxylate (**9**) as a white powder (3.31 g, 17.5 mmol, 94%). Mp 123−124 °C (Lit. mp 122−123 °C[12]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (br s, 1H, NH), 7.69 (dd, J = 8.0, 0.8 Hz, 1H), 7.43 (dd, J = 8.3, 0.9 Hz, 1H), 7.32 (ddd, J = 8.3, 7.0, 0.8 Hz, 1H), 7.24 (dd, J = 2.0, 0.8 Hz, 1H), 7.15 (ddd, J = 8.0, 7.0, 0.9 Hz, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 136.9, 127.5 (2C), 125.3, 122.6, 120.8, 111.9, 108.7, 61.1, 14.4.

*Ethyl 1-(Prop-2-yn-1-yl)-1H-indole-2-carboxylate (**10a**).*[13] To a stirred solution of ethyl 1*H*-indole-2-carboxylate (**9**) (4.0 g, 21.14 mmol) in dry DMF (20 mL), solid NaH was added (0.528 g, 22 mmol) piecewise. After a while, at the end of the release of H_2 gas, propargyl bromide (80 wt % in toluene) (2.45 mL, 22 mmol) was diluted in a 1:3 ratio with dry DMF and added to the stirring solution over a 30 min period. After completion of the reaction (4 h), water was added and the resulting mixture was extracted with ethyl acetate and brine solution. The organic extracts were combined, dried over with $MgSO_4$, and filtered. After the evaporation of the solvent, the product ethyl-1-(prop-2-yn-1-yl)-1*H*-indole-2-carboxylate (**10a**) was obtained as a white powder (4.51 g, 19.9 mmol, 94%). Mp 64−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.31 (ddd, J = 8.4, 7.0, 1.0 Hz, 1H), 7.26 (d, J = 0.7 Hz, 1H), 7.10 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 5.35 (d, J = 2.5 Hz, 2H), 4.31 (q, J = 7.1 Hz, 2H), 2.17 (t, J = 2.5 Hz, 1H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 139.0, 127.0, 126.3, 125.5, 122.8, 121.2, 111.4, 110.5, 78.8, 72.0, 60.8, 33.9, 14.3.

*Ethyl 1-(But-2-yn-1-yl)-1H-indole-2-carboxylate (**10b**).* To a stirred solution of ethyl-1*H*-indole-2-carboxylate (**9**) (4.0 g, 21.14 mmol) in dry DMF (20 mL), solid NaH was added (0.528 g, 22 mmol) piecewise. After a while, at the end of the release of H_2 gas, 1-bromobut-2-yne (1.86 mL, 21 mmol) was diluted in a 1:3 ratio with dry DMF and added to the stirring solution over 30 min. After completion of the reaction (2 h), water was added (100 mL) and the mixture was extracted with ethyl acetate (3 × 30 mL). The collected organic phases were washed with brine, dried over $MgSO_4$, and filtrated. After evaporation of the solvent, the product, ethyl 1-(but-2-yn-1-yl)-1*H*-indole-2-carboxylate (**10b**), was obtained as a white solid (4.56 g, 90%) from petroleum ether. Mp 66−68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dt, J = 8.0, 0.9 Hz 1H), 7.51 (d, J = 8.3, 0.7 Hz 1H), 7.38 (ddd, J = 8.3, 7.0, 0.9 Hz, 1H), 7.32 (d, J = 0.9 Hz, 1H), 7.18 (ddd, J = 8.0, 7.0, 0.7 Hz, 1H), 5.38 (q, $^5J_{8,9}$ = 2.3 Hz, 2H), 4.39 (q, J = 7.1 Hz, 2H), 1.75 (t, ^5J = 2.4 Hz, 3H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 139.0, 127.0, 126.2, 125.2, 122.6, 120.9, 111.0, 110.8, 79.7, 74.1, 60.7, 34.2, 14.4, 3.6. IR (ATR) 1698, 1317, 1195, 766. HRMS Calcd for ($C_{15}H_{15}NO_2$) [M + H]$^+$: 242.11756; Found: 242.1174.

*1-(Prop-2-yn-1-yl)-1H-indole-2-carboxylic Acid (**11a**).*[14] To a stirred solution of 4.51 g (19.9 mmol) of ethyl-1-(prop-2-yn-1-yl)-1*H*-indole-2-carboxylate (**10a**) in 50 mL of MeOH, 3.02 g (21.85 mmol) of K_2CO_3 were added. This mixture was refluxed for 12 h. After completion of the reaction, solvent was evaporated and water (100 mL) was added. The mixture was extracted with EtOAc (3 × 50 mL). The combined organic phase was washed with 1 N HCl and brine and dried over $MgSO_4$. Evaporation of solvent gave 1-(prop-2-yn-1-yl)-1*H*-indole-2-carboxylic acid (**11a**) as a white solid from hexane/CH_2Cl_2 (3.52 g, 17.7 mmol, 89%). Mp 193−195 °C (Lit. mp 190−193 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.60 (dd, J = 8.0, 0.9 Hz, 1H), 7.51 (dd, J = 8.4, 0.8 Hz, 1H), 7.28 (ddd, J = 8.4, 7.0, 0.9 Hz, 1H), 7.24 (d, J = 0.9 Hz, 1H), 7.06 (ddd, J = 8.0, 7.0, 0.8 Hz, 1H), 5.44 (d, J = 2.5 Hz, 2H), 2.63 (t, J = 2.5 Hz, 2H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 163.2, 140.1, 127.8, 127.2, 126.1, 123.5, 121.9, 112.2, 111.8, 80.0, 73.4, 34.2; IR (ATR, cm^{-1}) 3275, 2962, 2920, 1656, 1518, 1270, 1207; HRMS Calcd for ($C_{12}H_9NO_2$) [M + H]$^+$: 200.0706; Found: 200.07235.

*1-(But-2-yn-1-yl)-1H-indole-2-carboxylic Acid (**11b**).* To a stirred solution of 4.83 g (20 mmol) of ethyl 1-(but-2-yn-1-yl)-1*H*-indole-2-carboxylate (**10b**) in 50 mL of MeOH, 3.04 g of K_2CO_3 (22 mmol) were added. This mixture was refluxed for 12 h. After completion of the reaction, solvent was evaporated. The crude product was added to 1 N HCl (reaction medium acidified) and extracted with EtOAc (3 × 50 mL). Organic layers were combined and dried over $MgSO_4$. Evaporation of solvent gave 1-(but-2-yn-1-yl)-1*H*-indole-2-carboxylic acid (**11b**) (3.41 g, 17.7 mmol, 90%) as white needles from EtOAc/*n*-hexane. Mp 190−192 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.31 (bs, 1H, −OH), 7.74 (dt, J = 8.0, 0.9 Hz, 1H), 7.64 (dd, J = 8.4, 0.8 Hz, 1H), 7.41 (ddd, J = 8.3, 7.0, 1.0 Hz, 1H), 7.37 (d, J = 1.0 Hz, 1H), 7.20 (ddd, J = 8.0, 7.0, 0.7 Hz, 1H), 5.50 (q, J = 2.4 Hz, 1H), 1.72 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 163.2, 140.1, 127.8, 127.2, 126.0, 123.4, 121.8, 111.92, 111.88, 79.9, 75.4, 34.5, 3.1. IR (ATR) 2851, 2513, 1654, 1518, 1264, 1206, 733. HRMS Calcd for ($C_{13}H_{11}NO_2$) [M + H]$^+$: 214.0863; Found: 214.0869.

*3-Phenyl-1-(1-(prop-2-yn-1-yl)-1H-indol-2-yl)prop-2-yn-1-one (**13a**).* To a solution of 1-(prop-2-yn-1-yl)-1*H*-indole-2-carboxylic acid (**11a**) (500 mg, 2.5 mmol) in THF (20 mL) was added triethylamine (100 μL). The reaction mixture was stirred at room temperature for 30 min. To this solution was then added a solution of thionyl chloride (800 μL, 11 mmol) in THF (2 mL) dropwise, and the resulting mixture was stirred at room temperature for 3 h. Afterward the solid was filtered off, and solvent was evaporated. The acyl chloride **12a** was dissolved in chloroform (5 mL) without purification, and trimethyl-(phenylethynyl)silane[15] (3.0 mmol, 523 mg, 1.2 equiv) was added to

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the solution at room temperature. The mixture was then added to a solution of aluminum chloride (450 mg, 3.4 mmol) in chloroform (15 mL) dropwise at 0 °C, and the mixture was stirred for 24 h at room temperature. After completion of the reaction (controlled by TLC), water (30 mL) was added, and the solution was extracted with dichloromethane. The combined organic extracts were dried over Na_2SO_4. The solvent was evaporated to give crude product, which was purified by column chromatography eluting with EtOAc/hexane to give **13a** as a yellow solid (0.45 g, 1.6 mmol, 63%) from EtOAc/*n*-hexane. Mp 99−101 °C, R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dt, J = 8.1, 1.0 Hz, 1H), 7.70−7.69 (m, 3H), 7.54−7.37 (m, 5H), 7.22 (ddd, J = 8.0, 6.8, 1.1 Hz, 1H), 5.49 (d, J = 2.5 Hz, 2H), 2.28 (t, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 140.3, 134.9, 133.0, 130.7, 128.7, 127.4, 126.4, 123.6, 121.7, 120.3, 117.7, 110.8, 90.2, 87.8, 78.5, 72.4, 34.2; IR (ATR, cm^{-1}) 2988, 2901, 2199, 2097, 1608; HRMS Calcd for ($C_{20}H_{13}NO$) [M + H]$^+$: 284.10699; Found: 284.10725.

*1-(1-(But-2-yn-1-yl)-1H-indol-2-yl)-3-phenylprop-2-yn-1-one (**13b**).* To a solution of 1-(but-2-yn-1-yl)-1*H*-indole-2-carboxylic acid (**11b**) (500 mg, 2.35 mmol) in THF (20 mL), triethylamine (100 μL) was added. This mixture was stirred at room temperature for 30 min. To this solution, a solution of thionyl chloride (800 μL, 11 mmol) in THF (2 mL) was then added dropwise, and the resulting mixture was stirred at room temperature for 3 h. Afterward, the formed solid was filtered out, and solvent was evaporated. The resulting acyl chloride **12b** was dissolved in chloroform (5 mL), and trimethyl(phenylethynyl)silane (3.0 mmol, 523 mg, 1.2 equiv) was added to the solution at room temperature. The mixture was then added to a suspension of aluminum chloride (450 mg, 3.4 mmol) in chloroform (15 mL) dropwise at 0 °C, and the mixture was stirred for 24 h at room temperature. After completion of the reaction (controlled by TLC), water (30 mL) was added, and the mixture was extracted with dichloromethane. The combined organic extracts were dried over Na_2SO_4. The solvent was evaporated to give crude product, which was purified by column chromatography eluting with EtOAc/hexane (1:5) to give **13b** as pale yellow needles (0.395 g, 1.33 mmol, 57%). Mp 150−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (bd, $J_{4,5}$ = 8.1 Hz, 1H, H-4), 7.51−7.47 (m, 2H, arom.), 7.39−7.31 (m, 4H, arom), 7.28 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H), 7.10 (ddd, J = 8.1, 6.9, 0.9 Hz, 1H), 6.98 (bs, 1H), 5.00 (q, ^5J = 1.5 Hz, 2H), 2.54 (t, ^5J = 1.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 139.9, 138.5, 134.3, 132.0, 131.7, 130.2, 129.6, 128.6, 125.2, 124.0, 122.0, 121.4, 110.5, 101.2, 99.8, 89.5, 47.0, 18.4. IR (ATR, cm^{-1}): 3056, 2917, 2849, 2197, 1682, 1607, 1148, 741; HRMS: Calcd for $C_{21}H_{15}NO$ [M − H]$^-$: 296.10809; found: 296.11096.

General Procedure for Sonogashira Coupling. A stirred mixture of CuI (17 mg, 0.09 mmol), PPh_3 (90 mg, 0.34 mmol), and $Pd(OAc)_2$ (17 mg, 0.08 mmol) was purged with nitrogen for 30 min and heated to 50 °C. Then a solution of α,β-acetylenic ketones (1.1 mmol), halide arenes (1.2 mmol), and DIPA (2 mL) in THF (15 mL) was added successively. The mixture was then refluxed for 2−4 h at 70 °C. After complete conversion (monitored by TLC) solvent was evaporated, and the residue was chromatographed on silica gel eluting with ethyl acetate/hexane to give pure product.

*3-Phenyl-1-(1-(3-phenylprop-2-yn-1-yl)-1H-indol-2-yl)prop-2-yn-1-one (**14a**).* A yellow solid (313 mg, 0.87 mmol, 79%) (mp 114−116 °C). R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.1 Hz, 1H), 7.74 (s, 1H), 7.73 (dd, J = 8.0, 1.5 Hz, 3H), 7.65 (d, J = 8.5 Hz, 1H), 7.52−7.44 (m, 4H), 7.40−7.38 (m, 2H), 7.30−7.23 (m, 4H), 5.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 140.5, 135.0, 133.0, 131.8, 130.6, 128.7, 128.4, 128.2, 127.3, 126.4, 123.5, 122.6, 121.6, 120.4, 117.6, 111.1, 90.1, 87.8, 84.1, 83.9, 35.1; IR (ATR, cm^{-1}) 3062, 2986, 2917, 2201, 1609, 1509; HRMS Calcd for ($C_{26}H_{17}NO$) [M + H]$^+$: 360.13829; Found: 360.13893.

*3-Phenyl-1-(1-(3-(p-tolyl)prop-2-yn-1-yl)-1H-indol-2-yl)prop-2-yn-1-one (**14b**).* A yellow colored viscous oil (329 mg, 0.88 mmol, 80%). R_f = 0.7 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.0 Hz, 1H), 7.75 (s, 1H), 7.73 (dd, J = 7.9, 1.5 Hz, 3H), 7.66 (d, J = 8.5 Hz, 1H), 7.56−7.42 (m, 4H), 7.35−7.21 (m, 3H), 7.09 (d, J = 8.0 Hz, 2H), 5.76 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 140.5, 138.5, 135.1, 133.0, 131.6, 130.6, 128.9, 128.7, 127.3, 126.4, 123.5, 121.6, 120.4, 119.5, 117.6, 111.2, 90.1, 87.9, 84.2, 83.3, 35.1, 21.5; IR (ATR, cm^{-1}) 3059, 3025, 2987, 2917, 2847, 2201, 1609, 1508; HRMS Calcd for ($C_{27}H_{19}NO$) [M + H]$^+$: 374.15394; Found: 374.15698.

*1-(1-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-1H-indol-2-yl)-3-phenylprop-2-yn-1-one (**14c**).* A yellow colored viscous oil (335 mg, 0.86 mmol, 78%). R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 1H), 7.62 (s, 1H), 7.61 (dd, J = 8.0, 1.5 Hz, 1H) 7.54 (d, J = 8.5 Hz, 1H), 7.42−7.32 (m, 4H), 7.24−7.19 (quasi d, J = 8.0 Hz, 2H), 7.14 (t, J = 7.5 Hz, 1H), 6.68 (quasi d, J = 8.0 Hz, 2H), 5.63 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 159.7, 140.5, 135.1, 133.3, 132.9, 130.6, 128.7, 127.2, 126.4, 123.5, 121.5, 120.4, 117.6, 114.7, 113.8, 111.2, 90.0, 87.9, 84.0, 82.6, 55.2, 35.1; IR (ATR, cm^{-1}) 2988, 2968, 2901, 2358, 2198, 1605, 1508; HRMS Calcd for ($C_{27}H_{19}NO_2$) [M + H]$^+$: 390.14886; Found: 390.15167.

*1-(1-(3-(3-Nitrophenyl)prop-2-yn-1-yl)-1H-indol-2-yl)-3-phenylprop-2-yn-1-one (**14d**).* A yellow colored solid (384 mg, 0.95 mmol, 86%) from EtOAc/*n*-hexane. Mp 115−117 °C, R_f = 0.4 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 1.6 Hz, 1H), 8.12 (dd, J = 8.3, 1.3 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.73 (s, 1H), 7.70 (dd, J = 7.6, 1.6 Hz, 2H), 7.63 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.52−7.47 (m, 2H), 7.46−7.41 (m, 3H), 7.25 (t, J = 7.5 Hz, 1H), 5.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 148.0, 140.4, 137.6, 135.0, 133.0, 130.7, 129.2, 128.7, 127.5, 126.7, 126.4, 124.3, 123.7, 123.1, 121.8, 120.2, 117.8, 110.7, 90.4, 87.7, 86.8, 81.6, 34.9; IR (ATR, cm^{-1}) 2988, 2968, 2901, 2355, 2191, 1607, 1522; HRMS Calcd for ($C_{26}H_{16}N_2O_3$) [M + H]$^+$: 405.12337; Found: 405.12613.

*1-(1-(3-(4-Fluorophenyl)prop-2-yn-1-yl)-1H-indol-2-yl)-3-phenylprop-2-yn-1-one (**14e**).* A yellow colored viscous oil (343 mg, 0.91 mmol, 83%). R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.1 Hz, 1H), 7.64 (s, 1H), 7.62 (dd, J = 8.5, 1.7 Hz, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.43−7.32 (m, 4H), 7.29−7.22 (m, 2H), 7.14 (t, J = 7.9 Hz 1H), 6.88−6.82 (m, 2H), 5.63 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 162.5 (d, $^1J_{C,F}$ = 248.0 Hz), 140.5, 135.0, 133.8 (d, $^3J_{C,F}$ = 9.0 Hz), 133.0, 130.6, 128.7, 127.3, 126.4, 123.6, 121.6, 120.3, 118.6 (d, $^4J_{C,F}$ = 4.0 Hz), 117.6, 115.44 (d, $^2J_{C,F}$ = 22.0 Hz), 111.0, 90.2, 87.8, 83.7, 83.0, 35.0; IR (ATR, cm^{-1}) 3059, 2983, 2919, 2850, 2198, 1608, 1505; HRMS Calcd for ($C_{26}H_{16}FNO$) [M + H]$^+$: 378.12887; Found: 378.12960.

*3-Phenyl-1-(1-(3-(pyridin-2-yl)prop-2-yn-1-yl)-1H-indol-2-yl)-prop-2-yn-1-one (**14f**).* A yellow colored solid (339 mg, 0.94 mmol, 85%). Mp 185−187 °C, R_f = 0.4 (ethyl acetate/hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68−7.55 (m, 6H), 7.44−7.28 (m, 7H), 7.13 (ddd, J = 8.0, 5.3, 2.5 Hz, 1H), 5.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 143.0, 140.2, 135.23, 135.17, 134.8, 133.0, 132.2, 132.1, 130.6, 128.7, 127.5, 126.3, 123.6, 121.8, 120.3, 117.8, 110.7, 90.3, 87.6, 73.5, 68.3, 34.8; IR (ATR, cm^{-1}) 3065, 2974, 2920, 2847, 2204, 1610, 1511, 1279; HRMS Calcd for ($C_{25}H_{16}N_2O$) [M + H]$^+$: 361.13354; Found: 361.13098.

General Procedure for the Synthesis of Pyrazoles. To a refluxing solution of ketones **13a,b** and **14a−g** (0.5 mmol) in methanol (15 mL) was added hydrazine monohydrate (1 mL) dropwise under a nitrogen atmosphere. Refluxing was continued for 3 h, water was added, and the mixture was extracted with ethyl acetate (3 × 20 mL). The combined extracts were dried over $MgSO_4$ and evaporated. The crude product was chromatographed on silica gel eluting with ethyl acetate/hexane to give pyrazole derivatives **15a−g**.

*2-(3-Phenyl-1H-pyrazol-5-yl)-1-(3-phenylprop-2-yn-1-yl)-1H-indole (**15a**).* A yellow solid (176 mg, 0.47 mmol, 94%). Mp 189−191 °C, R_f = 0.5 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.78 (bs, 1H), 7.62 (dd, J = 7.9, 1.3 Hz, 2H), 7.51 (d, J = 7.8 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.31−7.20 (m, 9H), 7.15 (t, J = 7.5 Hz, 1H), 6.86 (s, 1H), 6.69 (s, 1H), 5.23 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 147.8, 137.7, 131.8, 130.7, 130.4, 129.0, 128.7, 128.5, 128.2, 128.0, 125.8, 122.7, 122.4, 121.0, 120.5, 110.2, 103.1, 103.0 84.5, 84.3, 34.9; IR (ATR, cm^{-1}) 2988, 2972, 2901, 1456, 1076; HRMS Calcd for ($C_{26}H_{19}N_3$) [M + H]$^+$: 374.16517; Found: 374.16830.

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*2-(3-Phenyl-1H-pyrazol-5-yl)-1-(3-(p-tolyl)prop-2-yn-1-yl)-1H-indole (**15b**).* A white solid (178 mg, 0.46 mmol, 92%) from CH_2Cl_2/*n*-hexane. Mp 208−210 °C, R_f = 0.4 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, Acetone-d_6) δ 12.73 (s, 1H), 7.83 (bd, J = 7.5 Hz, 2H), 7.59 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.43 (bt, J = 7.6 Hz, 2H), 7.32 (bt, J = 7.3 Hz, 1H), 7.22−7.10 (m, 4H), 7.06−7.02 (m, 3H), 6.85 (d, J = 0.6 Hz, 1H), 5.73 (bs, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 138.5, 137.9, 131.4 (2C), 129.1 (2C), 129.0, 128.4, 128.24, 128.15, 125.4, 122.1, 120.5, 120.1, 119.7, 110.2, 102.2, 102.0, 84.5, 83.4, 34.6, 20.4; IR (ATR, cm^{-1}) 2988, 2901, 1456, 1075; HRMS Calcd for ($C_{27}H_{21}N_3$) [M + H]$^+$: 388.1808; Found: 388.1812.

*1-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-2-(3-phenyl-1H-pyrazol-5-yl)-1H-indole (**15c**).* A yellow colored solid (182 mg, 0.45 mmol, 90%). Mp 158−160 °C, R_f = 0.3 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.87−7.81 (m, 2H), 7.59 (bd, J = 8.2 Hz, 1H), 7.54 (bd, J = 7.8 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.32 (tt, J = 7.3, 1.2 Hz, 1H), 7.25−7.14 (m, 3H), 7.13 (s, 1H), 7.04 (dt, J = 7.1, 0.7 Hz, 1H), 6.84 (s, 1H), 6.79−6.73 (m, 2H), 5.70 (s, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 159.9, 143.1, 142.1, 137.9, 133.0, 132.1, 131.8, 129.0, 128.3, 128.2, 125.5, 122.1, 120.5, 120.1, 114.6, 114.0, 110.3, 102.2, 102.0, 83.6, 83.3, 54.7, 34.6; IR (ATR, cm^{-1}) 2988, 2968, 2901, 1606, 1508, 1247; HRMS Calcd for ($C_{27}H_{21}N_3O$) [M + H]$^+$: 404.17574; Found: 404.17865.

*1-(3-(3-Nitrophenyl)prop-2-yn-1-yl)-2-(3-phenyl-1H-pyrazol-5-yl)-1H-indole (**15d**).* A yellow colored solid (193 mg, 0.46 mmol, 92%). Mp 199−201 °C, R_f = 0.5 (ethyl acetate/hexane, 1:2). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.11 (ddd, J = 8.3, 2.3, 1.0 Hz, 1H), 8.06 (t, J = 1.7 Hz, 1H), 7.83 (bd, J = 8.3, 2H), 7.71−7.64 (m, 1H), 7.61 (d, J = 8.3 Hz, 1H), 7.58−7.48 (m, 2H), 7.46−7.39 (m, 2H), 7.36−7.29 (m, 1H), 7.20 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H), 7.14 (s, 1H), 7.06 (td, J = 7.6, 0.8 Hz, 1H), 6.87 (d, J = 0.7 Hz, 1H), 5.82 (s, 2H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 148.2, 137.9, 137.4, 132.3, 130.3, 130.0, 129.0, 128.4, 128.3, 126.0, 125.5 (2C), 124.3, 123.1, 122.2, 120.53, 120.51, 120.3, 110.1, 102.3, 102.2, 88.0, 81.0, 34.6; IR (ATR, cm^{-1}) 3059, 2974, 2926, 2893, 1523, 1347; HRMS Calcd for ($C_{26}H_{18}N_4O_2$) [M + H]$^+$: 419.15025; Found: 419.15322.

*1-(3-(4-Fluorophenyl)prop-2-yn-1-yl)-2-(3-phenyl-1H-pyrazol-5-yl)-1H-indole (**15e**).* A yellow colored solid (172 mg, 0.44 mmol, 88%). Mp 183−185 °C, R_f = 0.4 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 8.0, 1.3 Hz, 2H), 7.53 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.34−7.19 (m, 6H), 7.10 (t, J = 7.5 Hz, 1H), 6.86−6.81 (m, 3H), 6.71 (s, 1H), 5.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.58 (d, $^1J_{C,F}$ = 249 Hz), 142.2, 137.7, 133.70 (d, $^3J_{C,F}$ = 8 Hz), 130.7, 130.3, 129.1, 128.7, 128.0, 125.7, 122.7, 121.0, 120.6, 118.5, 118.4, 115.50 (d, $^2J_{C,F}$ = 22 Hz), 110.1, 103.1, 103.0, 84.0, 83.4, 34.8; IR (ATR, cm^{-1}) 3138, 3101, 3056, 2932, 2890, 2850, 1597, 1505; HRMS Calcd for ($C_{26}H_{18}FN_3$) [M + H]$^+$: 392.15575; Found: 392.15673.

*1-(But-2-yn-1-yl)-2-(3-phenyl-1H-pyrazol-5-yl)-1H-indole (**15g**).* Pale yellow solid (128 mg, 0.41 mmol, 92%). Mp 120−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.66 (d, J = 7.4 Hz, 2H), 7.50 (d, $J_{4,5}$ = 8.0 Hz, 1H), 7.37 (d, $J_{7,6}$ = 8.3 Hz, 1H), 7.32 (t, J = 7.4 Hz, 2H), 7.27 (d, J = 6.9 Hz, 1H), 7.20 (ddd, $J_{5,4}$ = 8.0, $J_{5,6}$ = 7.0, and $J_{5,7}$ = 0.9 Hz, 1H), 7.07 (t, J = 7.4 Hz, 1H), 6.84 (s, 1H), 6.67 (s, 1H), 4.97 (d, J = 1.5 Hz, 2H), 1.68 (t, J = 2.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 141.5, 137.6, 130.6, 130.2, 129.0, 128.7, 127.8, 125.8, 122.7, 121.0, 120.4, 110.3, 110.0, 102.9, 80.8, 74.4, 34.4, 3.6. IR (ATR, cm^{-1}) 3055, 2918, 2851, 1456, 1335, 788; HRMS Calcd for ($C_{21}H_{17}N_3$) [M + H]$^+$: 312.1483; Found: 312.1495.

*2-(3-Phenyl-1H-pyrazol-5-yl)-1-(prop-2-yn-1-yl)-1H-indole (**15h**).* A light yellow colored solid (137 mg, 0.46 mmol, 92%). Mp 164−166 °C. R_f = 0.4 (ethyl acetate/hexane, 1:4); ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.83 (d, J = 7.1 Hz, 2H), 7.52 (bt, J = 8.9 Hz, 2H), 7.44−7.40 (m, 2H), 7.34 (bt, J = 7.3 Hz, 1H), 7.18 (bt, J = 7.1 Hz, 1H), 7.10 (bs, 1H), 7.05 (bt, J = 7.3 Hz, 1H), 6.84 (bs, 1H), 5.52 (bd, J = 2.0 Hz, 2H), 2.71 (bt, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 145.5, 143.8, 137.8, 132.1, 130.3, 129.0, 128.3 (2C), 125.5, 122.1, 120.5, 120.2, 110.2, 102.2, 102.1, 79.5, 72.7, 33.8; IR (ATR, cm^{-1}) 3269, 2972, 2901, 1454, 1075; HRMS Calcd for ($C_{20}H_{15}N_3$) [M + H]$^+$: 298.1339; Found: 298.1343.

*2-Phenyl-5-(pyridin-2-ylmethyl)pyrazolo[5′,1′:3,4]pyrazino[1,2-a]indole (**16f**).* A yellow colored needles (127 mg, 0.34 mmol, 85%). Mp 159−161 °C, R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 4.0 Hz, 1H), 7.92 (dd, J = 7.1, 1.3 Hz, 2H), 7.67−7.57 (m, 2H), 7.51 (s, 1H), 7.47−7.38 (m, 3H), 7.36−7.30 (m, 2H), 7.24 (t, J = 7.6 Hz, 1H), 7.13−7.09 (m, 2H), 6.90 (s, 1H), 6.77 (s, 1H), 5.93 (d, J = 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 153.8, 149.1, 136.6, 136.4, 134.7, 132.4, 132.3, 128.8, 128.7, 128.6, 126.2, 125.7, 125.6, 122.9, 121.3, 121.1, 120.7, 112.4, 109.6, 99.8, 98.3, 42.9; IR (ATR, cm^{-1}) 3050, 2962, 2919, 2847; HRMS Calcd for ($C_{25}H_{18}N_4$) [M + H]$^+$: 375.16042; Found: 375.16123.

*General Procedure for the Synthesis of Pyrazoloindolopyrazine **16h** and Pyrazolo-diazepinoindoles **17a−g** via $AuCl_3$-Catalyzed Cyclization.* To a solution of pyrazole **15a−h** (0.4 mmol) in acetonitrile (10 mL) was added a solution of gold trichloride (3 mg, 2.5 mmol %) in acetonitrile (1 mL) dropwise at room temperature under a nitrogen atmosphere. The reaction mixture was stirred for 8−24 h. The solvent was evaporated. The residue was chromatographed on silica gel eluting with ethyl acetate/hexane to give pyrazoloindolopyrazine and pyrazolodiazepinoindoles.

*5-Methyl-2-phenylpyrazolo[5′,1′:3,4]pyrazino[1,2-a]indole (**16h**).* White solid (103 mg, 0.34 mmol, 87%) from EtOAc/*n*-hexane. Mp 125−127 °C. R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.86 (m, 2H), 7.70−7.67 (m, 1H), 7.58−7.56 (m, 1H), 7.37 (bt, J = 7.5 Hz, 2H), 7.29 (tt, J = 7.4, 1.2 Hz, 1H), 7.28 (d, J = 1.1 Hz, 1H), 7.25−7.21 (m, 2H), 7.00 (s, 1H), 6.83 (bs, 1H), 2.56 (d, J = 1.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 133.7, 133.0, 131.1, 128.8, 128.6, 128.3, 126.5, 126.2, 122.2, 121.7, 121.1, 120.4, 109.7, 107.3, 97.4, 94.4, 14.9; IR (ATR, cm^{-1}) 2988, 2968, 2922, 2901, 2358, 1507, 1456, 1078; HRMS Calcd for ($C_{20}H_{15}N_3$) [M + H]$^+$: 298.1339; Found: 298.1348.

*2,5-Diphenyl-7H-pyrazolo[5′,1′:3,4][1,4]diazepino[1,2-a]indole (**17a**).* A white solid (123 mg, 0.33 mmol, 83%). Mp 211−213 °C, R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.84 (m, 2H), 7.73 (d, J = 7.9 Hz, 1H), 7.48−7.35 (m, 9H), 7.34−7.29 (m, 1H) 7.18 (t, J = 7.4 Hz, 1H), 7.10 (s, 1H), 6.98 (s, 1H), 6.15 (t, J = 7.6 Hz, 1H), 4.85 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 145.8, 140.2, 136.5, 135.9, 132.5, 129.14, 129.08, 128.6, 128.34, 128.3, 128.26, 127.8, 126.1, 122.5, 121.3, 120.1, 113.8, 108.9, 104.2, 101.8, 39.1; IR (ATR, cm^{-1}) 2988, 2971, 2918, 2901, 2358, 1456, 1076; HRMS Calcd for ($C_{26}H_{19}N_3$) [M + H]$^+$: 374.16517; Found: 374.16797.

*2-Phenyl-5-(p-tolyl)-7H-pyrazolo[5′,1′:3,4][1,4]diazepino[1,2-a]-indole (**17b**).* A white colored solid (124 mg, 0.32 mmol, 80%). Mp 142−144 °C, R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.3 Hz, 2H), 7.61 (d, J = 7.9 Hz, 1H), 7.36−7.12 (m, 8H), 7.09−7.00 (m, 3H), 6.97 (s, 1H), 6.85 (s, 1H), 6.00 (t, J = 7.6 Hz, 1H), 4.72 (d, J = 7.6 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 145.7, 140.2, 139.1, 135.9, 133.7, 132.6, 129.2, 128.8, 128.6, 128.3, 128.2, 127.8, 126.1, 122.5, 121.3, 120.1, 113.1, 108.9, 104.3, 101.8, 39.1, 21.3; IR (ATR, cm^{-1}) 2988, 2971, 2901, 2356, 1456, 1243, 1080; HRMS Calcd for ($C_{27}H_{21}N_3$) [M + H]$^+$: 388.18082; Found: 388.18366.

*5-(4-Methoxyphenyl)-2-phenyl-7H-pyrazolo[5′,1′:3,4][1,4]-diazepino[1,2-a]indole (**17c**).* A yellow colored viscous oil (129 mg, 0.32 mmol, 80%). R_f = 0.5 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, J = 8.2, 1.2 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.37−7.12 (m, 8H), 7.06 (t, J = 7.5 Hz, 1H), 6.97 (s, 1H), 6.85 (s, 1H), 6.81−6.71 (m, 2H), 5.95 (t, J = 7.6 Hz, 1H), 4.71 (d, J = 7.6 Hz, 2H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 152.1, 145.4, 140.2, 135.9, 132.6, 129.6, 129.2, 129.0, 128.6, 128.3, 127.8, 126.1, 122.5, 121.3, 120.1, 113.5, 112.3, 108.9, 104.3, 101.7, 55.3, 39.1; IR (ATR, cm^{-1}) 2988, 2971, 2901, 2356, 1509, 1456, 1252, 1066; HRMS Calcd for ($C_{27}H_{21}N_3O$) [M + H]$^+$: 404.17574; Found: 404.17888.

*5-(3-Nitrophenyl)-2-phenyl-7H-pyrazolo[5′,1′:3,4][1,4]diazepino-[1,2-a]indole (**17d**).* A yellow colored solid (138 mg, 0.33 mmol, 83%). Mp 118−120 °C, R_f = 0.5 (ethyl acetate/hexane, 1:4). ^{1}H NMR

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(400 MHz, $CDCl_3$) δ 8.25 (t, J = 1.7 Hz, 1H), 8.17 (bd, J = 8.2 Hz, 1H), 7.73 (bd, J = 7.0 Hz, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.57 (bd, J = 7.8 Hz, 1H), 7.50−7.40 (m, 2H), 7.39−7.28 (m, 4H), 7.24 (t, J = 7.7 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.03 (s, 1H), 6.91 (s, 1H), 6.17 (t, J = 7.4 Hz, 1H), 4.81 (d, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9, 148.2, 143.7, 140.3, 138.2, 136.0, 134.4, 134.2, 132.2, 129.0, 128.7, 128.6, 127.8, 126.1, 123.9, 123.3, 122.9, 121.4, 120.3, 115.4, 108.9, 104.7, 102.4, 39.0; IR (ATR, cm^{-1}) 2988, 2971, 2901, 2357, 1526, 1455, 1348, 1080; HRMS Calcd for ($C_{26}H_{18}N_4O_2$) [M + H]$^+$: 419.15025; Found: 419.15305.

*5-(4-Fluorophenyl)-2-phenyl-7H-pyrazolo[5′,1′:3,4][1,4]-diazepino[1,2-a]indole (**17e**).* A yellow colored viscous oil (121 mg, 0.31 mmol, 78%). R_f = 0.5 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.3, 1.3 Hz, 2H), 7.70 (d, J = 7.9 Hz, 1H), 7.45−7.38 (m, 3H), 7.37−7.33 (m, 3H), 7.29 (ddd, J = 8.1, 7.0, 1.0 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.06 (s, 1H), 7.04 (bt, J = 8.7 Hz, 2H), 6.95 (s, 1H), 6.08 (t, J = 7.6 Hz, 1H), 4.82 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.25 (d, $^1J_{C,F}$ = 247.0 Hz), 152.3, 144.8, 140.3, 135.9, 132.6, 132.4, 130.15 (d, $^3J_{C,F}$ = 8.0 Hz), 129.0, 128.7, 128.5, 127.8, 126.0, 122.6, 121.3, 120.2, 115.14 (d, $^2J_{C,F}$ = 22.0 Hz), 113.5, 108.9, 104.4, 102.0, 39.0; IR (ATR, cm^{-1}) 2987, 2968, 2919, 2853, 1507, 1451, 1234; HRMS Calcd for ($C_{26}H_{18}FN_3$) [M + H]$^+$: 392.15575; Found: 392.15650.

*5-Methyl-2-phenyl-7H-pyrazolo[5′,1′:3,4][1,4]diazepino[1,2-a]-indole (**17g**).* White solid (111 mg, 0.36 mmol, 89%). Mp 109−111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.82 (m, 2H, arom.), 7.59 (dt, J = 8.0, 1.0 Hz, 1H), 7.41−7.35 (m, 2H, arom.), 7.34−7.27 (m, 2H, arom), 7.19 (ddd, J = 8.2, 7.0, 1.0 Hz, 1H), 7.06 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 6.93 (s, 1H), 6.79 (s, 1H), 5.66 (tq, J = 7.2, 1.2 Hz, 1H), 4.59 (d, J = 7.2 Hz, 2H), 2.35 (d, J = 1.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 142.2, 138.8, 135.8, 132.6, 129.4, 128.7, 128.3, 127.9, 125.9, 122.4, 121.2, 120.0, 110.6, 108.9, 104.0, 101.7, 39.1, 21.0. IR (ATR, cm^{-1}) 2959, 2918, 2850, 1710, 1455, 734, 692; HRMS Calcd for ($C_{21}H_{17}N_3$) [M + H]$^+$: 312.14952; Found: 312.14935.

*General Procedure for the Synthesis of Pyrazoloindolopyrazines **16a−h** via NaH-Promoted Cyclization.* To a solution of pyrazole **15a−h** (0.4 mmol) in DMF (10 mL) was added sodium hydride (1.1 equiv) at room temperature under nitrogen atmosphere. The reaction mixture was stirred for 10−15 min. After complete conversion (monitored by TLC) water (50 mL) was added, and the mixture was extracted with ethyl acetate (2 × 20 mL). The combined extracts were dried over $MgSO_4$, and evaporated. The crude product was chromatographed on silica gel eluting with ethyl acetate/hexane to give pyrazoloindolopyrazines **16a−h**.

*5-Benzyl-2-phenylpyrazolo[5′,1′:3,4]pyrazino[1,2-a]indole (**16a**).* A white colored solid (135 mg, 0.36 mmol, 90%) (mp 141−143 °C). R_f = 0.8 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.2 Hz, 2H), 7.66−7.64 (m, 1H), 7.38−7.17 (m, 11H), 6.97 (d, J = 7.4 Hz, 2H), 6.80 (s, 1H), 4.31 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 135.2, 132.0, 131.4, 129.7, 128.1, 127.2, 127.1, 126.7, 125.6, 125.5, 124.8, 124.6, 122.6, 120.7, 120.2, 119.5, 108.1, 106.7, 95.8, 93.0, 33.1; IR (ATR, cm^{-1}) 3093, 3062, 3025, 2956, 2920, 2847, 1451, 1069; HRMS Calcd for ($C_{26}H_{19}N_3$) [M + H]$^+$: 374.16517; Found: 374.16611.

*5-(4-Methylbenzyl)-2-phenylpyrazolo[5′,1′:3,4]pyrazino[1,2-a]-indole (**16b**).* White solid (124 mg, 0.32 mmol, 80%) from CH_2Cl_2/*n*-hexane. Mp 163−165 °C, R_f = 0.7 (ethyl acetate/hexane, 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (bd, J = 8.1, 2H), 7.70−7.66 (m, 1H), 7.50−7.45 (m, 1H), 7.39 (bt, J = 7.7 Hz, 2H), 7.32−7.25 (m, 3H), 7.24−7.17 (m, 2H), 7.12 (bd, J = 7.8 Hz, 2H), 7.05 (s, 1H), 7.03, (s, 1H), 6.86 (bs, 1H), 4.32 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 136.64, 133.59, 133.6, 133.0, 131.3, 129.6, 129.4, 128.8, 128.7, 128.3, 126.4, 126.2, 124.5, 122.2, 121.7, 121.0, 109.7, 108.2, 97.4, 94.5, 34.2, 21.1; IR (ATR, cm^{-1}) 3053, 3020, 2956, 2917, 2847, 1456; HRMS Calcd for ($C_{27}H_{21}N_3$) [M + H]$^+$: 388.18082; Found: 388.18153.

*5-(4-Methoxybenzyl)-2-phenylpyrazolo[5′,1′:3,4]pyrazino[1,2-a]-indole (**16c**).* A yellow colored solid (125 mg, 0.31 mmol, 78%). Mp 146−148 °C). R_f = 0.7 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (bd, J = 7.8 Hz, 2H), 7.71−7.68 (m, 1H), 7.50−7.48 (m, 1H), 7.40 (bt, J = 7.6 Hz, 2H), 7.35−7.27 (m, 3H), 7.23−7.20 (m, 2H), 7.07 (s, 1H), 7.02 (bs, 1H), 6.91 (s, 1H), 6.90−6.83 (bd, 2H), 4.31 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 152.3, 133.7, 133.0, 131.3, 130.8, 128.8, 128.7, 128.6, 128.3, 126.4, 126.2, 124.7, 122.2, 121.7, 121.1, 114.1, 109.7, 108.2, 97.4, 94.5, 55.3, 33.8; IR (ATR, cm^{-1}) 2962, 2917, 2847, 1508, 1250; HRMS Calcd for ($C_{27}H_{21}N_3O$) [M + H]$^+$: 404.17574; Found: 404.17648.

*5-(3-Nitrobenzyl)-2-phenylpyrazolo[5′,1′:3,4]pyrazino[1,2-a]-indole (**16d**).* A yellow solid (155 mg, 0.37 mmol, 93%). Mp 219−221 °C, R_f = 0.5 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.07 (bd, J = 8.2 Hz, 1H), 7.88 (bd, J = 7.2 Hz, 2H), 7.80 (bd, J = 7.6 Hz, 1H), 7.73 (dd, J = 6.6, 1.9 Hz, 1H), 7.62 (bd, J = 7.1 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.40 (t, J = 7.2 Hz, 2H), 7.38 (bs, 1H), 7.34−7.23 (m, 3H), 7.07 (s, 1H), 6.92 (s, 1H), 4.44 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 148.4, 139.5, 135.5, 133.7, 132.7, 131.4, 129.4, 128.8, 128.5, 126.3, 126.14, 126.09, 124.5, 122.6, 122.15, 122.13, 122.1, 121.2, 109.7, 108.5, 97.6, 95.2, 34.6; IR (ATR, cm^{-1}) 2971, 2920, 2847, 1526, 1456, 1346; HRMS Calcd for ($C_{26}H_{18}N_4O_2$) [M + H]$^+$: 419.15025; Found: 419.14975.

*5-(4-Fluorobenzyl)-2-phenylvpyrazolo[5′,1′:3,4]pyrazino[1,2-a]-indole (**16e**).* White colored solid (145 mg, 0.37 mmol, 93%). Mp 145−147 °C, R_f = 0.7 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, J = 8.2, 1.0 Hz, 2H), 7.7−7.67 (m, 1H), 7.51−7.48 (m, 1H), 7.40−7.35 (m, 4H), 7.29 (tt, J = 7.3, 1.1 Hz, 1H), 7.24−7.20 (m, 2H), 7.05 (s, 1H), 7.04 (s, 1H), 6.9t (bt, J = 7.7 Hz, 2H) 6.87 (bs, 1H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.98 (d, $^1J_{C,F}$ = 244 Hz), 152.4, 133.6, 132.9, 132.52 (d, $^4J_{C,F}$ = 3 Hz), 131.3, 131.10 (d, $^3J_{C,F}$ = 8 Hz), 128.8, 128.7, 128.4, 126.3, 126.1, 123.9, 122.4, 121.9, 121.1, 115.53 (d, $^2J_{C,F}$ = 21 Hz), 109.7, 108.2, 97.4, 94.7, 33.9; IR (ATR, cm^{-1}) 2990, 2965, 2917, 2850, 1507, 1456; HRMS Calcd for ($C_{26}H_{18}FN_3$) [M + H]$^+$: 392.15575; Found: 392.15641.

*3-Bromo-1-(prop-2-yn-1-yl)-1H-indole (**20**).* To a solution of indole (**1**) (4.0 mmol) in dimethylformamide (20 mL) (DMF), bromine (4.0 mmol) was added dropwise at 0 °C under stirring within a few minutes. After completion of the reaction (controlled by TLC), the mixture was poured into ice water (50 mL) containing ammonia (0.5%) and sodium bisulphite (0.1%). Afterward the white solid precipitated was filtered off, washed with cold water, and dried. The product, 3-bromoindole **19**,[21] was dissolved in dry DMF (5 mL) without purification, and solid NaH was added (0.098 g, 4.1 mmol) piecewise. After a while, at the end of the release of H_2 gas, propargyl bromide (80 wt % in toluene) (500 μL, 4.5 mmol) was added dropwise within a few minutes into the stirring solution at 0 °C. After completion of the reaction (controlled by TLC), water (100 mL) was added and the mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with brine and water, dried over with $MgSO_4$, and filtrated. The solvent was evaporated to give crude product, which was purified by column chromatography eluting with EtOAc/hexane (1:7) to give **20** as a light yellow colored solid (725 mg, 3.1 mmol, 77%). Mp 40−42 °C, R_f = 0.7 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.9 Hz, 1H), 7.19−7.14 (m, 2H), 7.09 (ddd, J = 7.9, 6.8, 1.5 Hz, 1H), 7.03 (s, 1H), 4.57 (d, J = 2.5 Hz, 2H), 2.25 (t, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 127.8, 126.3, 123.2, 120.8, 119.7, 109.7, 90.8, 77.3, 74.3, 36.1; IR (ATR, cm^{-1}) 3054, 2990, 2923, 2362, 1457, 1320, 1249, 1188, 736; HRMS Calcd for ($C_{11}H_8BrN$): 232.9840; Found: 232.9840.

*1-(Prop-2-yn-1-yl)-2-(1H-pyrrol-2-yl)-1H-indole (**21**).* A solution of pyrrole (2.5 mmol) in methylene chloride (5 mL) was added to a solution of 3-bromo-1-(prop-2-yn-1-yl)-1*H*-indole (**13**) (500 mg, 2.1 mmol) in methylene chloride (25 mL) dropwise at room temperature while stirring. Trifluoroacetic acid (2 mmol) was then added into the reaction mixture, and the resulting mixture was stirred at room temperature for 1 h. After completion of the reaction (controlled by TLC), aqueous ammonia (10 mL) was added to the mixture and extracted with ethyl acetate (3 × 50 mL). The combined organic phase was washed with a brine solution, dried over $MgSO_4$, and filtered. Evaporation of solvent gave **21** as yellow needles (397 mg, 1.8 mmol, 86%). Mp 89−90 °C, R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR

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(400 MHz, $CDCl_3$) δ 8.49 (bs, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.1 Hz, 1H), 7.09 (t, J = 7.4 Hz, 1H), 6.88 (bs, 1H), 6.53 (bs, 1H), 6.45 (bs, 1H), 6.32−6.31 (m, 1H), 4.88 (d, J = 2.4 Hz, 2H), 2.31 (t, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 133.1, 128.2, 123.0, 122.1, 120.53, 120.49, 119.4, 110.0, 109.6, 109.4, 100.4, 79.2, 72.8, 33.8; IR (ATR, cm^{-1}) 3384, 3284, 2987, 2971, 2902, 1460, 1341; HRMS Calcd for ($C_{15}H_{12}N_2$) [M + H]$^+$: 221.10732; Found: 221.11055

1-(3-Phenylprop-2-yn-1-yl)-2-(1H-pyrrol-2-yl)-1H-indole (**22a**). Synthesized as described above (Sonogashira coupling). A yellow colored oil (122 mg, 0.41 mmol, 82%), R_f = 0.5 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.6 (bs, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.58 (d, J = 7.9 Hz, 1H), 7.43−7.41 (m, 2H), 7.37−7.35 (m, 3H), 7.23 (ddd, J = 8.2, 7.0, 8.2 Hz, 1H), 7.11 (ddd, J = 7.9, 7.0, 0.9 Hz, 1H), 7.03 (dd, J = 4.2, 2.6 Hz, 1H), 6.71−6.69 (m, 1H), 6.64 (s, 1H) 6.35−6.33 (m, 1H), 5.38 (s, 2H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 138.3, 134.7, 132.5, 129.5, 129.41, 129.36, 123.9, 123.4, 122.4, 121.0, 120.9, 120.5, 110.7, 110.2, 109.4, 100.4, 85.9, 84.5, 35.1; IR (ATR, cm^{-1}) 3408, 3053, 2968, 2920, 1436, 1338; HRMS Calcd for ($C_{21}H_{16}N_2$) [M + H]$^+$: 297.13862; Found: 297.14279.

1-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-2-(1H-pyrrol-2-yl)-1H-indole (**22b**). A yellow colored viscous oil (144 mg, 0.44 mmol, 88%). R_f = 0.4 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (bs, 1H), 7.54 (bd, J = 7.8 Hz, 1H), 7.45 (bd, J = 8.2 Hz, 1H), 7.28 (bd, J = 8.8 Hz, 2H), 7.14 (t, J = 7.2 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 6.89 (bs, 1H), 6.74 (bd, J = 8.8 Hz, 2H), 6.60 (bs, 1H), 6.48 (bs, 1H), 6.32 (dt, J = 5.9, 2.8 Hz, 1H), 5.09 (s, 2H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 137.3, 133.3, 128.2, 123.3, 121.9, 120.38, 120.35, 119.4, 114.4, 113.9 (2C), 110.0, 109.8, 109.4, 100.1, 84.5, 83.1, 55.3, 34.7; IR (ATR, cm^{-1}) 3414, 3053, 2965, 2911, 2838, 2243, 1508, 1246; HRMS Calcd for ($C_{22}H_{18}N_2O$) [M + H]$^+$: 327.1492; Found: 327.1502.

1-(3-(3-Nitrophenyl)prop-2-yn-1-yl)-2-(1H-pyrrol-2-yl)-1H-indole (**22c**). A yellow colored solid (157 mg, 0.46 mmol, 92%). Mp 160−162 °C, R_f = 0.3 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.56 (bs, 1H), 8.18 (bs, 2H), 7.77 (d, J = 7.5 Hz, 1H), 7.62−7.58 (m, 3H), 7.24 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.4 Hz, 1H), 7.04 (d, J = 1.2 Hz, 1H), 6.69 (s, 1H), 6.36 (dd, J = 3.0, 2.1 Hz, 1H), 5.41 (s, 2H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 149.1, 138.4, 138.3, 134.6, 130.9, 129.4, 127.0, 125.0, 124.2, 123.8, 122.5, 121.1, 121.0, 120.7, 110.7, 110.3, 109.5, 100.7, 88.5, 82.3, 35.1; IR (ATR, cm^{-1}) 3402, 2972, 2902, 1526, 1345; HRMS Calcd for ($C_{21}H_{15}N_3O_2$) [M − H]$^-$: 340.10915; Found: 340.11150.

5-Benzylpyrrolo[2′,1′:3,4]pyrazino[1,2-a]indole (**23a**). A yellow colored solid (107 mg, 0.36 mmol, 90%). Mp 117−119 °C, R_f = 0.7 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (bd, J = 7.8 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.31−7.22 (m, 5H), 7.18−7.12 (m, 4H), 7.00 (bs, 1H), 6.76 (bd, J = 3.4 Hz, 1H), 6.47 (bs, 1H), 4.09 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 132.0, 129.2, 129.0, 128.7, 127.3, 123.6, 122.3, 121.23, 121.20, 121.18, 120.7, 115.18, 115.16, 112.2, 109.5, 108.5, 104.7, 36.1; IR (ATR, cm^{-1}) 2966, 2918, 2850, 1457, 1380, 1048; HRMS Calcd for ($C_{21}H_{16}N_2$) [M + H]$^+$: 297.1386; Found: 297.1391

5-(4-Methoxybenzyl)pyrrolo[2′,1′:3,4]pyrazino[1,2-a]indole (**23b**). A yellow colored solid (111 mg, 0.34 mmol, 85%). Mp 153−155 °C, R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, J = 6.8, 2.0 Hz, 1H), 7.59 (d, J = 7.3 Hz, 1H), 7.30−7.19 (m, 6H), 7.12 (bs, 1H), 6.90 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 3.4 Hz, 1H), 6.58 (bs, 1H), 4.11 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 131.4, 130.1, 129.8, 129.3, 127.8, 123.6, 121.8, 120.6, 120.3, 115.9, 114.6, 114.4, 114.0, 111.6, 109.2, 108.0, 103.9, 55.3, 35.2; IR (ATR, cm^{-1}) 3102, 3044, 2999, 2938, 2865, 1509, 1243; HRMS Calcd for ($C_{22}H_{18}N_2O$) [M + H]$^+$: 327.1492; Found: 327.1497.

5-(3-Nitrobenzyl)pyrrolo[2′,1′:3,4]pyrazino[1,2-a]indole (**23c**). A yellow colored solid (123 mg, 0.36 mmol, 90%). Mp 147−150 °C, R_f = 0.3 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.05 (dd, J = 8.2, 1.3 Hz, 1H), 7.61 (dd, J = 6.5, 2.3 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.46 (d,, J = 8.5 Hz, 1H), 7.41 (t, J = 7.9 Hz, 1H), 7.2−7.11 (m, 3H), 6.83 (dd, J = 2.8, 1.3 Hz, 1H), 6.72 (dd, J = 3.7, 1.3 Hz, 1H), 6.70 (s, 1H), 6.43 (dd, J = 3.6, 3.0 Hz, 1H), 4.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 138.5, 134.4, 131.3, 130.0, 129.3, 128.5, 123.7, 123.4, 122.5, 122.0, 120.8, 120.4, 118.4, 114.3, 111.9, 109.1, 108.7, 104.1, 92.1, 35.8; IR (ATR, cm^{-1}) 3108, 3050, 2941, 2865, 1519, 1344; HRMS Calcd for ($C_{21}H_{15}N_3O_2$) [M + H]$^+$: 342.12370; Found: 342.12567.

5-Methylpyrrolo[2′,1′:3,4]pyrazino[1,2-a]indole (**23d**). A yellow colored solid (77 mg, 0.35 mmol, 88%). Mp 118−120 °C). R_f = 0.6 (ethyl acetate/hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 6.3, 2.7 Hz, 1H), 7.57−7.50 (m, 1H), 7.25 (bs, 1H), 7.20−7.13 (m, 3H), 7.06 (bs, 1H), 6.78 (bd, J = 3.1 Hz, 1H), 6.61−6.49 (m, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.1, 123.69, 123.66, 129.64, 121.8, 120.74, 120.66, 120.4, 114.1, 111.8, 109.27, 109.24, 106.7, 104.2, 15.8; HRMS Calcd for ($C_{15}H_{12}N_2$) [M + H]$^+$: 221.10732; Found: 221.11047.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02419.

Spectroscopic data (1D and 2D NMR spectra) of the products and Cartesian Coordinates for the Optimized Structures of **15h** + $AuCl_3$ and **15a** + $AuCl_3$ complexes; NBO charges and distances in Å (PDF)

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Notes

The authors declare no competing financial interest.

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