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Novel regio- and stereo-selectivity: synthesis of dihydropyrrolo[1,2-*f*] phenanthridines via isocyanide-based multicomponent reaction

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ABSTRACT

The novel one-pot three-component reactions of the zwitterions generated in situ from three isocyanides and 2-arylidenemalononitriles with phenanthridine via 1,3-dipolar cycloaddition are described. The reactions afforded the corresponding dihydropyrrolo[1,2-*f*]phenanthridine derivatives in good yields without using any catalyst and activation. The stereochemistry of the final products was confirmed by single-crystal X-ray diffraction analysis.

1. Introduction

Heterocycle rings are present as fundamental components in the skeleton of more than half of the biologically active compounds produced by nature.[1] One of the reasons for the widespread use of heterocyclic compounds in nature as well as in the pharmaceutical industry is their implication in a wide range of reaction types allowing subtle structural modification.[2–4] As an important kind of these heterocycles, nitrogen-containing heterocycles as recognized pharmacophores have received great attention in drug discovery and lead optimization.[5]

Polycyclic phenanthridine derivatives have attracted considerable attention in medicinal chemistry due to their biological activity and their presence in a variety of significant alkaloids.[6] A class of dihydro-imidazo-phenanthridinium (DIP) have been shown to exhibit tuneable anti-cancer activity.[7] Also, pyrrolophenanthridine derivatives display high anti-tumor and anti-leukemic activities.[8] Almerico[9] reported that substituted 3-methylpyrrolo[1,2-*f*]phenanthridines (Fig. 1, **A**) demonstrated anti-neoplastic and anti-HIV activities. Besides of pharmaceutical applications, Cronin[10] reported that some phenanthridine derivatives (Fig. 1, **B**) can be used as molecular scale devices which undergo reversible ring-opening/closing under pH control. Therefore, the synthesis of new pyrrolophenanthridine derivatives may be of great significance.

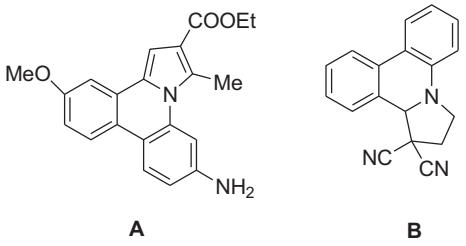

Fig. 1. Structures of compounds **A** and **B**.

Efficient and elegant assembly of complex structures with multiple stereocenters has become an important topic in chemical sciences. The multicomponent reaction (MCR) has thus emerged as a powerful tool for this purpose, in which a series of chemical processes can be controlled in a one-pot operation.[11] Moreover, the rich and fascinating chemistry that stems from MCR provides a robust approach for the synthesis of diverse and complex 'drug-like' heterocyclic compounds. They offer significant advantages over conventional linear-step syntheses due to their flexible, convergent, and atom efficient nature.[12]

Isocyanide-based multicomponent reactions (IMCRs) play an important role in this realm due to their diversity of bond-forming processes, functional group tolerance, and high levels of chemo-, regio-, and stereo-selectivities.[13] Apart from their well known and much exploited reactivity in Passerini and Ugi reactions,[14] isocyanides are known to form zwitterions with activated acetylene compounds, such as dimethyl acetylenedicarboxylate (DMAD), and

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develop novel protocols for the synthesis of heterocycles and carbocycles.[15] The success of these reactions provided us with a conceptual framework for designing novel multicomponent reactions.

As part of ongoing study on the chemistry of isocyanides, and based on our previous endeavors in exploring novel and practical multicomponent reactions to synthesize useful heterocyclic compounds,[16] this paper reports the results of our studies involving the reactions of phenanthridine with zwitterions generated in situ from 2-arylidenemalononitriles and isocyanides, which constitute a novel synthesis of dihydropyrrolo[1,2-*f*]phenanthridine derivatives.

2. Results and discussion

In an initial experiment, a solution of isocyanocyclohexane **1a** (1 equiv), 2-benzylidenemalononitrile **2a** (1 equiv), and phenanthridine **3** (1 equiv) in dry dichloromethane under argon was stirred at room temperature for 72 h to afford [(2*S**,12b*S**,*E*)-3-(cyclohexylimino)-2-phenyl-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-1,1(12b*H*)-dicarbonitrile **4a** in 40.0% yield (Table 1, entry 1). Full characterization involving IR, ^{1}H NMR, ^{13}C NMR, and HRMS proved the identity of **4a**, and the structure was further confirmed unambiguously by single-crystal X-ray analysis (Fig. 2). It is worthwhile to note that this reaction proceeded selectively to generate a single diastereomer.

Table 1
Optimization of solvents for formation of **4a**

Entry	Solvent	Time (h)	Isolated yield (%)
1	CH_2Cl_2	72	40
2	C_2H_5OH	48	48
3	$C_2H_5OC_2H_5$	48	64
4	CH_3CN	48	50
5	THF	72	35
6	Toluene	72	20

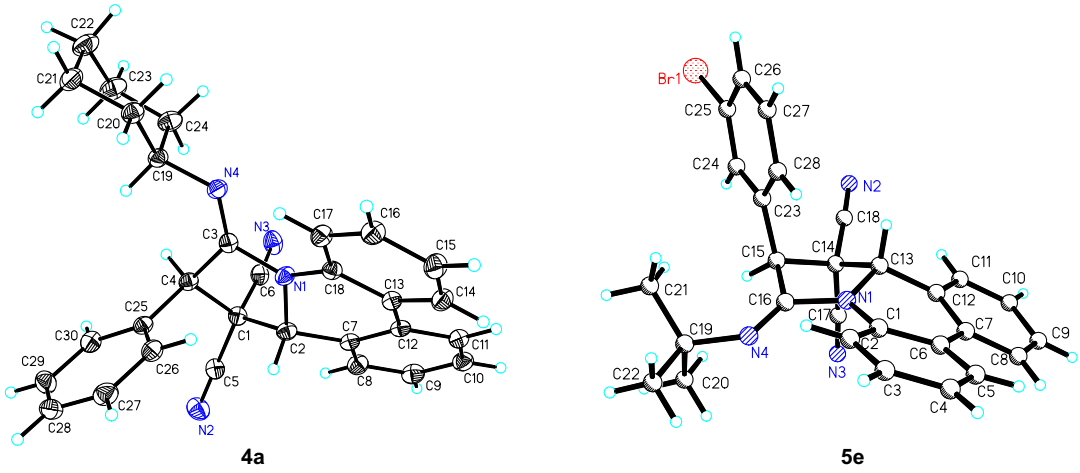


Fig. 2. ORTEP diagram of **4a** and **5e**.

Our approach toward the design and development of new domino and multicomponent procedures involves the use of cyclohexyl isocyanide **1a**, 2-benzylidenemalononitrile **2a**, and phenanthridine **3**. Two directions of the reaction are outlined in Scheme 1.

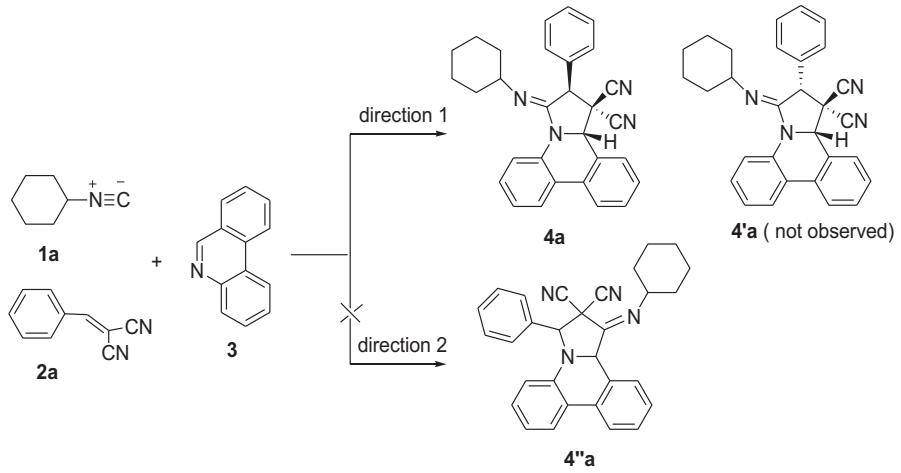
This basic reaction involves the formation of zwitterionic intermediate as a crucial step. It has been known that triphenyl phosphine,[17] pyridine,[18] quinoline, isoquinoline,[19] benzothiazole,[20] imidazole,[21] and isocyanides[22] can invoke the formation of zwitterions. Of special interest to us has been the addition of nucleophilic carbenes, such as isocyanides to 2-arylidenemalononitriles, which has received only scant attention.[23]

According to Mironov reaction[23] of isocyanides, 2-arylidenemalononitriles and isoquinoline, the key step in this reaction may be the formation of zwitterions generated from 2-arylidenemalononitriles and phenanthridine, which is attacked by isocyanide giving the final product **4″a**. But during our investigation, we did not trace any **4″a** or **4′a**, only **4a** was obtained exclusively. Our target compounds own two chiral centers, but only a single diastereomer was achieved. This result indicated that this transformation might provide a highly regio- and diastere-oselective method for the preparation of pyrrolophenanthridine derivatives.

Encouraged by this interesting result, we continued to focus on the optimization of reaction conditions. To search for the optimal solvent, the reaction of compounds **1a**, 2-benzylidenemalononitrile **2a** and **3** was examined using acetonitrile, ethanol, diethyl ether, THF, and toluene (Table 1). As can be seen, the reaction using diethyl ether as the solvent resulted in higher yield of 64% and needed shorter reaction time (Table 1, entry 3). So diethyl ether could be used as the solvent for further studies.

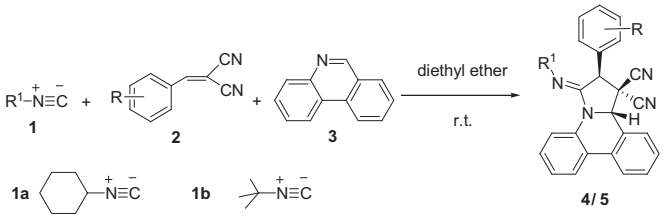
Having established the optimal reaction conditions, we tested the scope of substrates **2**, and found all reactions of **1a** and various 2-arylidenemalononitriles **2a**–**k** with phenanthridine **3** proceeded well and led to the corresponding dihydropyrrolo[1,2-*f*]phenanthridines **4a**–**k** (Table 2). Encouraged by the success of this reaction, we employed *tert*-butyl isocyanide **1b** instead of cyclohexyl isocyanide **1a** to investigate this MCR, and found that except **2k** the reactions involving **1b** proceeded well and just obtained single diastereomers **5** without any **5′** being observed. The experimental results are summarized in Table 2. As shown in Table 2, this reaction is tolerant of a variety of arylidenemalononitriles with electronically different substituents. And the substituents had some influence on the yields of products **4**/**5**. The arylidenemalononitriles with electron-withdrawing groups, such as fluoro, chloro, bromo, and nitro groups (Table 2, entries 2–9 and 13–18) reacted faster and gave higher yields than those with electron-rich groups, such as methyl and methoxyl groups (Table 2, entries 10, 11, and 19). What is more, the substrates **2** with substituents at *para*- and *ortho*-positions afforded higher yields than those counterparts at *meta*-position (Table 2, entries 2, 5, and 7), which should be also related to electronic effects.

The identification of dihydropyrrolo[1,2-*f*]phenanthridines **4** and **5** was unequivocally ascertained by their IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectra. For example, in the IR spectrum of **4a**, the C=N double bond showed strong absorption at 1666 cm^{-1} and the cyano group displayed its characteristic signal at 2254 cm^{-1}. Its ^{1}H NMR spectrum exhibited characteristic signals at δ 1.04–1.77 (series of multiplets) for the five CH_2 groups of the cyclohexyl moiety, and



Scheme 1. Two directions for the reactions of **1a**, **2**, and **3**.

Table 2
Synthesis of compounds **4** and **5**



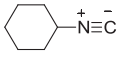
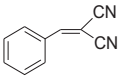
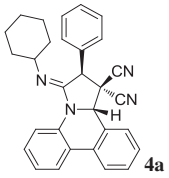
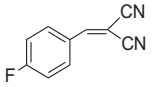
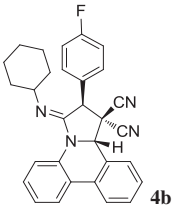
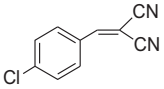
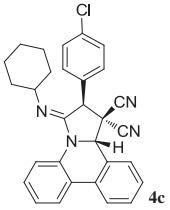
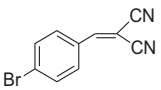
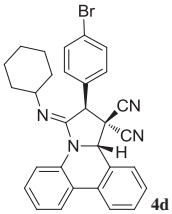
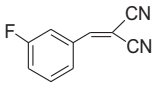
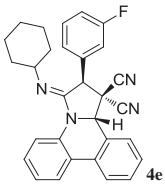
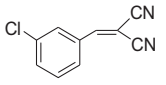
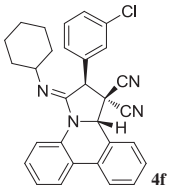
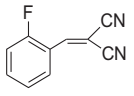
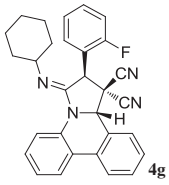
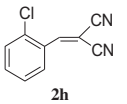
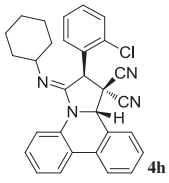
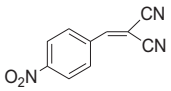
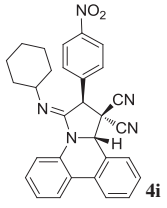
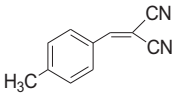
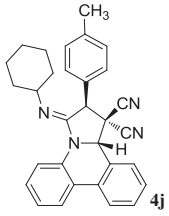
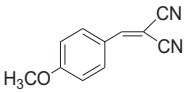
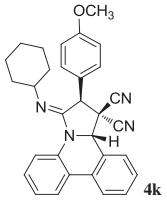
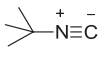
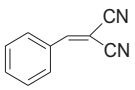
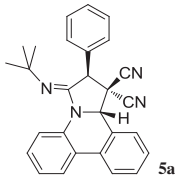
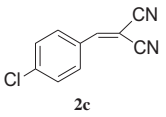
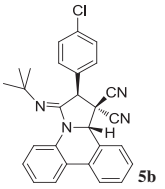
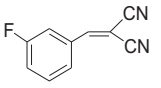
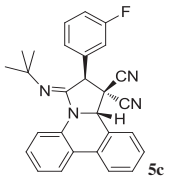
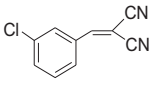
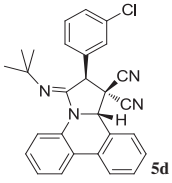
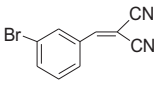
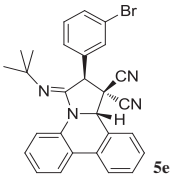
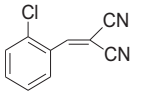
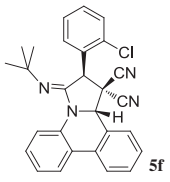
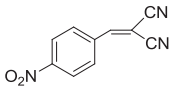
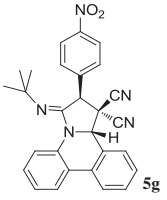
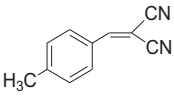
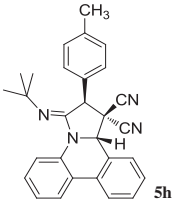
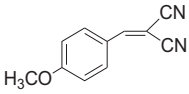
Entry	Precursor **1**	Precursor **2**	Product **4**/**5**	Time (h)	Isolated yield (%)
1	 **1a**	 **2a**	 **4a**	48	64
2	**1a**	 **2b**	 **4b**	36	74
3	**1a**	 **2c**	 **4c**	48	71
4	**1a**	 **2d**	 **4d**	48	69

Table 2 (*continued*)

Entry	Precursor **1**	Precursor **2**	Product **4**/**5**	Time (h)	Isolated yield (%)
5	**1a**	 **2e**	 **4e**	36	62
6	**1a**	 **2f**	 **4f**	48	65
7	**1a**	 **2g**	 **4g**	48	71
8	**1a**	 **2h**	 **4h**	48	68
9	**1a**	 **2i**	 **4i**	48	80[a]
10	**1a**	 **2j**	 **4j**	72	56
11	**1a**	 **2k**	 **4k**	72	51
12	 **1b**	 **2a**	 **5a**	48	60

(*continued on next page*)

Table 2 (*continued*)

Entry	Precursor **1**	Precursor **2**	Product **4**/**5**	Time (h)	Isolated yield (%)
13	**1b**	 **2c**	 **5b**	48	74
14	**1b**	 **2e**	 **5c**	36	70
15	**1b**	 **2f**	 **5d**	48	66
16	**1b**	 **2l**	 **5e**	48	60
17	**1b**	 **2h**	 **5f**	48	68
18	**1b**	 **2i**	 **5g**	48	46
19	**1b**	 **2j**	 **5h**	72	30
20	**1b**	 **2k**	—	96	No reaction

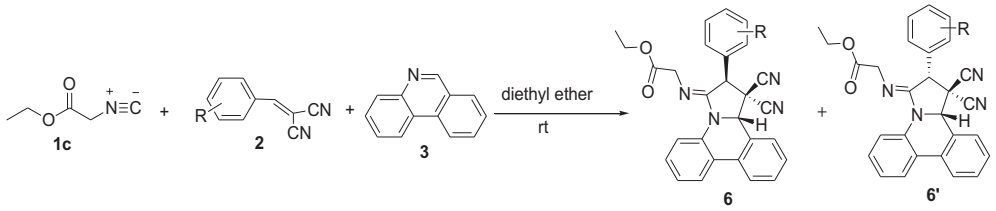
[a] Combined yield, the ratio (20:1) of **4b** to **4b′** was determined by ^{1}H NMR spectroscopy.

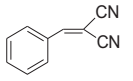
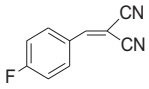
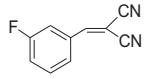
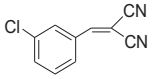
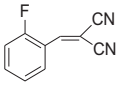
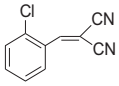
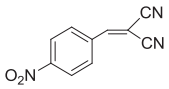
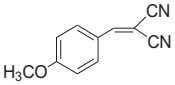
a symmetric multiplet at δ 3.09 for CH in cyclohexyl group. The C2-H signal displayed a singlet at δ 4.90, the H-atom from NCH can be observed at δ 5.50 as sharp singlet. The ^{13}C NMR spectrum was also in good agreement with the assigned structure. The two cyano carbons can be found to resonate at δ 112.4 and 113.4. In its HRMS spectra, 443.2222 was found while 443.2230 calcd for $C_{30}H_{27}N_4$ ($[M+H]^+$). Finally, the structures and stereochemistry of **4** and **5** were ascertained by the single-crystal X-ray diffraction analysis of **4a** and **5e** (Fig. 2).[24] The structures and stereochemistry of other compounds were concluded by their IR, ^{1}H NMR, ^{13}C NMR spectra in contrast with that of **4a** or **5e** and the crystal structures of **4a** or **5e**.

Next, this reaction was also extended by using ethoxycarbonylmethyl isocyanide **1c**, and similar reactivity was observed, **1c** underwent facile reactions with various arylidenemalononitriles **2** and phenanthridine **3** yielding the corresponding new dihydropyrrolo[1,2-*f*]phenanthridine-1,1(12b*H*)-dicarbonitrile derivatives **6** in moderate to good yields (Table 3). As can be seen from Tables 2 and 3, ethoxycarbonylmethyl isocyanide **1c** led to slightly higher yields than cyclohexyl isocyanide **1a** and *tert*-butyl isocyanide **1b**. For example, the yields of **4f** and **5d** were 65% and 66%, respectively (Table 2, entries 9 and 14), the yield of **6d** is 70% (Table 3, entry 4). Unfortunately, however, in all cases of **1c**, relatively moderate selectivity was observed; the reactions gave a mixture of two diastereomers of a compound with ratio of 13:1 up to 25:1, whereas both **1a** and **1b** gave one diastereomer of a compound with remarkable diastereoselectivity.

It may be concluded from the experimental results above, that in contrast to arylidenemalononitriles with electron-withdrawing groups, those with electron-donating groups produced lower yields in this IMCR. However, in some cases, arylidenemalononitriles with stronger electron-withdrawing group or stronger electron-donating group, such as *p*-nitro arylidenemalononitrile **2i** or *p*-methoxyl

Table 3
Synthesis of compounds **6**



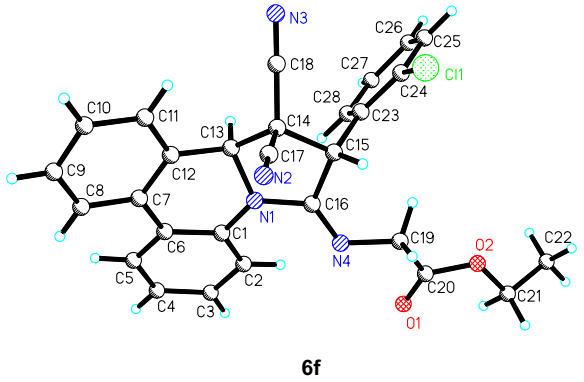
Entry	Precursor **2**	Product **6**/**6′**	Time (h)	Isolated yield[a] (%)(ratio)
1	 **2a**	**6a**/**6′a**	48	73 (14:1)
2	 **2b**	**6b**/**6′b**	36	82 (13:1)
3	 **2e**	**6c**/**6′c**	36	73 (14:1)
4	 **2f**	**6d**/**6′d**	48	70 (14:1)
5	 **2g**	**6e**/**6′e**	36	75 (25:1)
6	 **2h**	**6f**/**6′f**	48	72 (25:1)
7	 **2i**	—	96	No reaction
8	 **2k**	—	96	No reaction

[a] Combined yield, the ratio was determined by ^{1}H NMR spectroscopy.

arylidenemalononitrile **2k**, gave aberrant results.[25] For example, the reactions of **2i** or **2k** with cyclohexyl isocyanide **1a** gave good yields of 80% or 51%, respectively (Table 2, entries 9 and 10). When *tert*-butyl isocyanide **1c** was used instead of **1a**, only the reaction of **2i** proceeded and afforded the desired product **5g** in 46% yield, whereas **2k** did not react (Table 2, entries 18 and 20). Even in case of ethoxycarbonylmethyl isocyanide **1c**, both **2i** and **2 k** did not react at all (Table 3, entries 7 and 8), even when the reaction time was prolonged to 96 h, or in other various solvents, such as CH_2Cl_2, CH_3CN, and toluene at room or reflux temperature. But in THF solvent, the reactions of **2i** or **2k** with **1c** could occur, but produced a complex mixture without expected product.

The main products **6** were characterized on the basis of their spectroscopic data. Take **6f**, for example. A strong absorption at 1743 cm^{-1} in the IR spectrum indicates the presence of ester carbonyl group, and the absorption at 2251 cm^{-1} corresponds to the cyano groups. The ^1H NMR spectrum exhibits a triplet at δ 1.26 for methyl group CH_3, a quartet at δ 4.15 for the OCH_2, two doublets at δ 3.94 and 4.08 for the methylene linked to carbonyl group, a singlet at δ 5.46 for the CH proton adjacent to the C=N double bond, and a singlet at δ 5.67 for the NCH proton in phenanthridine ring. In the ^{13}C NMR spectrum of **6f**, six distinct saturated carbons resonance can be found, and two cyano group carbons were observed at δ 111.9 and 112.7, respectively. In HRMS spectra, 481.1440 ($[M+H]^+$) is found while 481.1431 calcd for $C_{28}H_{23}ClN_4O_2$. X-ray crystallographic analysis of **6f** [24] reveals the relative configuration of the main diastereomer as depicted in Fig. 3.

It is noteworthy that all the isolated products only need washing with diethyl ether twice rather than column chromatography or recrystallization. The ease of purification makes this methodology facile, practical, and rapid to execute. Significantly, this operationally simple domino reaction generated two chiral centers, but in most cases, the target products were obtained in good yields with excellent diastereoselectivity.



6f

Fig. 3. ORTEP diagram of **6f**.

Although the mechanistic detail of this reaction is unknown, the formation of these heterocycles is outlined in Scheme 2. The reaction may proceed via initial formation of a highly reactive zwitterion intermediate **7**/**7′** or **8**/**8′** from isocyanide **1** and arylidenemalononitrile **2**, followed by its trapping with phenanthridine **3** to give the intermediate **9** or **9′**. It is clear that **9′** has more steric hindrance than **9** to proceed intra-cyclization, therefore, final products **4**/**5**/**6** were obtained as a major diastereomer. It is worth mentioning that there is a big difference in the formation of zwitterion compared with the Mironov reaction,[23] and in our reaction the zwitterion was generated from 2-arylidenemalononitrile and isocyanide, not from 2-arylidenemalononitrile and phenanthridine as the Mironov reaction which should give compounds **4″**/**5″**/**6″**.

3. Conclusion

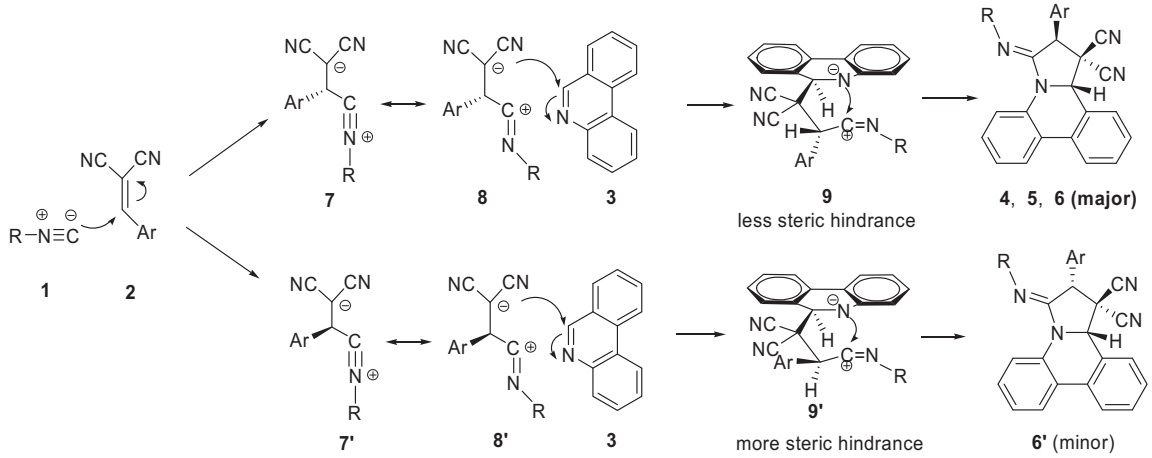
In summary, we have developed a novel three-component synthesis of dihydropyrrolo[1,2-*f*]phenanthridines via 1,3-dipolar cycloaddition, which may be of interest in the potential synthetic and pharmaceutical chemistry. The advantages of the present procedure are as follows: (1) simple mixing of the starting materials; (2) mild reaction conditions; (3) easy workup procedure; (4) highly regio- and stereo-selectivity;[26] (5) good yield of the product; and (6) good functional groups tolerance. Undoubtedly, this novel method is complementary to the classical 1,3-dipolar cycloaddition. We hope this approach may be of value to others seeking novel synthetic fragments with unique properties for medicinal chemistry. Further work is under way in this area.

4. Experimental section

4.1. General

All the reagents were purchased from local suppliers and used without purification.

Melting points were recorded on a RY-1 microscopic melting apparatus and uncorrected. ^1H NMR spectra were recorded on 500 MHz and ^{13}C NMR spectra were recorded on 125 MHz in $CDCl_3$ by using a Bruker Avance 500 spectrometer. Chemical shifts are reported in δ (ppm) relative to TMS as internal standard. IR spectra were recorded on a Nicolet iS10 FT-IR spectrometer and only major peaks are reported in cm^{-1}. HRMS were performed on Ultima Global and Varian spectrometer with an ESI source. The X-ray



Scheme 2. Possible mechanism.

single-crystal diffraction was performed on Rigaku Saturn 724+ CCD instrument.

4.2. General procedure for the preparation of products 4a–k, 5a–h, and 6a–f

A mixture of isocyanides **1** (1.0 mmol), 2-arylidenemalononitriles **2** (1.0 mmol), and phenanthridine **3** (1.0 mmol) was stirred in dry diethyl ether for the appropriate reaction time at room temperature. After completion of the reaction, as indicated by TLC (petroleum ether/EtOAc, 10:1, v/v), the products were precipitated directly from the solution. The precipitates were filtered and washed with diethyl ether (2×1 mL) to get the products **4a–k**, **5a–h**, and **6a–f**.

4.2.1. (2S,12bS*,E)-3-(Cyclohexylimino)-2-phenyl-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4a**).* White powder; mp 184–186 °C; IR (KBr, cm^{-1}): 2924, 2849, 2254, 1666, 1602, 1490, 746, 727, 701; δ_H (500 MHz, $CDCl_3$) 1.04–1.08 (m, 1H, CH), 1.17–1.30 (m, 3H, CH_2, CH), 1.39–1.45 (m, 2H, CH_2), 1.54–1.69 (m, 3H, CH_2, CH),1.75–1.77 (m, 1H, CH), 3.09 (m, 1H, =NCH), 4.90 (s, 1H, CH), 5.50 (s, 1H, NCH), 7.20–7.23 (t, *J*=7.5 Hz, 1H, ArH), 7.39–7.45 (m, 4H, ArH), 7.48–7.53 (m, 4H, ArH), 7.64–7.66 (d, *J*=7.5 Hz, 1H, ArH), 7.82–7.84 (d, *J*=7.5 Hz, 1H, ArH), 7.88–7.89 (d, *J*=7.5 Hz, 1H, ArH), 8.93–8.95 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.3, 34.6, 43.0, 52.6, 60.3, 62.3, 112.4, 113.4, 120.0, 123.5, 123.8, 124.1, 125.2, 128.2, 128.6, 129.1, 129.7, 129.9, 130.0, 131.7, 131.8, 135.9, 151.1; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{27}N_4$, 443.2230; found 443.2222.

4.2.2. (2S,12bS*,E)-3-(Cyclohexylimino)-2-(4-fluorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4b**).* White powder; mp 202–204 °C; IR (KBr, cm^{-1}): 2923, 2850, 2254, 2031, 1662, 1509, 1490, 839, 748; δ_H (500 MHz, $CDCl_3$) 1.02–1.11 (m, 1H, CH), 1.23–1.32 (m, 3H, CH_2, CH), 1.40–1.45 (m, 2H, CH_2), 1.56–1.68 (m, 3H, CH, CH_2), 1.75 (m, 1H, CH), 3.07 (m, 1H, =NCH), 4.90 (s, 1H, CH), 5.47 (s, 1H, NCH), 7.18–7.23 (m, 3H, ArH), 7.39–7.46 (m, 4H, ArH), 7.52 (t, *J*=8.0 Hz, 1H, ArH), 7.64–7.65 (d, *J*=7.5 Hz, 1H, ArH), 7.83–7.84 (d, *J*=8.0 Hz, 1H, ArH), 7.88–7.90 (d, *J*=8.0 Hz, 1H, ArH), 8.92–8.93 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.4, 34.6, 42.9, 51.7, 60.3, 62.2, 112.4, 113.2, 116.8, 117.0, 120.0, 123.4, 123.8, 123.9, 124.1, 125.1, 127.7, 128.3, 129.1, 129.7, 130.0, 130.5, 130.6, 131.7, 135.8, 150.8, 162.3, 164.3; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}FN_4$, 461.2136; found 461.2135.

4.2.3. (2S,12bS*,E)-2-(4-Chlorophenyl)-3-(cyclohexylimino)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4c**).* White powder; mp 201–203 °C; IR (KBr, cm^{-1}): 2936, 2922, 2849, 2257, 2027, 1666, 1491, 835, 747, 735; δ_H (500 MHz, $CDCl_3$) 1.04–1.12 (m, 1H, CH), 1.24–1.26 (m, 2H, CH_2), 1.34 (m, 1H, CH), 1.41–1.44 (m, 2H, CH_2), 1.57–1.68 (m, 3H, CH_2, CH), 1.76 (m, 1H, CH), 3.06 (m, 1H, =NCH), 4.88 (s, 1H, CH), 5.46 (s, 1H, NCH), 7.21–7.28 (m, 1H, ArH), 7.33–7.35 (m, 1H, ArH), 7.40–7.48 (m, 4H, ArH), 7.50–7.54 (m, 1H, ArH), 7.63–7.65 (d, *J*=7.5 Hz, 1H, ArH), 7.83–7.84 (dd, J_1=7.8 Hz, J_2=1.2 Hz, 1H, ArH), 7.88–7.90 (d, *J*=7.5 Hz, 1H, ArH), 8.91–8.92 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.4, 34.6, 42.9, 51.7, 60.3, 62.2, 112.3, 113.2, 120.0, 123.4, 123.8, 123.9, 124.1, 125.1, 128.3, 129.1, 129.6, 129.9, 130.0, 130.3, 131.6, 135.8, 136.2, 150.5; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}ClN_4$, 477.1841; found 477.1832.

4.2.4. (2S,12bS*,E)-2-(4-Bromophenyl)-3-(cyclohexylimino)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4d**).* White powder; mp 186–188 °C; IR (KBr, cm^{-1}): 2933, 2848, 2254, 2023, 1668, 1489, 829, 747, 735; δ_H (500 MHz, $CDCl_3$) 1.05–1.11 (m, 1H, CH), 1.22–1.30 (m, 2H, CH_2), 1.32–1.35 (m, 1H, CH), 1.40–1.46 (m, 2H, CH_2), 1.56–1.58 (m, 1H, CH), 1.65–1.68 (m, 2H, CH_2), 1.75–1.78 (m, 1H, CH), 3.05 (m, 1H, =NCH), 4.86 (s, 1H, CH), 5.45 (s, 1H, NCH), 7.20–7.24 (m, 1H, ArH), 7.27–7.28 (m, 2H, ArH), 7.40–7.45 (m, 2H, ArH), 7.51–7.54 (m, 1H, ArH), 7.62–7.64 (m, 3H, ArH), 7.83–7.84 (dd, J_1=8.0 Hz, J_2=1.2 Hz, 1H, ArH), 7.88–7.90 (d, *J*=7.5 Hz, 1H, ArH), 8.90–8.91 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.4, 34.6, 42.8, 51.8, 60.3, 62.2, 112.3, 113.1, 120.0, 123.4, 123.8, 124.0, 124.1, 124.4, 125.1, 128.3, 129.2, 129.6, 130.0, 130.2, 130.8, 131.6, 133.0, 135.7, 150.5; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}BrN_4$, 521.1335; found 521.1332.

4.2.5. (2S,12bS*,E)-3-(Cyclohexylimino)-2-(3-fluorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4e**).* White powder; mp 188–190 °C; IR (KBr, cm^{-1}): 2928, 2854, 2026, 1673, 1490, 1445, 1359, 753, 718; δ_H (500 MHz, $CDCl_3$) 1.03–1.10 (m, 1H, CH), 1.20–1.33 (m, 3H, CH_2, CH), 1.37–1.46 (m, 2H, CH_2), 1.54–1.59 (m, 1H, CH), 1.64–1.67 (m, 2H, CH_2), 1.74–1.77 (m, 1H, CH), 3.07 (m, 1H, =NCH), 4.89 (s, 1H, CH), 5.49 (s, 1H, NCH), 7.10–7.11 (d, *J*=9.0 Hz, 1H, ArH), 7.19–7.23 (m, 3H, ArH), 7.39–7.53 (m, 4H, ArH), 7.63–7.65 (d, *J*=7.5 Hz, 1H, ArH), 7.81–7.83 (d, *J*=8.0 Hz, 1H, ArH), 7.87–7.89 (d, *J*=7.5 Hz, 1H, ArH), 8.89–8.91 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.5, 25.6, 34.4, 34.7, 42.9, 52.1, 60.4, 62.4, 112.3, 113.2, 115.7, 115.9, 117.2, 117.4, 120.2, 123.5, 123.9, 124.0, 124.1, 124.6, 125.0, 128.3, 129.2, 129.8, 120.0, 131.5, 131.7, 134.3, 135.8, 150.5, 162.0, 164.1; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}FN_4$, 461.2142; found 461.2159.

4.2.6. (2S,12bS*,E)-2-(3-Chlorophenyl)-3-(cyclohexylimino)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4f**).* White powder; mp 187–189 °C; IR (KBr, cm^{-1}): 2929, 2854, 2254, 1672, 1490, 1445, 752, 711; δ_H (500 MHz, $CDCl_3$) 1.04–1.11 (m, 1H, CH), 1.18–1.33 (m, 3H, CH_2, CH), 1.39–1.46 (m, 2H, CH_2), 1.54–1.77 (m, 4H, 2× CH_2), 3.05 (m, 1H, =NCH), 4.86 (s, 1H, CH), 5.49 (s, 1H, NCH), 7.21 (t, *J*=7.0 Hz, 1H, ArH), 7.27–7.29 (m, 1H, ArH), 7.39–7.53 (m, 6H, ArH), 7.63–7.65 (d, *J*=8.0 Hz, 1H, ArH), 7.82–7.83 (dd, J_1=7.9 Hz, J_2=1.2 Hz, 1H, ArH), 7.88–7.89 (d, *J*=7.5 Hz, 1H, ArH), 8.90–8.91 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.5, 25.6, 34.4, 34.7, 43.0, 51.9, 60.4, 62.4, 112.3, 113.2, 120.2, 123.6, 123.9, 124.1, 124.2, 125.2, 126.9, 128.4, 128.8, 129.3, 129.7, 130.0, 130.4, 131.1, 131.7, 133.9, 135.7, 135.8, 150.4; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}ClN_4$, 477.1846; found 477.1831.

4.2.7. (2R,12bS*,E)-3-(Cyclohexylimino)-2-(2-fluorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4g**).* White powder; mp 186–188 °C; IR (KBr, cm^{-1}): 2928, 2853, 2254, 1673, 1491, 756, 723; δ_H (500 MHz, $CDCl_3$) 1.05–1.13 (m, 1H, CH), 1.20–1.35 (m, 3H, CH_2, CH), 1.39–1.48 (m, 2H, CH_2), 1.56–1.58 (m, 1H, CH), 1.65–1.71 (m, 2H, CH_2), 1.77–1.80 (m, 1H, CH), 3.05 (m, 1H, =NCH), 4.86 (s, 1H, CH),3.04 (m, 1H, =NCH), 5.25 (s, 1H, CH), 5.54 (s, 1H, NCH), 7.22–7.25 (m, 3H, ArH), 7.34 (t, *J*=9.0 Hz, 1H, ArH), 7.41–7.47 (m, 2H, ArH), 7.51–7.55 (m, 2H, ArH), 7.67–7.68 (d, *J*=8.0 Hz, 1H, ArH), 7.84–7.86 (dd, J_1=8.0 Hz, J_2=1.2 Hz, 1H, ArH), 7.90–7.92 (d, *J*=7.5 Hz, 1H, ArH), 8.97–8.99 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.3, 34.6, 42.1, 46.0, 60.5, 62.7, 112.2, 113.0, 116.6, 116.8, 119.5, 120.0, 123.5, 123.8, 123.9, 124.1, 125.0, 125.2, 128.3, 129.1, 129.7, 129.9, 131.6, 132.2, 135.9, 150.3, 159.8, 161.7; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}FN_4$, 461.2141; found 461.2138.

4.2.8. (2R,12bS*,E)-2-(2-Chlorophenyl)-3-(cyclohexylimino)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4h**).* White powder; mp 189–191 °C; IR (KBr, cm^{-1}):2929, 2854, 2254, 1688, 1600, 1491, 751, 728; δ_H (500 MHz, $CDCl_3$) 1.08–1.13 (m, 1H, CH), 1.19–1.27 (m, 2H, CH_2), 1.31–1.45 (m, 3H, CH_2, CH), 1.56–1.58 (m, 1H, CH), 1.64–1.66 (m, 1H, CH), 1.70–1.73 (m, 1H, CH), 1.78–1.80 (m, 1H, CH), 2.92 (m, 1H, =NCH), 5.45 (s, 1H, CH), 5.59 (s, 1H, NCH), 7.24 (t, *J*=8.0 Hz, 2H, ArH), 7.35 (t, *J*=7.5 Hz, 1H, ArH), 7.42–7.48 (m, 3H, ArH), 7.54 (t, *J*=7.5 Hz, 1H, ArH), 7.67–7.68 (d,

J=8.0 Hz, 2H, ArH), 7.85–7.86 (d, *J*=7.5 Hz, 1H, ArH), 7.91–7.92 (d, *J*=8.0 Hz, 1H, ArH), 8.99–9.00 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.2, 34.6, 41.7, 49.4, 60.8, 62.9, 112.0, 113.1, 120.0, 123.6, 123.7, 123.9, 124.1, 125.1, 128.0, 128.1, 128.3, 129.1, 129.7, 129.9, 130.2, 130.8, 131.3, 131.6, 135.3, 135.8, 151.1; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}ClN_4$, 477.1846; found 477.1839.

4.2.9. (2S,12bS*,E)-3-(Cyclohexylimino)-2-(4-nitrophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4i**).* White powder; mp 186–188 °C; IR (KBr, cm^{-1}): 2924, 2852, 2254, 1661, 1524, 1490, 852, 742; δ_H (500 MHz, $CDCl_3$) 1.02–1.05 (m, 1H, CH), 1.22–1.29 (m, 3H, CH_2, CH), 1.40–1.43 (m, 2H, CH_2), 1.53–1.56 (m, 1H, CH), 1.64–1.66 (m, 2H, CH_2), 1.75 (m, 1H, CH), 3.00 (m, 1H, =NCH), 4.99 (s, 1H, CH), 5.48 (s, 1H, NCH), 7.24 (t, *J*=7.5 Hz, 1H, ArH), 7.40–7.46 (q, *J*=7.5 Hz, 2H, ArH), 7.53 (t, *J*=8.0 Hz, 1H, ArH), 7.60–7.62 (m, 3H, ArH), 7.84–7.85 (d, *J*=8.0 Hz, 1H, ArH), 7.89–7.91 (d, *J*=8.0 Hz, 1H, ArH), 8.36–8.37 (d, *J*=9.0 Hz, 1H, ArH), 8.89–8.91 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.4, 25.5, 34.4, 34.7, 42.7, 51.7, 60.7, 62.4, 112.1, 112.8, 120.1, 123.5, 124.0, 124.2, 124.6, 124.9, 125.1, 128.5, 129.3, 129.4, 129.9, 130.2, 131.3, 131.7, 135.6, 138.9, 148.9, 149.7, 156.8; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{30}H_{26}N_5O_2$, 488.2087; found 488.2089.

4.2.10. (2S,12bS*,E)-3-(Cyclohexylimino)-2-(p-tolyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4j**).* White powder; mp 184–186 °C; IR (KBr, cm^{-1}): 2925, 2854, 2251, 1669, 1601, 1514, 1492, 820, 754, 738; δ_H (500 MHz, $CDCl_3$) 1.05–1.12 (m, 1H, CH), 1.19–1.30 (m, 2H, CH_2), 1.32–1.36 (m, 1H, CH), 1.40–1.45 (m, 2H, CH_2), 1.53–1.59 (m, 1H, CH), 1.65–1.70 (m, 2H, CH_2), 1.76–1.78 (m, 1H, CH), 2.40 (s, 3H, CH_3), 3.09 (m, 1H, =NCH), 4.85 (s, 1H, CH), 5.47 (s, 1H, NCH), 7.19 (t, *J*=7.5 Hz, 1H, ArH), 7.21–7.26 (m, 2H, ArH), 7.38–7.43 (q, *J*=8.0 Hz, 4H, ArH), 7.50 (t, *J*=7.5 Hz, 1H, ArH), 7.63–7.65 (d, *J*=7.5 Hz, 1H, ArH), 7.81–7.83 (dd, J_1=8.0 Hz, J_2=1.0 Hz, 1H, ArH), 7.86–7.88 (d, *J*=8.0 Hz, 1H, ArH), 8.92–8.94 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 21.4, 24.6, 25.6, 34.4, 34.7, 43.1, 52.4, 60.2, 62.3, 112.7, 113.6, 120.1, 123.5, 123.8, 124.1, 125.2, 128.3, 128.5, 128.8, 129.2, 129.9, 130.0, 130.4, 131.0, 131.8, 136.1, 140.1, 151.4; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{31}H_{29}N_4$, 457.2392; found 457.2398.

4.2.11. (2S,12bS*,E)-3-(Cyclohexylimino)-2-(4-methoxyphenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**4k**).* White powder; mp 215–217 °C; IR (KBr, cm^{-1}): 2924, 2848, 2250, 1673, 1609, 1514, 1490, 835, 751, 738; δ_H (500 MHz, $CDCl_3$) 1.02–1.13 (m, 1H, CH), 1.20–1.30 (m, 2H, CH_2), 1.35–1.46 (m, 3H, CH_2, CH), 1.57–1.79 (m, 5H, 2× CH_2, CH), 3.12 (m, 1H, =NCH), 3.87 (s, 3H, OCH_3), 4.88 (s, 1H, CH), 5.49 (s, 1H, NCH), 6.99–7.01 (d, *J*=9.0 Hz, 2H, ArH), 7.23 (t, *J*=8.0 Hz, 1H, ArH), 7.32 (t, *J*=8.5 Hz, 2H, ArH), 7.41–7.46 (m, 2H, ArH), 7.53 (t, *J*=8.0 Hz, 1H, ArH), 7.66–7.67 (d, *J*=7.5 Hz, 1H, ArH), 7.84–7.85 (dd, J_1=7.9 Hz, J_2=1.0 Hz, 1H, ArH), 7.89–7.91 (d, *J*=7.5 Hz, 1H, ArH), 8.94–8.96 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 24.5, 25.5, 34.4, 34.7, 43.1, 52.1, 55.3, 60.1, 62.2, 112.6, 113.5, 115.0, 120.0, 123.5, 123.7, 124.1, 125.1, 128.2, 129.1, 129.8, 129.9, 131.7, 136.0, 151.3, 160.6; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{31}H_{29}N_4O$, 473.2336; found 473.2330.

4.2.12. (2S,12bS*,E)-3-(tert-Butylimino)-2-phenyl-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5a**).* White powder; mp 158–160 °C; IR (KBr, cm^{-1}): 2970, 2250, 1682, 1600, 1491, 1444, 1356, 1302, 1212, 1179, 774, 752, 737, 728, 697; δ_H (500 MHz, $CDCl_3$) 1.20 (s, 9H, 3× CH_3), 4.83 (s, 1H, CH), 5.33 (s, 1H, NCH), 7.18 (t, *J*=7.5 Hz, 1H, ArH), 7.36–7.41 (m, 4H, ArH), 7.44–7.49 (m, 4H, ArH), 7.49 (t, *J*=7.5 Hz, 1H, ArH), 7.60–7.62 (d, *J*=7.5 Hz, 1H, ArH), 7.80–7.81 (d, *J*=7.0 Hz, 1H, ArH), 7.84–7.85 (d, *J*=8.0 Hz, 1H, ArH), 8.72–8.73 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.7, 43.4, 54.0, 54.9, 60.5, 112.7, 113.4, 120.4, 123.4, 123.6, 123.8, 124.2, 125.6, 128.2, 128.9, 129.7, 129.8, 129.9, 130.2, 132.0, 132.4, 135.9, 147.7; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{25}N_4$, 417.2079; found 417.2065.

4.2.13. (2S,12bS*,E)-3-(tert-Butylimino)-2-(4-chlorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5b**).* White powder; mp 167–169 °C; IR (KBr, cm^{-1}): 2969, 2251, 1675, 1600, 1490, 1444, 1356, 1299, 1213, 1181, 826, 748, 728; δ_H (500 MHz, $CDCl_3$) 1.20 (s, 9H, 3× CH_3), 4.80 (s, 1H, CH), 5.29 (s, 1H, NCH), 7.18 (t, *J*=7.5 Hz, 1H, ArH), 7.31–7.33 (m, 2H, ArH), 7.36–7.44 (m, 4H, ArH), 7.48 (t, *J*=7.5 Hz, 1H, ArH), 7.59–7.61 (d, *J*=7.5 Hz, 1H, ArH), 7.80–7.82 (d, *J*=8.0 Hz, 1H, ArH), 7.84–7.86 (d, *J*=7.5 Hz, 1H, ArH), 8.67–8.69 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.7 (2C), 43.2, 53.2, 54.9, 60.5, 112.5, 113.1, 120.4, 123.4, 123.8, 123.9, 124.2, 125.5, 128.3, 128.8, 129.9, 130.0, 130.2, 130.9, 131.9, 135.7, 136.1, 147.2; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{24}ClN_4$, 451.1689; found 451.1680.

4.2.14. (2S,12bS*,E)-3-(tert-Butylimino)-2-(3-fluorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5c**).* White powder; mp 161–163 °C; IR (KBr, cm^{-1}): 2968, 2251, 1678, 1591, 1489, 1445, 1355, 1299, 1213, 1186, 783, 750, 730; δ_H (500 MHz, $CDCl_3$) 1.23 (s, 9H, 3× CH_3), 4.84 (s, 1H, CH), 5.36 (s, 1H, NCH), 7.10–7.12 (d, *J*=9.0 Hz, 1H, ArH), 7.15–7.22 (m, 3H, ArH), 7.38–7.45 (m, 2H, ArH), 7.47–7.52 (m, 2H, ArH),7.62–7.64 (d, *J*=7.5 Hz, 1H, ArH), 7.81–7.83 (d, *J*=7.5 Hz, 1H, ArH), 7.86–7.88 (d, *J*=8.0 Hz, 1H, ArH), 8.69–8.71 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.7, 43.3, 53.4, 54.9, 60.6, 112.5, 113.1, 115.9, 116.1, 117.0, 117.2, 120.5, 123.4, 123.9, 124.2, 124.8, 125.5, 128.3, 128.9, 129.9, 130.0, 131.4, 131.5, 131.9, 134.7, 134.8, 135.6, 147.0, 162.2, 164.2; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{24}FN_4$, 435.1985; found 435.1975.

4.2.15. (2S,12bS*,E)-3-(tert-Butylimino)-2-(3-chlorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5d**).* White powder; mp 158–160 °C; IR (KBr, cm^{-1}): 2968, 2250, 1673, 1599, 1489, 1444, 1354, 1299, 1213, 1181, 780, 747, 723; δ_H (500 MHz, $CDCl_3$) 1.20 (s, 9H, 3× CH_3), 4.79 (s, 1H, CH), 5.33 (s, 1H, NCH), 7.18 (t, *J*=7.5 Hz, 1H, ArH), 7.25–7.27 (m, 1H, ArH), 7.37–7.44 (m, 5H, ArH), 7.48 (t, *J*=7.5 Hz, 1H, ArH), 7.60–7.61 (d, *J*=7.5 Hz, 1H, ArH), 7.80–7.82 (d, *J*=8.0 Hz, 1H, ArH), 7.85–7.86 (d, *J*=8.0 Hz, 1H, ArH), 8.66–8.68 (d, *J*=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.7 (2C), 43.3, 53.3, 54.9, 60.5, 112.4, 113.1, 120.5, 123.4, 123.8, 124.2, 125.5, 127.0, 128.3, 128.9, 129.0, 129.9, 130.2, 131.0, 131.9, 134.4, 135.6, 135.7, 146.9; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{24}ClN_4$, 451.1689; found 451.1685.

4.2.16. (2S,12bS*,E)-2-(3-Bromophenyl)-3-(tert-butylimino)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5e**).* White powder; mp 154–156 °C; IR (KBr, cm^{-1}): 2967, 2251, 1664, 1592, 1493, 1445, 1361, 1307, 1212, 1187, 782, 755, 730; δ_H (500 MHz, $CDCl_3$) 1.20 (s, 9H, 3× CH_3), 4.79 (s, 1H, CH), 5.33 (s, 1H, NCH), 7.19 (t, *J*=7.5 Hz, 1H, ArH), 7.30–7.36 (m, 2H, ArH), 7.37–7.44 (m, 2H, ArH), 7.49 (t, *J*=8.0 Hz, 1H, ArH), 7.55 (s, 1H, ArH), 7.60 (t, *J*=8.0 Hz, 2H, ArH), 7.80–7.82 (d, *J*=8.0 Hz, 1H, ArH), 7.85–7.86 (d, *J*=8.0 Hz, 1H, ArH), 8.66–8.67 (d, *J*=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.7, 31.9, 43.3, 53.2, 54.9, 60.5, 112.4, 113.0, 120.5, 123.4, 123.7, 123.8, 124.2, 125.5, 127.3, 128.0, 128.3, 128.6, 128.8, 129.9, 131.0, 131.1, 131.9, 132.6, 133.2, 133.4, 134.6, 135.6, 137.2, 146.9, 157.9; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{24}BrN_4$, 495.1184; found 495.1190.

4.2.17. (2R,12bS*,E)-3-(tert-Butylimino)-2-(2-chlorophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5f**).* White powder; mp 158–160 °C; IR (KBr, cm^{-1}): 2970, 2249, 1669, 1600, 1491, 1444, 1359, 1302, 1212, 1181, 776, 749, 730; δ_H (500 MHz, $CDCl_3$) 1.21 (s, 9H, 3× CH_3), 5.39 (s, 1H, CH), 5.41 (s, 1H, NCH), 7.19 (t, *J*=7.5 Hz, 1H, ArH), 7.20–7.25 (m, 1H, ArH), 7.31 (t,

J=8.0 Hz, 1H, ArH), 7.36–7.43 (m, 3H, ArH), 7.49 (t, J=7.5 Hz, 1H, ArH), 7.61–7.63 (m, 2H, ArH), 7.80–7.82 (dd, J_1=7.9 Hz, J_2=1.2 Hz, 1H, ArH), 7.84–7.86 (d, J=8.0 Hz, 1H, ArH), 8.71–8.73 (d, J=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.3, 42.0, 50.6, 54.7, 61.0, 112.3, 113.0, 120.4, 123.5, 123.8, 124.2, 125.6, 128.2, 128.2, 128.3, 128.8, 129.9, 130.0, 131.0, 131.3, 131.9, 135.5, 135.8, 147.3; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{24}ClN_4$, 451.1689; found 451.1675.

4.2.18. (2S,12bS*,E)-3-(tert-Butylimino)-2-(4-nitrophenyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5g**).* Yellow powder; mp 156–158 °C; IR (KBr, cm^{-1}): 2973, 2930, 2250, 2257, 1675, 1601, 1525, 1489, 1444, 1352, 1301, 838, 752, 739, 728; δ_H (500 MHz, $CDCl_3$) 1.19 (s, 9H, 3× CH_3), 4.92 (s, 1H, CH), 5.31 (s, 1H, NCH), 7.22 (t, J=7.5 Hz, 1H, ArH), 7.39–7.44 (q, J=8.0 Hz, 2H, ArH), 7.51 (t, J=7.5 Hz, 1H, ArH), 7.59 (t, J=7.5 Hz, 3H, ArH), 7.82–7.84 (d, J=8.0 Hz, 1H, ArH), 7.87–7.88 (d, J=7.5 Hz, 1H, ArH), 8.34–8.36 (d, J=8.5 Hz, 2H, ArH), 8.66–8.67 (d, J=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 31.7, 43.0, 53.1, 55.0, 60.5, 112.2, 112.6, 120.4, 123.3, 123.9, 124.1, 124.3, 124.8, 125.5, 128.4, 128.9, 129.5, 130.1, 131.8, 135.3, 139.4, 146.2, 148.7; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{24}N_5O_2$, 462.1930; found 462.1946.

4.2.19. (2S,12bS*,E)-3-(tert-Butylimino)-2-(p-tolyl)-2,3-dihydropyrrolo[1,2-f]phenanthridine-1,1(12bH)-dicarbonitrile (**5h**).* White powder; mp 162–164 °C; IR (KBr, cm^{-1}): 2969, 2926, 2250, 2227, 1671, 1632, 1490, 1444, 1357, 1302, 823, 750, 728; δ_H (500 MHz, $CDCl_3$) 1.21 (s, 9H, 3× CH_3), 2.38 (s, 3H, CH_3), 4.81 (s, 1H, CH), 5.33 (s, 1H, NCH), 7.19 (t, J=7.0 Hz, 1H, ArH), 7.20–7.26 (m, 2H, ArH), 7.27–7.42 (m, 4H, ArH), 7.49 (t, J=7.0 Hz, 1H, ArH), 7.62–7.63 (d, J=7.5 Hz, 1H, ArH), 7.80–7.82 (dd, J_1=8.0 Hz, J_2=1.2 Hz, 1H, ArH), 7.85–7.86 (d, J=8.0 Hz, 1H, ArH), 8.73–8.74 (d, J=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 21.3, 31.7, 43.4, 53.8, 54.8, 60.5, 112.8, 113.6, 120.4, 123.4, 123.6, 123.8, 124.2, 125.6, 128.2, 128.7, 128.8, 129.3, 129.8, 130.2, 130.4, 130.9, 132.0, 136.0, 140.0, 148.0, 159.8; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{29}H_{27}N_4$, 431.2236; found 431.2245.

4.2.20. Ethyl 2-((E)-((2S,12bS*)-1,1-dicyano-2-phenyl-1,12b-dihydropyrrolo[1,2-f]phenanthridin-3(2H)-ylidene)amino)acetate (**6a**).* White powder; mp 172–174 °C; IR (KBr, cm^{-1}): 1747, 1672, 1490, 1445, 1381, 1369, 1196, 1070, 1049, 749, 704; δ_H (500 MHz, $CDCl_3$) 1.24 (t, J=7.5 Hz, 3H, CH_3), 4.09 (d, J=22.0 Hz, 1H, =NCH_2), 4.11 (d, J=22.0 Hz, 1H, =NCH_2), 4.12 (q, J=7.5 Hz, 2H, OCH_2), 4.88 (s, 1H, CH), 5.61 (s, 1H, NCH), 7.25–7.27 (m, 2H, ArH), 7.38–7.45 (m, 2H, ArH), 7.49–7.52 (m, 4H, ArH), 7.64–7.66 (d, J=9.0 Hz, 1H, ArH), 7.83–7.85 (d, J=9.5 Hz, 1H, ArH), 7.90–7.92 (d, 1H, J=8.0 Hz, ArH), 9.02–9.03 (d, 1H, J=8.5 Hz, ArH); δ_C (125 MHz, $CDCl_3$) 14.1, 43.3, 52.7, 53.3, 61.1, 63.2, 112.3, 113.0, 120.6, 123.7, 123.9, 124.2, 124.7, 125.3, 128.5, 128.8, 129.3, 129.8, 130.0, 130.1, 130.4, 131.6, 135.2, 156.6, 170.1; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{23}N_4O_2$, 447.1821; found 447.1832.

4.2.21. Ethyl 2-((E)-((2S,12bS*)-1,1-dicyano-2-(4-fluorophenyl)-1,12b-dihydropyrrolo[1,2-f]phenanthridin-3(2H)-ylidene)amino)acetate (**6b**).* White powder; mp 177–179 °C; IR (KBr, cm^{-1}): 1750, 1670, 1603, 1511, 1447, 1384, 1369, 1225, 1183, 1162, 1071, 1051, 848, 792, 755, 723; δ_H (500 MHz, $CDCl_3$) 1.25 (t, J=7.0 Hz, 3H, CH_3), 4.04 (d, J=16.50 Hz, 1H, =NCH_2), 4.12 (d, J=16.50 Hz, 1H, =NCH_2), 4.15 (q, J=7.0 Hz, 2H, OCH_2), 4.89 (s, 1H, CH), 5.57 (s, 1H, NCH), 7.20 (t, J=8.5 Hz, 2H, ArH), 7.24–7.27 (m, 1H, ArH), 7.38–7.41 (m, 2H, ArH), 7.42–7.46 (m, 2H, ArH), 7.53 (t, J=7.5 Hz, 1H, ArH), 7.63–7.65 (d, J=7.5 Hz, 1H, ArH), 7.83–7.84 (d, J=8.0 Hz, 1H, ArH), 7.90–7.91 (d, 1H, J=7.5 Hz, ArH), 9.00–9.02 (d, 1H, J=8.5 Hz, ArH); δ_C (125 MHz, $CDCl_3$) 14.2, 43.3, 52.4, 52.7, 61.2, 63.1, 112.3, 112.9, 117.1, 117.3, 120.6, 123.7, 123.9, 124.2, 124.8, 125.3, 126.1, 128.5, 129.3, 129.6, 130.2, 130.8 (2C), 131.5, 135.1, 156.3, 162.6, 164.6, 170.0; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{22}FN_4O_2$, 465.1727; found 465.1741.

4.2.22. Ethyl 2-((E)-((2S,12bS*)-1,1-dicyano-2-(3-fluorophenyl)-1,12b-dihydropyrrolo[1,2-f]phenanthridin-3(2H)-ylidene)amino)acetate (**6c**).* White powder; mp 169–171 °C; IR (KBr, cm^{-1}): 1751, 1674, 1591, 1489, 1446, 1368, 1302, 1192, 1048, 786, 754, 721; δ_H (500 MHz, $CDCl_3$) 1.25 (t, J=7.0 Hz, 3H, CH_3), 4.05 (d, J=17.0 Hz, 1H, =NCH_2) 4.12 (d, J=17.0 Hz, 1H, =NCH_2), 4.14 (q, J=7.0 Hz, 2H, OCH_2), 4.90 (s, 1H, CH), 5.60 (s, 1H, NCH), 7.10–7.12 (d, J=9.0 Hz, 1H, ArH), 7.20–7.26 (m, 3H, ArH), 7.44–7.46 (m, 2H, ArH), 7.49–7.53 (m, 2H, ArH), 7.63–7.65 (d, J=8.0 Hz, 1H, ArH), 7.83–7.84 (d, J=8.0 Hz, 1H, ArH), 7.90–7.91 (d, J=8.0 Hz, 1H, ArH), 8.98–9.00 (d, J=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 14.2, 43.1, 52.7, 52.8, 61.3, 63.2, 112.1, 112.8, 115.9, 116.0, 117.6, 117.8, 120.7, 123.7, 123.9, 124.2, 124.7, 124.9, 125.3, 128.6, 129.4, 129.6, 130.2, 131.5, 131.8, 131.9, 132.4, 132.5, 135.0, 156.0, 162.2, 164.2, 170.0; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{22}FN_4O_2$, 465.1727; found 465.1750.

4.2.23. Ethyl 2-((E)-((2S,12bS*)-2-(3-chlorophenyl)-1,1-dicyano-1,12b-dihydropyrrolo[1,2-f]phenanthridin-3(2H)-ylidene)amino)acetate (**6d**).* White powder; mp 174–176 °C; IR (KBr, cm^{-1}): 1740, 1660, 1600, 1491, 1445, 1369, 1303, 1190, 1101, 1040, 753, 713; δ_H (500 MHz, $CDCl_3$) 1.26 (t, J=7.5 Hz, 3H, CH_3), 4.08 (d, J=17.0 Hz, 1H, =NCH_2), 4.12 (d, J=17.0 Hz, 1H, =NCH_2), 4.15 (q, J=7.5 Hz, 2H, OCH_2), 4.87 (s, 1H, CH), 5.61 (s, 1H, NCH), 7.25–7.30 (m, 2H, ArH), 7.38 (s, 1H, ArH), 7.44–7.54 (m, 5H, ArH), 7.63–7.65 (d, J=7.5 Hz, 1H, ArH), 7.83–7.85 (dd, J_1=8.0 Hz, J_2=1.2 Hz, 1H, ArH), 7.90–7.92 (d, J=7.5 Hz, 1H, ArH), 8.97–8.99 (d, J=8.0 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 14.2, 43.2, 52.6, 52.8, 61.2, 63.2, 112.1, 112.8, 123.7, 123.9, 124.2, 124.9, 125.3, 127.0, 128.6, 128.9, 129.4, 129.5, 130.2, 130.7, 131.3, 131.5, 135.0, 136.0, 155.9, 169.9; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{22}ClN_4O_2$, 481.1431; found 481.1451.

4.2.24. Ethyl 2-((E)-((2R,12bS*)-1,1-dicyano-2-(2-fluorophenyl)-1,12b-dihydropyrrolo[1,2-f]phenanthridin-3(2H)-ylidene)amino)acetate (**6e**).* White powder; mp 175–177 °C; IR (KBr, cm^{-1}): 1747, 1674, 1602, 1492, 1446, 1383, 1293, 1196, 1097, 1070, 1049, 769, 752, 724; δ_H (500 MHz, $CDCl_3$) 1.28 (t, J=7.5 Hz, 3H, CH_3), 3.68 (d, J=18.0 Hz, 1H, =NCH_2), 3.94 (d, J=18.0 Hz, 1H, =NCH_2), 4.15 (q, J=7.5 Hz, 2H, OCH_2), 5.22 (s, 1H, CH), 5.61 (s, 1H, NCH), 7.23–7.27 (m, 3H, ArH), 7.32 (t, J=9.0 Hz, 1H, ArH), 7.42–7.46 (q, J=7.5 Hz, 2H, ArH), 7.51–7.54 (m, 2H, ArH), 7.64–7.66 (d, J=8.0 Hz, 1H, ArH), 7.82–7.84 (d, J=8.0 Hz, 1H, ArH), 7.90–7.91 (d, J=8.0 Hz, 1H, ArH), 9.01–9.05 (d, J=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 14.1, 42.5, 46.8, 52.8, 61.1, 63.5, 112.1, 112.7, 116.9, 117.0, 118.0, 120.6, 123.7, 123.9, 124.2, 124.8, 125.2, 125.5, 128.5, 129.3, 129.6, 130.2, 131.5, 132.6, 135.2, 155.7, 160.0, 162.0, 169.9; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{22}FN_4O_2$, 465.1727; found 465.1740.

4.2.25. Ethyl 2-((E)-((2R,12bS*)-2-(2-chlorophenyl)-1,1-dicyano-1,12b-dihydropyrrolo[1,2-f]phenanthridin-3(2H)-ylidene)amino)acetate (**6f**).* White powder; mp 167–169 °C; IR (KBr, cm^{-1}): 2253, 1743, 1672, 1602, 1492, 1445, 1383, 1369, 1303, 1197, 1071, 1049, 768, 753, 731; δ_H (500 MHz, $CDCl_3$) 1.27 (t, J=7.0 Hz, 3H, CH_3), 3.96 (d, J=17.0 Hz, 1H, =NCH_2), 4.10 (d, J=17.0 Hz, 1H, =NCH_2), 4.17 (q, J=7.0 Hz, 2H, OCH_2), 5.46 (s, 1H, CH), 5.67 (s, 1H, NCH), 7.26–7.28 (m, 2H, ArH), 7.30–7.39 (m, 1H, ArH), 7.45–7.50 (m, 3H, ArH), 7.54–7.57 (m, 1H, ArH), 7.68–7.69 (m, 2H, ArH), 7.86–7.87 (d, J=7.5 Hz, 1H, ArH), 7.93–7.95 (d, J=8.0 Hz, 1H, ArH), 9.07–9.09 (d, J=8.5 Hz, 1H, ArH); δ_C (125 MHz, $CDCl_3$) 14.1, 42.0, 50.1, 52.8, 61.0, 63.6, 111.9, 112.7, 120.6, 123.8, 124.1, 124.7, 125.2, 128.0, 128.2, 128.4, 128.6, 129.2, 129.5, 130.1, 131.0, 131.4, 131.7, 135.1, 135.7, 156.3, 169.8; HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{28}H_{22}ClN_4O_2$, 481.1431; found 481.1440.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.03.085.

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24. Crystallographic data for **4a**, **5e**, and **6f** have been deposited in the Cambridge Crystallographic Data Centre with the deposition numbers CCDC 783837, 795218, and 795217, respectively. Copies of these data can be obtained free of charge via www.ccdc.cam.ac.uk (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; fax: +44-(0)1223-336033; or e-mail: deposit@ccdc.cam.ac.uk).
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