Iranian Journal of Organic Chemistry Vol. 8, No. 3 (2016) 1859-1863

Efficient one-pot synthesis of new derivatives of 1,7-phenanthrolines at room temperature

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Received: July 2016; Revised: July 2016; Accepted: September 2016

Abstract: A new class of N-heterocyclic compounds has been isolated in excellent yields from the 1:1:1 addition reaction between 1,7-phenanthroline and acetylenic esters such as dialkyl acetylenedicaboxylates in the presence of heterocyclic CH compound, 1,3- dimethyl barbituric acid. The structures of compounds were confirmed by elemental analyses, mass, IR, ^{1}HNMR and^{13}CNMR spectra.

Keywords: 1,7-Phenanthroline, 1,3- Dimethyl barbituric acid, Dialkyl acetylenedicarboxylate, Three component, Macromolecules.

Introduction

The development of simple synthetic routes for widely used organic compounds from readily available reagents is one of the major tasks in organic chemistry [1]. Nowadays heterocycles have received considerable attention in the literatures as a consequence of their exciting biological properties and their role as pharmacophores [2-4]. Among heterocycles, the five- and six-membered N-heterocycles are one of the most common structural motifs, spread across natural products, from simple alkaloid to complex biologically compounds[5,6]. In recent years, much attention has been focused on multi-component reactions (MCRs);specially the reactions between N-heterocycles ,acetylenic esters and NH or CH acid has been accomplished [7-9].These reactions prove a very elegant and economic way to build up complex structures in a single synthetic operation from simple starting materials, most of the time in one-pot [10,11].

Bridgehead N-heterocycles have been the subject of great consideration because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activity [12]. For example, the esters of pyrrole-2-carboxylic acids have been extensively utilized as intermediates in the total synthesis of porphyrins[13].

Phenanthrolines are important core structures found in a variety of organic products and biologically important molecules with a wide range of biological activities and applications, including antibacterial, anticancer, antimicrobial, anti-inflammatory, antiviral, antioxidant and also with industrial applications [14-16]. While a variety of new substituted derivatives of 1,10-phenanthrolines have been synthesized and characterized ,there are a few report of 1,7-phenanthrolinederivatives in literatures[17,18].

Owing to the increasing importance of these N-heterocycles in the field of technology, the synthesis of new derivatives of these heterocycles is highly desirable. In continuing our interest in [1,10]

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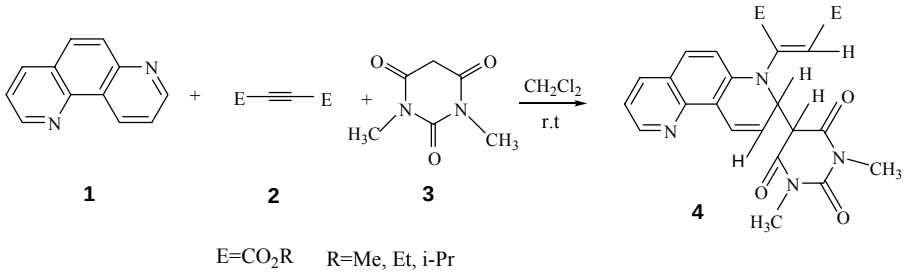
phenanthroline [19-24] and 1,7-phenanthroline reactions [25], herein, we report the first multi component reaction of 1,7-phenanthrolines with acetylenic esters and CH acid compound. We succeed in contribution of 1,7-phenanthrolinium in a multi-component one-pot condensation at room temperature to give novel stable macromolecules (Scheme **1**).

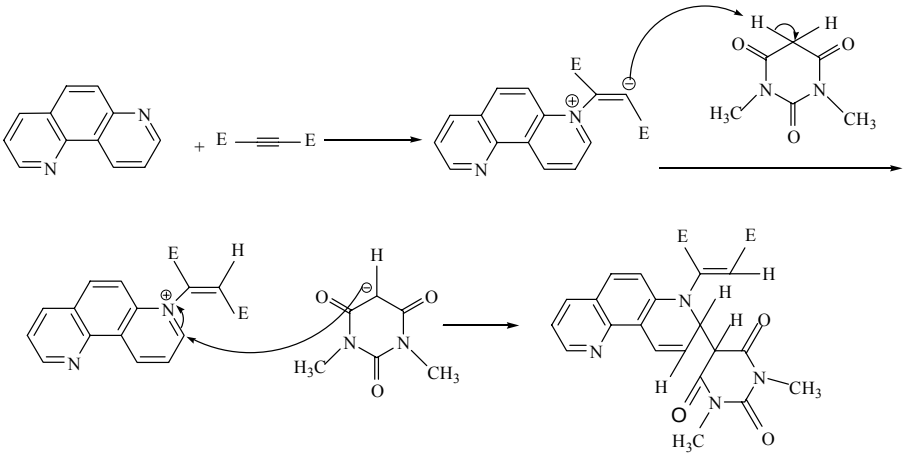


Scheme 1: Reaction of 1,7-phenanthrolines with acetylenic esters and CH acid.

Results and discussion

An efficient synthesis of a new class of N-heterocycles from reaction between 1,7-phenanthroline**1**and activated acetylenic esters **2** in the presence of heterocyclic CH acid compound such as 1,3-dimethylbarbituric acid **3** was undertaken at ambient temperature. Reactions were carried out by first mixing the 1, 7-phenanthroline and 1, 3-dimethylbarbituric acid and then the acetylenic ester was added slowly.

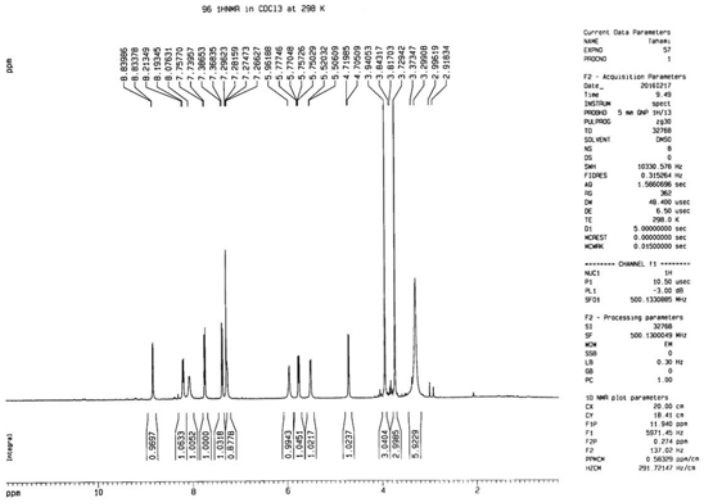
The proposed mechanism is showed in Scheme **2**. At first, 1, 7-phenanthroline reacts with acetylenic ester to give a zwitterion, which react with acidic hydrogen. Then stable anionic component attacked to intermediate to attain desired product.



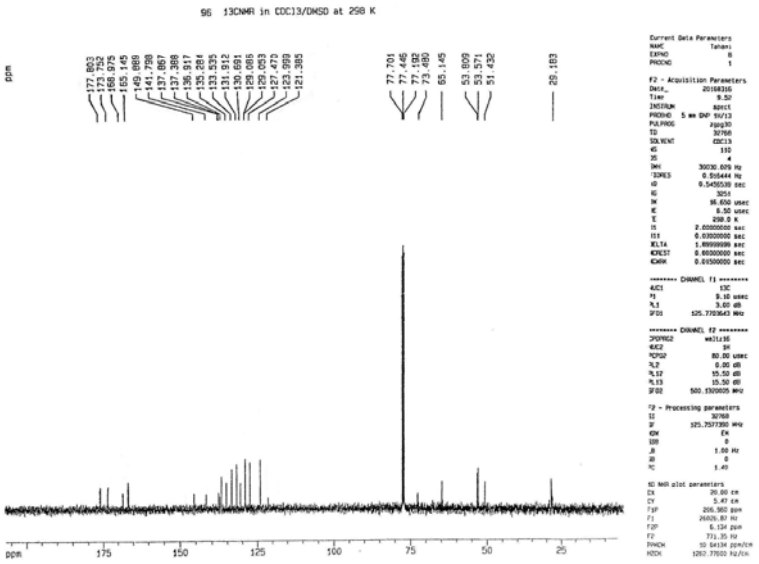
Scheme 2: Proposed mechanism for formation of product.

The structures of compounds were confirmed by elemental analyses, mass, IR, ^{1}H NMR and ^{13} CNMR spectra.

The ^{1}HNMR spectrum of **4a** presented in Scheme 3, exhibited two distinct signals at 3.29 and 3.37 arising from two "N-CH_3" groups. Also four characteristic signals at 4.70, 5.51, 5.76, and 5.96 arising from four C-H that confirm proposed structure. In ^{13}CNMR spectrum of **4a** presented in Scheme **4**, the close values of the chemical shifts at 149.88, 165.14, 168.97 of the three carbonyl groups of barbituric acid and 173.75,177.80 of two ester groups of acetylenic esters, represent strong evidence that they are grafted on compound. Also the ^{13}CNMR spectrum showed 11 distinct resonances in aromatic area in agreement with the proposed structure.

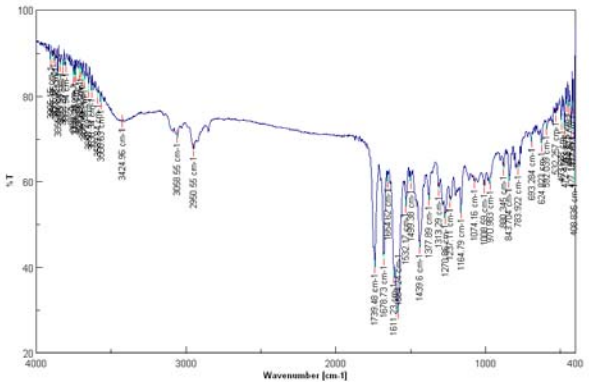


Scheme 3: The [1]HNMR spectrum of **4a.**



Scheme 4: The [13]CNMR spectrum of **4a.**

The IR spectrum of **4a** presented in Scheme 5, showed CO absorption at ν = 1678and 1739 cm^{-1} that is relevant to ketone and ester group respectively.



Scheme 5: The IR spectrum of **4a.**

The mass spectrum of **4a** displayed the molecular ion [M^+] signal at m/z 478 which is consistent with the product structure. Any initial fragmentation involves ring fragmentation.

This multi-component reaction (MCR) show special attributes such as high selectivity, high yielding and methodological simplicity due to the formation of carbon-carbon and carbon-heteroatom bonds in a single step. Moreover this reaction consisting of two synthetic steps, which are carried out without isolation of any intermediate, allow to reduce time, save money, energy and raw materials.

Conclusion

In summary, we have developed a facile and efficient synthetic method for preparation of substituted1,7-phenanthrolines via a new multi-component reaction. This reaction by contrast to the multi-step synthesis requires minimal work-up and generated products in excellent yields.

Experimental

Melting points and IR spectra of all compounds were measured on an Electro thermal 9100 apparatus and a JASCO FT-IR spectrometer, respectively. The ^{1}H and ^{13}CNMR 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. In addition, the mass spectra were recorded on a GCMS-QP5050A mass spectrometer operating at an ionization potential of 70 eV. Elemental analysis for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. 1,7-phenanthroline, 1,3-dimethylbarbituric acid and dialkyl acetylene dicarboxylates were purchased from Fluka, (Buchs, Switzerland) companies and used without further purification.

General synthetic procedure, exemplified by Dimethyl-8- (1,3-dimethyl-2,4,6-tri oxo-hexahydropyrimidine-5-yl) 1,7-phenanthroline, (8-H) 7-yl fomarate **(4a)**

To a magnetically stirred solution of 1,7-phenanthroline (0.18 g, 1 mmol) and 1,3- dimethyl barbituric acid(0.15 g, 1 mmol) in CH_2Cl_2 (15 mL) was added, drop wise, a mixture of dimethyl acetylene dicarboxylate (0.142gr, 1 mmol) in CH_2Cl_2 (5 mL) at -10 °Cover 10 min. The reaction mixture were allowed to attain room temperature, and then stirred for about 1hour. The solvent was then removed under reduced pressure and product washed with cold diethyl ether (2×5 mL). Then the product was recrystallized from acetonitrile to give the desired product. Yellow crystals, 80% yield, (0.38g), m.p: 151–153 °C. IR(KBr): (ν_{max}, cm^{-1}):1439,1611 (C=C), 1678 (C=O ketone), 1739 (C=O ester).^{1}H NMR (500.1 MHz, $CDCl_3$) : δ, ppm (J, Hz): 3.29- 3.37 (6H, s, 2NC*H*$_3$), 3.72, 3.94 (6H, s, 2 CO_2-C*H*$_3$), 4.70 (1H, d, J=7.3, O=C-C*H*-C=O),5.51(1H, dd, J=7.2, J=3.4, N-C*H*-CH), 5.76 (1H, dd, J=10.1 ,J=3.4, N-CH-C*H*),5.96 (1H, s, C=C*H*-CO_2-CH_3),7.29-8.83(6H aromatic). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ, ppm : 29.18 (2NCH_3), 51.43 (CH), 53.57, 53.80 (2 OCH_3), 65.14 (CH), 73.48 (CH), 123.99 (C), 127.47, 129.05, 129.08, 130.69, 131.91, 133.53, 135.28,136.91, 137.38, 137.86, 141.79 (11 C aromatic), 149.88, 165.14, 168.97 (3 C=O), 173.75, 177.80 (2 O-C=O). Mass, m/z(%): 478 (M^+ ,41), 419 (16), 387 (22), 334 (100), 239 (60), 180 (100), 150(40). Anal.Calcd.for $C_{24}H_{22}N_4O_7$ (478.44) C, 60.24; H, 4.63; N, 11.71. Found: C, 60.94; H, 4.13; N, 11.80.

Diethyl-8- (1,3-dimethyl-2,4,6-tri oxo-hexahydropyrimidine-5-yl) 1,7-phenanthroline,(8-H) 7-yl fomarate **(4b)**:Orange crystals, 72% yield, (0.36g), m.p: 165–168 °C. IR(KBr): (ν_{max}, cm^{-1}):1435,1615 (C=C), 1670 (C=O ketone), 1746 (C=O ester).^{1}H NMR (500 MHz, $CDCl_3$) : δ, ppm (J, Hz): 1.2,1.6 (6H, t, J=7.2Hz, 2CH_3), 3.31, 3.40 (6H, s, 2NCH_3), 3.77, 4.10 (2 CH_2, q, J=7.2, CO_2-C*H*$_2$-CH_3), 4.72 (1H, d, J=7.3, O=C-C*H*-C=O),5.55(1H, dd, J=7.2, J=3.4, N-C*H*-CH), 5.70 (1H, dd, J=10.1 ,J=3.4, N-CH-C*H*),5.91 (1H, s, N-C=C*H*-CO_2-CH_3), 7.33-8.80 (6H aromatic). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ, ppm :13.7, 14.0 (2 CH_3), 27.5 (2 NCH_3), 53.1 (CH), 58.2, 59.3 (2 OCH_2), 61.0 (CH), 71.1 (CH), 124.1 (C), 126.6, 129.8, 130.2, 131.5,132.2,133.4, 134.2, 137.8, 138.5, 139.1, 140.2 (11 C aromatic), 151.1, 164.7, 170.27 (3 C=O), 173.2,

176.9 (2 O-C=O). Mass, m/z(%): 506 (M^+,40), 480 (50), 420 (26), 387 (20), 334 (100), 310 (55), 239 (68), 180 (100), 155 (40).Anal. Calcd. For $C_{26}H_{26}N_4O_4$ (506.52): C, 61.65; H, 5.17; N, 11.06. Found: C, 61.42; H, 5.23; N, 11.28.

*Diisopropyl-8- (1,3-dimethyl-2,4,6-tri oxo-hexahydropyrimidine-5-yl) 1,7-phenanthroline,(8-H) 7-yl fomarate***(4c)**. Orange crystals, 70% yield, (0.37g), m.p. 155-158 °C. IR(KBr): (ν_{max}, cm^{-1}):1430,1625 (C=C), 1675 (C=O ketone), 1756 (C=O ester). ^{1}HNMR (500 MHz, $CDCl_3$) : δ, ppm (J, Hz) 1.15 (6H, d,J=6.3 Hz, CH*Me*$_2$), 1.58 (6H, d, J=6.3 Hz, CH*Me*$_2$),3.29, 3.37 (6H, s, 2N*CH*$_3$), 4.15 (1H,m, C*H*Me$_2$), 4.62 (1H, m, C*H*Me$_2$), 4.70 (1H, d, J=7.3, O=C-C*H*-C=O),5.53(1H, dd, J=7.2, J=3.4, N-C*H*-CH), 5.80 (1H, dd, J=10.1,J=3.4, N-CH-C*H*),5.90 (1H, s, N-C=C*H*-CO_2-CH_3), 7.32-8.73 (6H aromatic). ^{13}CNMR (125.8 MHz, $CDCl_3$): δ, ppm (J, Hz):21.3(2CH_3), 23.8 (2 CH_3), 28.5 (2 NCH_3), 69.1, 69.5 (2 CH), 54.1 (CH), 62.1 (CH), 70.9 (CH), 125.7 (C), 127.2, 131.1, 129.4, 130.9, 133.1, 134.1, 134.6, 136.8, 138.5, 138.7,141.2 (11 C aromatic), 152.1, 163.9, 171.2 (3 C=O), 173.3, 175.9 (2 O-C=O). Mass, m/z(%): 534 (M^+,46), 491 (36),475 (50), 448(60), 419(42), 379(52), 360 (45), 335(61), 199(65), 180(100), 155(45). Anal.Calcd. For $C_{28}H_{30}N_4O_7$ (534.56) C, 62.85; H, 5.61; N, 10.47. Found: C, 62.94; H, 5.47; N, 10.29.

Acknowledgment

We gratefully acknowledge financial support from the Young Researchers and Elite Club of Islamic Azad University of Sirjan.

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