

Friedel-Crafts Chemistry. Part 68. Synthesis and biological evaluation of some quinoline fused heterocycles via Jourdan-Ullmann and Friedel–Crafts approaches

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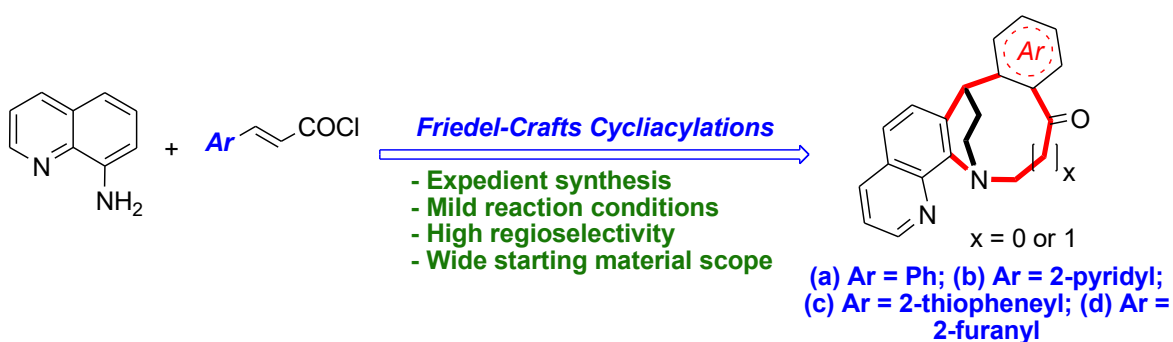
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Abstract

A facile procedure for synthesis of quinoline fused medium-sized N-heterocyclic systems from readily available starting materials is described. The key reaction in this synthesis is the use of Friedel-Crafts cyclizations of synthesized heterocyclic esters mediated by $\text{AlCl}_3/\text{CH}_3\text{NO}_2$ or trifluoromethanesulfonic acid (TfOH) or polyphosphoric acid (PPA) catalysts. Structures of synthesized compounds without stereochemical implications are established using both spectral and analytical data. A plausible mechanism for this type of Friedel–Crafts ring closure of ester moiety promoted by Lewis and Brønsted acids is proposed. Our developed strategy, involving a five-step route, offers easy access to fused quinoline systems in short reaction times and the products are obtained in moderate to good yields. Most of the synthesized pentacyclic compounds have shown promising antimicrobial activity.



Keywords: Friedel-Crafts cyclizations; regioselectivity; phenanthrolinones; azocino[3,2-*g*]quinolinones; pyrido[2',3':5,6]azonino[3,2-*h*]quinolinones; furo[2',3':5,6]azonino[3,2-*h*]quinolinones

Introduction

Polycyclic systems containing quinoline moiety are common structural motifs in large array of biologically active natural alkaloids¹ and are often incorporated into drugs² (Fig.1). Famous examples of well-studied quinoline alkaloids are, Topotecan, Codeine, Lysergic acid diethylamide and Glaucine showing diverse pharmacological activities.³ Furthermore, several industrial applications of this class of compounds have been reported in different fields such as the manufacture of dyestuffs⁴, agrochemicals⁵, polymers⁶, electroluminescent devices⁷, biosensors⁸ and laser technologies.⁹ There are various robust methodologies for the synthesis of quinoline fused to five or six-membered heteroaromatics possessing [6,6,(5/6)]-ring systems available in the literature, included, Doebner-von Miller¹⁰, Skraup¹¹, Combes¹², Friedlander¹³, Conrad-Limpach-Knorr¹⁴, Fitzinger¹⁵, Diels–Alder¹⁶, Friedel–Crafts¹⁷, alkynes cycloaddition¹⁸, Wittig reaction¹⁹, Wolff-rearrangement²⁰, Heck²¹, Povarov²², Mukaiyama-Aldol²³ and Sakurai-Hosomi allylations synthesis.²⁴

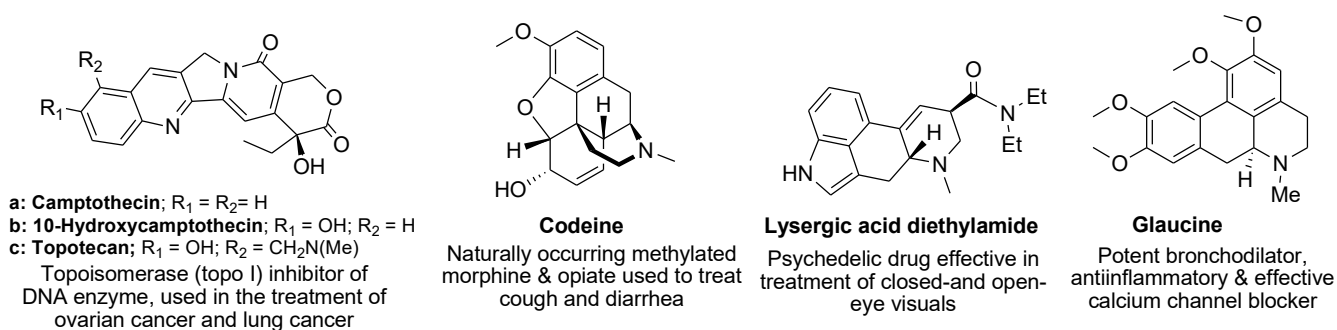


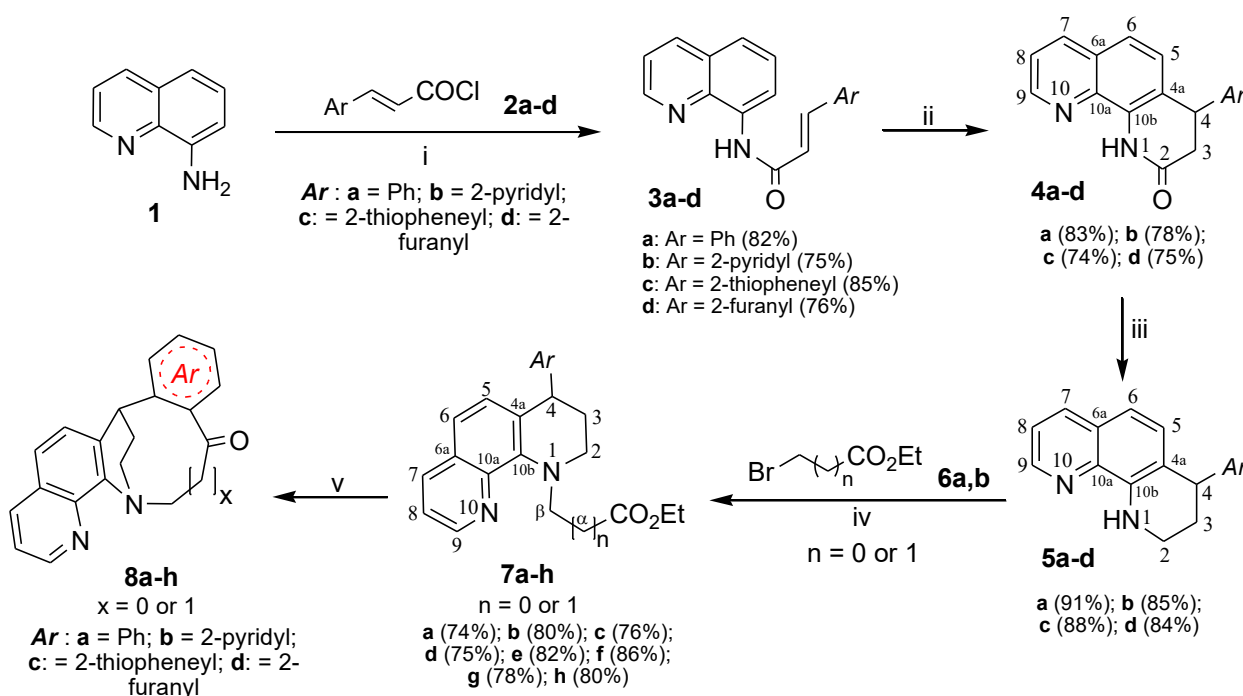
Figure 1. Examples of polycyclic quinoline drugs containing natural products.

Despite these accomplishments, access to quinoline fused to seven-or higher membered carbo-or heterocyclic ring systems remains challenging, mostly because the construction and functionalization of such ring systems have high enthalpic and less entropically favored as well as transannular interaction barriers.²⁵ It is noteworthy that, there are many ingenious strategies for synthesis of regioisomeric azepino[1,2-*a*], [2,3-*b*], [3,2-*b*], [4,3-*b*], and [4,5-*b*]quinolines have been described in the literature included; (i) cyclization of *N*-substituted pyrrolidinone amidines²⁶, (ii) condensation of anthranilic esters with lactams followed by TsOH-mediated cyclization of amidines²⁷, (iii) sequential steps starting with Wittig reaction of quinolines and acetaldehyde²⁸, (iv) organocatalytic oxidative of 3-arylpropanal enamines followed by 1,5-hydride transfer–cyclization sequences²⁹, (v) spontaneous macrocyclizations of benzoazepine carboxamides with silicate and aluminosilicate³⁰, (vi) Povarov multicomponent reaction between formylbenzonitriles and substituted anilines³¹ and (vii) nucleophilic displacement reactions of chlorine atoms of azepinoquinolines with *N*-alkyl-4-piperidinylmethanolates.³² Given the combination of intriguing molecular complexity and biological activity profiles of quinoline polycycles, has made the synthesis of these scaffolds are of considerable interest both synthetically and pharmacologically.

In recent years, our research program has been interested in the development of concise and efficient protocols for the synthesis of various bioactive *carb*-and heterocycles^{33–36} via intramolecular Friedel–Crafts^{37–40} methodology with broad functional group compatibility. Based on these findings, we sought a flexible strategy to synthesize complex quinoline polycycles, specifically quinoline fused to medium-sized *N*-heterocycles from readily available acyclic precursors which would be much more attractive and are valuable for medicinal chemistry and drug discovery.

Results and Discussion

The vast majority of research has been focused on the improvement of the Intramolecular Friedel-Crafts Acylation reactions both new substrates and reaction conditions (Scheme 1). In order to develop a facile acyclic precursor route to the polycyclic systems containing medium-sized N-heterocyclic rings fused to quinoline, we conceptually propose to synthesize acrylamides **3a-d** through acylations of aminoquinoline **1** with several (hetero)aryl-substituted acryloyl halides [**2a** (Ar = Ph), **2b**⁴¹ (Ar = 2-Pyridyl), **2c**⁴² (Ar = 2-thiophenyl), and **2d**⁴³ (Ar = 2-furanyl) under reflux conditions. Cyclizations of resulting amides **3a-d** to the corresponding phenanthrolinones **4a-d** were carried out by heating with AlCl₃/NaCl at 80-90°C for 1h following literature procedures.⁴⁴ Reduction of the latter lactams **4a-d** with LiAlH₄ in THF/Et₂O for 6h under reflux conditions to furnish the desired phenanthrolines **5a-d**.



Scheme 1. Reagents and conditions: (i) cinnamoyl chloride or 3-(pyridin-2-yl)acryloyl chloride or 3-(thiophen-2-yl)acryloyl chloride or 3-(furan-2-yl)acryloyl chloride/PhH, 10 h, reflux, (ii) AlCl₃/NaCl, 2h, 80-90°C, NaOH, (iii) LiAlH₄/THF/Et₂O, reflux, 7 h, NaOH, (iv) BrCH₂CO₂Et or BrCH₂CH₂CO₂Et/K₂CO₃/DMF, reflux, 8-10 h, (vii) Cyclizations of esters **8a-h** mediated by AlCl₃/CH₃NO₂ or TfOH or PPA promoters (Table 1).

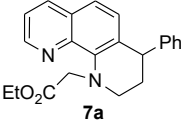
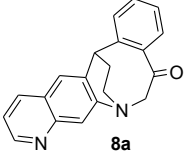
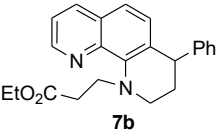
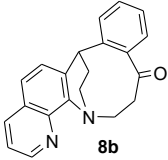
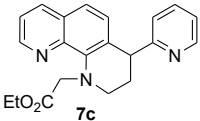
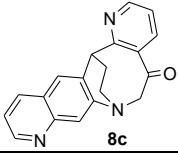
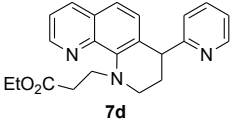
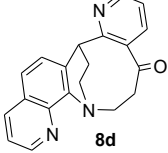
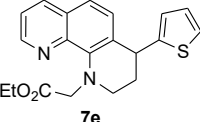
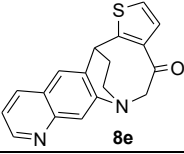
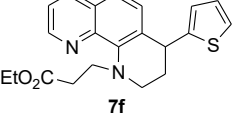
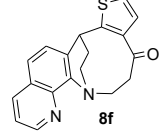
Once the key intermediates **5a-d** formed, the requisite highly electrophilic precursors phenanthroline-based carboxylic esters **7a-h** were readily obtained in moderate yield through the Jourdan-Ullmann⁴⁵ coupling reactions of (hetero)aryl-phenanthroline **5a-d** with α - or β -halo-aliphatic esters **6a,b** using DMF/K₂CO₃ at high temperature. Ring closure progress of precursors **7a-h** has been conducted by using AlCl₃/CH₃NO₂ or TfOH (trifluoromethanesulfonic acid) or PPA (polyphosphoric acid) catalysts to generate heteroarenes **8a-h**. The **conditions and results are summarized in Scheme 1 and Table 1. The constitutions of the products without** stereochemical assignment were appropriately established by both elemental and spectral analyses.

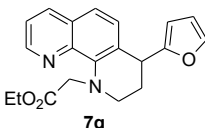
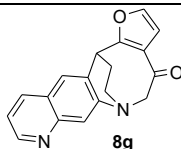
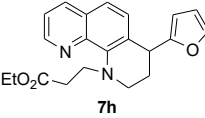
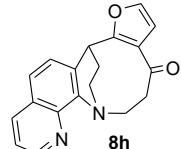
The versatility of this approach was demonstrated by the attempted cyclization of electron rich nucleophiles **7a-h** using $\text{AlCl}_3/\text{CH}_3\text{NO}_2$ or TfOH or PPA catalysts to pentacyclic quinoline fused medium-sized *N*-heterocycles **8a-h** (Scheme 1, Table 1). Interestingly, the choice of Brønsted and Lewis acids was based on their degree of oxophilicity, chemical yield as well as the acidity extents. Upon extensive optimization efforts of cyclization conditions, a systematic investigation of the scope and limitations of the Friedel-Crafts cyclization was commenced. To optimize the cyclization process, we evaluated several variables, including catalyst type, molar ratios, stoichiometric loadings, solvents, temperature, and reaction times.

The current state-of-the-art of the intramolecular Friedel-Crafts reactions has increasingly become a notable strategy for the assembly of medium-sized polycyclic scaffolds; however, its handicapped variant remains relatively underexplored. Literary, the apparent catalytic inhibition⁴⁶ difficulties of heteroatoms in substrates are the most commonly associated with Friedel-Crafts reactions in the synthesis of heterocyclic systems.

The regioselectivity of Friedel-Crafts cyclizations of highly electron-rich π -nucleophilic heterocycles with broad functional group compatibility in the presence of electron-deficient catalyst proceeded conceived to coordinating abilities of highly oxophilic catalysts to the sp^2 or sp^3 -hybridized nitrogen containing functionalities.⁴⁷ This renders the formation of Lewis acid-substrate complex or protonation of heteroatoms with Brønsted-catalyst that leads to inhibit both the catalyst activity and substrate nucleophilicity. Intuitively, these could be slow the cyclization rates in comparison of heteroaromatics with carbocyclic analogous.

Table 1. Optimization of Friedel-Crafts cyclizations of precursors **7a-h**.

Entry	Substrate	Methods	Time, h	Product	Yield (%) ^A
1		I*	12		86
		II**	8		79
		III***	8		75
2		I	15		90
		II	5		82
		III	7		77
3		I	18		85
		II	6		80
		III	10		73
4		I	11		88
		II	8		79
		III	12		72
5		I	16		92
		II	10		84
		III	10		81
6		I	18		90
		II	7		85
		III	10		72

7	 7g	I	18	 8g	91
		II	6		86
		III	8		74
8	 7h	I	15	 8h	87
		II	6		81
		III	10		72

^AIsolated yield refer to substrate.

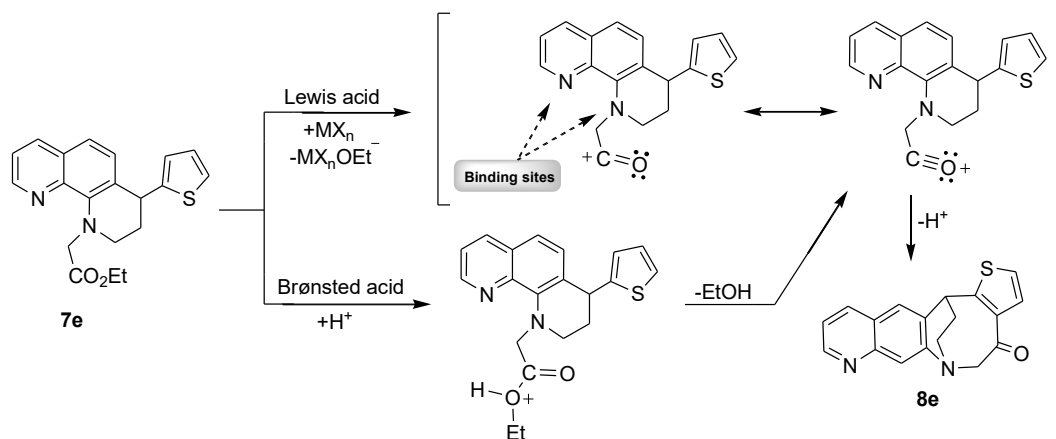
Method I*: esters **7a–h** (3 mmol) in CH₂Cl₂ (20 ml), AlCl₃ (10 mmol), MeNO₂ (100 mmol), room temperature.

Method II**: esters **7a–h** (3 mmol), TfOH (1 ml, 12 mmol), 1,2-DCE (20 ml), reflux.

Method III***: esters **7a–h** (3 mmol), PPA (10 g), PhCl (15 mL), reflux.

Consequently, the ease of cyclization process depends mainly on binding modes of catalysts on nucleophilic heteroatoms. Due to the low propensity of mild catalysts to binds less effectively with the substrate heteroatoms, uses of such promoters are therefore favored and are significant for the yield enhancement.

Given the above results shown in Table 1, there are some interesting results were observed in cyclization processes in the most of cases. The success of the cyclization and acceptable yields of condensed quinolines required the loading of Lewis or Brønsted acid promoters would be more than five-fold stoichiometric excess and reactions were carried out at high temperatures for longer reaction times. This trend is consistent with the observations discussed above that substituent's nature and mildness of oxophilic promoters are greatly improve cyclization yields. These results clearly demonstrate a significant impact of the catalyst and the more electron rich precursors. Interestingly, from the classical valence bond theory⁴⁸, it can be conceived that intramolecular Friedel-Crafts acylations of highly electron-rich ester precursors would enable a rapid intramolecular and diverted into two different pathways depends on the nature of the acylating agent, binding strength, type and strength of the oxophilic promoters. These results may give some insight into the proposed intramolecular Friedel-Crafts acylation mechanisms⁴⁹ at work which could benefit from a synthetic standpoint and for the future substrate design. Based on the numerous studies on the Friedel-Crafts acylation mechanisms reported in the literature, a mechanism was postulated to explain these findings (Scheme 2). Mechanistically³⁷⁻⁴⁰, the generations of acyl-cations by the treatment of ester-precursor **7e** have many subtleties depending on the choice acidic catalysts. This would lead to the formation of a catalyst–substrate complex either by reaction with Lewis acid or protonation of heteroatoms of the substrate with Brønsted acid proton. Subsequently, the removal of EtOH molecule leads to the formation acyl-cation. Electrophilic cyclization of the acyl-cation takes place by loss of electron-rich (hetero)aromatic proton to produce cyclic ketone.



Scheme 2. Proposed mechanism for cyclizations of ester **7e** by Lewis or Brønsted acids

The generation of asymmetric centers in both acyclic precursors and products leads to additional stereochemical complexity. Thus, the diastereotopic⁴⁹ hydrogens (Ha and Hb) of CH_2 group adjacent to new stereogenic carbon showed unresolved signals with largest change in chemical shifts in 1H NMR spectra. It is known that electronegative atoms such as oxygen, nitrogen and sulfur deshield the hydrogen atoms. The extent of deshielding is proportional to the electronegativity of the heteroatom and its proximity to the hydrogen. This trend has been observed by chemical shifts of diastereotopic hydrogens of CH_2 group obtained in each ester precursors and fused heterocycles products. In addition to the geometric factor, another competing parameter commonly occurs in medium-ring systems is the transannular interactions. These interactions imply the presence of inequivalent protons (*pseudo-axial* and *pseudo-equatorial*) in the cyclic structures. The assignment of the diastereotopic protons of the methylene groups was made on the basis of *J*-values that were obtained by direct inspection of the 1H NMR spectrum. Therefore, the axial-H atoms displayed higher vicinal coupling constants than the equatorial-H atoms.

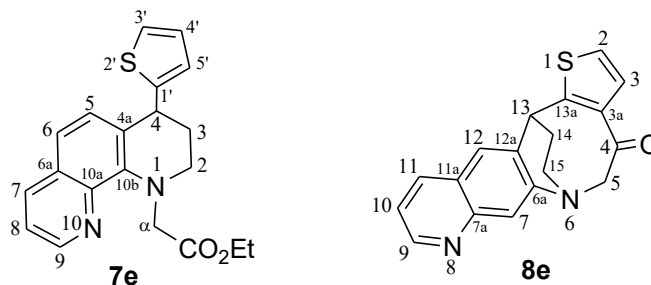


Figure 3. Structures of pentacyclic compound **8e** and its ester precursor **7e**.

For example, the 1H NMR spectra of pentacyclic ketone **8e** and its ester precursor **7e** displayed several distinct signals (Fig. 3). The 1H NMR spectrum of compound **8e** showed one of the diastereotopic *bridged- $C^{14}Ha$* protons appeared as a doublet of doublet of doublet of doublets at 2.16 ppm with coupling constants 13.6, 8.1, 3.5, 1.4 Hz. The other *bridged- $C^{14}Hb$* proton appeared at 2.33 ppm with coupling constants 13.6, 8.1, 5.9, 3.4 Hz. The *bridged- $NC^{15}Ha,Hb$* protons showed two sets of signals as doublet of doublet of doublets near in the range of 3.54-3.70 ppm with a geminal coupling constant 12.2, 8.1, 3.4 Hz and inner signals overlapping. The peaks that appear as a doublet (d at 4.71 ppm, *J* 16.9 Hz) and doublet of doublets (dd at 4.86 ppm, *J* 5.9, 1.4 Hz) were integrating for the *pseudo-axial* C^5Hb and *pseudo-equatorial* C^5Hb , respectively. Another feature is the appearance of one doublet at 5.04 ppm with coupling constant 16.9 Hz assigned to $C^{13}H$ proton. The IR spectrum showed the absorption bands at 1700 ($C=O$) characteristic for ketone skeleton. Whilst, the 1H NMR spectrum of **7b** exhibited eight aliphatic signals at 1.17, 2.04, 2.12, 3.26, 3.32, 3.95, 4.10 and 4.38 ppm related

to $\text{CH}_3\text{CH}_2\text{O}$, C^3Ha , C^3Hb , C^2Ha , C^3Hb , $\text{C}^\alpha\text{H}_2$, $\text{CH}_3\text{CH}_2\text{O}$, C^4H , respectively. Meanwhile, ten aromatic protons appeared at an average of δ 6.92–8.72 ppm with different values of coupling constants.

Over the last few decades, Friedel–Crafts processes have held the interests of chemists, both as subject to investigate the construction of more strained complex carbo- and heterocyclic scaffoldings (Fig. 2).⁵⁰ As being rich in potential areas of exploration, these reactions were considered as one of the macrocyclization strategies (e.g. carbocyclizations, macrolactonizations and macrolactamizations) applied for the constructions of complex scaffolds.

Furthermore, transannular interactions in medium-rings are an important property in drug design. Numerous experimental studies have been done until now to control the transannular interactions in medium-rings lead to significant changes in geometry, electron density distribution and molecular orbital energies. It was anticipated that, medium-ring systems have a large number of conformations with low energy barriers as well as transannular interactions (non-bonded repulsions). This leads to a considerable amount of Pitzer, Prelog and Baeyer strains. It was also concluded⁴⁸ that, regioselectivity and regiospecificity of cyclization process of positive charge precursor enabling a relatively small entropic strain at the transition state. This takes place at the cost of minimized these penalties substantial in seven- and higher-membered rings which could be relieve or surmount circumvented by sustainable adoption of low strength catalysts and suitable conditions.

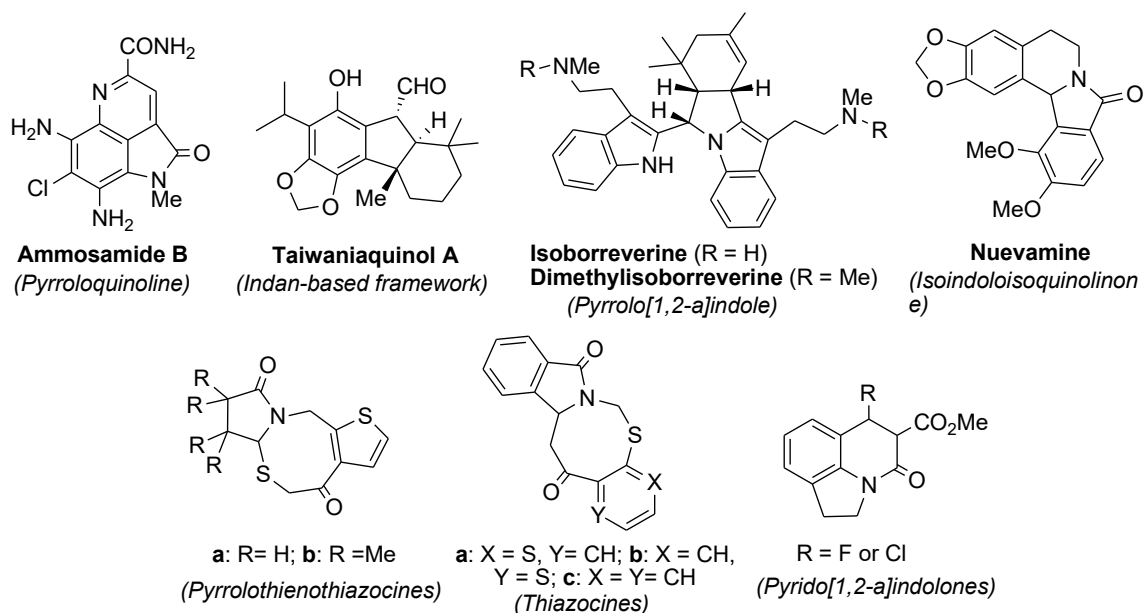


Figure 2. Representative examples of biological and industrial heterocycles prepared by Friedel–Crafts processes

Antimicrobial activity

All newly synthesized compounds **8a–h** were screened *in vitro* for antibacterial activity against Gram-positive bacteria (*Bacillus Subtilis*, *Micrococcus luteus*) and Gram-negative bacteria (*Escherichia coli* & *Pseudomonas aeruginosa*). The antifungal activity was determined against *Aspergillus flavus*, *Candida albicans*, *Geotrichum candidum* and *Scopulariopsis brevicaulis*. Chloramphenicol (0.001 mole/ml) and Clotrimazole (0.001 mole/ml) were used as standard for antibacterial and antifungal activities, respectively. All tests were carried out using disc diffusion method.⁵¹ Discs were incubated at 5 °C for 1 hour to permit good diffusion and the incubated at 28 °C for 24 hours, the zones of inhibition were measured in mm. Compounds were dissolved in DMF/H₂O solution and activity cited on 1000 ppm. Agar plates were surface inoculated uniformly from fresh broth

culture of the gram (+ve) and gram (–ve) bacteria and fungi. Minimum inhibitory concentrations (MICs) for compounds were recorded by measuring the diameter of the inhibition zone at the end of 24 hours for bacteria and 48 hours for fungi activity. Each experiment was repeated thrice and the average of the three independent determinations was recorded. The results are compiled in Table 1.

To our delight, the preliminary results from Table 1, indicated that these compounds showed good to excellent activities against both antibacterial and fungal strains as compared to standard. Comparative studies between activities of compounds and standard drug showed that compounds **8a** and **8b** displayed a lowest activity against *M.luteus* and *P.aeruginosa*. On the other hand, it was observed that almost all compounds **8a-h** showed good activity for four fungal strains as compared to the standard. Only compounds **8a** & **8b** showed low antifungal activities against four strains and compound **8h** against *C. albicans*.

Table 2. Antimicrobial activity of synthesized compounds **8a-h**, (MIC, 50 mole/ml)

Compd. ^A no.	Antibacterial activity zone of inhibition in mm ^B					Antifungal activity zone of inhibition in mm			
	Gram positive (+ve)		Gram negative (-ve)						
	<i>B.</i>	<i>M.</i>	<i>E.</i>	<i>P.</i>	<i>A.</i>	<i>C.</i>	<i>G.</i>	<i>S.</i>	
	<i>subtilis</i>	<i>luteus</i>	<i>coli</i>	<i>aeruginosa</i>	<i>flavus</i>	<i>albicans</i>	<i>candidum</i>	<i>brevicaulis</i>	
8a	20	6	15	5	17	15	16	15	
8b	25	9	20	7	34	30	15	21	
8c	44	36	40	58	38	65	33	45	
8d	45	39	50	48	47	40	36	32	
8e	66	56	61	64	72	80	75	76	
8f	78	76	80	71	78	86	86	60	
8g	48	44	52	62	45	48	62	66	
8h	51	52	55	40	50	32	24	54	
Standard ^C	20	20	20	20	26	26	20	24	

^AChemical compounds tested at 20 mg.

^BMinimal inhibitory concentrations (MIC, mole/ml) for each pore in DMF/H₂O

^CStandard for antibacterial: Chloramphenicol (0.001 mole/ml). Standard for antifungal: Clotrimazole (0.001 mole/ml).

Referring back to Table 2, it is apparent that the contiguous molecular scaffolds containing nucleophilic pyridyl (**8c,d**), 2-thiophenyl (**8e,f**) and 2-furanyl (**8g,h**) moieties that are appended in diverse pentacyclic ring systems exhibited the highest potent inhibitory activity towards all the tested microorganisms in comparing with compounds **8a,b** incorporating Ph-moiety in an eight-or nine-membered ketonic structures. Likely this occurs through the increasing of ring size from azocines and azonines the insertion of more electron-rich heteroatoms in their complex structures.

Conclusions

We have developed an expedient and efficient synthetic procedure for the heteroannulation of quinolin-8-amine, affording novel azocino[3,2-*g*]quinolinones, as well as pyrido-, thieno-, and furo-fused azonino[3,2-*h*]quinolinones in good to excellent yields. This method utilizes intramolecular Friedel-Crafts cyclizations of easily prepared esters, such as ethyl 2-(4-phenyl-3,4-dihydro-1,10-phenanthroline-1(2*H*)-yl)acetate.

Characterized by operational simplicity and widely available precursors, this collective protocol seamlessly merges bioactive quinoline and medium-sized N-heterocyclic scaffolds into unique fused polycycles, offering a powerful new tool for pharmaceutical discovery.

Experimental Section

General. All commercially chemicals used were of reagent grade and solvents were freshly distilled and dried by standard procedures before use. Melting points were taken on a digital Gallenkamp capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were obtained on a Perkin-Elmer 1600 FT-IR spectrophotometer using KBr wafer and thin film techniques (ν cm^{-1}) and are in cm^{-1} . ^1H NMR and ^{13}C NMR spectra were recorded on JEOL LA 400 MHz FT-NMR (400 MHz for ^1H NMR, 100 MHz for ^{13}C NMR) using CDCl_3 solvent with tetramethylsilane (Me_4Si , TMS) as internal standard. Chemical shifts are given in parts per million (δ), and the coupling constants (J) are given in Hertz (Hz), respectively. Mass spectra were measured on a Perkin Elmer PE SCIEX-API 2000 mass spectrometer at an ionizing potential of 70 eV using the direct inlet system. Elemental analyses were carried out by a GmbH Vario EL III, 2400, CHNOS-elemental analyzer. Antimicrobial screenings were performed at Assiut University Mycological Center (AUMC) in DMF by disc diffusion method. The progress of reactions were monitored by thin-layer chromatography (TLC) analysis on precoated silica plates (Silufol, UV-254 TLC, aluminium sheets) and plates were visualized with UV light (at 254 and/or 360 nm). Flash column chromatography, where necessary, was performed on silica gel (230–400 mesh) or basic alumina using AcOEt and hexane as eluents. Syntheses of (hetero)aryl-acryloyl chlorides **2a-d** were obtained by following their literature procedures

General procedure for the synthesis of quinoline-based arylamides 3a-d. To a solution of quinolin-8-amine **1** (30 mmol) in dry benzene (30 mL) containing a catalytic amount of pyridine (0.5 mL) was added dropwise (hetero)aryl-acid chlorides **2a**, **2b**, **2c** or **2d** (33 mmol) in benzene (30 mL) with stirring over a 40-min period. The mixture was stirred at ambient temperature for 2 h and then refluxed on a steam bath for 8 h. After standing overnight the solvent was then concentrated in *vacuo*. After cooling to ambient temperature a yellow precipitated was filtered to give the crude amides. The residue was purified by crystallization to afford pure amides **3a-d**. Crystallization solvents and yields are given together with the spectral data of each product.

N-(Quinolin-8-yl)cinnamamide (3a). Yellow crystals; 82%; mp 130–132 °C (ethanol); IR (KBr, ν , cm^{-1}): 3277, 3087, 2982, 1670, 1600, 1480, 1450, 1385, 1283, 1150, 795. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 5.21 (1H, s, NH), 6.78 (1H, d, J 15.7 Hz, $\text{CH}^2=$), 7.30 (1H, dd, J 8.3, 1.3 Hz), 7.43 (2H, dddd, J 8.1, 7.2, 2.0, 0.5 Hz), 7.44 (1H, tt, J 7.2, 1.6 Hz), 7.44 (1H, ddd, J 8.0, 4.7, 0.5 Hz), 7.52 (1H, dddd, J 8.1, 2.4, 1.6, 0.5 Hz), 7.63 (1H, d, J 15.7 Hz, $\text{CH}^3=$), 7.69 (2H, dddd, J 8.1, 1.5, 1.3, 0.5 Hz), 7.84 (1H, ddd, J 8.3, 8.1, 0.4 Hz), 8.05 (1H, dddd, J 8.0, 1.7, 1.5, 0.4 Hz), 8.85 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 118.1, 120.0, 122.0, 123.0, 125.8, 128.1 (2C), 128.4 (2C), 128.7 (2C), 132.8, 136.0, 138.9, 140.1, 141.1, 149.5, 162.2. Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}$ (274); C, 78.83; H, 5.10; N, 10.21. Found; C, 78.90; H, 5.17; N, 10.14%.

3-(Pyridin-2-yl)-N-(quinolin-8-yl)acrylamide (3b). Yellow plates, 75%, mp 112–15 °C (Acetone); IR (KBr, ν , cm^{-1}): 3240, 3030, 2980, 1674, 1600, 1480, 1380, 1285, 1137, 899. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 5.70 (1H, s, NH), 6.86 (1H, d, J 15.9 Hz, $\text{CH}^2=$), 7.38 (1H, ddd, J 8.4, 4.7, 0.5 Hz), 7.47 (1H, dd, J 8.1, 1.4 Hz), 7.51 (1H, d, J 15.9 Hz, $\text{CH}^3=$), 7.55 (ddd, J 7.4, 4.7, 1.4 Hz), 7.71 (2H, ddd, J 8.0, 1.5, 1.4, 0.5 Hz), 7.81 (1H, ddd, J 8.1, 8.0, 0.4 Hz), 7.90 (1H, ddd, J 7.7, 7.4, 1.9 Hz), 8.03 (1H, dddd, J 8.4, 1.7, 1.5, 0.4 Hz), 8.70 (1H, ddd, J 4.7, 1.9, 0.5

Hz), 8.86 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 118.1, 118.7, 120.0, 122.0, 122.5 (2C), 125.8, 128.1, 132.2, 136.0, 136.6, 138.9, 140.1, 149.5, 149.7, 155.3, 162.2. Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{N}_3\text{O}$ (275); C, 74.18; H, 4.72; N, 15.27. Found; C, 74.20; H, 4.65; N, 15.33%.

***N*-(Quinolin-8-yl)-3-(thiophen-2-yl)acrylamide (3c).** Yellow plates; 85%; mp 134–37 °C (ethanol); IR (KBr, ν , cm^{-1}): 3244, 3028, 2950, 1665, 1605, 1585, 1480, 1440, 1375, 1260, 1160, 789. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 5.54 (1H, s, NH), 6.74 (1H, d, J 15.6 Hz, $\text{CH}^2=$), 7.25 (1H, dd, J 7.4, 4.4 Hz), 7.35 (1H, dd, J 8.1, 1.4 Hz), 7.41 (1H, dd, J 7.4, 1.2 Hz), 7.43 (1H, ddd, J 8.4, 4.7, 0.5 Hz), 7.55 (1H, dd, J 4.4, 1.2 Hz), 7.68 (1H, d, J 15.6 Hz, $\text{CH}^3=$), 7.71 (1H, dddd, J 8.0, 1.5, 1.4, 0.5 Hz), 7.81 (1H, ddd, J 8.1, 8.0, 0.4 Hz), 8.03 (1H, dddd, J 8.4, 1.7, 1.5, 0.4 Hz), 8.83 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 118.1, 120.0, 121.3, 122.0, 125.8, 128.1, 128.6 (2C), 132.3, 136.0, 138.6, 138.9, 139.8, 140.1, 149.5, 164.7. Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{OS}$ (280); C, 68.57; H, 4.28; N, 10.00; S, 11.42. Found; C, 68.49; H, 4.30; N, 9.91; S, 11.48%.

3-(Furan-2-yl)-*N*-(quinolin-8-yl)acrylamide (3d). Yellow crystals; 76%; mp 150–52 °C (ethanol); IR (KBr, ν , cm^{-1}): 3260, 3069, 2982, 1690, 1605, 1585, 1440, 1370, 1263, 1120, 790. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 4.91 (1H, s, NH), 6.31 (1H, dd, J 3.4, 1.8 Hz), 6.79 (1H, d, J 15.7 Hz, $\text{CH}^2=$), 7.02 (1H, dd, J 3.4, 0.9 Hz), 7.31 (1H, d, J 15.7 Hz, $\text{CH}^3=$), 7.45 (1H, ddd, J 8.4, 4.7, 0.5 Hz), 7.48 (1H, dd, J 8.1, 1.4 Hz), 7.69 (1H, dd, J 1.8, 0.9 Hz), 7.71 (1H, dddd, J 8.0, 1.5, 1.4, 0.5 Hz), 7.81 (1H, ddd, J 8.1, 8.0, 0.4 Hz), 8.07 (1H, dddd, J 8.4, 1.7, 1.5, 0.4 Hz), 8.81 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 112.5, 115.9, 118.1, 120.0, 121.3, 122.0, 125.8, 128.1, 129.9, 136.0, 138.9, 140.1, 145.0, 149.5, 150.9, 164.7. Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$ (264); C, 72.72; H, 4.54; N, 10.60. Found; C, 72.70; H, 4.62; N, 10.64%.

General procedure for synthesis of phenanthrolinones 4a-d. A mixture of amide **3a**, **3b**, **3c** or **3d** (25 mmol) with anhydrous AlCl_3 (60 mmol) and anhydrous NaCl (5 g) was warmed briefly at 80–90 °C for 1h and then stirred for 2h at ambient temperature. After which TLC analysis (EtOAc/n -hexane, 1/2) indicated that the reaction was complete, the resulting mixture was quenched with excess of well-stirred ice water (150 mL). The mixture was made alkaline with NaOH solution (40 mL, 20%) and extracted with EtOAc (3×30 mL). The organics were washed sequentially with H_2O and saturated brine solution, dried over MgSO_4 , filtered, and concentrated, yielding crude oils which crystallized upon standing. The resulting light tan solid was collected, washed with H_2O and then with cold Et_2O to afford crude products **4a-d**. Crystallization solvents and yields are given together with the spectral data of each product.

3,4-Dihydro-4-phenyl-1,10-phenanthrolin-2(1H)-one (4a). Yellowish brown plates; 83%; mp 122–125 °C (acetone); IR (KBr, ν , cm^{-1}): 3360, 3036, 2975, 1690, 1600, 1585, 1480, 1340, 1280, 1124, 779. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.82 (1H, dd, J 16.3, 1.9 Hz, C^3Ha), 3.07 (1H, dd, J 16.3, 4.1 Hz, C^3Hb), 4.82 (1H, dd, J 4.1, 1.9 Hz, C^4H), 7.19 (1H, tt, J 7.7, 1.5 Hz), 7.26 (2H, dddd, J 7.8, 7.7, 1.9, 0.5 Hz), 7.27 (2H, dddd, J 7.8, 1.5, 1.3, 0.5 Hz), 7.40 (1H, ddd, J 8.4, 4.7, 0.4 Hz), 7.48 (1H, dd, J 8.1, 0.4 Hz), 7.99 (1H, dddd, J 8.4, 1.7, 1.6, 0.4 Hz), 8.26 (1H, ddd, J 8.1, 1.6, 0.4 Hz), 8.78 (1H, dd, J 4.7, 1.7 Hz), 9.85 (1H, s, NH). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 38.0, 45.4, 122.0, 126.8 (3C), 127.6, 127.8, 128.2 (2C), 128.6 (2C), 133.9, 136.0, 137.8, 140.1, 149.5, 169.1. Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}$ (274); C, 78.83; H, 5.10; N, 10.21. Found; C, 78.87; H, 5.20; N, 10.09%.

3,4-Dihydro-4-(pyridin-2-yl)-1,10-phenanthrolin-2(1H)-one (4b). Yellow crystals; 78%, mp 115–17 °C (acetone); IR (KBr, ν , cm^{-1}): 3310, 3050, 2984, 1678, 1600, 1490, 1450, 1260, 1145, 1080, 795. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.86 (1H, dd, J 16.4, 1.9 Hz, C^3Ha), 3.07 (1H, dd, J 16.4, 4.1 Hz, C^3Hb), 4.87 (1H, dd, J 4.1, 1.9 Hz, C^4H), 7.14 (1H, ddd, J 7.4, 4.9, 1.2 Hz), 7.28 (1H, ddd, J 7.6, 1.2, 0.6 Hz), 7.43 (1H, ddd, J 8.4, 4.7,

0.4 Hz), 7.68 (1H, ddd, J 7.6, 7.4, 1.9 Hz), 7.79 (1H, dd, J 8.5, 0.4 Hz), 8.00 (1H, dddd, J 8.4, 1.7, 1.6, 0.4 Hz), 8.26 (1H, ddd, J 8.5, 1.6, 0.4 Hz), 8.52 (1H, ddd, J 4.9, 1.9, 0.6 Hz), 8.78 (1H, dd, J 4.7, 1.7 Hz), 9.92 (1H, s, NH). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 38.0s, 45.4, 114.1, 122.0, 122.2, 126.8, 127.6, 128.1 (2C), 133.9, 136.0 (2C), 140.1, 147.8, 149.5, 160.7, 169.1. Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{N}_3\text{O}$ (275); C, 74.18; H, 4.72; N, 15.27. Found; C, 74.25; H, 4.68; N, 15.31%.

3,4-Dihydro-4-(thiophen-2-yl)-1,10-phenanthroline-2(1H)-one (4c). Brownish needles; 74%, m.p. 175°C *dec.* (AcOEt); IR (KBr, ν , cm^{-1}): 3340, 3020, 2965, 1700, 1590, 1480, 1440 1382, 1260, 1170, 796. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.76 (1H, dd, J 16.3, 1.9 Hz, C^3Ha), 2.98 (1H, dd, J 16.3, 4.1 Hz, C^3Hb), 4.95 (1H, dd, J 4.1, 1.9 Hz, C^4H), 7.16 (2H, dd, J 8.1, 5.0 Hz), 7.38-7.49 (2H, m), 7.58 (1H, dd, J 8.1, 0.4 Hz), 7.99 (1H, dddd, J 8.4, 1.7, 1.6, 0.4 Hz), 8.26 (1H, ddd, J 8.1, 1.6, 0.4 Hz), 8.79 (1H, dd, J 4.7, 1.7 Hz), 9.63 (1H, s, NH). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): δ 40.5, 73.2, 122.0, 126.3, 126.7 (2C), 127.2, 127.6, 128.2 (2C), 133.9, 136.0, 139.8, 140.1, 149.5, 169.7. Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{OS}$ (280); C, 68.57; H, 4.28; N, 10.00; S, 11.42. Found; C, 68.53; H, 4.36; N, 10.12; S, 11.39%.

4-(Furan-2-yl)-3,4-dihydro-1,10-phenanthroline-2(1H)-one (4d). Yellow crystal; 75%, m.p. 155-57 °C (AcOEt); IR (KBr, ν , cm^{-1}): 3280, 3040, 2975, 1677, 1600, 1590, 1445, 1373, 1260, 1160, 795. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.78 (1H, dd, J 16.3, 1.9 Hz, C^3Ha), 2.99 (1H, dd, J 16.3, 4.1 Hz, C^3Hb), 4.89 (1H, dd, J 4.1, 1.9 Hz, C^4H), 6.15 (1H, dd, J 3.4, 1.8 Hz), 6.28 (1H, dd, J 3.4, 1.2 Hz), 7.33 (1H, dd, J 1.8, 1.2 Hz), 7.43 (1H, ddd, J 8.4, 4.7, 0.4 Hz), 7.75 (1H, dd, J 8.5, 0.4 Hz), 8.04 (1H, dddd, J 8.4, 1.7, 1.6, 0.4 Hz), 8.26 (1H, ddd, J 8.5, 1.6, 0.4 Hz), 8.78 (1H, dd, J 4.7, 1.7 Hz), 9.88 (1H, s, NH). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 40.5, 73.2, 106.3, 110.5, 122.0, 126.8, 127.6, 128.1 (2C), 133.9, 136.0, 140.1, 141.9, 149.5, 156.3, 169.7. Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$ (264); C, 72.72; H, 4.54; N, 10.60. Found; C, 72.81; H, 4.55; N, 10.52%.

General procedure for synthesis of phenanthrolines 5a-d. To an ice-cold stirred suspension of LiAlH_4 (30 mmol) in ether (40 mL) and THF (30 mL) was added a solution of lactams **4a**, **4b**, **4c** or **4d** (10 mmol) in THF (30 mL) dropwise with efficient stirring over a period of 30 min. The mixture was stirred at room temperature for 2 h and then refluxed for 4 h on water bath. After cooling in ice-bath, excess hydride was carefully destroyed by dropwise addition of cold water (5 mL). This was followed by the addition of aqueous NaOH solution (20 mL, 10%) with efficient stirring. After filtration and washing the precipitate with AcOEt, the precipitate was discarded and the filtrate was extracted with AcOEt (3×50 mL). The combined organic phase was washed with water, NaHCO_3 (30 mL, 5%), and dried over anhydrous MgSO_4 . Removal of the solvent gave quantitative yields of crude products **5a-d**. Purification was accomplished by flash column chromatography (basic alumina, EtOAc/*n*-hexane, 1/1) to afford the target amines **5a-d**.

Crystallization solvents and yields are given together with the spectral data of each product.

1,2,3,4-Tetrahydro-4-phenyl-1,10-phenanthroline (5a). Yellow plates; 91%; mp 151-54 °C (ethanol); IR (KBr, ν , cm^{-1}): 3420, 3050, 2980, 1700, 1605, 1580, 1475, 1440, 1370, 1255, 1147, 790. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 1.98 (1H, dddd, J 13.8, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.14 (1H, dddd, J 13.8, 4.6, 3.9, 1.9 Hz, C^3Hb), 3.31 (1H, ddd, J 13.3, 10.0, 1.9 Hz, C^2Ha), 3.40 (1H, ddd, J 13.3, 3.9, 1.9 Hz, C^2Hb), 4.01 (1H, dd, J 9.7, 4.6 Hz, C^4H), 7.14 (1H, tt, J 7.7, 1.3 Hz), 7.26 (2H, dddd, J 7.8, 7.7, 1.9, 0.5 Hz), 7.25 (2H, dddd, J 7.8, 1.3, 1.2, 0.5 Hz), 7.39 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.53 (1H, dd, J 8.8, 0.5 Hz), 7.95 (1H, dddd, J 8.3, 1.7, 1.5, 0.5 Hz), 8.41 (1H, ddd, J 8.8, 1.5, 0.5 Hz), 8.71 (1H, dd, J 4.7, 1.7 Hz), 9.60 (1H, s, NH). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5,

42.9, 45.4, 122.0, 126.8 (3C), 127.6, 127.8, 128.2 (2C), 128.6 (2C, s), 133.9, 136.0, 137.8, 140.1, 149.5. Anal. Calcd. for $C_{18}H_{16}N_2$ (260); C, 83.07; H, 6.15; N, 10.76. Found; C, 83.00; H, 6.22; N, 10.77%.

1,2,3,4-Tetrahydro-4-(pyridin-2-yl)-1,10-phenanthroline (5b). Yellow crystals; 85%; mp 137-40 °C (ethanol); IR (KBr, ν , cm^{-1}): 3370, 3045, 2966, 1690, 1600, 1590, 1470, 1440, 1370, 1260, 1125, 796. 1H NMR (400 MHz, $CDCl_3$, δ , ppm): 2.01 (1H, dddd, J 13.5, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.34 (1H, dddd, J 13.5, 4.6, 3.9, 1.9 Hz, C^3Hb), 3.31 (1H, ddd, J 13.2, 10.0, 1.9 Hz, C^2Ha), 3.40 (1H, ddd, J 13.2, 3.9, 1.9 Hz, C^2Hb), 4.02 (1H, dd, J 9.7, 4.6 Hz, C^4H), 7.18 (ddd, J 7.4, 4.5, 1.2 Hz), 7.26 (ddd, J 7.6, 1.2, 0.6 Hz), 7.39 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.52 (1H, dd, J 8.7, 0.4 Hz), 7.68 (1H, ddd, J 7.6, 7.4, 1.9 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.5, 0.4 Hz), 8.37 (1H, ddd, J 8.7, 1.5, 0.5 Hz), 8.54 (1H, ddd, J 4.5, 1.9, 0.6 Hz), 8.74 (1H, dd, J 4.7, 1.7 Hz), 9.80 (1H, s, NH). ^{13}C NMR (100 MHz, $CDCl_3$, δ , ppm): 28.5, 42.9, 45.4, 114.1, 122.0, 122.2, 126.8, 127.6, 128.1 (2C), 133.9, 136.0 (2C), 140.1, 147.8, 149.5, 160.7. Anal. Calcd. for $C_{17}H_{15}N_3$ (261); C, 78.16; H, 5.74; N, 16.09. Found; C, 78.20; H, 5.78; N, 16.01%.

1,2,3,4-Tetrahydro-4-(thiophen-2-yl)-1,10-phenanthroline (5c). Yellow crystals; 88%; mp 125-27 °C (benzene); IR (KBr, ν , cm^{-1}): 3430, 3050, 2970, 1699, 1600, 1590, 1470, 1440, 1353, 1272, 1125, 789. 1H NMR (400 MHz, $CDCl_3$, δ , ppm): 1.94 (1H, dddd, J 14.2, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.14 (1H, dddd, J 14.2, 4.6, 3.9, 1.9 Hz, C^3Hb), 3.21 (1H, ddd, J 13.2, 10.0, 1.9 Hz, C^2Ha), 3.39 (1H, ddd, J 13.2, 3.9, 1.9 Hz, C^2Hb), 4.27 (1H, dd, J 9.7, 4.6 Hz, C^4H), 6.90 (1H, dd, J 8.2, 1.3 Hz), 7.17 (1H, dd, J 8.2, 5.0 Hz), 7.38 (2H, dd, J 5.0, 1.3 Hz), 7.55 (1H, dd, J 8.8, 0.5 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.5, 0.5 Hz), 8.42 (1H, ddd, J 8.8, 1.5, 0.5 Hz), 8.71 (1H, dd, J 4.7, 1.7 Hz), 9.52 (1H, s, NH). ^{13}C NMR (100 MHz, $CDCl_3$, δ , ppm): 28.5, 42.9, 73.2, 122.0, 126.3, 126.8 (2C), 127.2, 127.6, 128.1 (2C), 133.9, 136.0, 139.8, 140.1, 149.5. Anal. Calcd. for $C_{16}H_{14}N_2S$ (266); C, 72.18; H, 5.26; N, 10.52; S, 12.03. Found; C, 72.10; H, 5.34; N, 10.48; S, 12.07%.

4-(Furan-2-yl)-1,2,3,4-tetrahydro-1,10-phenanthroline (5d). Yellow crystals; 84%; mp 120-22 °C (ethanol); IR (KBr, ν , cm^{-1}): 3440, 3052, 2984, 1696, 1600, 1580, 1470, 1440, 1385, 1258, 1170, 795. 1H NMR (400 MHz, $CDCl_3$, δ , ppm): 2.23 (1H, dddd, J 13.5, 3.9, 1.9, 1.6 Hz, C^3Ha), 2.44 (1H, dddd, J 13.5, 10.0, 4.5, 1.9 Hz, C^3Hb), 3.22 (1H, ddd, J 13.0, 10.0, 1.9 Hz, C^2Ha), 3.38 (1H, ddd, J 13.0, 3.9, 1.9 Hz, C^2Hb), 4.16 (1H, dd, J 4.5, 1.6 Hz, C^4H), 6.24 (2H, dd, J 3.4, 1.8 Hz), 7.32-7.43 (2H, m), 7.60 (1H, dd, J 8.7, 0.4 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.6, 0.4 Hz), 8.41 (1H, ddd, J 8.7, 1.6, 0.5 Hz), 8.71 (1H, dd, J 4.7, 1.7 Hz), 9.73 (1H, s, NH). ^{13}C NMR (100 MHz, $CDCl_3$, δ , ppm): 28.5, 42.9, 73.2, 106.3, 110.5, 122.0, 126.8, 127.6, 128.2 (2C), 133.9, 136.0, 140.1, 141.9, 149.5, 156.3. Anal. Calcd. for $C_{16}H_{14}N_2O$ (250); C, 76.80; H, 5.60; N, 11.20. Found; C, 76.91; H, 5.52; N, 11.15%.

General procedure for the synthesis of phenanthroline-based esters 7a-h. To a mixture of phenanthrolines **5a**, **5b**, **5c** or **5d** (15 mmol) and K_2CO_3 (40 mol) in DMF (30 mL) was added dropwise a solution of ethyl 2-chloroacetate **6a** or ethyl 3-chloropropanoate **6b** (20 mmol) in DMF (25 mL) over a 20-min period with efficient stirring at ambient temperature. The reaction mixture was then refluxed for 8–10 h. After which TLC analysis (AcOEt/hexane, 1/2) showed the reaction to be complete, the solvent was removed in *vacuo* and the residue was diluted with water (150 mL) and extracted with AcOEt (3×30 mL). The organic layer was washed with three portions of 25 mL of H_2O , followed by saturated brine, dried over Na_2SO_4 and evaporated to dryness. The residue was purified by flash chromatography column to afford crude ester **7a–h**. Crystallization solvents and yields are given together with the spectral data of each product.

Ethyl 2-(4-phenyl-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)acetate (7a). Yellow crystals; 74%, mp 137-40 °C (acetone); IR (KBr, ν , cm^{-1}): 3075, 2960, 1740, 1600, 1590, 1480, 1440, 1368, 1285, 1192, 798. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 1.17 (3H, t, J 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}-$), 1.96 (1H, dddd, J 13.8, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.17 (1H, dddd, J 13.8, 4.6, 3.9, 1.9 Hz, C^3Hb), 3.24-3.37 (2H, m, $\text{N}-\text{C}^2\text{Ha}$ & $\text{N}-\text{C}^2\text{Hb}$), 3.96 (2H, s, $\text{C}^\alpha\text{H}_2$), 4.11 (2H, q, J 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}-$), 4.23 (1H, dd, J 9.7, 4.6 Hz, C^4H), 7.19 (1H, tt, J 7.7, 1.3 Hz), 7.26 (2H, dddd, J 7.8, 7.7, 1.9, 0.5 Hz), 7.25 (2H, dddd, J 7.8, 1.3, 1.2, 0.5 Hz), 7.38 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.54 (1H, dd, J 8.8, 0.5 Hz), 7.87 (1H, dddd, J 8.3, 1.7, 1.6, 0.5 Hz), 8.43 (1H, ddd, J 8.8, 1.6, 0.5 Hz), 8.73 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 14.1, 28.5, 45.4, 47.3, 50.0, 61.2, 122.0, 126.8 (3C), 127.6, 127.8, 128.1 (2C), 128.6, 136.0, 137.8, 138.1, 140.1, 149.5, 167.1. MS (EI, 70 eV) m/z (%), 348 ($\text{M}^+ + 2$, 3), 347 ($\text{M}^+ + 1$, 7), 346 (M^+ , 14), 324 (M^+ , 25), 306 (30), 301 (100), 280 (6), 239 (55), 222 (33), 195 (18), 166 (11), 156 (34), 148 (13), 109 (88), 105 (30), 98 (14), 92 (45), 76 (64). Anal. Calcd. for $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_2$ (346); C, 76.30; H, 6.35; N, 8.09. Found; C, 76.32; H, 6.40; N, 7.98%.

Ethyl 3-(4-phenyl-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)propanoate (7b). Pale yellow crystals; 80%, mp 114-15 °C (benzene); IR (KBr, ν , cm^{-1}): 3030, 2965, 1740, 1600, 1590, 1475, 1440, 1390, 1275, 1140, 796. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 1.15 (3H, t, J 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}-$), 1.96 (1H, dddd, J 13.7, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.19 (1H, dddd, J 13.7, 4.6, 3.9, 1.9 Hz, C^3Hb), 2.51 (2H, t, J 6.7 Hz, $\text{C}^\alpha\text{H}_2$), 3.22 (1H, ddd, J 13.6, 3.9, 1.9 Hz, C^2Ha), 3.42 (ddd, J 13.6, 10.0, 1.9 Hz, C^2Hb), 3.62 (2H, t, J 6.7 Hz, C^βH_2), 4.10 (2H, q, J 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 4.25 (1H, dd, J 9.7, 4.6 Hz, C^4H), 7.13 (1H, tt, J 7.7, 1.3 Hz), 7.26 (2H, dddd, J 7.8, 7.7, 1.9, 0.5 Hz), 7.25 (2H, dddd, J 7.8, 1.3, 1.2, 0.5 Hz), 7.42 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.53 (1H, dd, J 8.8, 0.5 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.5, 0.5 Hz), 8.42 (1H, ddd, J 8.8, 1.5, 0.5 Hz), 8.71 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 14.1, 28.5, 32.2, 45.4, 50.0, 50.3, 60.3, 122.0, 126.8 (3C), 127.6, 127.8, 128.1 (2C), 128.6 (2C), 136.0, 137.8, 138.1, 140.1, 149.5, 172.6. MS (EI, 70 eV) m/z (%), 361 ($\text{M}^+ + 1$, 5), 360 (M^+ , 16), 315 (86), 287 (100), 262 (2), 246 (13), 235 (70), 212 (15), 199 (16), 176 (10), 165 (67), 136 (6), 123 (4), 105 (5), 99 (31), 92 (2), 75 (8). Anal. Calcd. for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_2$ (360); C, 76.66; H, 6.66; N, 7.77. Found; C, 76.60; H, 6.71; N, 7.71%.

Ethyl 2-(4-(pyridin-2-yl)-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)acetate (7c). Greenish crystals; 76%, mp 130-32 °C (AcOEt); IR (KBr, ν , cm^{-1}): 3060, 2974, 1737, 1605, 1590, 1480, 1445, 1365, 1258, 1175, 794. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 1.17 (3H, dd, J 7.1, 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 2.12 (1H, dddd, J 13.6, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.41 (1H, dddd, J 13.6, 4.6, 3.9, 1.9 Hz, C^3Hb), 3.22-3.35 (2H, m, C^2Ha & C^2Hb), 3.94 (2H, s, $\text{C}^\alpha\text{H}_2$), 4.13 (2H, q, J 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 4.24 (1H, dd, J 9.7, 4.6 Hz, C^4H), 7.16-7.26 (2H, m), 7.38 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.62 (1H, dd, J 8.5, 0.4 Hz), 7.68 (1H, ddd, J 7.6, 7.4, 1.9 Hz), 7.87 (1H, dddd, J 8.3, 1.7, 1.6, 0.4 Hz), 8.41 (1H, ddd, J 8.5, 1.6, 0.5 Hz), 8.52 (1H, ddd, J 4.5, 1.9, 0.6 Hz), 8.72 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 14.1, 28.5, 45.4, 47.3, 50.0, 61.2, 114.1, 122.0, 122.2, 126.8, 127.6, 128.1 (2C), 136.0 (2C), 138.1, 140.1, 147.8, 149.5, 160.7, 174.8. MS (EI, 70 eV) m/z (%), 349 ($\text{M}^+ + 2$, 4), 348 ($\text{M}^+ + 1$, 20), 347 (M^+ , 44), 315 (M^+ , 86), 328 (19), 319 (37), 302 (100), 285 (17), 276 (64), 246 (12), 233 (7), 217 (5), 199 (56), 183 (21), 169 (10), 141 (5), 115 (12), 102 (2), 90 (27), 78 (7). Anal. Calcd. for $\text{C}_{21}\text{H}_{21}\text{N}_3\text{O}_2$ (347); C, 72.62; H, 6.05; N, 12.10. Found; C, 72.59; H, 6.10; N, 12.16%.

Ethyl 3-(4-(pyridin-2-yl)-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)propanoate (7d). Buff crystals; 75%, mp 119-21 °C (acetone); IR (KBr, ν , cm^{-1}): 3025, 2970, 1738, 1605, 1590, 1480, 1445, 1373, 1186, 785. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 1.15 (3H, t, J 7.1, 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 2.07 (1H, dddd, J 13.6, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.41 (1H, dddd, J 13.6, 4.6, 3.9, 1.9 Hz, C^3Hb), 2.51 (2H, t, J 6.7 Hz, $\text{C}^\alpha\text{H}_2$), 3.26 (1H, ddd, J 13.4, 3.9, 1.9 Hz, C^2Ha), 3.35 (1H, ddd, J 13.4, 10.0, 1.9 Hz, C^2Hb), 3.62 (2H, t, J 6.7 Hz, C^βH_2), 4.06 (2H, q, J 7.1 Hz, $\text{CH}_3\text{CH}_2\text{O}$),

4.22 (1H, dd, J 9.7, 4.6 Hz, C⁴H), 7.20 (1H, ddd, J 7.4, 4.5, 1.2 Hz), 7.26 (1H, ddd, J 7.6, 1.2, 0.6 Hz), 7.38 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.64 (2H, dd, J 8.5, 0.4 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.5, 0.4 Hz), 8.40 (1H, ddd, J 8.5, 1.5, 0.5 Hz), 8.52 (1H, ddd, J 4.5, 1.9, 0.6 Hz), 8.72 (1H, dd, J 4.7, 1.7 Hz). ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 14.1, 28.5, 32.2, 45.4, 50.0, 50.3, 60.3, 114.1, 122.0, 122.2, 126.8, 127.6, 128.2 (2C), 136.1 (2C), 138.1, 140.1, 147.8, 149.5, 160.7, 178.9. MS (EI, 70 eV) m/z (%), 363 (M⁺+2, 7), 362 (M⁺+1, 15), 361 (M⁺, 9), 332 (41), 316 (100), 302 (6), 280 (5), 258 (2), 239 (68), 222 (29), 214 (15), 195 (13), 166 (9), 156 (30), 148 (17), 109 (85), 105 (82), 92 (45), 76 (84). Anal. Calcd. for C₂₂H₂₃N₃O₂ (361); C, 73.13; H, 6.37; N, 11.63. Found; C, 73.22; H, 6.38; N, 11.57%.

Ethyl 2-(4-(thiophen-2-yl)-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)acetate (7e). Pale yellow needles; 82%, mp 142–44 °C (acetone); IR (KBr, ν , cm⁻¹): 3030, 2965, 1740, 1600, 1585, 1460, 1485, 1338, 1274, 790. ¹H NMR (400 MHz, CDCl₃, δ , ppm): 1.17 (3H, dd, J 7.1, 7.1 Hz, CH₃CH₂O), 2.04 (1H, dddd, J 13.7, 10.0, 9.7, 1.9 Hz, C³Ha), 2.12 (1H, dddd, J 13.7, 4.6, 3.9, 1.9 Hz, C³Hb), 3.26 (1H, ddd, J 16.5, 10.0, 1.9 Hz, C²Ha), 3.32 (1H, ddd, J 16.5, 3.9, 1.9 Hz, C²Hb), 3.95 (2H, s, C ^{α} H₂), 4.10 (2H, q, J 7.1 Hz, CH₃CH₂O), 4.38 (1H, dd, J 9.7, 4.6 Hz, C⁴H), 6.92 (1H, dd, J 8.2, 1.3 Hz), 7.17 (1H, dd, J 8.2, 5.0 Hz), 7.38 (2H, ddd, J 8.3, 4.7, 0.5 Hz), 7.56 (1H, dd, J 8.8, 0.5 Hz), 7.87 (1H, dddd, J 8.3, 1.7, 1.6, 0.5 Hz), 8.43 (1H, ddd, J 8.8, 1.6, 0.5 Hz), 8.72 (1H, dd, J 4.7, 1.7 Hz). ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 14.1, 28.5, 47.3, 50.0, 61.2, 73.2, 122.0, 126.3, 126.7 (2C), 127.2, 127.6, 128.1 (2C), 136.0, 138.1, 139.8, 140.1, 149.5, 172.7. MS (EI, 70 eV) m/z (%), 354 (M⁺+2, 6), 353 (M⁺+1, 10), 352 (M⁺, 29), 324 (12), 306 (100), 294 (25), 280 (22), 271 (6), 240 (2), 224 (5), 197 (7), 186 (40), 164 (3), 153 (68), 136 (12), 117 (84), 106 (41), 90 (23), 77 (70). Anal. Calcd. for C₂₀H₂₀N₂O₂S (352); C, 68.18; H, 5.68; N, 7.95; S, 9.09. Found; C, 68.21; H, 5.56; N, 8.03; S, 9.11%.

Ethyl 3-(4-(thiophen-2-yl)-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)propanoate (7f). Yellow needles; 86%, mp 133–35 °C (acetone); IR (KBr, ν , cm⁻¹): 3040, 2975, 1737, 1605, 1580, 1470, 1440, 1370, 1275, 1145, 788. ¹H NMR (400 MHz, CDCl₃, δ , ppm): 1.15 (3H, t, J 7.1 Hz, CH₃CH₂O), 2.04 (1H, dddd, J 13.7, 10.0, 9.7, 1.9 Hz, C³Ha), 2.16 (ddddd, J 13.7, 4.6, 3.9, 1.9 Hz, C³Hb), 2.51 (2H, t, J 6.7 Hz, C ^{α} H₂), 3.30 (2H, ddd, J 13.3, 3.9, 1.9 Hz, C²Ha & C²Hb), 3.62 (2H, t, J 6.7 Hz, C ^{β} H₂), 4.11 (2H, q, J 7.1 Hz, CH₃CH₂O), 4.37 (1H, dd, J 9.7, 4.6 Hz, C⁴H), 6.92 (1H, dd, J 8.2, 1.3 Hz), 7.17 (1H, dd, J 8.2, 5.0 Hz), 7.38 (2H, ddd, J 8.3, 4.7, 0.5 Hz), 7.55 (1H, dd, J 8.8, 0.5 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.5, 0.5 Hz), 8.42 (1H, ddd, J 8.8, 1.5, 0.5 Hz), 8.71 (1H, dd, J 4.7, 1.7 Hz). ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 14.1, 28.5, 32.2, 50.0, 50.3, 60.3, 73.2, 122.0, 126.3, 126.7 (2C), 127.2, 127.6, 128.2 (2C), 136.0, 138.1, 139.8, 140.1, 149.5, 170.26. MS (EI, 70 eV) m/z (%), 367 (M⁺+1, 12), 366 (M⁺, 19), 344 (M⁺, 37), 321 (64), 302 (29), 293 (100), 285 (61), 267 (28), 242 (20), 227 (27), 109 (7), 199 (11), 173 (14), 163 (53), 145 (30), 105 (49), 106 (41), 91 (64), 79 (39). Anal. Calcd. for C₂₁H₂₂N₂O₂S (366); C, 68.85; H, 6.01; N, 7.65; S, 8.74. Found; C, 68.78; H, 6.08; N, 7.59; S, 8.66%.

Ethyl 2-(4-(furan-2-yl)-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)acetate (7g). Brownish needles; 78%, mp 100–102 °C (ethanol); IR (KBr, ν , cm⁻¹): 3040, 2975, 1736, 1600, 1580, 1470, 1440, 1360, 1274, 1130, 799. ¹H NMR (400 MHz, CDCl₃, δ , ppm): 1.17 (3H, dd, J 7.1, 7.1 Hz, CH₃CH₂O), 2.07 (1H, dddd, J 13.6, 10.0, 9.7, 1.9 Hz, C³Ha), 2.28 (1H, dddd, J 13.6, 4.6, 3.9, 1.9 Hz, C³Hb), 3.30 (1H, ddd, J 16.5, 3.9, 1.9 Hz, C²Ha), 3.28 (1H, ddd, J 16.5, 10.0, 1.9 Hz, C²Hb), 3.96 (2H, s, C ^{α} H₂), 4.13 (2H, q, J 7.1 Hz, CH₃CH₂O), 4.20 (1H, dd, J 9.7, 4.6 Hz, C⁴H), 6.13 (1H, dd, J 3.4, 1.8 Hz), 6.26 (1H, dd, J 3.4, 1.2 Hz), 7.36 (2H, dd, J 1.8, 1.2 Hz), 7.58 (1H, dd, J 8.5, 0.4 Hz), 7.87 (1H, dddd, J 8.3, 1.7, 1.6, 0.4 Hz), 8.43 (1H, ddd, J 8.5, 1.6, 0.5 Hz), 8.72 (1H, dd, J 4.7, 1.7 Hz). ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 14.1, 28.5, 47.3, 50.0, 61.2, 73.2, 106.3, 110.5, 122.0, 126.8, 127.6, 128.1 (2C), 136.0, 138.1, 140.1, 141.9, 149.5, 156.3, 165.12. MS (EI, 70 eV) m/z (%), 338 (M⁺+2, 6), 337 (M⁺+1,

26), 336 (M^+ , 53), 321 (18), 307 (23), 291 (100), 269 (3), 259 (8), 243 (12), 217 (4), 204 (5), 191 (3), 177 (2), 168 (50), 139 (11), 115 (6), 102 (3), 92 (39), 77 (23). Anal. Calcd. for $C_{20}H_{20}N_2O_3$ (336); C, 71.42; H, 5.95; N, 8.33. Found; C, 71.45; H, 5.90; N, 8.44%.

Ethyl 3-(4-(furan-2-yl)-3,4-dihydro-1,10-phenanthrolin-1(2H)-yl)propanoate (7h). Pale yellow needles; 80%, mp 115–17 °C (ethanol); IR (KBr, ν , cm^{-1}): 3060, 2970, 1735, 1600, 1580, 1470, 1445, 1350, 1276, 784. 1H NMR (400 MHz, $CDCl_3$, δ , ppm): 1.15 (3H, dd, J 7.1, 7.1 Hz, CH_3CH_2O), 2.07 (1H, dddd, J 13.5, 10.0, 9.7, 1.9 Hz, C^3Ha), 2.30 (1H, dddd, J 13.5, 4.6, 3.9, 1.9 Hz, C^3Hb), 2.50 (2H, t, J 6.7 Hz, $C^{\alpha}H_2$), 3.24 (1H, ddd, J 13.4, 3.9, 1.9 Hz, C^2Ha), 3.38 (1H, ddd, J 13.4, 10.0, 1.9 Hz, C^2Hb), 3.62 (2H, t, J 6.7 Hz, $C^{\beta}H_2$), 4.75 (2H, q, J 7.1 Hz, CH_3CH_2O), 4.15 (1H, dd, J 9.7, 4.6 Hz, C^4H), 6.18 (1H, dd, J 3.4, 1.8 Hz), 6.28 (1H, dd, J 3.4, 1.2 Hz), 7.34 (1H, dd, J 1.8, 1.2 Hz), 7.41 (1H, ddd, J 8.3, 4.7, 0.5 Hz), 7.57 (1H, dd, J 8.5, 0.5 Hz), 7.96 (1H, dddd, J 8.3, 1.7, 1.6, 0.5 Hz), 8.42 (1H, ddd, J 8.5, 1.6, 0.5 Hz), 8.71 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ , ppm): 14.1, 28.5, 32.2, 50.0, 50.3, 60.3, 73.2, 106.3, 110.5, 122.0, 126.8, 127.6, 128.1 (2C), 136.0, 138.1, 140.1, 141.9, 149.5, 156.3, 178.8. MS (EI, 70 eV) m/z (%), 351 ($M^+ + 1$, 12), 350 (M^+ , 28), 337 (2), 306 (100), 294 (25), 277 (52), 240 (2), 224 (5), 203 (2), 197 (8), 186 (41), 170 (21), 153 (59), 117 (82), 106 (43), 95 (16), 77 (52). Anal. Calcd. for $C_{21}H_{22}N_2O_3$ (350); C, 72.00; H, 6.28; N, 8.00. Found; C, 72.11; H, 6.19; N, 8.06%.

General procedure for the synthesis of heterocycles 8a-h

Method I. General Procedure for $AlCl_3/CH_3NO_2$ -mediated cyclizations of esters 7a-h.

A solution of ester **7a**, **7b**, **7c**, **7d**, **7e**, **7f**, **7g** or **7h** (3 mmol) in DCM (20 mL) was added dropwise to a solution of $AlCl_3$ (10 mmol) in CH_3NO_2 (100 mmol) over a 10-15 min period with constant stirring at ambient temperature. The mixture was stirred for a certain time at the required temperature (Table 1). Afterwards, the mixture was quenched with ice-cold HCl solution (30 mL, 20 %) and extracted with EtOAc (3×30 mL). The combined extract was washed with H_2O and Na_2CO_3 solution (30 mL, 5%). After drying over $MgSO_4$, the solution was filtrated and evaporated under reduced pressure to give the crude products **8a-h**.

Method II. General Procedure for TfOH-mediated cyclizations of esters 7a-h.

To a solution of esters **7a**, **7b**, **7c**, **7d**, **7e**, **7f**, **7g** or **7h** (3 mmol) in DCM (20 mL) was added TfOH (12 mmol) dropwise over 10 min at ambient temperature. The resulting solution was refluxed at the required temperature and time as shown in Table 1. After which TLC analysis indicated that the reaction was complete, the mixture was cooled in ice-bath and quenched cautiously by the stepwise addition of aqueous $NaHCO_3$ solution (30 mL, 20%). The product was extracted with EtOAc (3×30 mL). The organics were washed sequentially with H_2O , Na_2CO_3 solution (30 mL, 5%), saturated brine solution, dried over anhydrous Na_2SO_4 , filtered and concentrated in *vacuo* to yield the crude products **8a-h**.

Method III: General Procedure for PPA-mediated cyclizations of esters 7a-h.

Freshly prepared PPA (10 g) was added to a solution of esters **7a**, **7b**, **7c**, **7d**, **7e**, **7f**, **7g** or **7h** (3 mmol) in PhCl (20 mL), and the mixture was refluxed for the required time presented in Table I. The solvent was evaporated under reduced pressure and the cold mixture was made alkaline with $NaHCO_3$ solution (40 mL, 20%) and extracted with EtOAc (3×40 mL). The combined organics was washed with water and Na_2CO_3 solution (30 mL, 5%). After drying over $MgSO_4$, the solution was filtered and concentrated in *vacuo* to afford the desired crude products **8a-h**.

In all procedures, the completion of the reaction was monitored by TLC-analysis. The crude product was subjected to flash chromatography (basic alumina, EtOAc/hexane, 1/2) to afford the pure pentacyclic products **8a-h**. Crystallization solvents and yields are given together with the spectral data of each product.

6,14-Dihydro-5H-7,14-ethanobenzo[5,6]azocino[3,2-g]quinolin-5-one (8a): Yield 0.76 g (86%, method I), 0.70 g (79%, method II), 0.66 g (75%, method III), Pale yellow crystals; mp 150-153 °C (AcOEt); IR (KBr, ν , cm^{-1}): 3060, 2983, 1695, 1600, 1590, 1470, 1440, 1365, 1289, 1136, 785. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.01 (2H, dddd, J 13.4, 7.9, 4.4, 1.4 Hz, *bridged- C^{15}H_2*), 3.45 (2H, ddd, J 12.0, 7.9, 2.7 Hz, *bridged- NC^{16}H_2*), 4.40 (1H, dd, J 6.7, 1.4 Hz, C^{14}H), 4.92 (2H, d, J 17.1 Hz, C^6H_2), 7.21 (1H, ddd, J 8.0, 1.4, 0.5 Hz), 7.35 (2H, ddd, J 8.5, 4.6, 0.4 Hz), 7.43 (1H, ddd, J 8.0, 7.3, 1.3 Hz), 7.46 (2H, dddd, J 8.5, 1.8, 1.5, 0.5 Hz), 7.67 (1H, ddd, J 1.5, 0.5, 0.4 Hz), 7.91 (1H, ddd, J 7.9, 1.3, 0.5 Hz), 8.87 (1H, ddd, J 4.6, 1.8, 0.5 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5, 32.9, 42.8, 50.0, 116.0 (2C), 121.6, 122.8, 124.6, 126.1, 126.8 (2C), 127.8, 128.0, 128.8, 135.3, 141.6, 148.5, 151.2, 206.5. MS (EI, 70 eV) m/z (%), 302 ($\text{M}^+ + 2$, 3), 301 ($\text{M}^+ + 1$, 18), 300 (M^+ , 100), 284 (15), 270 (59), 265 (12), 242 (55), 228 (22), 214 (21), 199 (17), 185 (29), 170 (11), 155 (12), 141 (12), 115 (39), 103 (13), 96 (36), 77 (10). Anal. Calcd. for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}$ (300); C, 80.00; H, 5.33; N, 9.33. Found; C, 80.08; H, 5.42; N, 9.27%.

6,7-Dihydro-5,13-ethanobenzo[5,6]azonino[3,2-h]quinolin-8(13H)-one (8b). Yield 0.84 g (90%, method I), 0.77 g (82%, method II), 0.72 g (77%, method III), Yellow solid; mp 134-36 °C (acetone); IR (KBr, ν , cm^{-1}): 3060, 2935, 1700, 1600, 1585, 1470, 1445, 1355, 1270, 1175, 795. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.42 (2H, dddd, J 14.1, 10.1, 4.9, 1.5 Hz, *bridged- C^{14}H_2*), 2.88 (2H, ddd, J 16.2, 5.5, 1.4 Hz, C^7H_2), 3.35 (2H, ddd, J 14.1, 9.1, 4.9 Hz, *bridged- NC^{15}H_2*), 3.86 (2H, ddd, J 13.5, 5.5, 1.4 Hz, C^6H_2), 4.78 (1H, dd, J 10.1, 3.3 Hz, C^{13}H), 7.20 (1H, ddd, J 8.2, 1.8, 0.5 Hz), 7.38 (2H, ddd, J 8.4, 4.7, 0.6 Hz), 7.47 (1H, ddd, J 8.2, 7.5, 1.3 Hz), 7.55 (1H, dd, J 8.9, 0.5 Hz), 7.82 (1H, ddd, J 7.9, 1.3, 0.5 Hz), 7.95 (1H, dddd, J 8.4, 1.7, 1.6, 0.5 Hz), 8.43 (1H, ddd, J 8.9, 1.6, 0.6 Hz), 8.76 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5, 35.9, 42.8, 50.0, 53.4, 122.0, 122.8, 124.6, 126.1, 126.8 (2C), 127.6, 127.8, 128.2 (2C), 128.8, 136.0, 138.1, 140.1, 149.5, 210.5. MS (EI, 70 eV) m/z (%), 315 ($\text{M}^+ + 1$, 37), 314 (M^+ , 100), 307 (8), 291 (13), 286 (70), 275 (19), 265 (56), 249 (38), 231 (7), 213 (16), 187 (14), 175 (9), 165 (18), 148 (20), 121 (45), 102 (27), 92 (46), 77 (67). Anal. Calcd. for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}$ (314); C, 80.25; H, 5.73; N, 8.91. Found; C, 80.30; H, 5.78; N, 8.84%.

6,14-Dihydro-5H-7,14-ethanopyrido[2',3':5,6]azocino[3,2-g]quinolin-5-one (8c). Yield 0.76 g (85%, method I), 0.72 g (80%, method II), 0.65 g (73%, method III), Brown crystals; mp 178 *dec.* °C (acetone); IR (KBr, ν , cm^{-1}): 3035, 2977, 1705, 1600, 1580, 1480, 1440, 1369, 1244, 1180, 780. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.07 (1H, dddd, J 13.4, 7.9, 4.4, 1.4 Hz, *bridged- C^{15}Ha*), 2.41 (1H, dddd, J 13.4, 8.0, 6.7, 2.7 Hz, *bridged- C^{15}Hb*), 3.43 (1H, ddd, J 12.3, 7.9, 2.7 Hz, *bridged- NC^{16}Ha*), 3.61 (1H, ddd, J 12.3, 8.0, 4.4 Hz, *bridged- NC^{16}Hb*), 4.79 (1H, dd, J 6.7, 1.4 Hz, C^{14}H), 4.98 (2H, d, J 17.2 Hz, C^6H), 7.25 (1H, dd, J 7.8, 4.5 Hz), 7.35 (1H, ddd, J 8.5, 4.6, 0.4 Hz), 7.46 (2H, dddd, J 8.5, 1.8, 1.5, 0.5 Hz), 7.71 (1H, ddd, J 1.5, 0.5, 0.4 Hz), 7.87 (1H, dd, J 7.8, 1.9 Hz), 8.71 (1H, dd, J 4.5, 1.9 Hz), 8.87 (1H, ddd, J 4.6, 1.8, 0.5 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5, 32.9, 45.4, 50.0, 116.0 (2C), 121.1, 121.6, 124.6, 126.8, 128.0, 128.8, 135.3, 141.6, 148.5, 149.2, 151.2, 154.6, 208.9. MS (EI, 70 eV) m/z (%), 304 ($\text{M}^+ + 3$, 4), 303 ($\text{M}^+ + 2$, 23), 302 ($\text{M}^+ + 1$, 100), 302 (M^+ , 52), 284 (16), 274 (69), 260 (9), 245 (31), 229 (40), 217 (18), 202 (29), 187 (22), 161 (38), 149 (26), 133 (25), 124 (87), 91 (72), 77 (45). Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}$ (301); C, 75.74; H, 4.98; N, 13.95. Found; C, 75.76; H, 5.04; N, 13.88%.

6,7-Dihydro-5,13-ethanopyrido[2',3':5,6]azonino[3,2-h]quinolin-8(13H)-one (8d). Yield 0.82 g (88%, method I), 0.74 g (79%, method II), 0.67 g (72%, method III), Yellow crystals; mp 122-24 °C (acetone); IR (KBr, ν , cm^{-1}):

3030, 2975, 1691, 1600, 1580, 1480, 1440, 1370, 1265, 1174, 794. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.36 (2H, dddd, J 14.7, 10.1, 5.0, 1.5 Hz, *bridged- C^{14}H_2*), 2.86–3.02 (2H, ddd, J 15.7, 5.4, 1.4 Hz, C^7H_2), 3.07 (1H, ddd, J 15.7, 9.3, 1.5 Hz, *bridged- NC^{15}Ha*), 3.33 (1H, ddd, J 14.5, 9.0, 5.0 Hz, *bridged- NC^{15}Hb*), 3.57 (1H, ddd, J 14.5, 5.3, 1.5 Hz, C^6H_a), 3.88 (2H, ddd, J 13.5, 5.4, 1.5 Hz, C^6H_b), 5.09 (1H, dd, J 10.1, 3.3 Hz, C^{13}H), 7.04 (1H, dd, J 7.9, 4.6 Hz), 7.38 (1H, ddd, J 8.4, 4.7, 0.5 Hz), 7.59 (1H, dd, J 8.6, 0.4 Hz), 7.88 (1H, dd, J 7.9, 1.9 Hz), 8.11 (1H, dddd, J 8.4, 1.7, 1.6, 0.4 Hz), 8.43 (1H, ddd, J 8.6, 1.6, 0.5 Hz), 8.74 (1H, dd, J 4.7, 1.7 Hz), 8.80 (1H, dd, J 4.6, 1.9 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5, 35.9, 45.4, 50.0, 53.4, 121.1, 122.0, 124.6, 126.8, 127.6, 128.1 (2C), 128.8, 136.0, 138.1, 140.1, 149.2, 149.5, 154.6, 202.6. MS (EI, 70 eV) m/z (%), 316 ($\text{M}^+ + 1$, 13), 315 (M^+ , 100), 302 (10), 292 (8), 287 (100), 275 (19), 265 (72), 249 (49), 231 (7), 213 (13), 202 (4), 187 (14), 175 (8), 165 (15), 148 (22), 129 (11), 115 (21), 92 (74), 77 (58). Anal. Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}$ (315); C, 76.19; H, 5.39; N, 13.33. Found; C, 76.24; H, 5.34; N, 13.40%.

5,13-Dihydro-4H-6,13-ethanothieno[2',3':5,6]azocino[3,2-g]quinolin-4-one (8e). Yield 0.83 g (92%, method I), 0.76 g (84%, method II), 0.73 g (81%, method III), Yellow solid; mp 164–67 °C (AcOEt); IR (KBr, ν , cm^{-1}): 3040, 2978, 1700, 1600, 1585, 1470, 1445, 1390, 1260, 1175, 783. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.16 (1H, dddd, J 13.6, 8.1, 3.5, 1.4 Hz, *bridged- C^{14}Ha*), 2.33 (1H, dddd, J 13.6, 8.1, 5.9, 3.4 Hz, *bridged- C^{14}Hb*), 3.54 (1H, ddd, J 12.2, 8.1, 3.4 Hz, *bridged- NC^{15}Ha*), 3.70 (1H, ddd, J 12.2, 8.1, 3.5 Hz, *bridged- NC^{15}Hb*), 4.71 (1H, d, J 16.9 Hz, C^5Ha), 4.86 (1H, dd, J 5.9, 1.4 Hz, C^5Hb), 5.04 (1H, d, J 16.9 Hz C^{13}H), 7.35 (1H, ddd, J 8.5, 4.6, 0.4 Hz), 7.46 (2H, dddd, J 8.5, 1.8, 1.5, 0.5 Hz), 7.59 (1H, d, J 8.0 Hz), 7.69 (2H, d, J 8.0 Hz), 8.87 (1H, ddd, J 4.6, 1.8, 0.5 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5, 32.9, 50.0, 73.2, 108.5, 116.0 (2C), 121.6, 126.8, 128.0, 128.5, 135.3, 137.4, 138.2, 141.6, 148.5, 151.2, 212.1. MS (EI, 70 eV) m/z (%), 308 ($\text{M}^+ + 2$, 9), 307 ($\text{M}^+ + 2$, 20), 306 (M^+ , 100), 290 (25), 278 (40), 265 (53), 249 (42), 231 (7), 213 (12), 187 (13), 165 (52), 148 (20), 121 (45), 115 (25), 92 (44), 77 (18). Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{OS}$ (306); C, 70.58; H, 4.56; N, 9.15; S, 10.45. Found; C, 70.65; H, 4.53; N, 9.21; S, 10.37%.

12,13-Dihydro-4,11-ethanothieno[2',3':5,6]azonino[3,2-h]quinolin-14(4H)-one (8f). Yield 0.85 g (90%, method I), 0.80 g (85%, method II), 0.68 g (72%, method III), Yellow plates, mp 170–73 °C (AcOEt); IR (KBr, ν , cm^{-1}): 3034, 2979, 1692, 1600, 1580, 1500, 1440, 1322, 1275, 1153, 794. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.17 (1H, dddd, J 13.6, 8.9, 5.4, 3.0 Hz, *bridged- C^{16}Ha*), 2.51 (1H, dddd, J 13.6, 10.2, 5.1, 1.5 Hz, *bridged- C^{16}Hb*), 2.80 (1H, ddd, J 15.9, 8.6, 1.4 Hz, C^{13}Ha), 2.93 (1H, ddd, J 15.9, 6.2, 1.4 Hz, C^{13}Hb), 3.50 (1H, ddd, J 14.2, 8.9, 5.1 Hz, C^{12}Ha), 3.59 (1H, ddd, J 13.8, 8.6, 1.4 Hz, *bridged- NC^{15}Ha*), 3.66 (1H, ddd, J 14.2, 5.4, 1.5 Hz, *bridged- NC^{15}Hb*), 3.84 (1H, ddd, J 13.8, 6.2, 1.4 Hz, C^{12}Hb), 5.15 (1H, dd, J 10.2, 3.0 Hz, C^4H), 7.39 (1H, ddd, J 8.4, 4.7, 0.5 Hz), 7.55 (2H, dd, J 8.9, 0.5 Hz), 7.69 (1H, d, J 8.3 Hz), 7.95 (1H, dddd, J 8.4, 1.7, 1.6, 0.5 Hz), 8.43 (1H, ddd, J 8.9, 1.6, 0.5 Hz), 8.77 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3 , δ , ppm): 28.5, 35.9, 50.0, 53.4, 73.2, 108.5, 122.0, 126.8, 127.6, 128.2 (2C), 128.5, 136.0, 137.4, 138.2 (2C), 140.1, 149.5, 205.6. MS (EI, 70 eV) m/z (%), 321 ($\text{M}^+ + 1$, 4), 320 (M^+ , 9), 315 (22), 292 (57), 274 (68), 265 (100), 257 (44), 225 (79), 215 (13), 197 (36), 181 (55), 168 (8), 152 (25), 127 (7), 115 (17), 93 (13), 76 (16). Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{OS}$ (320); C, 71.25; H, 5.00; N, 8.75; S, 10.00. Found; C, 71.33; H, 5.05; N, 8.70; S, 10.10%.

5,13-Dihydro-4H-6,13-ethanofuro[2',3':5,6]azocino[3,2-g]quinolin-4-one (8g). Yield 0.78 g (91%, method I), 0.74 g (86%, method II), 0.63 g (74%, method III), Yellow needles, mp 144–46 °C (AcOEt); IR (KBr, ν , cm^{-1}): 3035, 2965, 1700, 1605, 1585, 1470, 1440, 1363, 1245, 1175, 787. ^1H NMR (400 MHz, CDCl_3 , δ , ppm): 2.18–2.33 (2H, m, *bridged- C^{14}H_2*), 3.55 (1H, ddd, J 15.1, 8.1, 3.5 Hz, *bridged- NC^{15}Ha*), 3.65 (1H, ddd, J 15.1, 8.1, 3.4 Hz, *bridged- NC^{15}Hb*), 4.51 (1H, dd, J 5.9, 1.4 Hz, C^5Ha), 4.62 (1H, d, J 16.9 Hz, C^5Hb), 5.08 (1H, d, J 16.9 Hz,

$C^{13}H$), 6.75 (1H, d, J 1.8 Hz), 7.28-7.61 (4H, 7.35 (1H, ddd, J 8.5, 4.6, 0.4 Hz), 7.46 (2H, dddd, J 8.5, 1.9, 1.5, 0.5 Hz), 7.56 (1H, d, J 1.8 Hz), 7.71 (1H, ddd, J 1.5, 0.5, 0.4 Hz), 8.87 (1H, ddd, J 4.6, 1.9, 0.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ , ppm): 28.5, 32.9, 50.0, 73.2), 108.5, 116.0 (2C), 121.6, 126.8, 128.0, 135.3, 138.1 (2C), 141.6, 142.0, 148.5, 151.2, 199.2. MS (EI, 70 eV) m/z (%), 292 ($M^{+}+2$, 5), 291 ($M^{+}+1$, 13), 292 (M^{+} , 27), 274 (44), 262 (100), 257 (27), 252 (69), 225 (31), 197 (34), 181 (26), 168 (10), 152 (24), 141 (16), 122 (45), 115 (10), 104 (30), 93 (27), 77 (25). Anal. Calcd. for $C_{18}H_{14}N_2O_2$ (290); C, 74.48; H, 4.82; N, 9.65. Found; C, 74.52; H, 4.84; N, 9.57%.

12,13-Dihydro-4,11-ethanofuro[2',3':5,6]azonino[3,2-*h*]quinolin-14(4*H*)-one (8h). Yield 0.76 g (87%, method I), 0.63 g (81%, method II), 0.56 g (72%, method III), Creamy powder; mp 138-41 °C (acetone); IR (KBr, ν , cm^{-1}): 3050, 2977, 1698, 1600, 1480, 1440, 1380, 1253, 1182, 770. 1H NMR (400 MHz, $CDCl_3$, δ , ppm): 2.39-2.51 (2H, m, *bridged- $C^{16}H_2$*), 2.72 (1H, ddd, J 15.9, 9.9, 4.3 Hz, $C^{13}Ha$), 2.89 (1H, ddd, J 15.9, 3.9, 1.8 Hz, $C^{13}Hb$), 3.43 (1H, ddd, J 15.3, 8.6, 5.4 Hz, *bridged- $NC^{15}Ha$*), 3.71 (1H, ddd, J 15.3, 5.7, 1.4 Hz, *bridged- $NC^{15}Hb$*), 3.74 (2H, ddd, J 13.5, 4.3, 1.8 Hz, $C^{12}H_2$), 4.64 (1H, dd, J 10.2, 2.8 Hz, C^4H), 6.74 (1H, d, J 1.8 Hz), 7.39 (1H, ddd, J 8.4, 4.7, 0.5 Hz), 7.51 (1H, d, J 1.8 Hz), 7.62 (1H, dd, J 8.7, 0.4 Hz), 7.96 (1H, dddd, J 8.4, 1.7, 1.6, 0.4 Hz), 8.43 (1H, ddd, J 8.7, 1.6, 0.5 Hz), 8.76 (1H, dd, J 4.7, 1.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ , ppm): 28.5, 35.9, 50.0, 53.4, 73.2, 108.5, 122.0, 126.8, 127.6, 128.1 (2C), 136.0, 138.2 (3C), 140.1, 142.0, 149.5, 203.4. MS (EI, 70 eV) m/z (%), 305 ($M^{+}+1$, 17), 304 (M^{+} , 13), 292 (M^{+} , 29), 290 (12), 276 (36), 265 (100), 240 (2), 224 (5), 197 (9), 186 (38), 170 (21), 153 (66), 136 (7), 117 (48), 106 (40), 90 (29), 77 (42). Anal. Calcd. for $C_{19}H_{16}N_2O_2$ (304); C, 75.00; H, 5.26; N, 9.21. Found; C, 74.92; H, 5.20; N, 9.28%.

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Conflicts of interest

The authors declare no conflicts of interest

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Supplementary Material

The data that support this study are available in the article and accompanying online supplementary material.

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