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Green methodology in diastereoselective one-pot synthesis of dicyano tetrahydropyrrolo 1,10-phenanthrolines

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Abstract: A green methodology in solvent –free condition has developed for synthesis of new pyrrolo phenanthrolines in high yields. The use of this green method improves the reaction performance and provides benefit like replacement of hazardous chemicals. The structures of compounds were established from spectroscopic data and melting points.

Keywords: Pyrrolo phenanthroline, Knoevenagel condensation, Green chemistry, Solvent free, Base.

Introduction

The synthesis of novel heterocycles has become the cornerstone of synthetic organic chemistry[1]. Exploitation of these heterocycles should allow the synthetic chemist to rapidly discover methodology for the preparation of complex molecules in a shorter time scale [2,3]. In the last decade, interest in substituted [1,10]phenanthrolines has been increased and, as result, chemistry, synthetic methods and properties of these *N*-heterocycles have been studied by several groups[4-6]. These polycyclic compounds are very interesting molecules not only from chemical properties: aromaticity,[7] basicity[8] and chelating capability,[9] but also for their biological[10] and industrial[11] application.

For instance some soluble pyrrolo[1,2-*a*][1,10]phenanthroline derivatives are very promising candidates for use in organic light emitting diodes (OLEDs)[12].

Owing to the increasing importance of these N-heterocycles in the field of biology and technology, we succeed in contribution of 1,10-phenanthrolinium *N*-ylide, in a multi-component one-pot diastereoselective Knoevenagel condensation [13,14,15].

Recently green chemistry is placed in the frontier areas of research and has been focused for considerable [16,17]. For instance solvent-free reactions using either organic or inorganic solid supports have received increasing attention. Grindstone Chemistry is a branch of green chemistry for solvent-free chemical reactions which can be probably conducted in high yield by just grinding solid/solid, solid/liquid, or even liquid/liquid together [18,19] .There are several advantages to performing synthesis in dry media: (i) short reaction times, (ii) increased safety, (iii) economic advantages due to the absence of solvent. Because of environmental concerns and increased restrictions on the use of hazardous organic solvents, it has recently become of significant interest to develop reactions in solvent-free method, which is an environmentally benign protocol [20,21].

In continuing our interest in [1,10]phenanthroline reactions we now report one efficient and clean

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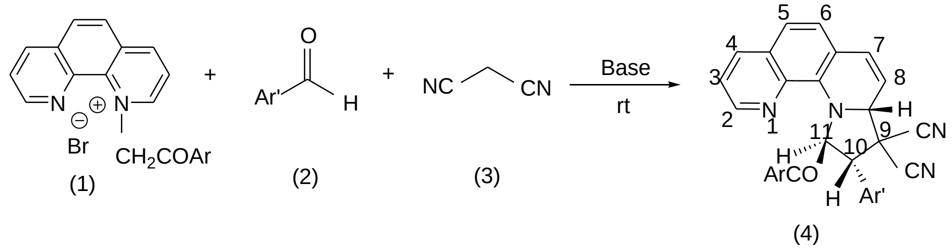
*Corresponding author. Tel: (+98) 34 41523307, Fax: (+98) 34 41523307, E-mail: tahamipour@yahoo.com synthetic route for pyrrolo phenanthrolines in good yield.

Results and discussion

We observed that three-component reaction of 1-phenacyl-1,10-phenanthrolinium bromide **1**, aromatic aldehydes **2** and CH acids such as malonitrile **3** in the presence of triethylamine as base, in green methodology, afforded chiefly a single diastereoisomer of trihydropyrrolo[1,2-*a*][1,10] phenanthroline derivatives **4a-h** as new macromolecules in excellent yields (Scheme **1**).



Ar=phenyl, 4-Methylphenyl

Ar'=4-pyridyl, Phenyl, 3-Pyridyl, 3-Chlorophenyl, 1-Naphthyl

Scheme 1: Reaction of 1-(phenacyl)-1,10-phenanthrolinium bromides 1, with aromatic aldehydes 2 and malonitrile 3.

In attempts to synthesize these new heterocycles we have reported a green method under solvent–free conditions using basic catalysts.

At first we examined different basic catalyst such as triethyl amine, DABCO, K_2CO_3, $Mg(OH)_2$, NaOH as catalyst (Table **1**).

Table 1: effect of different base on reaction.

Base	Yields (%)	Time/min
Et_3N	90	15
DABCO	85	15
K_2CO_3	30	60
$Mg(OH)_2$	35	60
NaOH	90	55

It's clear that lewis base such as triethyl amine and DABCO are good basic catalyst. Also NaOH is good basic catalyst but the reaction took about one hours to complete. In the presence of weak base the reaction gave poor yields.

To establish the generality of this process, various aldehydes were treated with malonitrile in solid state at room temperature (Table **2**).

All of the aldehydes gave expected products in quantitative yields and purity. The isolated product was completely characterized by IR, ^{1}H NMR and elemental analyses. The melting points of the known compounds were in agreement with those of literature reported.

Conclusion

This reaction is very clean, without any side product in every run. Also work-up procedure is done by washing with water. Therefore, the products obtained in high purity with remarkable yields and do not require any chromatographic separation.

Table 2: Synthesis of dicyano tetrahydropyrrolo 1,10-phenanthrolines using basic catalyst.

Entry	Ar	Ar'	Yield%	m.p(°C) obs	mp (° C) (ref)
a	Phenyl	Phenyl	87	162-164	163-165(14)
b	Phenyl	4-Pyridyl	85	152-154	154-156(15)
c	Phenyl	3-Chlorophenyl	88	150-152	149-151(14)
d	Phenyl	3-Pyridyl	86	153-155	153-155(14)

e	4- Methylphenyl	3- Methyl	85	148-150	147-149(13)
f	4- Methylphenyl	Phenyl	85	139-141	138-140(13)
g	4- Methylphenyl	3-Chlorophenyl	88	142-144	141-143(15)
h	4- Methylphenyl	1-Naphthyl	85	141-143	140-142(15)

Experimental

Melting points and IR spectra of all compounds were measured on an Electro thermal 9100 apparatus and a JASCO FT-IR spectrometer, respectively. Also, the ^{1}H and ^{13}C NMR spectra were obtained with a BRUKER DRX-500 AVANCE instrument using $CDCl_3$ as the applied solvent and TMS as internal standard at 500.1 and 125.8 MHz, respectively. Malonitrile, and aldehyde derivatives were purchased from Merck companies and used without further purification. 1-phenacyl-1,10-phenanthrolinium bromide , prepared according to literatures [6].

General synthetic procedure exemplified by 9,9-dicyano-11-benzoyl-10-phenyl-8a,9,10,11-tetrahydro pyrrolo[1,2-a][1,10] phenanthroline (4a):

A mixture of 1,10-phenanthrolinium bromide (2 mmol, 0.75g) benzaldehyde (2.2 mmol, 0.23g) malonitrile (2.2mmol, 0.14g) and triethylamine (2.5 mmol, 0.25g) or another base was added and the mixture was pulverized in a mortar (or the mixture can be also stirred by a magnet in a test tube) at room temperature. Then the reaction was continued and a color change occurred from yellow to brown. The reaction was monitored in TLC. After completion of reaction, the residue washed with water and air dried to afford desired product.

Yellow crystal 87% yield, (0.75g), mp: 162-164 °C, IR (KBr) (ν_{max}, cm^{-1}): 1454 (s, C=C), 1688(s, C=O), 2247 (m, CN). ^{1}H NMR (500.1MHz; $CDCl_3$): δ_H 3.81 (1H, d, J = 8.3 Hz, C-10-H), 5.93 (1H, dd, J_1 = 9.9, J_2 = 1.8 Hz, C-8-H), 6.26 (1H, dd, J_1 = 1.8, J_2 = 1.4 Hz, C-8a-H), 6.71 (1H, d, J = 8.3 Hz, C-11-H), 6.84(1H, dd, Hz, C-7-H), 7.02 (1H, C-3-H), 7.12 (1H, C-5-H), 7.20 (1H, C-6-H), 7.29-7.33 (2H, m, C-3'-H, C-5'-H), 7.39-7.42 (3H, m, C-2'-H, C-6'-H, C-4'-H), 7.46-7.49 (2H, m, C-3''-H, C-5''-H), 7.53-7.54 (1H, m, C-4''-H), 7.55 (1H, C-2-H), 7.71 (2H, d, C-2''-H, C-6''-H), 7.91 (1H, dd, J_1 = 8.1, J_2 = 1.3 Hz, C-4-H).

9,9-dicyano-11-benzoyl-10-(4-pyridyl)-8a,9,10,11-tetrahydropyrrolo[1,2-a][1,10] phenanthroline (4b):

This compound was obtained as dark yellow powder in 88% yield (0.75g), mp: 152-154 °C, IR (KBr) (ν_{max}, cm^{-1}): 1455 (s, C=C), 1655(s, C=O), 2248 (m, CN). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.72 (d, 1H, J = 8.4 Hz, C-10-H), 5.90 (dd, 1H, J_1 = 9.9, J_2 = 2.0 Hz, C-8-H), 6.22 (dd, 1H, J_1 = 2.0, J_2 = 1.59 Hz, C-8a-H), 6.70 (d, 1H, J = 8.4 Hz, C-11-H), 6.83 (dd, 1H, J_1 =9.9, J_2 = 1.59 Hz, C-7-H), 7.02 (dd, 1H, J_1 = 8.4, J_2 = 4.1 Hz, C-3-H), 7.11 (d, 1H, J = 8.2 Hz, C-5-H), 7.17 (d, 1H, J = 8.2 Hz, C-6-H), 7.29-7.33 (m, 2H, C-3''-H, C-5''-H), 7.44 (d, 2H, J = 5.9 Hz, C-6'-H, C-2'-H), 7.46-7.49 (m, 1H, C-4''-H), 7.51 (dd, 1H, J_1 = 4.1, J_2 = 1.46 Hz, C-2-H), 7.68 (d, 2H, J = 7.3 Hz, C-2''-H, C-6''-H), 7.89 (dd, 1H, J_1 = 8.2, J_2 = 1.46 Hz, C-4-H), 8.63 (d, 2H, J = 5.9 Hz, C-3'-H, C-5'-H).

9,9-Dicyano-11-benzoyl-10-(3-chlorophenyl)-8a,9,10, 11-tetrahydropyrrolo[1,2-a][1,10]phenanthroline (4c):

This compound was obtained as bright yellow crystal in 86% yield, (0.83g), mp: 150-152 °C. IR (KBr) (ν_{max}, cm^{-1}): 1459 (s, C=C), 1683 (s, C=O), 2245 (m, CN) .^{1}H NMR (500.1 MHz, $CDCl_3$): 3.76 (1H, d, J = 8.4 Hz, C-10-H), 5.92 (1H, dd, J_1 = 9.9, J_2 = 2.0 Hz, C-8-H) 6.26(1H, dd, J_1 = 2.0, J_2 = 1.6 Hz, C-8a-H), 6.69 (1H, d, J = 8.4 Hz, C-11-H), 6.84 (1H, dd, C-7-H), 7.02 (1H, dd, C-3-H), 7.12 (1H, d, C-5-H), 7.19 (1H, d, C-6-H), 7.33-7.35 (3H, m, C-3''-H, C-5''-H, C-6'-H), 7.40-7.41 (1H, m, C-5'-H), 7.45-7.46 (1H, m, C-4''-H), 7.50 (1H, dd, C-2-H), 7.51-7.53 (2H, m, C-2'-H, C-4'-H), 7.73 (2H, d, C-2''-H, C-6''-H), 7.91 (1H, dd, J_1= 8.1, J_2=1.4 Hz, C-4-H) .

9,9-Dicyano-11-benzoyl-10-(3-pyridyl)-8a,9,10,11-tetrahydropyrrolo[1,2-a][1,10]phenanthroline (4d):

This compound was obtained as dark yellow crystal in 85% yield (0.75g) mp:153-155 °C, IR (KBr) (ν_{max}, cm^{-1}): 1450 (s, C=C), 1679(s, C=O), 2248 (w, CN). ^{1}H NMR (500.1 MHz, $CDCl_3$): 3.81 (1H, d, J = 8.5 Hz, C-10-H), 5.93 (1H, dd, J_1 = 9.9, J_2 = 2.1 Hz, C-8-H), 6.27 (1H, dd, J_1 = 2.1, J_2 = 1.4 Hz, C-8a-H) 6.71(1H, d, J = 8.5 Hz, C-11-H), 6.85(1H, dd, C-7-H), 7.04 (1H, dd, C-3-H), 7.13 (1H, d, C-5-H), 7.20 (1H, d, C-6-H), 7.32-7.35 (2H, m, C-3''-H, C-5''-H), 7.38-7.39 (1H, m, C-5'-H), 7.48-7.49 (1H, m, C-4''-H), 7.53 (1H, dd, C-2-H), 7.71 (2H, d, C-2''-H, C-6''-H), 7.92 (1H, dd, C-4-H), 7.99 (1H, d, C-6'-H), 8.66-8.68 (2H, m, H-2', H-4') .

9,9-Dicyano-10-(3-methylphenyl)-11-(4-methyl benzoyl)-8a,10,11-tetrahydro pyrrolo [1,2-a][1,10] phenanthroline, (4e):

This compound was obtained as bright yellow powder in 85% yield (0.78g), mp: 148-150 °C, IR (KBr) (ν_{max}, cm^{-1}): 1453, 1606 (s, C=C), 1686 (s, C=O), 2245 (m, CN). ^1H NMR (500.1 MHz, $CDCl_3$): δ_H 2.37(3H, s, CH_3), 2.39 (3H, s, CH_3), 3.77 (1H, d, *J* = 8.4 Hz, C-10-H), 5.91 (1H, dd, J_1 = 9.9, J_2 = 2.2 Hz, C-8-H) 6.26 (1H, dd, J_1 = 2.2, J_2 = 1.6 Hz, C-8a-H), 6.71 (1H, d, *J* = 8.4 Hz, C-11-H), 6.82 (1H, dd, J_1 =9.9, J_2 = 1.6 Hz, C-7-H), 7.01 (1H, dd, J_1 = 8.2, J_2 = 4.1 Hz, C-3-H), 7.10 (2H, d, J_2 = 8.0 Hz, C-3''-H, C-5''-H), 7.12 (1H, d, *J* = 8.2 Hz, C-5-H), 7.17 (1H, d, *J* = 8.2 Hz, C-6-H), 7.23(1H, d, *J*=7.7, C-4'-H), 7.29-7.31 (2H, m, C-2'-H, C-5'-H), 7.38 (1H, d, *J*=7.8, C-6'-H), 7.49 (1H, dd, J_1 = 4.1, J_2 = 1.46 Hz, C-2-H), 7.62 (2H, d, *J* = 8.0 Hz, C-2''-H, C-6''-H), 7.88 (1H, dd, J_1 = 8.2 , J_2 = 1.46 Hz, C-4-H).

9,9-dicyano-10-(phenyl) -11-(4-methylbenzoyl)-8a,10, 11-tetrahydropyrrolo[1,2-a][1,10]phenanthroline (4f):

This compound was obtained as bright orange powder in 85% yield, (0.78g), mp: 139-141 °C, IR (KBr) (ν_{max}, cm^{-1}): 1453, 1605 (s, C=C), 1686(s, C=O), 2247 (m, CN). ^1H NMR (500.1MHz; $CDCl_3$): δ_H 2.38 (3H, s, CH_3), 3.81 (1H, d, *J* = 8.3 Hz, C-10-H), 5.92 (1H, dd, J_1 = 9.9, J_2 = 2.2 Hz, C-8-H), 6.27 (1H, dd, J_1 = 2.2, J_2 = 1.4 Hz, C-8a-H), 6.73 (1H, d, *J* = 8.4 Hz, C-11-H), 6.84 (1H, dd, J_1 = 9.9, J_2 = 1.4 Hz, C-7-H), 7.02 (1H, dd, J_1 = 8.2, J_2 = 3.8 Hz, C-3-H), 7.11(2H, m, C-3''-H, C-5''-H), 7.12 (1H, d, *J* = 8.2 Hz, C-5-H), 7.18 (1H, d, *J* = 8.2 Hz, C-6-H), 7.40-7.43 (3H, m, C-3'-H, C-4'-H, C-5'-H), 7.51 (1H, dd, J_1 = 3.8 , J_2 = 1.3 Hz, C-2-H), 7.55-7.57(2H, m, C-2'-H, C-6'-H), 7.62 (2H, d, J_1 = 7.2 Hz, C-2''-H, C-6''-H), 7.88 (1H, dd, J_1 = 8.1, J_2 = 1.3 Hz, C-4-H).

9,9-Dicyano-10-(3-chlorophenyl)-11-(4-methylbenzoyl)-8a,10,11-tetrahydropyrrolo[1,2-a][1,10]phenanthroline (4g):

This compound was obtained as dark yellow powder in 88% yield (0.96 g), mp: 142-144 °C, IR (KBr) (ν_{max}, cm^{-1}): 1125, 1282 (s, C-O), 1454, 1509 (s, C=C), 1686 (s, C=O ketone), 2203 (m, CN). ^1H NMR (500 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 3.77 (d, 1H, *J* = 8.4 Hz, C-10-H), 5.91 (dd, 1H, J_1 = 9.9, J_2 = 2.2 Hz, C-8-H), 6.25 (dd, 1H, J_1 = 2.2, J_2 = 1.6 Hz, C-8a-H), 6.70 (d, 1H, *J* = 8.4 Hz, C-11-H), 6.83 (dd, 1H, J_1 =9.9, J_2 = 1.6 Hz, C-7-H), 7.03 (dd, 1H, J_1 = 8.2, J_2 = 4.1 Hz, C-3-H), 7.10 (d, 2H, J_2 = 8.0 Hz, C-3''-H, C-5''-H), 7.12-7.18 (m, 2H, C-5-H, C-6-H), 7.29-7.47 (m, 4H, C-2'-H, C-4'-H, C-5'-H, C-6'-H), 7.54 (dd, 1H, J_1 = 4.1, J_2 = 1.46 Hz, C-2-H), 7.63 (d, 2H, *J* = 8.0 Hz, C-2''-H, C-6''-H), 7.90 (dd, 1H, J_1 = 8.2, J_2 = 1.46 Hz, C-4-H).

9,9-Dicyano-10-(1-naphthyl)-11-(4-methylbenzoyl)-8a, 10,11-tetrahydropyrrolo [1,2-a][1,10] phenanthroline (4h):

This compound was obtained as dark yellow powder in 85% yield (0.95g), mp: 141-143 °C, IR (KBr) (ν_{max}, cm^{-1}): 1124, 1290 (s, C-O), 1454, 1509 (s, C=C), 1674 (s, C=O ketone), 2248 (m, CN). ^1H NMR (500 MHz, $CDCl_3$): δ 2.25 (s, 1H, CH_3), 4.94 (d, 1H, *J* = 8.4 Hz, C-10-H), 5.96 (dd, 1H, J_1 = 9.9, J_2 = 2.2 Hz, C-8-H), 6.48 (dd, 1H, J_1 = 2.2, J_2 = 1.6 Hz, C-8a-H), 6.85 (dd, 1H, J_1 =9.9, J_2 = 1.6 Hz, C-7-H), 6.93 (d, 1H, *J* = 8.4 Hz, C-11-H), 6.95(d, 2H, J_2 = 8.0 Hz, C-3''-H, C-5''-H), 7.02 (dd, 1H, J_1 = 8.3, J_2 = 4.1 Hz, C-3-H), 7.13(d, 1H, *J* = 8.2 Hz, C-5-H), 7.20 (d, 1H, *J* = 8.2 Hz, C-5-H), 7.49-7.58 (m, 5H, 5H naphthyl), 7.64(dd, 1H, J_1 = 3.5, J_2 = 1.4 Hz, C-2-H), 7.87 (m, 1H, 1H naphthyl), 7.93 (d, 2H, *J* = 8.0 Hz, C-2''-H, C-6''-H), 8.06(m, 1H, 1H naphthyl), 8.17(dd, 1H, J_1 = 8.2, J_2 = 1.46 Hz, C-4-H).

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