



Synthesis of functionalized pyrrole derivatives *via* diverse cyclization of azomethine ylide and olefins

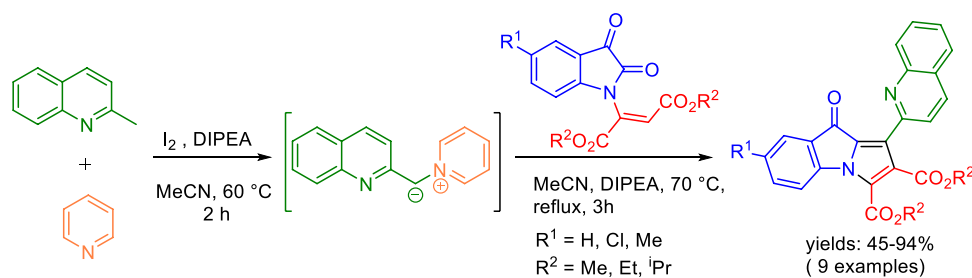
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Abstract

The azomethine ylides are generally used in 1,3-dipolar cycloadditions with various dipolarophiles. In this work, a new and diverse route has been developed for the azomethine ylides, for synthesis of novel pyrrole derivatives. The azomethine ylide, produced via C–H activation of unreactive C(*sp*³)–H bond of 2-methylquinoline, by molecular iodine, in the presence of pyridine. Herein, we represent novel pyrrole derivatives, synthesized from the reaction of pyridinium ylide with olefins, which formed via a reaction of isatin, dialkyl acetylenedicarboxylate derivatives and pyridine as a base in moderate to excellent yields. Various features of this cyclization, discussed.

Graphic abstract



Keywords Diverse cyclization reaction · Azomethine ylide · Pyrrole-based scaffolds · Pyridine · Tandem reaction

Introduction

Pyrrole is one of the most important nitrogen-containing, five-membered heterocycles in organic chemistry [1]. This compound is the key structural fragment of numerous natural products such as heme, chlorophyll, bile pigments, vitamin B₁₂ and various cytochrome enzymes [2]. Pyrrole and its derivatives demonstrate numeral biological activities such as antibacterial, antiviral, anti-inflammatory, antitumour and antioxidant [3]. These privileged structural motifs are not only wide spread in a vast variety of natural compounds,

but also utilized as building blocks in a number of pharmaceuticals, including the blockbuster drug, atorvastatin, used as a cholesterol lowering agent, being the top selling medicine worldwide, the non-steroidal anti-inflammatory compound, Tolmetin and the anticancer drug candidate, Tallimustine [4].

Moreover, many researchers have been concentrated on the biological and pharmaceutical activities of fluorazone (9*H*-pyrrolo[1,2-*a*]indole-9-one) and its derivatives [5]. They show a wide range of biological activities, including anti-tubulin [6], psychostimulant [7] and antidiabetic [8]. In addition, novel chromophores exhibit the promising application of dyes having a fluorazone linker as a photosensitizer for solar cells [9]. Also, considerable interest pertaining to fluorazone, arises from the fact that, this fused tricyclic unit, represents the chemical precursor of 9*H*-pyrrolo[1,2-*a*]indole (fluorazene), the basic skeleton of cytostatic

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mitomycin, which serves as cancer chemotherapeutic agents [10] (Fig. 1).

A wealth of synthetic approaches, have been applied for the preparation of pyrrole ring, including the Hantzsch procedure [11], a Paal–Knorr synthesis [12] and the Clauson–Kaus reaction [13]. Despite the existence of these synthetic methods, synthesis of functionalized pyrroles remains intriguing [14, 15] because the above-mentioned routes have some drawbacks such as multi-step synthetic operation, inaccessible starting materials and limited scope [16]. In an attempt to provide access to a broader range of pyrroles, the application of multi-component reactions, specially 1,3-dipolar cycloadditions, has been recently reviewed [17].

C–H bond activations are of practical importance in organic synthesis due to their energy efficient and step-economic process, albeit their low acidities [18]. In the past, C–H bond activation was restricted to the metal-catalyzed methods, involving the scission of a C–H in favor of a metal to build complex structures [19]. Metal-catalyzed C–H bond functionalization is more prevalent and used to transformations where cleavage of a C–H bond is accompanied by a new bond formation at the carbon center [20]. By rising environmental concerns, particularly in the area of pharmaceuticals, recognition of routes that do not need transition-metal catalysts, have been highlighted to solve the problem of metallic impurities elimination from pharmaceutical moieties [21, 22]. In 2011, Kumar and co-workers reported the first molecular iodine-promoted metal-free C–H bond activation of alkylazaarene pyridinium zwitterion [21]. Recently the key role of sp^3 C–H bond activation

in 1,3-dipolar cycloaddition reactions of azomethine ylides with various alkynes and olefins has been addressed [18, 23, 24]. In 2016, indolizine derivatives were synthesized through 1,3-dipolar cycloaddition reaction of chalcone with an azomethine ylide, generated in-situ by the C–H bond activation of 2-methylquinoline in the presence of iodine and pyridine by Yavari et al. [18]. Also, recently the above-mentioned group, applied the same methodology to alkyne and arylidene pyrazolone derivatives [25].

These reactions lead to the formation of indolizine and spirocyclopropane-linked pyrazolone derivatives, respectively [18, 25]. Herein, we report an innovative pyrrole derivatives synthetic protocol in which, an azomethine ylide undergoes a diverse cyclization reaction with olefin.

Results and discussion

We commenced our studies by exploring a pilot experiment. Initially, 2-methylquinoline (**1**) and pyridine (**2**) treated to afford azomethine ylide (**4**) through an iodine-promoted, metal-free C–H activation of 2-methylazaarene. Then, azomethine ylide (**4**) underwent cyclization reaction with olefin [26] (**3a**), which formed in-situ, via a reaction of isatin [27, 28] and DMAD in the presence of pyridine as a base, which led to the construction of pyrrole (**5a**), through a one-pot procedure.

To optimize conditions, the reaction was carried out in various solvents and bases at different temperatures (Table 1). Remarkably, control experiments disclosed that

Fig. 1 Some drugs containing pyrrole and fluorazene structure

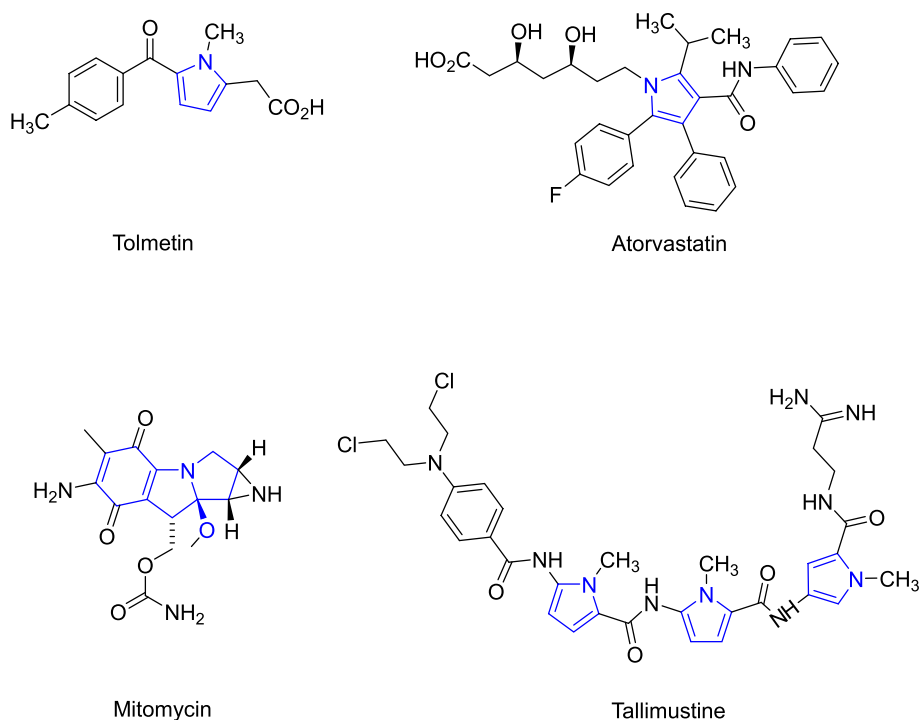
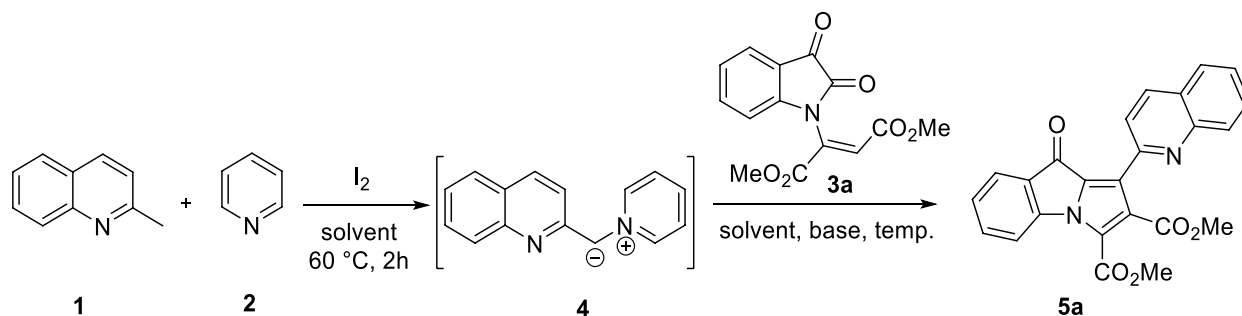


Table 1 Optimization of the reaction conditions for dimethyl 9-oxo-1-(quinolin-2-yl)-9H-pyrrolo [1,2-*a*]indole-2,3-dicarboxylate (**5a**)

Entry	Base (×equivalents)	Solvent	Temp	Yield (%) ^{a,b}
1	Et ₃ N (1.0)	H ₂ O	60 °C	Trace
2	Et ₃ N (1.0)	MeOH	60 °C	10
3	Et ₃ N (1.0)	DMF	r.t	N.R
4	Et ₃ N (1.0)	MeCN	r.t	N.R
5	(ⁱ Pr) ₂ NEt (1.0)	MeCN	r.t	N.R
6	K ₂ CO ₃ (2.0)	MeCN	60 °C	10
7	DBU (2.0)	MeCN	60 °C	20
8	(ⁱ Pr) ₂ NEt (1.0)	MeCN	60 °C	40
9	(ⁱ Pr) ₂ NEt (2.0)	MeCN	60 °C	50
10	(ⁱ Pr) ₂ NEt (2.0)	MeCN	70 °C	55

^a Isolated yield ^b Reaction conditions (i): **1** (0.143 g, 1 mmol), **2** (0.158 g, 2 mmol), I₂ (0.253 g, 1 mmol), solvent (5 ml), 60 °C, 2 h, DIPEA (2.2 mmol), (ii): **3a** (0.289 g, 1 mmol), base (x equivalent), solvent (5 ml)

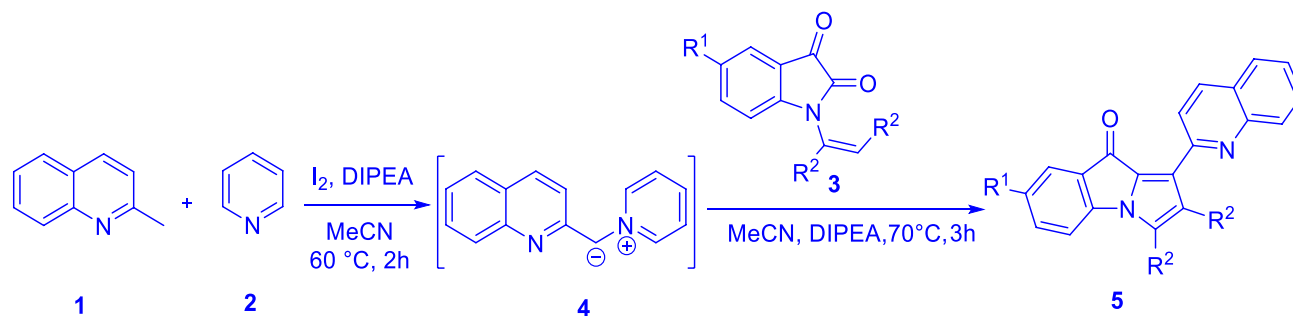
no reaction occurred at ambient temperature (Table 1, entries 3–5). We screened a number of solvents such as H₂O, MeOH, DMF and MeCN and found the latter to be the most effective solvent (Table 1, entries 6–10). Base screening studies exploited that surprisingly, the use of DIPEA, instead of DBU, duplicated the yield of product (**5a**), (Table 1, entry 8). This dramatic increase, promoted us to further optimize the reaction conditions by raising DIPEA loading. Using 2 equivalents of DIPEA, reached the yield to 50% (Table 1, entry 9). To further extend the reaction scope, we gradually elevated the temperature to 70 °C under reflux condition. Thereupon, the yield of product **5a** has slightly improved (Table 1, entry 10).

With the optimized condition in hand, we then investigated the reactions scopes, not only with unsubstituted substrates, but also with a wide range of substrates bearing electron-withdrawing and electron-donating functional groups. The reactions proceeded smoothly, affording functionalized pyrrole derivatives (**5**) in moderate to excellent yields (Table 2).

The structure of product (**5a**) was elucidated unambiguously on the basis of its spectroscopic data such as ¹H NMR, ¹³C NMR, IR as well as mass spectrometry. The mass of pyrrole (**5a**), depicted molecular ion peak at *m/z* = 413. The ¹H NMR spectrum of (**5a**) exhibited two singlet signals at

about 3.09 and 3.13 ppm which could be ascribed to the protons of methyl groups attached to the carbonyl groups in the aliphatic region, beside 10 aromatic protons. The observation of 24 distinct signals in the ¹H decoupled ¹³C NMR spectrum of product (**5a**) is in agreement with the proposed structure.

Also, in the IR spectrum, the absorption band at 1751 cm⁻¹ (C=O), was the most significant stretching frequency, proved the presence of ketone carbonyl group in the structure. As a result, the conversion proceeded in 55% yield to afford pyrrole (**5a**) using MeCN as a solvent and 2 equivalents of DIPEA as a base, under reflux condition at 70 °C for 3 h (Table 2, entry 1). Therefore, we aimed to propose operationally benign conditions that can be applied to present a wide variety of pyrrole scaffolds (Table 1). After reaction completion (monitored by TLC), the reaction solvent evaporated gradually, and then the precipitate was recrystallized from *n*-hexane–EtOAc (3:1), washed with distilled water and dried at ambient temperature. The structures of pyrrole derivatives (**5a–5i**) were confirmed on the basis of their spectroscopic data such as ¹H NMR, ¹³C NMR, IR and Mass as shown in supporting information. Regarding the scopes of pyrrole derivatives, the yields of substrates bearing electron-withdrawing groups and unsubstituted substrates were in the same range, and they gave

Table 2 Synthesis of pyrrole derivatives (**5a–5i**)

Entry	R ¹	R ²	Product	Yield (%) ^{a,b}
1	H	Me	5a	55
2	H	Et	5b	90
3	H	iPr	5c	48
4	Cl	Me	5d	57
5	Cl	Et	5e	60
6	Cl	iPr	5f	94
7	Me	Me	5g	45
8	Me	Et	5h	48
9	Me	iPr	5i	50

^aIsolated yield ^bReaction conditions (i): **1** (0.143 g, 1 mmol), **2** (0.158 g, 2 mmol), I₂ (0.253 g, 1 mmol), MeCN (5 ml), 60 °C, 2 h, DIPEA (2.2 mmol), (ii): **3** (1 mmol), DIPEA (2 equivalent), MeCN (5 ml), Reflux, 3 h

higher yields, as compared to substrates bearing electron-donating groups (Table 2, entries 1–9). We were surprised to find that product (**5f**) was obtained in 94% yield, the highest yield among other pyrrole derivatives (Table 2, entry 6). Pleasurably, the above-mentioned result, outlined that the reaction proceeded almost complete in this case (Table 2, entry 6). To our delight, the reaction exploited compatibility toward various functional groups, leading to obtain the corresponding substituted pyrrole derivatives (**5a–i**) in moderate to excellent yields (Table 2, entries 1–9).

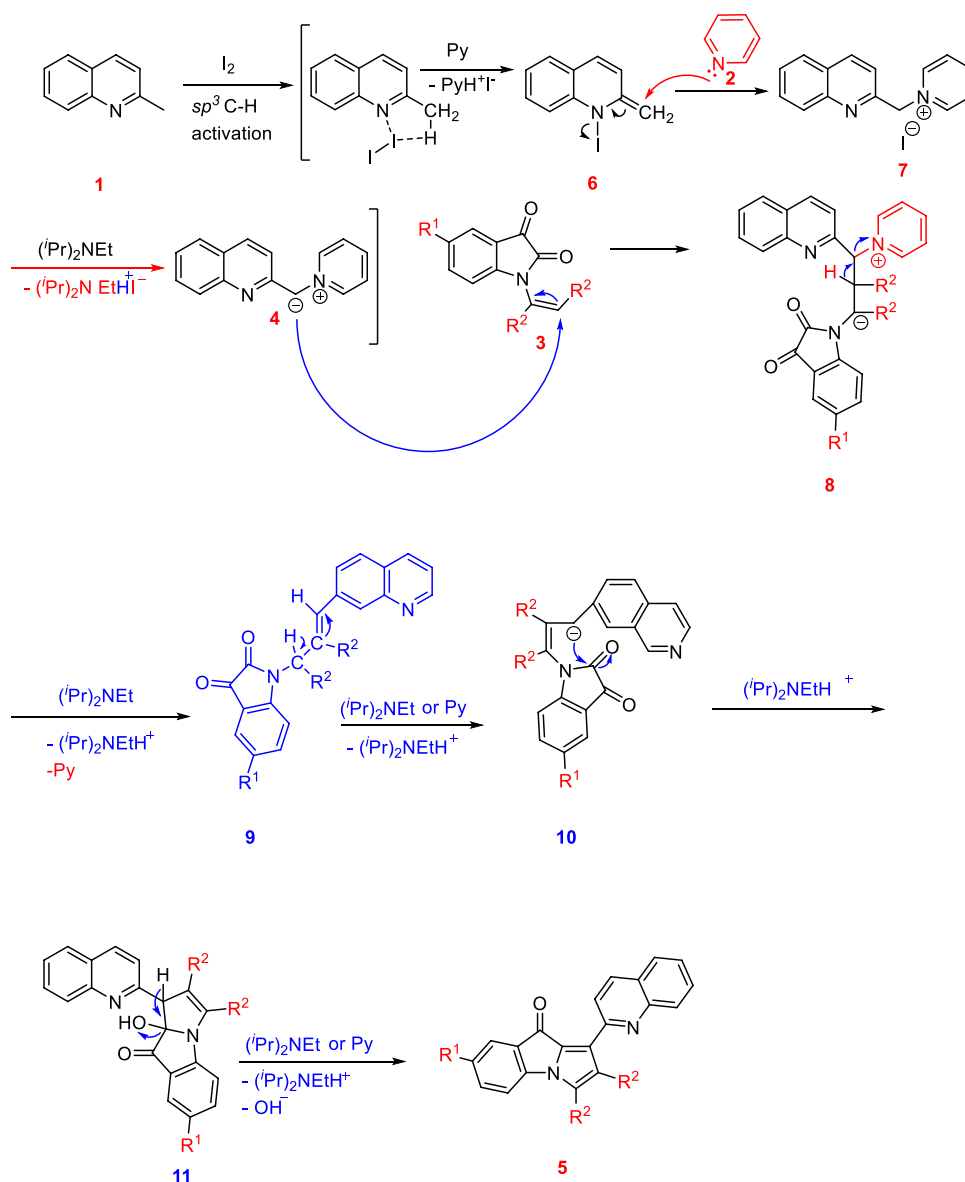
Intrigued to take a closer inception of the reaction procedure, our attention was turned to envision a reasonable mechanism for the formation of product (**5**). Accordingly, a mechanistic rationalization was proposed (Scheme 1). To gain insight into the reaction mechanism, firstly, the C–H activation of 2-methylquinoline (**1**) by coordination to iodine leads to the formation of intermediate (**6**). This intermediate is attacked by pyridine to obtain 1-(quinolin-2-ylmethyl) pyridinium iodide (**7**), which is converted to azomethine ylide (**4**) by DIPEA. Then, azomethine ylide (**4**) undergoes a cyclization reaction with olefin [26] (**3**) to afford the intermediate (**8**). Then, DIPEA, attacks to intermediate (**8**) and takes the proton which is attached to the adjacent carbon of 2-methylquinoline. The driving force of this attack causes the elimination of pyridine and affords

the intermediate (**9**). Further attack of DIPEA to the intermediate (**9**), elimination of the proton and charge transferring, leads to the formation of intermediate (**10**). Finally, intermediate (**10**) undergoes an intramolecular cycloaddition in order to gain the intermediate (**11**), and this intermediate converts to the target pyrrole (**5**) by DIPEA, through an elimination of water. Significantly, the reaction proceeds via the elimination of the pyridine and protonated DIPEA. It is worth mentioning that olefin [26] (**3**) was prepared in-situ and has two *E* and *Z* isomers. Notably, we did not isolate the isomers, but TLC monitoring elucidated that the *Z* isomer reacts with the azomethine ylide, and the *E* isomer remains almost unreacted. Remarkably, driving forces of this cyclization are reactivity of isatin carbonyl group and also aromatic stability of pyrrole product (**5**) (Scheme 1).

Conclusion

Totally, azomethine ylides react differently with various dipolarophiles. *N*-metalled azomethine ylides underwent 1,3-dipolar cycloaddition reactions with quinolyl α,β -unsaturated esters and led to the synthesis of polysubstituted 3-pyrrolidinylquinolyl derivatives [29]. Also, the reactions of azomethine ylides with chalcones and arylidene pyrazolones have been

Scheme 1 A possible mechanistic pathway for the formation of product 5



recently reviewed and led to synthesis of indolizines through 1,3-dipolar cycloaddition reactions and spirocyclopropane derivatives via elimination of pyridine [18],25. In the present work, we have successfully accomplished an elegant approach in order to synthesize novel poly substituted pyrrole derivatives with aromatic stabilization, comprising the diverse cyclization reaction of azomethine ylides generated in-situ through the iodine-mediated reaction of 2-methylquinoline and pyridine with in-situ prepared olefins. Apart from the moderate to excellent yields of the desired products and short reaction time, the present work is bestowed with several advantages over previous key protocols for synthesis of pyrrole-based scaffolds [16, 17, 30], such as, one pot procedure, toleration of an array of functional groups, simple work-up procedure, besides straight-forward isolation and purification of target pyrroles, since all derivatives were purified by recrystallization

without using silica gel column chromatography. It is worth mentioning that the reaction is catalyst-free and proceeds well without the formation of any side products, irradiation, metals or ligands. We hope our novel protocol provides a new access to pyrrole-based scaffolds of pharmaceutical applications.

Experimental section

General remarks

All reagents were purchased from Merck and Fluka companies and used without further purifications. The melting points were recorded on an Electro thermal type 9100 melting point apparatus. The IR spectra were obtained on Avatar 370 FT-IR Thermo Nicolet, and only noteworthy absorptions

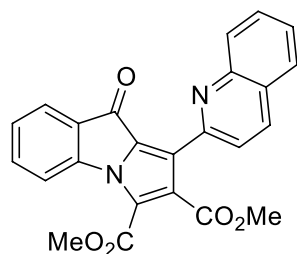
are mentioned. The ^1H NMR (300 MHz) and the ^{13}C NMR (75 MHz) spectra were recorded on a Bruker DRX-300 Avance, using CDCl_3 as applied solvent and TMS as internal standard at 300 and 75 MHz, respectively; δ in ppm, J in Hz. The mass spectra were scanned on a Varian Mat CH-7 at 70 eV and AB SCIEX 3200 QTRAP apparatuses.

General procedure for the synthesis of pyrrole 5a–i

1. A mixture of quinaldine (**1**) (0.143 g, 1 mmol), pyridine (**2**) (0.158 g, 2 mmol) and I_2 (0.253 g, 1 mmol) in the presence of DIPEA (0.258 g, 2 mmol) in MeCN (3 mL) was warmed to 60 °C to afford azomethine ylide (**4**). Then, the formed azomethine ylide (**4**) was added dropwise to the mixture of olefin [26] (**3**) (1 mmol) which is prepared *in-situ*, through a one pot procedure. The reaction mixture was settled under reflux conditions at 70 °C for 3 h. The reaction solvent was evaporated gradually, and the precipitate was recrystallized from *n*-hexane–EtOAc (3:1). Finally, the precipitate was filtered, washed with distilled water repeatedly and dried at ambient temperature, to give the pyrroles **5a–c**. It is noteworthy to mention that in the cases of products **5d**, **5e**, **5h** and **5i**, a gum-shaped product was gained after recrystallization. So, the formed gum was dissolved in the minimum amount of EtOAc in order to remove the impurities. In the case of product **5g**, in order to more purification after recrystallization, the precipitate was washed with boiling *n*-hexane. Moreover, in the case of product **5f** in which the reaction proceeded almost completely, the precipitate was purified only by washing with EtOAc in 50 °C.

Complete spectroscopic and analytical data for products **5a–i** are given below.

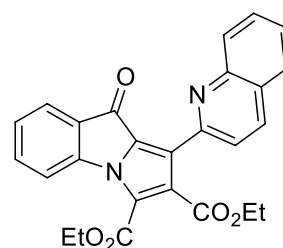
Dimethyl 9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-*a*]indole-2,3-dicarboxylate (**5a**)



Yellow powder; mp 178–180 °C; yield: 0.22 g (55%). FT-IR (KBr, ν (cm^{-1})): 1258, 1445, 1596, 1697, 1729, 1751, 2953, 3047. ^1H NMR (300 MHz, CDCl_3) δ ppm:

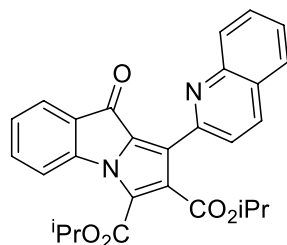
3.99 (s, 3H), 4.06 (s, 3H), 7.30 (d, $J = 6.0$ Hz, 1H), 7.49–7.64 (m, 2H), 7.65–7.78 (m, 2H), 7.83 (d, $J = 9.0$ Hz, 1H), 7.98 (d, $J = 12.0$ Hz, 1H), 8.26 (d, $J = 9.0$ Hz, 1H), 8.34 (d, $J = 9.0$ Hz, 1H), 8.82 (d, $J = 9.0$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ ppm = 52.4 (CH_3), 52.9 (CH_3), 116.6 (CH), 121.6 (CH), 123.5 (CH), 124.8 (C), 126.2 (C), 126.8 (C), 126.9 (C), 127.5 (CH), 127.9 (CH), 128.8 (CH), 129.0 (CH), 129.6 (C), 129.7 (CH), 132.0 (CH), 132.7 (C), 135.9 (CH), 136.8 (C), 147.7 (C), 148.5 (C), 159.2 (C=O), 163.9 (C=O), 178.7 (C=O). MS m/z (%) = 412 [M] $^+$, Chemical formula, $\text{C}_{24}\text{H}_{16}\text{N}_2\text{O}_5$, Exact Mass = 412.

Diethyl 9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-*a*]indole-2,3-dicarboxylate (**5b**)



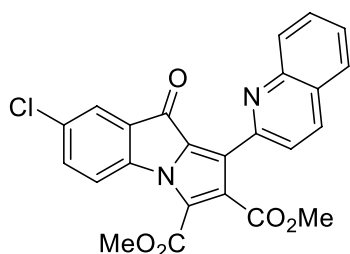
Yellow powder; mp 180–182 °C; Yield: 0.39 g (90%); FT-IR (KBr, ν (cm^{-1})): 1249, 1468, 1597, 1695, 1724, 2896, 2978, 3051; ^1H NMR (300 MHz, CDCl_3) δ ppm: 1.41 (t, $J = 6$ Hz, 3H), 1.43 (t, $J = 6$ Hz, 3H), 4.43 (q, $J = 6.0$ Hz, 2H), 4.54 (q, $J = 6.0$ Hz, 2H), 7.16–7.25 (m, 1H), 7.46–7.52 (m, 2H), 7.63–7.69 (m, 2H), 7.78 (d, $J = 6.0$ Hz, 1H), 7.96 (d, $J = 9.0$ Hz, 1H), 8.22 (d, $J = 9.0$ Hz, 1H), 8.27 (d, $J = 9.0$ Hz, 1H), 8.76 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ ppm: 14.0 (CH_3), 14.2 (CH_3), 61.4 (CH_2), 62.1 (CH_2), 116.6 (CH), 121.7 (CH), 123.7 (CH), 124.6 (C), 126.6 (C), 126.7 (C), 127.4 (C), 127.5 (CH), 127.7 (CH), 128.8 (CH), 129.3 (CH), 129.5 (C), 129.5 (CH), 130.6 (CH), 135.7 (C), 136.7 (CH), 143.7 (C), 147.5 (C), 149.2 (C), 158.9 (C=O), 165.2 (C=O), 179.8 (C=O). Synthesis of compound (**5b**) with chemical formula ($\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_5$) was confirmed with LC/MS/MS [$\text{M} + \text{H}$] $^+$ ion at $m/z = 441.145$.

Diisopropyl 9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5c)



Yellow powder; mp 182–184 °C; Yield: 0.22 g (48%); FT-IR (KBr, ν (cm⁻¹)): 1258, 1468, 1695, 1613, 1726, 2851, 2920, 2953; ¹H NMR (300 MHz, CDCl₃) δ ppm: 1.22 (d, $J=6.0$ Hz, 6H), 1.37 (d, $J=6.0$ Hz, 6H), 5.23–5.31 (m, 2H), 7.44–7.51 (m, 3H), 7.63 (t, $J=9.0$ Hz, 2H), 7.77 (d, $J=6.0$ Hz, 1H), 7.98 (d, $J=6.0$ Hz, 1H), 8.20 (d, $J=6.0$ Hz, 1H), 8.22 (d, $J=6.0$ Hz, 1H), 8.60 (d, $J=6.0$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ ppm: 21.7 (2 CH₃), 22.0 (2 CH₃), 69.6 (CH), 70.8 (CH), 117.9 (CH), 121.7 (CH), 124.5 (CH), 124.8 (C), 126.9 (CH), 127.6 (C), 127.7 (C), 128.3 (CH), 129.2 (CH), 129.5 (CH), 129.6 (CH), 130.4 (C), 130.5 (CH), 132.6 (CH), 135.0 (C), 136.7 (CH), 142.1 (C), 147.7 (C), 149.2 (C), 158.7 (C=O), 164.1 (C=O), 178.5 (C=O). Synthesis of compound (5c) with chemical formula (C₂₈H₂₄N₂O₅) was confirmed with LC/MS/MS [M + H]⁺ ion at $m/z=469.178$ and LC/MS/MS [M + Na]⁺ adduct ion at $m/z=491.169$.

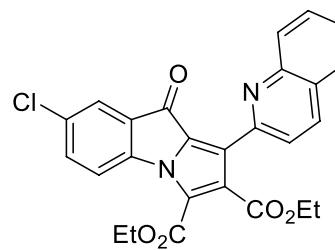
Dimethyl 7-chloro-9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5d)



Yellow powder; mp 184–186 °C; Yield: 0.25 g (57%); FT-IR (KBr, ν (cm⁻¹)): 837, 1292, 1468, 1595, 1696, 1726, 2923, 3080; ¹H NMR (300 MHz, CDCl₃) δ ppm: 3.99

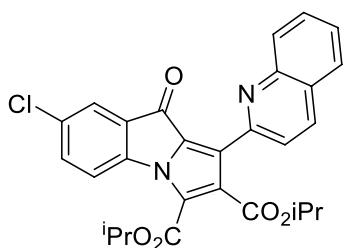
(s, 3H), 4.06 (s, 3H) 7.50–7.57 (m, 2H), 7.67–7.73 (m, 2H), 7.82 (d, $J=9.0$ Hz, 1H), 7.97 (d, $J=9.0$ Hz, 1H), 8.27 (d, $J=9.0$ Hz, 1H), 8.32 (d, $J=9.0$ Hz, 1H), 8.76 (d, $J=9.0$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ ppm: 61.5 (CH₃), 62.3 (CH₃), 117.9 (CH), 121.6 (CH), 123.9 (CH), 124.8 (C), 126.9 (C), 127.5 (C), 127.8 (C), 128.1 (CH), 129.5 (CH), 129.5 (CH), 129.6 (C), 130.3 (CH), 130.5 (C), 132.6 (CH), 135.1 (C), 136.8 (CH), 142.0 (C), 147.6 (C), 148.9 (C), 158.9 (C=O), 165.0 (C=O), 178.5 (C=O). Synthesis of compound (5d) with chemical formula (C₂₄H₁₅ClN₂O₅) was confirmed with LC/MS/MS [M + H]⁺ ion at $m/z=447.060$ and LC/MS/MS [M + Na]⁺ adduct ion at $m/z=469.062$.

Diethyl 7-chloro-9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5e)



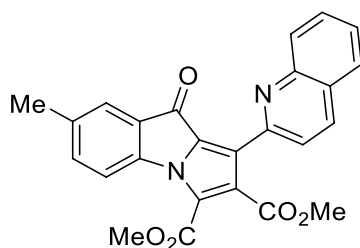
Yellow powder; mp 183–185 °C; Yield: 0.28 g (60%); FT-IR (KBr, ν (cm⁻¹)): 839, 1469, 1597, 1699, 1723, 1740, 2974, 3072; ¹H NMR (300 MHz, CDCl₃) δ ppm: 1.40 (t, $J=9.0$ Hz, 3H), 1.43 (t, $J=9.0$ Hz, 3H), 4.44 (q, $J=6.0$ Hz, 2H), 4.53 (q, $J=6.0$ Hz, 2H), 7.56–7.48 (m, 2H), 7.65–7.72 (m, 2H), 7.82 (d, $J=12.0$ Hz, 1H), 7.96 (d, $J=9.0$ Hz, 1H), 8.25 (d, $J=9.0$ Hz, 1H), 8.31 (d, $J=9.0$ Hz, 1H), 8.73 (d, $J=9.0$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ ppm: 13.9 (CH₃), 14.2 (CH₃), 61.5 (CH₂), 62.3 (CH₂), 117.9 (CH), 121.6 (CH), 123.9 (CH), 124.8 (C), 126.9 (C), 127.5 (C), 127.8 (C), 128.1 (CH), 129.5 (CH), 129.6 (CH), 129.67 (C), 130.3 (CH), 130.5 (C), 132.6 (CH), 135.1 (C), 136.8 (CH), 142.0 (C), 147.6 (C), 148.9 (C), 158.9 (C=O), 165.0 (C=O), 178.5 (C=O). Synthesis of compound (5e) with chemical formula (C₂₆H₁₉ClN₂O₅) was confirmed with LC/MS/MS [M + H]⁺ ion at $m/z=475.088$.

Diisopropyl 7-chloro-9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5f)



Yellow powder; mp 184–186 °C; Yield: 0.47 g (94%); FT-IR(KBr, ν (cm⁻¹)): 835, 1470, 1598, 1697, 1718, 1734, 2982, 3076; ¹H NMR (300 MHz, CDCl₃) δ ppm: 1.29 (d, J =6.0 Hz, 6H), 1.43 (d, J =6.0 Hz, 6H), 5.28–5.40 (m, 2H), 7.47–7.56 (m, 2H), 7.65–7.71 (m, 2H), 7.82 (d, J =9.0 Hz, 1H), 8.03 (d, J =9.0 Hz, 1H), 8.25 (d, J =6.0 Hz, 1H), 8.28 (d, J =6.0 Hz, 1H), 8.62 (d, J =9.0 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ ppm: 21.8 (2CH₃), 22.1 (2CH₃), 69.7(CH), 70.9 (CH), 118.0 (CH), 121.8 (CH), 124.6 (CH), 124.8 (C), 127.0 (C), 127.7 (C), 127.8 (C), 128.0 (CH), 129.3 (CH), 129.5 (CH), 129.7 (C), 130.4 (CH), 130.5 (C), 132.7 (CH), 135.1 (CH), 136.8 (C), 142.2 (C), 147.8 (C), 149.3 (C), 159.2 (C=O), 164.6 (C=O), 178.2 (C=O). Synthesis of compound (5f) with chemical formula (C₂₈H₂₃ClN₂O₅) was confirmed with LC/MS/MS [M+H]⁺ ion at m/z =503.133 and LC/MS/MS [M+Na]⁺ adduct ion at m/z =525.129.

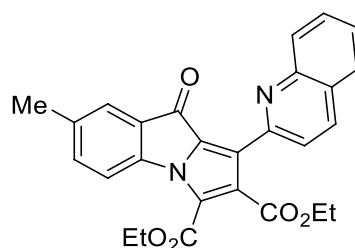
Dimethyl 7-methyl-9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5g)



Yellow powder; mp 181–183 °C; Yield: 0.19 g (45%); FT-IR (KBr, ν (cm⁻¹)): 1458, 1593, 1706, 1727, 1744, 2853, 2924,

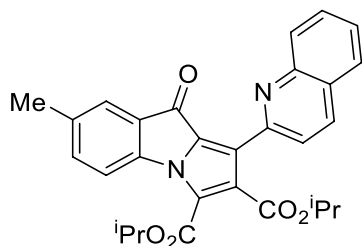
2956; ¹H NMR (300 MHz, CDCl₃) δ ppm: 2.40 (s, 3H), 3.98 (s, 3H), 4.02 (s, 3H), 7.36 (d, J =9.0 Hz, 1H), 7.53 (s, 1H), 7.67 (t, J =9.0 Hz, 1H), 7.83 (t, J =9.0 Hz, 1H), 7.91 (d, J =9.0 Hz, 1H), 7.94 (d, J =9.0 Hz, 1H), 8.50 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ ppm: 21.0 (CH₃), 69.4 (CH₃), 70.5 (CH₃), 116.3 (CH), 121.9 (CH), 124.1 (CH), 125.3 (C), 126.8 (C), 127.4 (C), 127.6 (C), 127.6 (CH), 128.6 (CH), 129.1 (CH), 129.4 (C), 129.5 (CH), 130.6 (CH), 136.1 (C), 136.7 (C), 136.9 (CH), 141.7 (C), 147.8 (C), 149.8 (C), 159.0 (C), 164.5 (C), 180.0 (C). Synthesis of compound (5g) with chemical formula (C₂₅H₁₈N₂O₅) was confirmed with LC/MS/MS [M+H]⁺ ion at m/z =427.126.

Diethyl 7-methyl-9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5h)



Yellow powder; mp 183–185 °C; Yield: 0.21 g (48%); IR (KBr, ν (cm⁻¹)): 1255, 1489, 1599, 1695, 1726, 2847, 2958, 3056; ¹H NMR (300 MHz, CDCl₃) δ ppm: 1.40 (t, J =6.0 Hz, 3H), 1.43 (t, J =6.0 Hz, 3H), 2.33 (s, 3H), 4.43 (q, J =6.0 Hz, 2H), 4.53 (q, J =6.0 Hz, 2H), 7.26–7.31 (m, 1H), 7.46–7.53 (m, 2H), 7.64–7.70 (m, 1H), 7.80 (d, J =9.0 Hz, 1H), 7.96 (d, J =9.0 Hz, 1H), 8.15 (d, J =9.0 Hz, 1H), 8.23 (d, J =9.0 Hz, 1H), 8.76 (d, J =9.0 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ ppm: 14.0 (CH₃), 14.2 (CH₃), 20.9 (CH₃), 61.4 (CH₂), 62.0 (CH₂), 116.4 (CH), 121.7 (CH), 123.5 (C), 125.2 (C), 126.7 (C), 127.2 (C), 127.5 (C), 127.7 (CH), 128.9 (CH), 128.9 (CH), 129.5 (C), 130.7 (CH), 136.0 (CH), 136.7 (C), 136.8 (C), 141.7 (CH), 147.6 (C), 149.4 (C), 159.0 (C), 161.0 (C=O), 165.3 (C=O), 180.1 (C=O). Synthesis of compound (5h) with chemical formula (C₂₇H₂₂N₂O₅) was confirmed with LC/MS/MS [M+H]⁺ ion at m/z =455.160.

Diisopropyl 7-methyl-9-oxo-1-(quinolin-2-yl)-9H-pyrrolo[1,2-a]indole-2,3-dicarboxylate (5i)



Yellow powder; mp 185–187 °C; Yield: 0.24 g (50%); IR (KBr, ν (cm^{-1})): 1218, 1477, 1600, 1697, 1723, 1744, 2924, 3080; ^1H NMR (300 MHz, CDCl_3) δ ppm: 1.22 (d, $J=6.0$ Hz, 6H), 1.35 (d, $J=9.0$ Hz, 6H), 2.28 (s, 3H), 5.20–5.33 (m, 2H), 7.18–7.24 (m, 1H), 7.39–7.46 (m, 2H), 7.56–7.62 (m, 1H), 7.73 (d, $J=9.0$ Hz, 1H), 7.95 (d, $J=9.0$ Hz, 1H), 8.04 (d, $J=9.0$ Hz, 1H), 8.16 (d, $J=9.0$ Hz, 1H), 8.57 (d, $J=9.0$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ ppm: 20.9 (CH_3), 21.7 (2 CH_3), 22.0 (2 CH_3), 69.4 (CH), 70.4 (CH), 116.3 (CH), 121.8 (CH), 124.1 (CH), 125.1 (C), 126.7 (C), 127.3 (C), 127.5 (C), 127.6 (CH), 128.6 (CH), 129.1 (CH), 129.4 (C), 129.4 (CH), 130.55 (CH), 135.9 (C), 136.5 (CH), 136.8 (C), 141.8 (C), 147.6 (C), 149.6 (C), 158.8 (C=O), 164.4 (C=O), 180.11 (C=O). Synthesis of compound (5i) with chemical formula ($\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_5$) was confirmed with LC/MS/MS [$\text{M} + \text{H}$] $^+$ ion at $m/z=483.198$.

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