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Rapid Access to Novel 1,2,3-Triazolo-Heterocyclic Scaffolds via Tandem Knoevenagel Condensation/Azide−Alkyne 1,3-Dipolar Cycloaddition Reaction in One Pot

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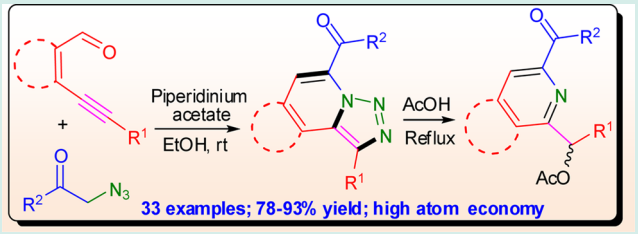
Supporting Information

ABSTRACT: An operationally simple, one-pot, two-step cascade method has been developed to afford biologically important fused 1,2,3-triazolo-heterocyclic scaffolds from 2-alkynyl aryl(heteroaryl) aldehydes and phenacyl azides. This unique atom economical transformation engages four reactive centers (aldehyde, alkyne, active methylene, and azide) under metal-free catalysis.



KEYWORDS: *Knoevenagel condensation, azide−alkyne cycloaddition, tandem reaction, triazole, pyrazolo-pyridine, β-carboline, isoquinoline*

INTRODUCTION

The azide−alkyne 1,3-dipolar cycloaddition reaction has attracted an enormous amount of interest over the past decade. Today it is widely used in classical organic/combinatorial synthesis,[1] medicinal chemistry/drug discovery programs,[2] and has also made a major impact in polymer/material science,[3] and in the field of chemical biology.[4] The ease and efficiency of this reaction has been recognized in organic/aqueous solvents over a range of temperature varying from ambient to heating.[5] Moreover, both terminal and internal alkynes have been efficiently used as compatible substrate with a high order of regioselectivity. In addition to the intermolecular format, many research groups have demonstrated intramolecular version of azide−alkyne 1,3-dipolar cycloaddition reaction.[6] However, most of the reported intramolecular strategies of the azide−alkyne 1,3-dipolar cycloaddition have largely utilized terminal alkyne in a multistep format to facilitate the reaction with limited applications to internal alkynes.[7] Intramolecular azide−alkyne cycloaddition provides an elegant access to interesting two annulated cyclic ring system. Thus, developing one pot, novel tandem process for intramolecular azide/internal alkyne 1,3-dipolar cycloaddition would open a rapid access to diverse heterocyclic scaffold.[8]

Efficient transformation of simple substrates into structurally novel and multifarious heterocycles constitutes a great challenge in organic chemistry. Tandem reactions which allow formation of multiple bonds in one pot operation have been recognized as a powerful tool to address these concerns.[9] Presented in this letter is a tandem process which involves an intermolecular Knoevenagel condensation-intramolecular azide/internal alkyne 1,3-dipolar cycloaddition reaction in one pot that eventually leads to very interesting fused 1,2,3-triazolo-heterocycles. The strategy has been generalized on three distinct substrates bearing indole, pyrazole, and benzene core motifs. We have also demonstrated efficient conversion of fused 1,2,3-triazolo-heterocycles into β-carboline, pyrazolo-pyridine, and isoquinolines. These heterocycles are very important scaffolds as they are found in numerous synthetic and natural products of biological and pharmacological interest (Figure 1).[10]

RESULTS AND DISCUSSION

Indole is considered as a privileged scaffold and is found in a plethora of synthetic and natural products of medicinal interest.[11] Starting from 2-(arylethynyl)-indole-3-carbaldehyde **1** and phenacyl azide **2**, the proposed tandem Knoevenagel condensation-azide/internal alkyne 1,3-dipolar cycloaddition reaction should lead to the formation of fused 1,2,3-triazolo-β-carbolines **3.** Thus, first we sought to optimize the reaction by taking 1-benzyl-2-(phenylethynyl)-1*H*-indole-3-carbaldehyde **1{1}** and 2-azido-1-phenylethanone **2{1}** as reaction partners (Table 1).

A number of base (piperidine, DBU, NaOH) and acid [*p*-TsOH, AcOH, $Sc(OTf)_3$] catalysts were attempted but none of them lead to a satisfactory yield of **3{1,1}** either at ambient temperature or under reflux condition (Table 1, entry 1−7). Under basic conditions, substrate **1{1}** remained largely unreacted whereas **2{1}** was fully consumed. A careful survey of the literature revealed that the anion obtained after deprotonation of active methylene **2{1}** with a base undergoes

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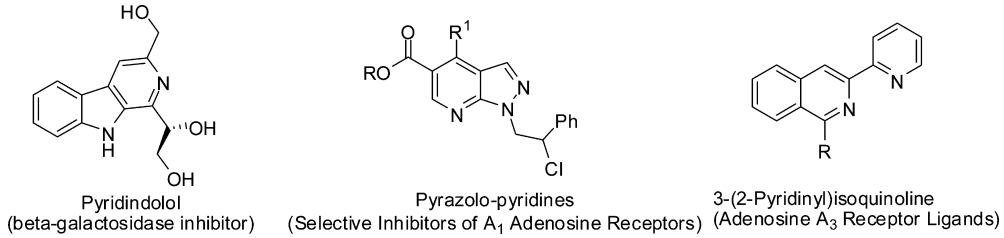
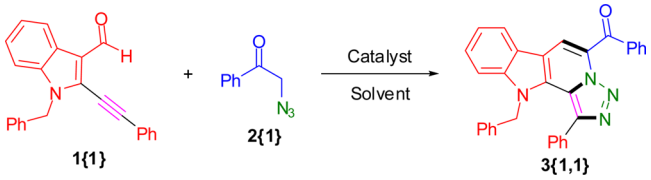


Figure 1. Chemical structure of some biologically important β-carboline, pyrazolo-pyridine, and isoquinoline.

Table 1. Optimization of One Pot, Tandem Knoevenagel Condensation-Azide/Internal Alkyne 1,3-Dipolar Cycloaddition Reaction[a]



entry	catalyst/ additive[d]	catalyst/ additive (mol %)	solvent	temperature[c]	yield of 3{1,1} (%)[b]
1	piperidine	20	ethanol	rt	12
2	piperidine	20	ethanol	reflux	NI
3	DBU	20	ethanol	rt	8
4	NaOH	20	ethanol	rt	NI
5	*p*-TsOH	20	ethanol	rt	NI
6	AcOH	20	ethanol	rt	NI
7	$Sc(OTf)_3$	20	ethanol	rt	NI
8	PA	20	ethanol	rt	35
9	PA	50	ethanol	rt	55
10	PA	100	ethanol	rt	88
11	PA	150	ethanol	rt	88
12	PA	100	ethanol	reflux	87
13	PA	100	acetonitrile	rt	81
14	PA	100	methanol	rt	87

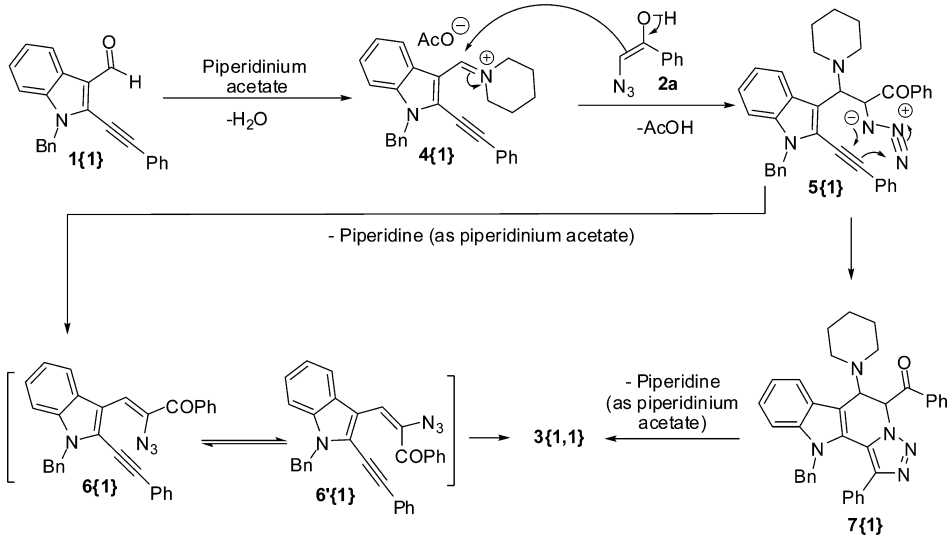
[a]{1} (0.20 mmol), 2{1} (0.20 mmol), solvent (2.0 mL), catalyst, stir, 24 h. [b]Isolated unoptimized yields. NI = Not isolated. [c]rt = room temperature. [d]PA = piperidinium acetate.

decomposition.[12] We were pleased to achieve complete conversion of both 1{1} and 2{1} (TLC) and high yield of 3{1,1} using piperidinium acetate as an additive (100 mol %) at ambient temperature (Table 1, entry 10).[13] The structure of 3{1,1} was assigned with the help of ESI-MS, ^{1}H NMR, ^{13}C NMR, IR, and HRMS data [IR spectra of 3{1,1} did not show any band corresponding to azide and alkyne; ^{13}C NMR of 3{1,1} did not show any alkyne carbon in typical acetylene region]. Refluxing the reaction mixture or further increasing the amount of the additive (150 mol %) did not lead to any improvement. Methanol and acetonitrile were also found suitable solvents for the reaction.

Piperidinium acetate mediated reaction can be explained as depicted in Scheme 1. Substrate 1{1} reacts with piperidinium acetate to yield an imininium acetate 4{1} which is attacked by enol 2{1} leading to the formation of 5{1}. The intermediate 5{1} might lead to the formation of 3{1,1} in two different pathways depending on whether piperidine is lost before or after azide/alkyne 1,3-dipolar cycloaddition reaction. It is not easy for the Knoevenagel adduct 6′{1} to undergo intramolecular azide/alkyne cycloaddition due to azide/alkyne proximity limitations. Since 6′{1} (and even 6{1}) was never isolated in our reaction conditions, it might be assumed either 6{1} was preferentially formed or reaction proceeded via alternative pathway where elimination of piperidine occurred after azide/alkyne cycloaddition. However, a possibility of piperidine mediated isomerization of 6′{1} to 6{1} cannot be ruled out.

Having optimized the tandem strategy with the substrates 1{1} and 2{1}, a series of fused 1,2,3-triazolo-β-carbolines 3

Scheme 1. Plausible Mechanism for Piperidinium Acetate Mediated Tandem Knoevenagel Condensation-Azide/Internal Alkyne 1,3-Dipolar Cycloaddition Reaction



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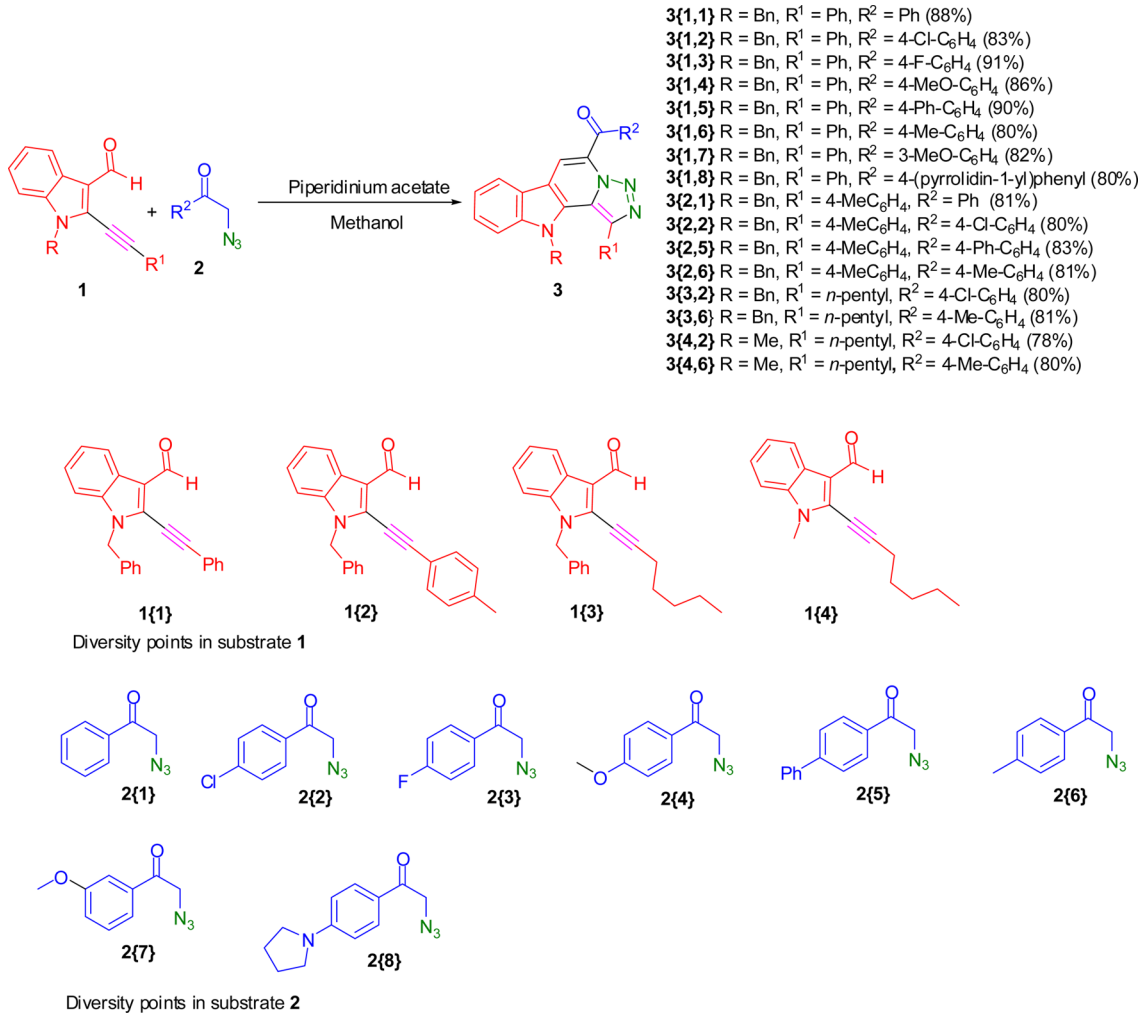
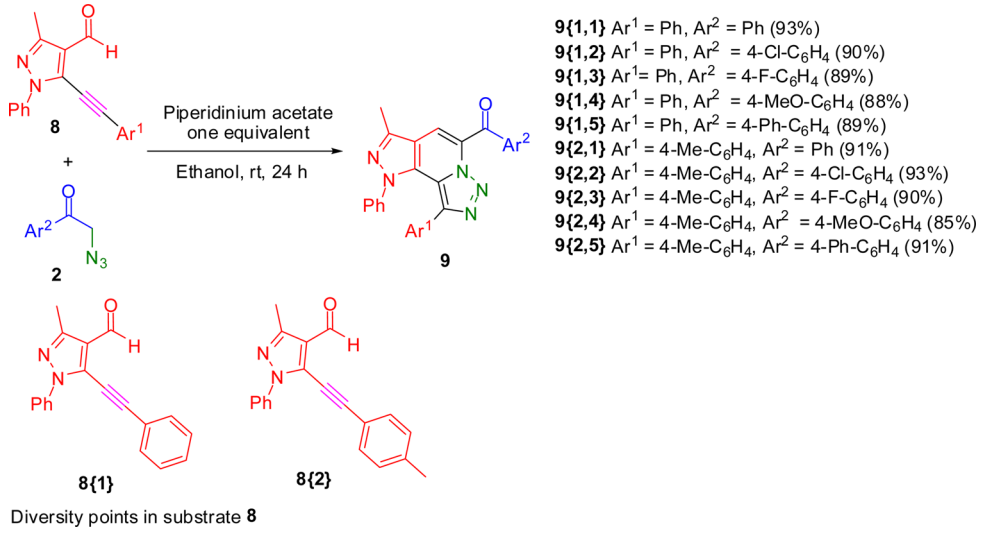


Figure 2. Synthesis of a library of fused 1,2,3-triazolo-β-carbolines **3** through tandem Knoevenagel condensation-azide/internal alkyne 1,3-dipolar cycloaddition reaction. Bn = $PhCH_2$, values in parentheses represent isolated unoptimized yields.

Scheme 2. Synthesis of Fused Pyrazole-1,2,3-triazolopyridyls Library through Tandem Knoevenagel Condensation-Azide/Internal Alkyne 1,3-Dipolar Cycloaddition Reaction[a]



[a]Values in parentheses represent isolated unoptimized yields.

(Figure 2) were synthesized in high yields following the same protocol. It should be noted that azide−alkyne click reaction smoothly proceeded without any metal catalyst at ambient temperature making the process environmentally benign. In all

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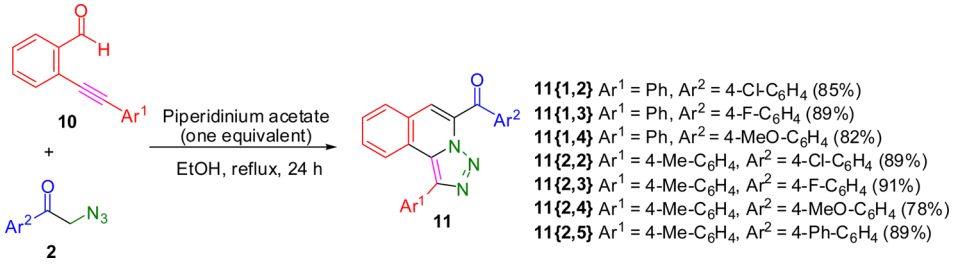
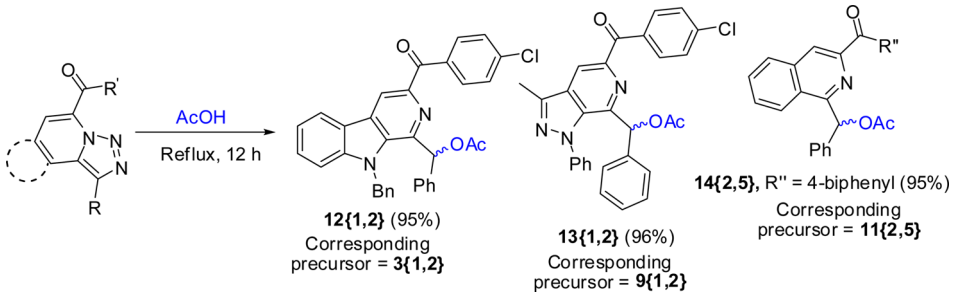
Scheme 3. Synthesis of 1,2,3-Triazoloisoquinoline Library through Tandem Knoevenagel Condensation-Azide/Internal Alkyne 1,3-Dipolar Cycloaddition[a]



[a]Values in parentheses represent isolated unoptimized yields.

Scheme 4. Conversion of Fused 1,2,3-Triazolo-heterocycles to Corresponding β-Carboline, Pyrazolo-Pyridine, and Isoquinoline[a]



[a]Values in parentheses represent isolated unoptimized yields.

of the reactions, a single new spot appeared on TLC and Knoevenagel adduct (corresponding to 6′{1} or 6{1}) was never obtained in any case.

Next, we focused our attention toward synthesizing fused pyrazole-1,2,3-triazolopyridyls **9** by reacting 5-(arylethynyl)-1*H*-pyrazole-4-carbaldehyde **8** with phenacyl azides **2** using piperidinium acetate as an additive (Scheme 2). To our delight, substrate **8** smoothly reacted with phenacyl azides **2** in ethanol at room temperature using one equivalent piperidinium acetate as an additive leading to high yields of fused pyrazole-1,2,3-triazolopyridyls **9**. All the reactions proceeded straightforwardly leading to a clean single spot on TLC with no side products. A series of fused pyrazole-1,2,3-triazolopyridyls **9** were successfully synthesized using the optimized protocol.

Next, we explored the scope of the tandem process using 2-(arylethynyl)benzaldehyde **10** as substrates. In contrast to indole and pyrazole substrates, the reaction of 2-(phenylethynyl)benzaldehyde **10**{1} with 2-azido-1-(4-fluorophenyl)ethanone **2**{3} in ethanol using 1 equiv of piperidinium acetate remained incomplete even after 96 h. However, refluxing the reaction mixture for 24 h led to the complete consumption of both substrates (**10**{1} and **2**{3}) yielding **11**{1,3} (89%) (Scheme 3). Next, a series of fused 1,2,3-triazoloisoquinolines **11** were synthesized by refluxing 2-alkynylaryl aldehydes **10** and phenacyl azides **2** in ethanol using one equivalent of piperidinium acetate as an additive.

Fused 1,2,3-triazolo-heterocycles **3**, **9**, and **11** are very interesting heterocycles in terms of their biological and pharmacological potentials since they bear privileged scaffolds (β-carboline, pyrazolo-pyridine, and isoquinoline) as a part of their chemical structure. Moreover we found that these fused 1,2,3-triazolo-heterocycles **3**, **9**, and **11** could be converted to β-carboline **12**, pyrazolo-pyridine **13** and isoquinoline **14** by refluxing the corresponding precursor in acetic acid. Thus, these new fused heterocycles provide efficient and alternative routes for β-carboline, pyrazolo-pyridine and isoquinoline (Scheme 4).

CONCLUSION

An atom economical, tandem, four-centered, one-pot, two-step method has been developed leading to the formation of structurally novel diverse heterocyclic scaffolds. The generality and scope of the strategy has been demonstrated on three distinct substrates (indole, pyrazole, and benzene). Furthermore, efficient conversion of these heterocyles into various other pharmacologically important β-carboline, pyrazolo-pyridine, and isoquinoline has been illustrated.

EXPERIMENTAL PROCEDURES

General Information. All the reagents and chemicals were purchased from commercial sources and used without further any purification. Anhydrous solvents were purchased from Sigma-Aldrich Company and used without further any purification. Common laboratory solvents (LR grade) were purchased from domestic suppliers. Analytical thin layer chromatography was performed with E. Merck silica gel 60 F aluminum plates and visualized under UV 254 nm. NMR spectra were measured with Bruker 300, 500, and 600 MHz, and Varian 400 MHz instruments. Chemical shifts are reported in δ units, parts per million (ppm) downfield from TMS. Coupling constants (*J*) are in hertz (Hz) and are unadjusted; therefore, due to limits in resolution, in some cases there are small differences (<1 Hz) in the measured *J* value of the same coupling constant determined from different signals. Splitting patterns are designed as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; dt, doublet of triplets; tt, triplet of triplets; m, multiplet; br, broad. IR spectra were recorded on a Perkin−Elmer FT-IR RXI spectrophotometer and values

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reported in cm^{-1}. ESI-MS spectra were obtained on a LCQ Advantage ion trap mass spectrometer (Finnigan Thermo Fischer Scientific) and high-resolution mass spectra (ESI-HRMS) were recorded on Agilent 6520 ESI-QTOP mass spectrometer. Melting points were determined on a Kofler block and are uncorrected. All the new compounds were fully characterized by ^1H NMR, ^{13}C NMR, mass spectroscopy, IR, and HRMS analysis. The chromatographic solvents are mentioned as v/v ratios.

General Experimental Procedure for the Synthesis of 2-Azido-1-arylethanone 2{1}−2{8}. To a stirred solution of sodium azide (0.65g, 10 mmol) in 20 mL of acetone−water (2:1, v/v) or DMSO was added 2-bromo-1-arylethanone (3 mmol) at room temperature. After 2 h of stirring, the mixture was poured onto ice−water (100g) and extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried ($MgSO_4$), filtered and evaporated in vacuum to yield corresponding 2-azido-1-arylethanone. **Caution!** Organic azides are potentially explosive substances that can and will decompose with the slightest input of energy from external sources (heat, light, pressure). They should not be heated too much when concentrating. They should be stored at low temperature in a refrigerator.

*2-Azido-1-phenylethanone **2{1}***. **2{1}** (0.440 g, 91%) was obtained as a yellow oil which solidifies in the refrigerator starting from 0.597 g of phenacyl bromide using DMSO as solvent. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.55 (s, 2H), 7.45−7.50 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.87 (d, J = 7.2 Hz, 2H) (found in accordance with those in literature).[14]

*2-Azido-1-(4-chlorophenyl)ethanone **2{2}***. **2{2}** (0.528 g, 90%) was obtained as a yellow solid starting from 0.701 g of 2-bromo-1-(4-chlorophenyl)ethanone bromide using DMSO as solvent. ^1H NMR (500 MHz, $CDCl_3$) δ: 4.53 (s, 2H), 7.47 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 2H) (found in accordance with those in literature).[14]

*2-Azido-1-(4-fluorophenyl)ethanone **2{3}***. **2{3}** (0.500 g, 93%) was obtained as a yellow solid starting from 0.651 g of 2-bromo-1-(4-fluorophenyl)ethanone bromide using DMSO as solvent. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.54 (s, 2H), 7.15 (t, J = 8.6 Hz, 2H), 7.93−7.98 (m, 2H) (found in accordance with those in literature).[12]

*2-Azido-1-(4-methoxyphenyl)ethanone **2{4}***. **2{4}** (0.522 g, 91%) was obtained as a yellow solid starting from 0.687 g of 2-bromo-1-(4-methoxyphenyl)ethanone using acetone−water (2:1) as solvent. ^1H NMR (500 MHz, $CDCl_3$) δ: 3.88 (s, 3H), 4.51 (s, 2H), 6.95 (d, J = 8.9 Hz, 2H), 7.88 (d, J = 8.9 Hz, 2H) (found in accordance with those in literature).[15]

*2-Azido-1-(biphenyl-4-yl)ethanone **2{5}***. **2{5}** (0.641 g, 90%) was obtained as a white solid starting from 0.825 g of 1-(biphenyl-4-yl)-2-bromoethanone using acetone−water (2:1) as solvent. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.60 (s, 2H), 7.42−7.51 (m, 3H), 7.61−7.64 (m, 2H), 7.71(d, J = 8.5 Hz, 2H), 7.97 (d, J = 8.5 Hz, 2H) (found in accordance with those in literature).[15]

*2-Azido-1-p-tolylethanone **2{6}***. **2{6}** (0.494 g, 94%) was obtained as a pale yellow solid starting from 0.639 g of 2-bromo-1-*p*-tolylethanone using acetone−water (2:1) as solvent. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.17 (s, 3H), 4.54 (s, 2H), 7.15−7.21 (m, 2H), 7.93−7.98 (m, 2H) (found in accordance with those in literature).[16]

*2-Azido-1-(3-methoxyphenyl)ethanone **2{7}***. **2{7}** (0.488 g, 85%) was obtained as a brown oil starting from 0.687g of 2-bromo-1-(3-methoxyphenyl)ethanone using acetone−water (2:1) as solvent. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.86 (s, 3H), 4.55 (s, 2H), 7.14−7.18 (m, 1H), 7.36−7.45 (m, 3H) (found in accordance with those in literature).[17]

*2-Azido-1-(4-(pyrrolidin-1-yl)phenyl)ethanone **2{8}***. **2{8}** (0.608 g, 88%) was obtained as a brown solid starting from 0.804 g of 2-bromo-1-(4-(pyrrolidin-1-yl)phenyl)ethanone bromide using acetone−water (2:1) as solvent. mp: 155−156 °C. ESI MS (m/z): 231(M + H). IR (KBr, cm^{-1}): 2140, 2103, 1662, 1604, 1549, 1530, 1423, 1397, 1247, 1229. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.00−2.09 (m, 4H), 3.30−3.40 (m, 4H), 4.44 (s, 2H), 6.50 (d, J = 8.9 Hz, 2H), 7.77 (d, J = 8.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 25.35, 47.53, 54.04, 110.89, 121.56, 130.23, 151.45, 190.58.

General Experimental Procedure for the Synthesis of 2-(Arylethynyl)-1*H*-indole-3-carboxyaldehyde 1{1}−1{4}. Compounds **1{1}−1{4}** were synthesized in three steps described as follows.

Step 1 (2-Oxindole to 2-Bromo-1H-indole-3-carboxyaldehyde). To a solution of DMF (3.655 g, 50 mmol) in dichloromethane (15 mL) was added dropwise a solution of phosphorus oxybromide (11.47 g, 40 mmol) in dichloromethane (25 mL) at 0 °C. The white thick mixture was refluxed during 15 min, and then 2-oxindole (2.66 g, 20 mmol) was added portion-wise. The mixture was stirred at reflux during 1 h. Next the reaction was quenched by addition of crushed ice to the media. The mixture was stirred for 20 min and allowed to stand for 10 min. Next the two layers (aqueous−organic) were separated. The aqueous layer was neutralized with solid potassium carbonate. The pale yellow precipitate which appeared was filtered and washed with cold water and purified with silica-gel column chromatography using hexane−ethyl acetate (3:1) as eluent. Yield: 3.63g (81%) as pale yellow solid, mp 186−188 °C, [Literature 186 °C].[18]

Step 2 (2-bromo-1H-indole-3-carboxyaldehyde to 1-alkyl-2-bromo-1H-indole-3-carboxyaldehyde). Sodium hydride [0.40 g (60% dispersion in mineral oil), 10 mmol] was added to a solution of 2-bromo-1*H*-indole-3-carboxyaldehyde (2.240 g, 10 mmol) in 30 mL of dry THF at 0−5 °C and stirred for 10 min. Next the benzyl bromide (2.052 g, 12 mmol) (or equivalent amount of MeI for methylation) in dry THF (10 mL) was added to it and stirring was further continued for 6 h at room temperature. When the starting materials were consumed completely as monitored by TLC, the reaction mixture was concentrated using a vacuum evaporator to yield a crude product. Pure 1-benzyl-2-bromo-1*H*-indole-3-carboxyaldehyde was isolated by purifying the crude through silica gel column chromatography using hexane−ethyl acetate in increasing polarity as eluent. Characterization data for both the compounds are as follows.

1-Benzyl-2-bromo-1H-indole-3-carboxyaldehyde. Yield: 2.357 g (75%) as white solid. ^1H NMR (500 MHz, $CDCl_3$) δ: 5.45 (s, 2H), 7.09 (d, J = 7.1 Hz, 2H), 7.21−7.35 (m, 6H), 8.32 (d, J = 7.6 Hz, 1H), 10.05 (s, 1H) (found in accordance with those reported in literature).[18]

2-Bromo-1-methyl-1H-indole-3-carboxyaldehyde. Yield: 2.023 g (85%) as a yellow solid. ^1H NMR (500 MHz, $CDCl_3$) δ: 3.81 (s, 3H), 7.27−7.37 (m, 3H), 8.30−8.33 (m, 1H), 10.01 (s, 1H) (found in accordance with those reported in literature).[19]

*Step 3 (1-Benzyl-2-bromo-1H-indole-3-carboxyaldehyde to 1-Benzyl-2-phenylethynyl-1H-indole-3-carboxyaldehyde **1a**).* CuI (23.8 mg, 0.125 mmol), $PdCl_2(PPh_3)_2$ (175.5 mg, 0.25 mmol), 1-benzyl-2-bromo-1*H*-indole-3-carboxyaldehyde

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(1.57 g, 5 mmol), were suspended in 10 mL of anhydrous DMF and 15 mL of Et_3N under nitrogen. Next phenyl acetylene (0.562 g, 5.5 mmol) was added to it, and the reaction mixture was stirred overnight at 40 °C and then it was diluted in EtOAc (100 mL). Filtration on Celite, evaporation of Et_3N, DMF, and EtOAc under reduced pressure and purification by flash chromatography on silica gel using hexane-ethyl acetate in increasing polarity afforded the desired product **1{1}** (1.107 g, 66%) as pale brown solid.

*1-Benzyl-2-(phenylethynyl)-1H-indole-3-carboxyaldehyde **1{1}***. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.54 (s, 2H), 7.23 (d, J = 6.9 Hz, 2H), 7.27−7.34 (m, 6H), 7.37−7.44 (m, 3H), 7.54 (dd, J = 7.8 and 1.5 Hz, 2H), 8.35−8.37 (m, 1H), 10.34 (s, 1H) (found in accordance with those reported in literature).[18]

*1-Benzyl-2-(p-tolylethynyl)-1H-indole-3-carboxyaldehyde **1{2}***. **1{2}** was also prepared in the same way and on the same scale, 1.345g (77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.39 (s, 3H), 5.55 (s, 2H), 7.19 (d, J = 7.9 Hz, 2H), 7.26−7.34 (m, 8H), 7.44 (d, J = 8.1 Hz, 2H), 8.34−8.36 (m, 1H), 10.33 (s, 1H) (found in accordance with those reported in literature).[18]

*1-Benzyl-2-(hept-1-ynyl)-1H-indole-3-carboxyaldehyde **1{3}***. **1{3}** was also prepared in the same way using 1-benzyl-2-bromo-1*H*-indole-3-carbaldehyde and 1-heptyne as substrates. Yield: 1.318 g (80%), light brown oil. ESI MS (*m/z*): 330 (M + H). IR (KBr, cm^{-1}): 2226, 1647, 1612, 1576, 1513, 1495, 1487, 1456, 1430, 1379, 1342, 1213, 1202, 1191. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.86 (t, J = 6.8 Hz, 3H), 1.28−1.46 (m, 4H), 1.68−1.69 (m, 2H), 2.52 (t, J = 7.6 Hz, 2H), 5.45 (s, 2H), 7.15−7.37 (m, 8H), 8.30−8.33 (m, 1H), 10.20 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 13.81, 19.67, 22.02, 27.75, 30.92, 48.19, 69.28, 103.81, 110.23, 119.59, 121.94, 123.25, 124.51, 124.66, 126.61, 127.74, 128.73, 132.90, 135.95, 136.44, 185.37. HRMS calculated for $C_{23}H_{24}ON$ (M + H): 330.18524; found 330.18500.

*1-Benzyl-2-(hept-1-ynyl)-1H-indole-3-carboxyaldehyde **1{4}***. **1{4}** was prepared in the same way using 1-methyl-2-bromo-1*H*-indole-3-carbaldehyde and 1-heptyne as substrates. Yield: 0.925 g (73%), %), light brown oil. ESI MS (*m/z*): 254 (M + H). IR (KBr, cm^{-1}): 2231, 1651, 1609, 1574, 1513, 1465, 1410, 1382, 1330, 1254, 1127. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.93 (t, J = 7.3 Hz, 3H), 1.35−1.51 (m, 4H), 1.67−1.73 (m, 2H), 2.57 (t, J = 7.0 Hz, 2H), 3.80 (s, 3H), 7.26−7.35 (m, 3H), 8.28 (d, J = 7.3 Hz, 1H), 10.13 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 13.91, 19.74, 22.09, 27.91, 30.89, 31.05, 69.20, 103.64, 109.51, 119.33, 121.92, 123.22, 124.27, 124.53, 133.16, 137.01, 185.24. HRMS calculated for $C_{17}H_{20}ON$ (M + H): 254.15394; found 254.15363.

General Experimental Procedure for the Synthesis of 3-Methyl-1-phenyl-5-(arylethynyl)-1*H*-pyrazole-4-carboxyaldehyde 8{1}−8{2}. Compounds **8{1}** and **8{2}** were synthesized in three steps.

Step 1 [Phenyl Hydrazine to 3-Methyl-1-phenyl-1H-pyrazol-5(4H)-one]. Phenyl hydrazine (9.73g, 90 mmol) was taken in 50 mL of glacial acetic acid, and methyl acetoacetate (10.45 g, 90 mmol) was added to it and stirred at reflux for 3 h. Thereafter, the reaction mixture was evaporated to dryness, and the residue was extracted with water (50 mL) and EtOAc (50 mL). The organic layer was separated whereas the aqueous layer was further extracted with EtOAc (2 × 50 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated over reduced pressure to afford pure 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one as a white solid (10.975g, 70%). mp: 127−128 °C [literature 127.5−128.5 °C].[20]

Step 2 [3-Methyl-1-phenyl-1H-pyrazol-5(4H)-one to 5-Chloro-3-methyl-1-phenyl-1H-pyrazole-4-carboxyaldehyde]. To a stirred solution of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (10 g, 57 mmol) in dry DMF (100 mL), $POCl_3$ (13.4 mL,144 mmol) was added dropwise at 0 °C. After addition, the reaction was continued at 100 °C for 6 h. Then the reaction mixture was poured into 150 g of ice−200 mL water and neutralized with saturated aqueous solution of $NaHCO_3$. Thereafter EtOAc (400 mL) was added to it and organic layer was separated whereas the aqueous layer was further extracted with EtOAc (2 × 200 mL). The pooled organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by column chromatography over silica gel (EtOAc/hexanes, 1:9) furnished pure product as a white solid (9.0 g, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.54 (s, 3H), 7.46−7.54 (m, 5H), 9.97 (s, 1H) (found in accordance with those in literature).[21]

Step 3 [5-Chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde to 3-Methyl-1-phenyl-5-(phenylethynyl)-1H-pyrazole-4-carboxyaldehyde]. Triethylamine (5.06g, 50 mmol), phenyl acetylene (1.53g, 15 mmol), $(PPh_3)_2PdCl_2$ (701 mg, 1 mmol), and CuI (380 mg, 2 mmol) were added under nitrogen to a solution of 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (2.21g, 10 mmol) in dry DMF (20 mL) and the reaction mixture was stirred at 80 °C for 4 h. DMF was evaporated under reduced pressure. The residue was dissolved in dichloromethane (20 mL), water (40 mL) was added, and the mixture was extracted with dichloromethane (3 × 40 mL). The organic layers were combined, washed with brine and dried with Na_2SO_4. The solvent was evaporated and the residue was purified by silica-gel column chromatography to yield 2.12 g (74%) of **8{1}**.

*3-Methyl-1-phenyl-5-(phenylethynyl)-1H-pyrazole-4-carboxyaldehyde **8{1}***. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.59 (s, 3H), 7.35−7.55 (m, 8H), 7.82 (d, J = 7.5 Hz, 2H), 10.17 (s, 1H) (found in accordance with those in literature).[22]

*3-Methyl-1-phenyl-5-(p-tolylethynyl)-1H-pyrazole-4-carboxyaldehyde **8{2}***. **8{2}** was also prepared in the same way and on the same scale, 1.952g (65%) - ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.38 (s, 3H), 2.58 (s, 3H), 7.17 (d, J = 7.9 Hz, 2H), 7.36−7.54 (m, 5H), 7.81 (d, J = 7.5 Hz, 2H), 10.16 (s, 1H) (found in accordance with those in literature).[22]

General Experimental Procedure for the Synthesis of 2-(Arylethynyl)benzaldehyde 11{1}−11{2}. $(Ph_3P)_2PdCl_2$ (152 mg, 0.22 mmol) and CuI (21 mg, 0.11 mmol) were added to a solution of 2-bromobenzaldehyde (2.00 g, 10.81 mmol) and phenylacetylene (1.32 g, 12.97 mmol) in triethylamine (45 mL). Next the reaction mixture was heated under nitrogen atmosphere at 50 °C until completion (TLC). The reaction mixture was concentrated under reduced pressure and purified by silica-gel column chromatography using *n*-hexane/ethyl acetate (24:1 v/v) as eluent to give **11{1}** (1.70g, 77%) as a yellow oil.

*2-(Phenylethynyl)benzaldehyde **11{1}***. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.37−7.41 (m, 3H), 7.44 (t, J = 7.5 Hz, 1H), 7.52−7.60 (m, 3H), 7.64 (d, J = 7.6 1H), 7.95 (dd, J = 7.8 and 0.9 Hz, 1H), 10.66 (s, 1H) (found in accordance with those in literature).[23]

*2-(p-Tolylethynyl)benzaldehyde **11{2}***. In the same way, **11{2}** was also prepared on the same scale. Yield: 1.55 g (65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.39 (s, 3H), 7.19 (d, J = 7.9 Hz, 2H), 7.42−7.47 (m, 3H), 7.56 (dt, J = 7.5 and 1.2 Hz, 1H),

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7.63 (d, J = 7.5 Hz, 1H), 7.94 (dd, J = 7.8 and 0.9 Hz, 1H), 10.66 (s, 1H) (found in accordance with those in literature).[24]

General Experimental Procedure for the Synthesis of Fused 1,2,3-Triazolo-β-carbolines 3. To a stirred solution of **1{1}**−**1{4}** (0.20 mmol) and 2-azido-1-(aryl)ethanone **2{1}**−**2{8}** (0.20 mmol) in ethanol (2.0 mL) was added 0.20 mmol of piperidinium acetate and stirring was further continued until complete consumption of the starting substrates (TLC). Next ethanol was evaporated in vacuum and residue was extracted with chloroform/water (15 mL each). The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated to yield crude which was purified through silica gel column chromatography using ethyl acetate/hexane as eluent in increasing polarity.

*Compound **3{1,1}***. mp: 196−198 °C; 84 mg (88%) of **3{1,1}** was obtained as a light yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 479 (M + H). IR (KBr, cm^{-1}): 1699, 1624, 1511, 1497, 1466, 1397, 1345, 1281, 1250, 1203. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.27 (s, 2H), 6.49 (d, J = 7.0 Hz, 2H), 7.09−7.17 (m, 3H), 7.21−7.28 (m, 3H), 7.31−7.45 (m, 5H), 7.51 (m, 2H), 7.64 (m, 1H), 7.97−8.03 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 50.00, 111.58, 114.44, 115.50, 119.84, 122.05, 123.28, 123.71, 125.54, 126.28, 127.40, 127.60, 128.37, 128.48, 128.67, 128.95, 130.04, 130.40, 130.92, 132.92, 133.57, 135.82, 136.99, 137.31, 140.42, 188.17. HRMS calculated for $C_{32}H_{23}ON_4$ (M + H): 479.18719, found 479.18609.

*Compound **3{1,2}***. mp: 126−128 °C; 85 mg (83%) of **3{1,2}** was obtained as a yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 513 (M + H). IR (KBr, cm^{-1}): 1657, 1624, 1586, 1543, 1508, 1496, 1485, 1399, 1278, 1253, 1234, 1208. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.28 (s, 2H), 6.50 (d, J = 7.3 Hz, 2H), 7.11−7.19 (m, 3H), 7.22−7.28 (m, 3H), 7.32−7.45 (m, 5H), 7.49 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.5 Hz, 2H), 8.03 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 50.00, 111.59, 114.56, 115.54, 119.82, 122.14, 123.19, 123.62, 125.50, 126.37, 127.20, 127.40, 128.37, 128.47, 128.99, 130.32, 131.00, 131.26, 132.35, 135.36, 135.72, 137.37, 139.94, 140.39, 186.99. HRMS calculated for $C_{32}H_{22}ON_4Cl$ (M + H): 513.14767, found 513.14795.

*Compound **3{1,3}***. mp: 200−202 °C; 90 mg (91%) of **3{1,3}** was obtained as a yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 497 (M + H). IR (KBr, cm^{-1}): 1673, 1644, 1622, 1596, 1567, 1504, 1299, 1278, 1252, 1232, 1215. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.28 (s, 2H), 6.50 (d, J = 6.9 Hz, 2H), 7.10−7.26 (m, 8H), 7.32−7.45 (m, 5H), 7.98−8.06 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 50.00, 111.63, 114.20, 115.55, 115.84, 116.08, 119.86, 122.14, 123.23, 125.54, 126.39, 127.45, 128.41, 129.03, 130.38, 130.93, 132.43, 132.63, 132.75, 133.31, 135.80, 137.37, 140.42, 164.80, 167.35, 186.80. HRMS calculated for $C_{32}H_{22}ON_4F$ (M + H): 497.17722, found 497.17666.

*Compound **3{1,4}***. mp: 123−125 °C; 87 mg (86%) of **3{1,4}** was obtained as a pale yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 509 (M + H). IR (KBr, cm^{-1}): 1621, 1598, 1510, 1468, 1417, 1254. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.90 (s, 3H), 5.27 (s, 2H), 6.49 (d, J = 6.8 Hz, 2H), 6.98 (d, J = 8.3 Hz, 2H), 7.05−7.31 (m, 6H), 7.32−7.40 (m, 3H), 7.43 (d, J = 7.6 Hz, 2H), 7.95−8.04 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 49.93, 55.55, 111.50, 113.09, 113.98, 115.58, 119.80, 121.89, 123.21, 123.70, 125.53, 126.17, 127.33, 127.91, 128.34, 128.44, 128.89, 129.52, 130.38, 130.50, 132.56, 135.90, 137.16, 140.35, 164.17, 186.89. HRMS calculated for $C_{33}H_{25}O_2N_4$ (M + H): 509.19720, found 509.19607.

*Compound **3{1,5}***. mp: 209−211 °C; 100 mg (90%) of **3{1,5}** was obtained as a yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 555 (M + H). IR (KBr, cm^{-1}): 1661, 1601, 1624, 1509, 1496, 1485, 1467, 1450, 1396, 1278, 1255. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.28 (s, 2H), 6.51 (d, J = 7.3 Hz, 2H), 7.11−7.18 (m, 3H), 7.22−7.26 (m, 3H), 7.33−7.50 (m, 8H), 7.66 (d, J = 7.5 Hz, 2H), 7.73 (d, J = 8.2H, 2H), 8.03−8.07 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 50.07, 110.43, 111.66, 114.33, 115.64, 116.95, 119.95, 122.13, 123.35, 123.79, 125.62, 126.38, 127.39, 127.48, 128.38, 128.47, 128.56, 129.02, 130.19, 130.48, 130.74, 132.57, 135.69, 135.92, 137.40, 139.85, 140.49, 146.42, 187.85. HRMS calculated for $C_{38}H_{27}ON_4$ (M + H): 555.21794, found 555.21720.

*Compound **3{1,6}***. mp: 174−176 °C; 79 mg (80%) of **3{1,6}** was obtained as a light yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 493 (M + H). IR (KBr, cm^{-1}): 1658, 1624, 1604, 1573, 1496, 1469, 1451, 1362, 1266, 1251, 1233. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.47 (s, 3H), 5.27 (s, 2H), 6.49 (d, J = 6.8 Hz, 2H), 7.00−7.27 (m, 6H), 7.30−7.40 (m, 5H), 7.43 (d, J = 7.6 Hz, 2H), 7.89 (d, J = 7.6 Hz, 2H), 7.98 (s, 1H), 8.02 (d, J = 6.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.32, 50.04, 111.57, 114.48, 115.35, 119.80, 122.01, 123.29, 123.73, 125.50, 126.20, 127.34, 127.57, 128.35, 128.65, 129.02, 129.40, 130.01, 130.16, 131.06, 133.53, 135.95, 136.99, 138.80, 140.43, 188.20. HRMS calculated for $C_{33}H_{25}ON_4$ (M + H): 493.20229, found 493.20186.

*Compound **3{1,7}***. mp: 89−91 °C; 83 mg (82%) of **3{1,7}** was obtained as a yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 509 (M + H). IR (KBr, cm^{-1}): 1660, 1622, 1595, 1495, 1485, 1466, 1428, 1395, 1268, 1240. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.88 (s, 3H), 5.27 (s, 2H), 6.49 (d, J = 6.8 Hz, 2H), 7.07−7.26 (m, 7H), 7.31−7.45 (m, 6H), 7.49 (d, J = 7.6 Hz, 1H), 7.59 (s, 1H), 8.00−8.03 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 49.95, 55.48, 111.54, 114.01, 114.42, 115.38, 119.80, 120.15, 122.01, 122.86, 123.21, 125.50, 126.23, 127.34, 128.33, 128.44, 128.91, 129.58, 130.33, 130.86, 132.46, 135.77, 137.29, 138.25, 140.37, 159.80, 187.87. HRMS calculated for $C_{33}H_{25}O_2N_4$ (M + H): 509.19720, found 509.19758.

*Compound **3{1,8}***. mp: 129−131 °C; 88 mg (80%) of **3{1,8}** was obtained as a yellow solid starting from 67 mg of **1{1}**. ESI MS (m/z): 548 (M + H). IR (KBr, cm^{-1}): 1633, 1590, 1543, 1530, 1505, 1495, 1463, 1316, 1237. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.00−2.13 (m, 4H), 3.30−3.47 (m, 4H), 5.25 (s, 2H), 6.48 (d, J = 6.6 Hz, 2H), 6.56 (d, J = 8.9 Hz, 2H), 7.08−7.16 (m, 3H), 7.20−7.26 (m, 3H), 7.30−7.40 (m, 3H), 7.43 (d, J = 7.0 Hz, 2H), 7.87 (s, 1H), 7.93 (d, J = 8.9 Hz, 2H), 8.00 (d, J = 8.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.45, 47.68, 49.92, 111.07, 111.45, 111.57, 115.79, 119.86, 121.69, 123.32, 123.64, 125.62, 126.03, 127.34, 128.38, 128.50, 128.85, 130.54, 132.11, 132.89, 133.04, 136.18, 140.39, 151.80, 186.22. HRMS calculated for $C_{36}H_{30}ON_5$ (M + H): 548.24449, found 548.24347.

*Compound **3{2,1}***. mp: 197−198 °C; 80 mg (81%) of **3{2,1}** was obtained as a light yellow solid starting from 70 mg of **1{2}**. ESI MS (m/z): 493 (M + H). IR (KBr, cm^{-1}): 1669, 1595, 1549, 1519, 1485, 1469, 1447, 1395, 1350, 1204. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 5.28 (s, 2H), 6.52 (d, J = 6.8 Hz, 2H), 6.99 (d, J = 7.7 Hz, 2H), 7.10−7.17 (m, 3H), 7.22−7.40 (m, 5H), 7.50 (t, J = 7.6 Hz, 2H), 7.63 (t, J = 7.3 Hz, 1H), 7.97−8.03 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.41, 50.13, 111.66, 114.57, 115.44, 119.90, 122.10, 123.38,

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123.82, 125.59, 126.29, 127.42, 127.66, 128.44, 128.73, 129.11, 129.49, 130.10, 130.25, 133.62, 136.04, 137.08, 138.89, 140.52, 188.28. HRMS calculated for $C_{33}H_{25}ON_4$ (M + H): 493.20229, found 493.20186.

*Compound **3{2,2}***. mp: 184−186 °C; 84 mg (80%) of **3{2,2}** was obtained as a yellow solid starting from 70 mg of **1{2}**. ESI MS (*m*/*z*): 527 (M + H). IR (KBr, cm^{-1}): 1681, 1660, 1645, 1633, 1599, 1556, 1531, 1519, 1496, 1485, 1397, 1279, 1267, 1251, 1232. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 5.28 (s, 2H), 6.52 (d, *J* = 7.0 Hz, 2H), 6.99 (d, *J* = 7.6 Hz, 2H), 7.10−7.19 (m, 3H), 7.24−7.40 (m, 5H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.88 (d, *J* = 8.5 Hz, 2H), 8.02−8.05 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.41, 50.20, 111.71, 114.65, 115.53, 119.89, 122.22, 123.32, 123.76, 125.56, 126.41, 127.45, 128.44, 129.11, 129.34, 130.22, 131.35, 135.48, 135.95, 137.58, 139.97, 140.02, 140.52, 187.15. HRMS calculated for $C_{33}H_{24}ON_4Cl$ (M + H): 527.16332, found 527.16341.

*Compound **3{2,5}***. mp: 113−115 °C; 94 mg (83%) of **3{2,5}** was obtained as a yellow solid starting from 70 mg of **1{2}**. ESI MS (*m*/*z*): 569 (M + H). IR (KBr, cm^{-1}): 1693, 1660, 1644, 1633, 1601, 1556, 1538, 1495, 1485, 1469, 1393, 1278, 1180. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 5.28 (s, 2H), 6.53 (d, *J* = 6.8 Hz, 2H), 7.00 (d, *J* = 7.7 Hz, 2H), 7.11−7.18 (m, 3H), 7.25−7.49 (m, 8H), 7.66 (d, *J* = 7.0 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 8.03−8.07 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.26, 50.09, 111.61, 114.21, 115.50, 119.86, 122.03, 123.36, 123.77, 125.54, 126.24, 126.88, 127.33, 127.77, 128.30, 128.39, 128.95, 129.05, 129.44, 130.21, 130.66, 131.07, 131.74, 135.68, 136.00, 137.42, 138.83, 139.83, 140.48, 146.33, 187.84. HRMS calculated for $C_{39}H_{29}ON_4$ (M + H): 569.23359, found 569.23323.

*Compound **3{2,6}***. mp: 196−198 °C; 82 mg (81%) of **3{2,6}** was obtained as a pale yellow solid starting from 70 mg of **1{2}**. ESI MS (*m*/*z*): 507 (M + H). IR (KBr, cm^{-1}): 1698, 1693, 1681, 1667, 1651, 1644, 1633, 1621, 1538, 1519, 1495, 1469, 1452, 1434, 1395, 1351, 1257, 1235, 1205. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 2.47 (s, 3H), 5.28 (s, 2H), 6.52 (d, *J* = 6.8 Hz, 2H), 7.00 (d, *J* = 7.7 Hz, 2H), 7.10−7.17 (m, 3H), 7.24−7.38 (m, 7H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.97 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.32, 50.04, 111.57, 114.48, 115.35, 119.80, 122.01, 123.29, 123.73, 125.50, 126.20, 127.34, 127.57, 128.35, 128.65, 129.02, 129.40, 130.01, 130.16, 131.06, 133.53, 135.95, 136.99, 138.80, 140.43, 188.20. HRMS calculated for $C_{34}H_{27}ON_4$ (M + H): 507.21794, found 507.21685.

*Compound **3{3,2}***. mp: 116−119 °C; 81 mg (80%) of **3{3,2}** was obtained as a pale yellow solid starting from 66 mg of **1{3}**. ESI MS (*m*/*z*): 507 (M + H). IR (KBr, cm^{-1}): 1660, 1620, 1604, 1586, 1537, 1495, 1487, 1470, 1452, 1401, 1360, 1278, 1251, 1229, 1205. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.81 (t, *J* = 6.8 Hz, 3H), 1.09−1.27 (m, 4H), 1.75−1.88 (m, 2H), 3.02 (t, *J* = 7.6 Hz, 2H), 5.95 (s, 2H), 7.07−7.10 (m, 2H), 7.30−7.46 (m, 8H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.97 (s, 1H), 8.03 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.95, 22.23, 27.99, 29.85, 31.54, 49.76, 110.94, 114.03, 114.62, 119.76, 122.18, 123.15, 123.33, 125.41, 126.25, 127.52, 127.99, 128.94, 129.24, 131.10, 131.50, 135.52, 135.93, 136.74, 139.79, 140.15, 187.28. HRMS calculated for $C_{31}H_{28}ON_4Cl$ (M + H): 507.19462, found 507.19406.

*Compound **3{3,6}***. mp: 129−130 °C; 79 mg (81%) of **3{3,6}** was obtained as a pale yellow solid starting from 66 mg of **1{3}**. ESI MS (*m*/*z*): 487 (M + H); IR (KBr, cm^{-1}): 1655, 1619, 1604, 1533, 1493, 1470, 1451, 1398, 1362, 1332, 1261, 1237. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.83 (t, *J* = 6.8 Hz, 3H), 1.16−1.34 (m, 4H), 1.76−1.90 (m, 2H), 2.46 (s, 3H), 3.04 (t, *J* = 7.6 Hz, 2H), 5.97 (s, 2H), 7.09 (d, *J* = 6.8 Hz, 2H), 7.28−7.47 (m, 8H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.93 (s, 1H), 8.01 (d, J = 7.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.02, 21.85, 22.34, 28.07, 30.05, 31.59, 49.75, 110.96, 113.53, 114.59, 119.77, 122.04, 123.21, 123.44, 125.47, 126.14, 128.00, 129.26, 129.37, 130.16, 131.26, 134.46, 136.12, 136.68, 140.14, 144.56, 188.20. HRMS calculated for $C_{32}H_{31}ON_4$ (M + H): 487.24924, found 487.25027.

*Compound **3{4,2}***. mp: 184−185 °C; 67 mg (78%) of **3{4,2}** was obtained as a pale yellow solid starting from 51 mg of **1{4}**. ESI MS (*m*/*z*): 431 (M + H). IR (KBr, cm^{-1}): 1649, 1623, 1605, 1585, 1500, 1485, 1397, 1247, 1182. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.90 (t, *J* = 6.8 Hz, 3H), 1.34−1.62 (m, 4H), 1.91−2.08 (m, 2H), 3.34 (t, *J* = 7.6 Hz, 2H), 4.29 (s, 3H), 7.28−7.45 (m, 3H), 7.52−7.60 (m, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.89 (s, 1H), 7.96 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.02, 22.50, 28.78, 29.88, 31.73, 33.62, 110.14, 114.19, 114.36, 119.72, 121.84, 122.80, 123.42, 126.05, 127.10, 128.89, 131.04, 131.38, 135.57, 136.64, 139.68, 140.48, 187.26. HRMS calculated for $C_{25}H_{24}ON_4Cl$ (M + H): 431.16332, found 431.16326.

*Compound **3{4,6}***. mp: 128−129 °C; 66 mg (80%) of **3{4,6}** was obtained as a pale yellow solid starting from 51 mg of **1{4}**. ESI MS (*m*/*z*): 411 (M + H). IR (KBr, cm^{-1}): 1650, 1623, 1605, 1573, 1501, 1455, 1380, 1248, 1184. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.90 (t, *J* = 6.8 Hz, 3H), 1.36−1.54 (m, 4H), 1.90−2.01 (m, 2H), 2.43 (s, 3H), 3.35 (t, *J* = 7.6 Hz, 2H), 4.28 (s, 3H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.33−7.37 (m, 1H), 7.49−7.57 (m, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.84 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.02, 21.74, 22.50, 28.77, 29.97, 31.73, 33.56, 110.08, 113.52, 114.26, 119.64, 121.61, 122.79, 123.44, 125.85, 127.62, 129.26, 129.99, 131.07, 134.47, 136.48, 140.43, 144.35, 188.10. HRMS calculated for $C_{26}H_{27}ON_4$ (M + H): 411.21794, found 411.21741.

General Experimental Procedure for the Synthesis of Fused Pyrazole-1,2,3-triazolopyridyls 9{1,1}−9{2,5}. To a stirred solution of **8{1}**/**8{2}** (0.20 mmol) and 2-azido-1-(aryl)ethanone **2{1}**−**2{5}** (0.20 mmol) in ethanol (2.0 mL) was added 0.20 mmol of piperidinium acetate and stirring was further continued for 24 h until complete consumption of the starting substrates (TLC). Next ethanol was evaporated in vacuum and residue was extracted with chloroform/water (15 mL each). The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated to yield crude, which was purified through silica gel column chromatography using ethyl acetate/hexane as eluent in increasing polarity.

*Compound **9{1,1}***. mp: 192−193 °C; 80 mg (93%) of **9{1,1}** was obtained as a white solid starting from 57 mg of **8{1}**. ESI MS (*m*/*z*): 430 (M + H). IR (KBr, cm^{-1}): 1667, 1595, 1580, 1558, 1530, 1512, 1501, 1459, 1447, 1398, 1318, 1302, 1285, 1251, 1222. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.64 (s, 3H), 6.85−7.12 (m, 6H), 7.16−7.32 (m, 4H), 7.37−7.55 (m, 3H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.76, 112.44, 118.20, 121.43, 123.81, 127.74, 127.75, 128.29, 128.53, 128.74, 129.71, 129.81, 130.59, 131.15, 133.94, 136.33, 139.42, 139.60, 146.59, 187.97. HRMS calculated for $C_{27}H_{20}ON_5$ (M + H): 430.16624, found 430.16646.

*Compound **9{1,2}***. mp: 206−206 °C; 84 mg (90%) of **9{1,2}** was obtained as a light yellow solid starting from 57 mg

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of **8{1}**. ESI MS (*m*/*z*): 464 (M + H). IR (KBr, cm^{-1}): 1661, 1633, 1587, 1529, 1496, 1461, 1320, 1303, 1283, 1275, 1258. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.65 (s, 3H), 6.91−6.99 (m, 4H), 7.00−7.10 (m, 2H), 7.18 (d, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.53 (s, 1H), 7.86 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.79, 112.70, 118.24, 121.41, 123.83, 127.80, 127.84, 128.30, 128.56, 129.13, 129.43, 130.67, 131.05, 131.16, 134.79, 139.54, 139.57, 140.43, 146.70, 186.87. HRMS calculated for $C_{27}H_{19}ON_5Cl$ (M + H): 464.12726, found 464.12842.

*Compound **9{1,3}**.* mp: 219−220 °C; 80 mg (90%) of **9{1,3}** was obtained as a white solid starting from 57 mg of **8{1}**. ESI MS (*m*/*z*): 448 (M + H). IR (KBr, cm^{-1}): 1666, 1634, 1594, 1558, 1530, 1499, 1461, 1285, 1257. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.65 (s, 3H), 6.89−7.00 (m, 4H), 7.02−7.10 (m, 2H), 7.17−7.25 (m, 6H), 7.51 (s, 1H), 7.95−7.98 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.76, 112.31, 115.94, 116.12, 118.22, 121.41, 123.82, 127.78, 128.73, 128.53, 129.52, 130.58, 131.06, 132.52, 132.61, 132.71, 139.48, 139.58, 146.60, 165.18, 167.23, 186.53. HRMS calculated for $C_{27}H_{19}ON_5F$ (M + H): 448.15681, found 448.15739.

*Compound **9{1,4}**.* mp: 174−176 °C; 81 mg (88%) of **9{1,4}** was obtained as a light yellow solid starting from 57 mg of **8{1}**. ESI MS (*m*/*z*): 460 (M + H). IR (KBr, cm^{-1}): 1647, 1626, 1596, 1569, 1525, 1445, 1422, 1304, 1258, 1213. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.64 (s, 3H), 3.90 (s, 3H), 6.90−7.08 (m, 8H), 7.16−7.25 (m, 4H), 7.44 (s, 1H), 7.94 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.77, 55.58, 111.28, 114.08, 118.28, 121.46, 123.83, 127.75, 128.30, 128.44, 128.52, 129.03, 130.05, 130.41, 131.24, 132.48, 139.38, 139.68, 146.39, 164.42, 186.57. HRMS calculated for $C_{28}H_{22}O_2N_5$ (M + H): 460.17680, found 460.17772.

*Compound **9{1,5}**.* mp: 186−188 °C; 90 mg (89%) of **9{1,5}** was obtained as a light yellow solid starting from 57 mg of **8{1}**. ESI MS (*m*/*z*): 506 (M + H). IR (KBr, cm^{-1}): 1658, 1632, 1599, 1530, 1512, 1496, 1461, 1445, 1317, 1301, 1273, 1257, 1228. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.66 (s, 3H), 6.96−8.02 (m, 20H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.76, 112.32, 118.24, 121.42, 123.52, 123.78, 127.23, 127.33, 127.72, 128.26, 128.34, 128.48, 128.90, 129.76, 130.06, 130.48, 131.13, 134.95, 139.41, 139.58, 146.58, 146.61, 187.50. HRMS calculated for $C_{33}H_{24}ON_5$ (M + H): 506.19754, found 506.19907.

*Compound **9{2,1}**.* mp: 204−204 °C; 81 mg (91%) of **9{2,1}** was obtained as a white solid starting from 60 mg of **8{2}**. ESI MS (*m*/*z*): 444 (M + H). IR (KBr, cm^{-1}): 1670, 1625, 1614, 1597, 1527, 1499, 1463, 1447, 1377, 1320, 1303, 1284, 1240. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.24 (s, 3H), 2.63 (s, 3H), 6.72 (d, *J* = 7.7 Hz, 2H), 6.92−6.97 (m, 2H), 7.00−7.09 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 2H),7.49 (s, 1H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.63−7.68 (m, 1H), 7.93 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.77, 21.15, 112.39, 118.10, 121.43, 123.86, 127.72, 128.09, 128.22, 128.45, 128.73, 129.72, 129.89, 130.70, 133.92, 136.38, 137.50, 139.55, 139.73, 146.55, 188.04. HRMS calculated for $C_{28}H_{22}ON_5$ (M + H): 444.18189, found 444.18204.

*Compound **9{2,2}**.* mp: 192−194 °C; 89 mg (93%) of **9{2,2}** was obtained as a white solid starting from 60 mg of **8{2}**. ESI MS (*m*/*z*): 478 (M + H). IR (KBr, cm^{-1}): 1660, 1633, 1530, 1499, 1483, 1318, 1302, 1282, 1255, 1147. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.25 (s, 3H), 2.64 (s, 3H), 6.72 (d, *J* = 7.8 Hz, 2H), 6.93−6.97 (m, 2H), 7.00−7.09 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.51 (s, 1H), 7.85 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.79, 21.17, 112.62, 118.14, 123.89, 127.80, 127.93, 128.22, 128.49, 129.13, 129.44, 130.72, 131.16, 134.85, 137.61, 139.67, 140.41, 146.64, 186.95. HRMS calculated for $C_{28}H_{21}ON_5Cl$ (M + H): 478.14291, found 478.14386.

*Compound **9{2,3}**.* mp: 179−183 °C; 83 mg (90%) of **9{2,3}** was obtained as a light yellow solid starting from 60 mg of **8{2}**. ESI MS (*m*/*z*): 462 (M + H). IR (KBr, cm^{-1}): 1662, 1625, 1593, 1558, 1499, 1463, 1446, 1319, 1301, 1271, 1252, 1227. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.24 (s, 3H), 2.63 (s, 3H), 6.71 (d, *J* = 7.4 Hz, 2H), 6.87−7.24 (m, 9H), 7.49 (s, 1H), 7.92−7.97 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 11.82, 21.21, 112.41, 115.93, 116.22, 118.17, 121.46, 123.90, 127.83, 128.03, 128.24, 128.53, 129.52, 130.74, 132.57, 132.72, 137.64, 139.67, 139.73, 146.65, 164.55, 167.95, 186.66. HRMS calculated for $C_{28}H_{21}ON_5F$ (M + H): 462.17247, found 462.17290.

*Compound **9{2,4}**.* mp: 167−168 °C; 81 mg (85%) of **9{2,4}** was obtained as a light yellow solid starting from 60 mg of **8{2}**. ESI MS (*m*/*z*): 474 (M + H). IR (KBr, cm^{-1}): 1647, 1596, 1523, 1450, 1434, 1422, 1400, 1378, 1260, 1228. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.24 (s, 3H), 2.62 (s, 3H), 3.88 (s, 3H), 6.71 (d, *J* = 7.5 Hz, 2H), 6.88−6.99 (m, 4H), 7.02−7.09 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.42 (s, 1H), 7.92 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.75, 21.14, 55.56, 111.24, 114.04, 118.16, 121.43, 123.85, 127.64, 128.14, 128.20, 128.41, 128.44, 129.03, 129.99, 130.48, 132.45, 137.42, 139.47, 139.76, 146.33, 164.37, 186.60. HRMS calculated for $C_{29}H_{24}O_2N_5$ (M + H): 474.19245, found 474.19347.

*Compound **9{2,5}**.* mp: 199−201 °C; 95 mg (91%) of **9{2,5}** was obtained as a yellow solid starting from 60 mg of **8{2}**. ESI MS (*m*/*z*): 520 (M + H). IR (KBr, cm^{-1}): 1645, 1598, 1557, 1524, 1463, 1447, 1317, 1306, 1275, 1259, 1225. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.25 (s, 3H), 2.65 (s, 3H), 6.72 (d, *J* = 7.9 Hz, 2H), 6.93−6.98 (m, 2H), 7.03−7.10 (m, 3H), 7.21 (d, *J* = 7.2 Hz, 2H), 7.39−7.51 (m, 3H), 7.53 (s, 1H), 7.63−7.68 (m, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 8.00 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.80, 21.17, 112.19, 118.19, 121.46, 123.89, 127.31, 127.41, 127.73, 128.11, 128.24, 128.38, 128.48, 128.96, 129.89, 130.53, 130.71, 135.07, 137.51, 139.59, 139.70, 139.77, 146.56, 146.56, 187.64. HRMS calculated for $C_{34}H_{26}ON_5$ (M + H): 520.21319, found 520.21443.

General Experimental Procedure for the Synthesis of Fused 1,2,3-Triazoloisoquinoline 11{1,2}−11{2,5}. To a stirred solution of **10{1}**−**10{2}** (0.20 mmol) and 2-azido-1-(aryl)ethanone **2{2}**−**2{5}** (0.20 mmol) in ethanol (2.0 mL) was added 0.20 mmol of piperidinium acetate and the reaction mixture was heated under reflux for 12−24 h until complete consumption of the starting substrates (TLC). Next ethanol was evaporated in vacuum and residue was extracted with chloroform/water (15 mL each). The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated to yield crude which was purified through silica gel column chromatography using ethyl acetate/hexane as eluent in increasing polarity.

*Compound **11{1,2}**.* mp: 184−186 °C; 65 mg (85%) of **11{1,2}** was obtained as a pale yellow solid starting from 41 mg of **10{1}**. ESI MS (*m*/*z*): 384 (M + H). IR (KBr, cm^{-1}): 1671, 1625, 1588, 1553, 1487, 1458, 1446, 1280, 1242, 1204. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.46−7.48 (m, 3H), 7.51−7.59 (m, 4H), 7.63 (dt, *J* = 7.5 and 0.7 Hz, 1H), 7.76 (d, *J* = 6.9 Hz, 2H), 7.85−7.89 (m, 3H), 8.24 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR

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(125 MHz, $CDCl_3$) δ: 119.18, 123.46, 124.48, 128.45, 128.50, 128.84, 128.94, 129.17, 129.40, 129.68, 130.07, 131.28, 131.67, 131.88, 134.34, 140.78, 140.90, 186.82. HRMS calculated for $C_{23}H_{15}ON_3Cl$ (M + H): 384.08982, found 384.09026.

Compound ***11{1,3}***. mp: 164−164 °C; 65 mg (89%) of **11{1,3}** was obtained as Tan color solid starting from 41 mg of **10{1}**. ESI MS (m/z): 368 (M + H). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.15 (t, J = 8.5 Hz, 2H), 7.45 (s, 1H), 7.49−7.66 (m, 5H), 7.76 (d, J = 6.6 Hz, 2H), 7.84 (d, J = 7.7 Hz, 1H), 7.95−8.00 (m, 2H), 8.23 (d, J = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 116.02, 116.20, 118.83, 123.47, 124.44, 128.52, 128.78, 128.85, 128.94, 129.39, 129.71, 129.97, 131.71, 132.05, 132.37, 132.71, 132.78, 140.90, 165.40, 167.44, 186.45. HRMS calculated for $C_{23}H_{15}ON_3F$ (M + H): 368.11937; found 368.11918.

Compound ***11{1,4}***. mp: 96−99 °C; 62 mg (82%) of **11{1,4}** was obtained as a pale yellow solid starting from 41 mg of **10{1}**. ESI MS (m/z): 380 (M + H). IR (KBr, cm^{-1}): 1659, 1597, 1573, 1509, 1475, 1458, 1420, 1256, 1207. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.90 (s, 3H), 6.97 (d, J = 8.9 Hz, 2H), 7.40 (s, 1H), 7.51−7.59 (m, 4H), 7.61−7.65 (m, 1H), 7.78 (d, J = 6.9 Hz, 2H), 7.83 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 9.0 Hz, 2H), 8.24 (d, J = 8.0 Hz, 1H. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 55.43, 113.97, 117.90, 123.16, 123.94, 128.33, 128.43, 128.62, 128.69, 129.15, 129.47, 131.62, 132.12, 132.38, 140.53, 164.47, 186.18. HRMS calculated for $C_{24}H_{18}O_2N_3$ (M + H): 380.13935; found 380.13995.

Compound ***11{2,2}***. mp: 183−183 °C; 71 mg (89%) of **11{2,2}** was obtained as a brown solid starting from 44 mg of **10{2}**. ESI MS (m/z): 398 (M + H). IR (KBr, cm^{-1}): 1675, 1630, 1588, 1508, 1478, 1456, 1421, 1321, 1284, 1178; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.49 (s, 3H), 7.37 (d, J = 7.9 Hz, 2H), 7.47 (s, 2H), 7.50 (s, 1H), 7.54−7.60 (m, 2H), 7.65 (d, J = 7.7 Hz, 2H), 7.84−7.90 (m, 3H), 8.27 (d, J = 7.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.44, 119.14, 123.50, 124.63, 128.43, 128.67, 128.81, 129.18, 129.31, 129.55, 130.03, 131.28, 131.94, 134.38, 138.87, 140.77, 140.99, 186.90. HRMS calculated for $C_{24}H_{17}ON_3Cl$ (M + H): 398.10547, found 398.10562.

Compound ***11{2,3}***. mp: 189−192 °C; 69 mg (91%) of **11{2,3}** was obtained as a pale yellow solid starting from 44 mg of **10{2}**. ESI MS (m/z): 382 (M + H). IR (KBr, cm^{-1}): 1665, 1626, 1598, 1504, 1480, 1460, 1295, 1250, 1152. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.49 (s, 3H), 7.15 (t, J = 8.3 Hz, 2H), 7.36 (d, J = 7.6 Hz, 2H), 7.45 (s, 1H), 7.54−7.61 (m, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.84 (d, J = 7.6 Hz, 1H), 7.95−8.01 (m, 2H), 8.26 (d, J = 8.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.40, 115.99, 116.16, 118.75, 123.46, 124.53, 128.38, 128.45, 128.71, 129.26, 129.53, 129.91, 132.05, 132.36, 132.69, 132.77, 138.82, 140.95, 165.26, 167.40, 186.49. HRMS calculated for $C_{24}H_{17}ON_3F$ (M + H): 382.13502, found 382.13506.

Compound ***11{2,4}***. mp: 169−171 °C; 61 mg (78%) of **11{2,4}** was obtained as a light gray solid starting from 44 mg of **10{2}**. ESI MS (m/z): 394 (M + H). IR (KBr, cm^{-1}): 1659, 1629, 1602, 1573, 1509, 1320, 1266, 1247, 1203. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.48 (s, 3H), 3.89 (s, 3H), 6.96 (d, J = 8.9 Hz, 2H), 7.36 (s, 1H), 7.38 (s, 2H), 7.52 (dt, J = 7.7 and 1.0 Hz, 1H), 7.60 (dt, J = 7.5 and 0.8 Hz, 1H), 7.65 (d, J = 7.9 Hz, 2H), 7.82 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 8.9 Hz, 2H), 8.25 (d, J = 8.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.43, 55.60, 114.12, 117.91, 123.44, 124.37, 128.41, 128.53, 128.63, 128.79, 128.89, 129.15, 129.52, 129.59, 132.61, 138.74, 140.88, 164.61, 186.48. HRMS calculated for $C_{25}H_{20}O_2N_3$ (M + H): 394.15500, found 394.15496.

Compound ***11{2,5}***. mp: 204−205 °C; 78 mg (89%) of **11{2,5}** was obtained as a brown solid starting from 44 mg of **10{2}**. ESI MS (m/z): 440 (M + H). IR (KBr, cm^{-1}): 1665, 1628, 1602, 1557, 1509, 1460, 1444, 1286, 1248, 1201. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.49 (s, 3H), 7.37 (d, J = 7.8 Hz, 2H), 7.39−7.42 (m, 1H), 7.46−7.49 (m, 3H), 7.55−7.58 (m, 1H), 7.62−7.65 (m, 3H), 7.67 (d, J = 7.9 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 7.8 Hz, 1H), 8.02 (d, J = 8.4 Hz, 2H), 8.27 (d, J = 8.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.44, 118.70, 123.51, 124.59, 127.01, 127.33, 127.46, 128.43, 128.60, 128.72, 128.89, 128.97, 129.22, 129.55, 129.62, 129.81, 130.65, 132.47, 134.69, 138.81, 139.66, 140.96, 147.00, 187.59. HRMS calculated for $C_{30}H_{22}ON_3$ (M + H): 440.17574, found 440.17565.

General Experimental Procedure for the Synthesis of *β*-Carboline 12{1,2}, Pyrazolo-pyridine 13{12}, and Isoquinoline 14{2,5}. Fifty milligrams of fused 1,2,3-triazolo-heterocycles (**3{1,2}**, **9{1,2}**, or **11{2,5}**) were taken in 2 mL of glacial acetic acid and heated under reflux until reaction was complete (12 h). Next most of the acetic acid was evaporated in vacuum and residue was treated with 10 mL of aqueous saturated solution of $NaHCO_3$ and extracted with ethyl acetate (3 × 8 mL). The combined organic layer was dried over Na_2SO_4 and evaporated in vacuum to yield the corresponding product (*β*-carboline, pyrazolo-pyridine, or isoquinoline). Next the compounds were crystallized from ethanol.

Compound ***12{1,2}***. mp: 199−200 °C; 50 mg (95%) of **12{1,2}** was obtained as a white solid starting from 50 mg of **3{1,2}**. ESI MS (m/z): 545 (M + H). IR (KBr, cm^{-1}): 1741, 1650, 1633, 1497, 1486, 1469, 1450, 1369, 1341, 1301, 1268, 1223, 1205, 1197. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.85 (s, 3H), 5.63 (d, J = 18.2 Hz, 1H), 5.85 (d, J = 18.2 Hz, 1H), 6.79−7.00 (m, 3H), 7.08−7.45 (m, 12H), 7.48−7.60 (m, 1H), 7.97 (d, J = 6.8 Hz, 2H), 8.21 (d, J = 6.1 Hz, 1H), 8.90 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.83, 47.44, 73.81, 109.38, 116.05, 120.40, 120.77, 124.68, 126.34, 126.74, 126.88, 127.02, 127.37, 128.15, 128.48, 130.68, 131.99, 134.57, 134.72, 135.59, 137.26, 138.25, 141.72, 143.20, 169.26, 190.28. HRMS calculated for $C_{34}H_{26}O_3N_2Cl$ (M + H): 545.16265, found 545.16351.

Compound ***13{1,2}***. mp: 317−319 °C (changing color from white to pink after 250 °C); 51 mg (96%) of **13{1,2}** was obtained as a white solid starting from 50 mg of **9{1,2}**. ESI MS (m/z): 518 (M + Na). IR (KBr, cm^{-1}): 1737, 1726, 1704, 1693, 1681, 1564, 1556, 1417, 1415, 1261, 1249. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.99 (s, 3H), 2.69 (s, 3H), 6.69 (d, J = 7.3 Hz, 2H), 6.81 (s, 1H), 7.09−7.13 (m, 2H), 7.18 (tt, J = 7.3 and 1.0 Hz, 1H), 7.40−7.41 (d, J = 8.7 Hz, 2H), 7.50−7.60 (m, 5H), 8.16 (d, J = 8.7 Hz, 2H), 8.56 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6 + CF_3COOD) δ: 11.43, 20.49, 73.44, 117.83, 124.29, 127.36, 127.70, 128.09, 128.25, 128.33, 129.44, 129.67, 129.95, 132.58, 135.08, 135.47, 136.74, 137.51, 139.55, 141.31, 143.60, 145.45, 169.34, 190.41. HRMS calculated for $C_{29}H_{22}ClN_3NaO_3$ (M + Na): 518.12474, found 518.12306.

Compound ***14{2,5}***. mp: 142−144 °C; 51 mg (95%) of **14{2,5}** was obtained as a brown solid starting from 50 mg of **11{2,5}**. ESI MS (m/z): 472 (M + H). IR (KBr, cm^{-1}): 1739, 1693, 1650, 1633, 1600, 1556, 1538, 1513, 1504, 1486, 1445, 1247. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.11 (s, 3H), 2.30 (s, 3H), 7.12 (d, J = 7.9 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.39−

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7.42 (m, 2H), 7.46−7.49 (m, 2H), 7.53 (s, 1H), 7.63−7.71 (m, 5H), 8.00 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 8.4 Hz, 2H), 8.49 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.20, 21.55, 75.79, 123.41, 124.95, 126.58, 126.78, 127.07, 127.31, 128.12, 128.97, 129.34, 129.43, 129.52, 130.54, 130.65, 132.08, 134.96, 135.72, 136.76, 138.48, 140.22, 145.14, 155.96, 170.57, 193.17. HRMS calculated for $C_{32}H_{26}O_3N$ (M + H): 472.19072, found 472.19072.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all new 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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