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New and Facile Synthesis of Pyrimidine, Coumarine, Pyrimido[1,6-*a*]Pyrimidine, 1,2,4-Triazine and Pyrimido[4,5-*c*] Pyridazine Derivatives

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Dedicated to the memory of Prof. A.A. Elagamey

Abstract

Condensation of cyanoacetylurea **1** with aromatic aldehydes gave the arylidenes **2**a-d. Compound **2**a cyclised to the pyrimidone **4** by boiling in DMF/Et_3N. Compound **1** condensed with 2,4-dihydroybenzaldehyde to give the arylidene **6** .Cyclisation of **6** yield the coumarine **7**.Coupling of **1** with aryl diazonium salts gave aryl hydrazones **9**a,b. Compound **9**a cyclised to **10** . Compound **10** reacted with malononitrile to give pyrimido [1,6-*a*] pyrimidine **11**. Reaction of **9**b with triethyl orthoformate and ethyl chloroformate afforded 1,2,4-triazines **13** and **15** respectively. Condensation of **1** with arylhydrazone **16** yielded pyrimido[4,5-*c*] pyridazine **19**.

*Keywords***:** Cyanoacetylurea, pyrimidine, coumarine, 1,2,4-triazine

Introduction

Active methylene nitriles are versatile reagents that extensively used for preparation of a variety of aromatic and heteroaromatic products [1,2]. These products gained interest as biodegradable agrochemicals [1,2], pharmaceuticals [3] and as nonpeptide human deficiency virus (HIV) protease inhibitors and blood anticoagulants [4,5]. Other derivatives such as hexahydro quinolines bearing an acyl group on C-3 have been exhaustively studied as interesting calcium antagonist modulators [1,6].

In the past few years, we have been involved in a program aimed of developing new accesses to the synthesis of functionally substituted heterocycles using readily available starting materials.

The present work aimed of synthesis of a variety of heterocycles using cyanoacetylurea *N*-carbamoyl-2-cyanoacetamide) **1** and other compounds as starting materials.

Materials and Methods

All melting points are uncorrected and measured on Griffin George MBF 010T (London) apparatus. Recorded yield correspond to the pure products. IR (KBr) spectra were recorded on a Perkin Elmer SP-880 spectrometer and ^{1}H-NMR spectra: were measured on Varian 270 MHz

spectrometer on DMSO-d_6 as solvent and TMS an internal standard. Chemical shifts are reported in δ units (ppm). Microanalyses were performed on a LECO CHN-932 elemental analyzer and carried out in the Microanalytical Data Unit at Cairo and Damietta Universities. Mass spectra were recorded on a MS 30(AEI) instrument at 70 eV ionization energy.

Synthesis of (E)-3-aryl-N-carbamoyl-2-cyanoacrylamides **2**a-d

A mixture of cyanoacetylurea **1** (0.01 mole) with an equimolecular amounts of the appropriate aldehydes were refluxed in acetic acid (20 ml) for 1h. Precipitate formed, were filtered off, recrystallized and then identified as ***2***a-d.

(*E*)-*N-carbamoyl-2-cyano-3-(4-methoxyphenyl) acrylamide* **2**a

Formed colorless crystals in 70 %yield, from ethanol/DMF, m.p. 227-229°C (lit. [7] m.p. 226°C).

(*E*)-*N-carbamoyl-2-cyano-3-(4-chlorophenyl) acrylamide* **2**b

Formed yellow crystals in 65 % yield, from CH_2Cl_2/DMF, m.p. 233-235°C; IR (ν/cm^{-1}): 3432, 3228 (NH_2, NH), 2210 (conjugated CN), 1700 (CO), 1680 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 7.54-7.96 (m, 6H, 4H, aromatic protons +2HNH_2), 8.35 (s, 1H, ylidenic H), 10.64 (s, 1H, NH). *Anal*. Calcd. for $C_{11}H_8N_3O_2Cl$ (249.56): C, 52.92; H, 3.23; N, 16.83.Found: C, 52.67; H, 3.39; N, 16.49; MS : M^+ = 249 (m/z).

(E)-N-carbamoyl-2-cyano-3-(4-phenoxyphenyl) acrylamide **2**c

Formed colorless crystals in 65 % yield , from CH_2Cl_2/ DMF, m.p. 233-235°C; IR (ν/cm^{-1}): 3432, 3228 (NH_2, NH), 2210 (conjugated CN), 1700 (CO), 1680 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 7.08-7.71 (m,11H,9H ,aromatic protons +2HNH_2), 8.32 (s, 1H, ylidenic H), 10.58 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) (δ, ppm) 106.77 (C-2), 115.25 (CN), 151.42 (C-3), 153.18 (CO), 163.40 (CO), 122.62, 124.22, 124.99, 130.26, 131.04, 133.25, 155.66, 157.34. *Anal*. Calcd. for $C_{17}H_{13}N_3O_3$ (307.30): C, 66.44; H, 4.26; N, 13.67. Found: C, 66.67; H, 4.39; N, 13.49.

(*E*)-*N-carbamoyl-2-cyano-3-(3-chlorophenyl) acrylamide* **2**d

Formed orange crystals in 75 % yield, from acetic acid, m.p. 223-225°C; IR (ν/cm^{-1}): 3437, 3325 (NH_2, NH), 2225 (conjugated CN), 1722 (CO), 1684 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 7.52-7.95 (m, 6H, 4H, aromatic protons + 2H, NH_2), 8.33 (s, 1H, ylidenic H), 10.63 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) (δ, ppm): 106.68 (C-2), 115.16 (CN), 150.65 (C-3), 153.17 (CO), 163.40 (CO), 122.62, 124.22, 124.99, 130.26, 131.04, 133.25, 155.66, 157.34. *Anal*. Calcd. for $C_{11}H_8N_3O_2Cl$ (249.56): C,52.92; H, 3.23; N, 16.83. Found: C, 52.67; H, 3.39; N, 16.49; MS: M^+ = 249 (m/z).

Formation of **6**-*(4-methoxyphenyl)-2,4-dioxo-1,2,3,4-tetrahydro pyrimidine -5-carbonitrile* **4**

Asolution of **2**a (0.01 mole) in dimethylforamide (20 ml) and few drops of triethylamine were heated under reflux for 2h.The reaction mixture was then left to cool to room temperature and the solid formed was collected by filtration and then recrystallised from to give **4** as colorless crystals in 75 % yield, from DMF, m.p. 204-206°C; IR (ν/cm^{-1}): 3444, 3364, 3303 (NH_2, NH), 2207 (conjugated CN), 1700(CO), 1680 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 3.85 (s, 3H, OCH_3), 7.12-7.15 (d, J= 7.5 Hz, 2H, aromatic protons), 7.64 (s, 1H, NH), 7.76 (s, 1H, NH), 7.49-7.97 (d, J= 7.5 Hz, 2H, aromatic protons), 8.10 (s, 1H, OH).

Anal. Calcd. for $C_{12}H_9N_3O_3$ (243.06): C,59.26; H, 3.73; N , 17.28. Found: C, 59.37; H, 3.61; N, 17.49.

Preparation of -N-carbamoyl-2-cyano-3-(2,4-dihydroxyphenyl) acrylamides **6**

This compound was prepared according to the method described for preparation of ***2***a-d. Compound **6** formed yellow crystals in 70 % yield, from $CHCl_3$/DMF, m.p. 277-279°C; IR (ν/cm^{-1}): 3225, 3043 (NH_2, NH), 2235 (conjugated CN), 1744 (CO), 1616 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 2.49 (s, 2H, NH_2), 6.73-6.90 (m, 2H, aromatic protons), 7.63-7.64 (d, J=7Hz, 1H, aromatic protons), 8.09 (s, 1H, ylidenic H), 8.77 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) (δ, ppm): 110.31 (C-2), 115.28 (CN), 131.84 (C-3), 153.31 (CO), 164.98 (CO),156.61, 156.67, 114.63, 102.51, 102.08

Anal. Calcd. for $C_{11}H_9N_3O_4$ (247.06): C,53.44; H, 3.63; N, 17.00. Found: C, 53.56; H, 3.59; N, 17.12; MS: M^+ = 247 (m/z).

Synthesis of N-carbamoyl-7-hydroxy-2-oxo-2H-chromene-3-carboxamide **7**A

Suspension of **6** (0.01 mole) in DMF (20 ml) containing few drops of triethylamine, was refluxed for 6h. then the solvent was concentrated to its half volume. The reaction mixture was left to cool to room temperature and the solid deposited was collected by filtration, recrystallized from DMF to give **7** as colorless crystals in 70 % yield, m.p. 285-287°C; IR (ν/cm^{-1}): 3438, 3324, 3243 (NH_2, NH) 1707 (CO), 1616 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 6.91 (brs, 2H, NH_2), 7.55-7.88 (m, 2H, aromatic protons), 8.91 (s, 1H, coumarin H-4), 10.38 (s, 1H, NH), 11.32 (s, 1H, OH); ^{13}C-NMR (DMSO-d_6) (δ, ppm): 112.31 (C-3), 114.83 (C-4), 156.82 (CO), 164.98 (CO), 206.56 (CO).

Anal. Calcd. for $C_{11}H_8N_2O_5$ (248.19): C, 53.23; H, 3.25; N, 11.29. Found: C, 53.46; H, 3.29; N, 11.13; MS: M^+ = 248 (m/z).

Preparation of N-aryl 2-oxo- 2-ureidoacetohydrazonoyl cyanide **9**a,b

An aqueous solution of $NaNO_2$ (0.7 g in 5 ml H_2O) was added to a cold solution of appropriate primary aromatic amines (0.01 mole) in concentrated HCl (2 ml).The resulting diazonium salt solution was then added to a cold solution of (0.01 mole) of compound 1 in ethanol (20 ml) containing CH_3CO_2Na (0.5 g). The reaction mixture was stirred at room temperature for 1h.and the solid product was collected by filtration and recrystallised from the proper solvents to give **9**a,b.

N-(4-methoxyphenyl)2-oxo-2-ureidoacetohydrazonoyl cyanide **9**a

Formed green crystals from CH_2Cl_2/DMF in 85 % yield, m.p. 218-220°C; IR (ν/cm^{-1}): 3421, 3270 (NH_2, NH), 2231 (conjugated CN), 1700 (CO), 1666 (CO).

Anal. Calcd. for $C_{11}H_{11}N_5O_3$ (261.24): C, 50.57; H, 4.24; N, 26.81. Found: C, 50.32; H, 4.42; N, 26.70.

N-(4-chlorophenyl)2-oxo-2-ureidoacetohydrazonoyl cyanide **9**b

Formed golden yellow crystals from isopropanol/DMF in 75 % yield, m.p. 225-227°C; IR (ν/cm^{-1}): 3478,3324 (NH_2, NH), 2221 (conjugated CN), 1700 (CO), 1670 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 7.42-7.78 (m,7H, 4H, aromatic protons+2NH_2 +NH), 8.91 (s, 1H, coumarin H-4), 10.03 (s, 1H, NH).

Anal. Calcd. for $C_{10}H_8N_5O_2Cl$ (265.66): C, 45.21; H, 3.04; N, 26.36. Found: C, 45.44; H, 3.29; N, 26.53; MS: M^+ = 265 (m/z).

6-amino-5-(2-(4-methoxyphenyl)hydrazonopyrimidine-2,4-(3*H*,5*H*)-*dione* **10**

A solution of *N*-(4-methoxyphenyl)2-oxo- 2-ureidoaceto hydrazonoyl cyanide **9**a (0.01 mole) in dimethylfornamide (20 ml) was treated with few drops triethylamine was heated under reflux for 3h. then left to cool to room temperature .The formed precipitate was collected by filtration, recrystallised from CH_3CO_2H to give red crystals of **10** in 75 % yield, m.p. > 300°C; IR (ν/cm^{-1}): 3454, 3014 (NH_2, NH), 1731 (CO), 1621 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 3.78 (s, 3H, OCH_3), 6.99-7.02 (d, J= 7Hz, 2H, aromatic protons), 7.33 (brs. 1H, NH), 7.06-7.63 d, J = 7Hz, 2H, aromatic protons), 10.42 (brs, 1H, NH), 10.82 (s, 2H, NH). *Anal*. Calcd. for $C_{11}H_{11}N_5O_3$ (261.24): C, 50.57; H, 4.24; N, 26.81. Found: C, 50.44; H, 4.29; N, 26.63.

2,4-diamino-9-(4-methoxyphenyl)diazenyl)-6H-pyrimido[1,6-a] pyrimidine-6,8(7H)-dione **11**

A solution of **10** (0.01 mole) and (0.01 mole) of malononitrile was refluxed for 6h. in ethanol/dimethylformamide mixture (1:1) (30 ml) and then the solution was concentrated in *vacuo* and then left to cool at room temperature .The formed solid was collected by filtration and recrystallised from EtOH/DMFto give **11** as yellow crystals in 65 % yield, m.p. 290-292°C; IR (ν/cm^{-1}): 3490, 3413, 3232 (NH_2, NH) 1724 (CO), 1620 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 3.78 (s, 3H, OCH_3), 6.99-7.04 (d, J = 7 Hz, 2H, aromatic protons), 7.41 (s, 1H, aromatic proton), 7.60-7.62 (d, J= 7Hz, 2H, aromatic protons), 10.41 (s, 1H, NH), 10.85 (s, 2H, NH_2); ^{13}C-NMR (DMSO-d_6) (δ, ppm): 55.36 (OCH_3), 79.14 (CH), 172.03 (CO), 161.15 (CO), 122.19 114.91 (aromatic carbons). *Anal*. Calcd. for $C_{14}H_{13}N_7O_3$ (327.30): C,51.38; H, 4.00; N, 29.96. Found: C, 51.46; H, 3.79; N, 29.63.

2-(4-Chlorophenyl)-6-cyano-3-ethoxy-5-oxo-2,3-dihydro-1,2,4-triazine-4(5H)-carboxamide **13**

A solution of *N'*-(4-chlorophenyl)-2-oxo- 2-ureidoacetohydrazonoyl cyanide **9**b (0.01 mole) in acetic anhydride (30 ml) was treated with (0.01 mole) of triethylorthoformate, was refluxed for 6h.The reaction mixture was concentrated under reduced pressure and then left to cool at room temperature. The solid deposited upon cooling was collected by filtration and recrystallised from EtOH/DMF to give **13** as faint green crystals in 60% yield, m.p. 294-296°C; IR (ν/cm^{-1}): 3398, 3151 (NH_2), 2206 (conjugated CN), 1700 (CO), 1635 (CO). *Anal*. Calcd. for $C_{13}H_{12}N_5O_3Cl$ (321.06): C, 48.53; H, 3.76; N, 21.77. Found: C, 48.44; H, 3.89; N, 21.53; MS: M^+ = 321 (m/z).

2-(4-Chlorophenyl)-6-cyano-3,5-dioxo-2,3-dihydro-1,2,4-triazine-4(5H)-carboxamide **15**

A suspension of N'-(4-chlorophenyl)-2-oxo- 2-ureidoacetohydrazonoyl cyanide **9**b (0.0 mole) in ethanol (50 ml) containing triethylamine (0.1 ml), was treated with (0.0 mole) of ethyl chloroformate and the reaction mixture was heated under reflux for 3h.The formed solid product was collected by filtration, recrystallised from EtOH / DMF to give **15** as brown crystals in 65% yield, m.p. > 300°C; IR (ν/cm^{-1}): 3494, 33441 (NH_2), 2214 (conjugated CN), 1743 (CO), 1674 (CO). *Anal*. Calcd. for $C_{11}H_6N_5O_3Cl$ (291.65): C,45.30; H, 2.07; N , 24.01. Found: C, 45.44; H, 2.17; N, 24.23.

3-Acetyl-1-(4-Chlorophenyl)-4-methylpyrimido[4,5-c]pyridazine-5,7-(1H,6H)-dione **19**

A mixture of cyanoacetylurea **1** (0.01 mole) and 3-(2-(4-chlorophenyl) hydrazono) pentane-2,4-dione **16** (0.01 mole) in ethanol (50 ml) was treated with few drops of piperidine .The reaction mixture was refluxed for 6h. and then left to cool to room temperature, the precipitate formed was collected by filtration, recrystallised from EtOH/DMF to give **19** as colorless crystals in 75 % yield, m.p. 146-148°C; IR (ν/cm^{-1}): 3421, 3317 (NH) 1724 (CO), 1666 (CO); ^{1}H-NMR (DMSO-d_6) (δ, ppm): 2.45 (s, 3H, CH_3), 3.35 (s, 3H, CH_3), 7.47-7.48 (d, J= 7Hz, 2H, aromatic protons), 7.60-7.62 (d, J= 7Hz, 2H, aromatic protons), 13.86 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) (δ, ppm): 26.35 (CH_3), 39.18(CH_3), 79.14 (CH), 196.36 (CO), 140.89(CO), 117.88, 128.92, 129.24, 129.58, 133.74 (aromatic carbons) . *Anal*. Calcd. for $C_{15}H_{11}N_4O_3Cl$ (330.73): C, 54.47; H, 3.35; N, 16.94. Found: C, 54.66; H, 3.49; N, 16.63; MS: M^+ = 331 (m/z).

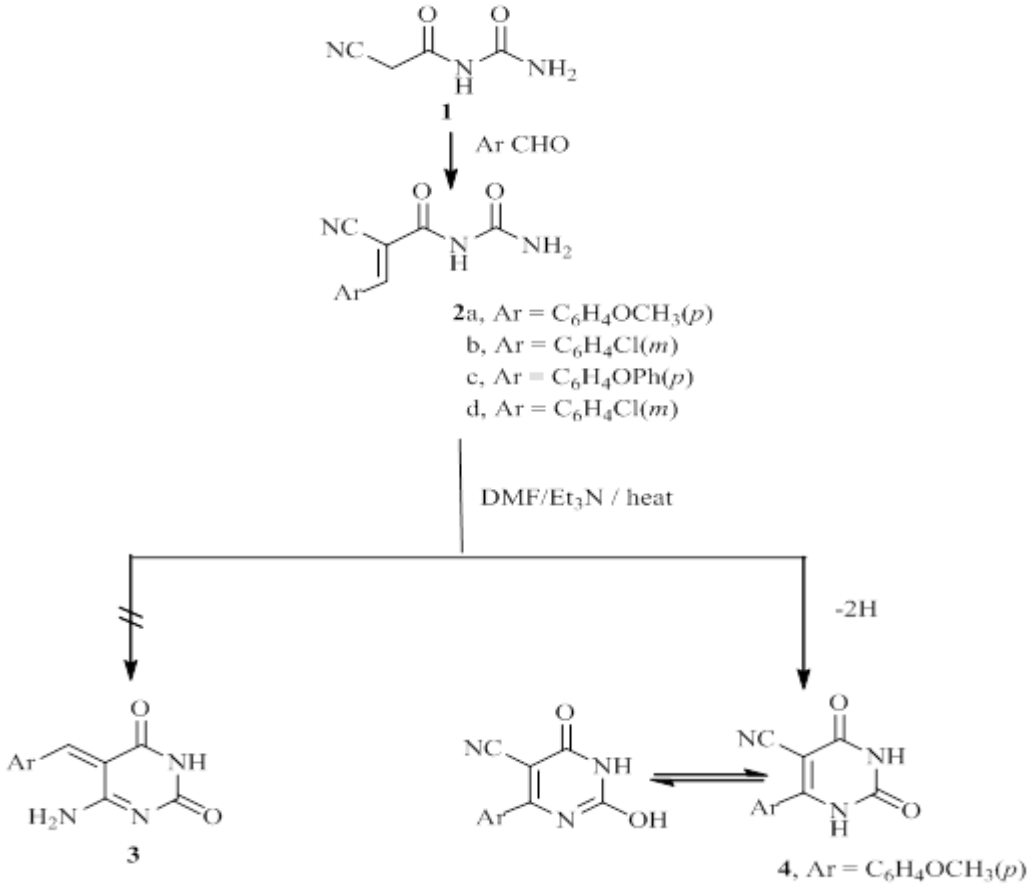
Results

In continuation of this effort, we describe here new procedures for synthesis of different heterocycles. These functionally substituted pyrimidine, coumarine, pyrimido[1,6-*a*]pyrimidine, 1,2,4-triazine and pyrimido[4,5-*c*] pyridazine derivatives of potential biological importance utilizing active methylene nitriles such as cyanoacetylurea as a key compound and other reagents.

It has been found that, cyanoacetylurea **1**prepared by reacting cyanoacetic acid and urea in acetic anhydride [7,8] condensed readily with aromatic aldehydes ,namely *p*-anisaldehyde,*p*-chlorobenzadehyde, *p*-phenoxy benzaldehyde and *m*- chlorobenzadehyde affording the corresponding (*E*)-3-aryl-*N*-carbamoyl-2-cyanoacrylamides **2**a-d .IR spectra of compounds showed the presence of two carbonyl functions at $\upsilon \approx$ 1780-1700 cm^{-1},cyano functions at $\upsilon \approx$ 2210-2217 cm^{-1} and amino groups were clearly observed in the region of $\upsilon \approx$ 3228-3432 cm^{-1}.^{1}-H-NMR spectra of the obtained products indicate in addition to aromatic protons, ylidenic protons at $\delta \approx$ 8.33ppm.^{13}C-NMR spectra of **2** c,d are compatible with structures **2** (*c.f.* Scheme 1).

Heating of (*E*)-*N*-carbamoyl-2-cyano-3-(4-methoxyphenyl) acrylamide **2**a in dimethylforamide containing drops of triethylamine was thought to afford two products,(*E*)-6-amino-5-(4-methoxybenzylidene)pyrimidine-2,4(3*H*,5*H*)-dione **3** and 6-(4-methoxyphenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile **4**. Structure **3** was readily eliminated by spectral data of the reaction product (*c.f.* Experimental). Similar behavior has been recently reported for similar systems [8].

On the other hand, condensation of cyanoacetylurea **1** with 2,4-dihydroxybenzaldehyde **5** in refluxing acetic acid to give (*E*)-*N*-carbamoyl-2-cyano-3-(2,4-dihydroxyphenyl)acrylamide **6**.Structure **6** was established by analytical and spectral data (*c.f.* Experimental).



Scheme 1. Formation of 5-cyanopyrimidine 4

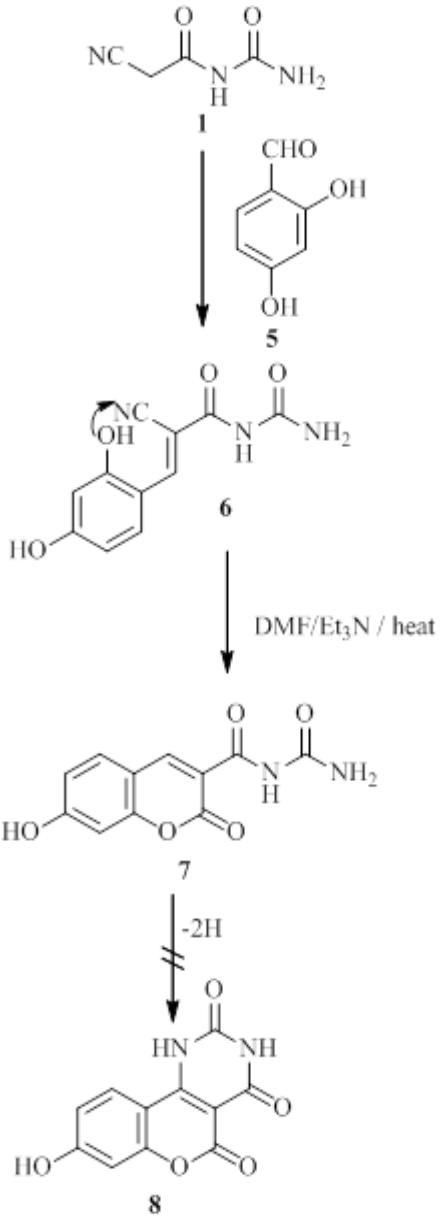
Boiling of **6** in dimethylformamide resulted in the formation of *N*-carbamoyl-7-hydroxy-2-oxo2*H*-chromene-3-carboxamide **7**. IR spectrum of **7** clearly indicates the absence of any signal due to cyano group and ^{1}H-NMR spectrum showed the presence of coumarin H-4 at δ ≈ 9.10ppm in addition to aromatic protons.

Trials to cyclize (*E*)-*N*-carbamoyl-2-cyano-3-(2,4-dihydroxyphenyl) acrylamide **6** to 8-hydroxy-1*H*-chromeno[4,3-d]pyrimidine-2,4,5(3*H*)-trione **8** under different conditions were found unsuccessful (*c.f.* Scheme 2).

Compound **1** coupled with aryl diazonium salts to give *N*-aryl 2-oxo- 2-ureidoacetohydrazonoyl cyanides **9**a,b. *N*-(4-methoxyphenyl)2-oxo- 2-ureidoacetohydrazonoyl cyanide **9**a was cyclised to 6-amino-5-(2-(4-methoxyphenyl) hydrazonopyrimidine-2,4-(3*H*,5*H*)-dione **10** by the effect of boiling of **9**a in dimethylforamide / triethylamine[8].IR spectrum of **10** clrealy indicates the absence of any signal due to cyano group.

6-Amino-5-(2-(4-methoxyphenyl) hydrazono-pyrimidine-2,4-(3*H*,5*H*)-dione **10**a as heterocyclic amidine cyclocondensed with malononitrile in refluxing ethanol/ dimethyl-foramide to give 2,4-diamino-9-(4-methoxy-phenyl) diazenyl)-6*H*-pyrimido[1,6-*a*] pyrimidine -6,8(7*H*)-dione **11** (*c.f.* Scheme 3). Structure **11** was supported from its analytical and spectral data. Thus, IR spectrum showed signals at ν = 3490, 3413, 3232cm^{-1} attributable to NH_2 and $_{NH}$), ν = 1724c m^{-1} and 1620 cm^{-1} for two carbonyl groups. ^{1}H-NMR spectrum showed signals in addition to aromatic protons, signals at δ, ppm = 3.78 attributable to OCH_3, signals at δ, ppm= 10.41, 10.85 attributable to NH, NH_2 respectively.

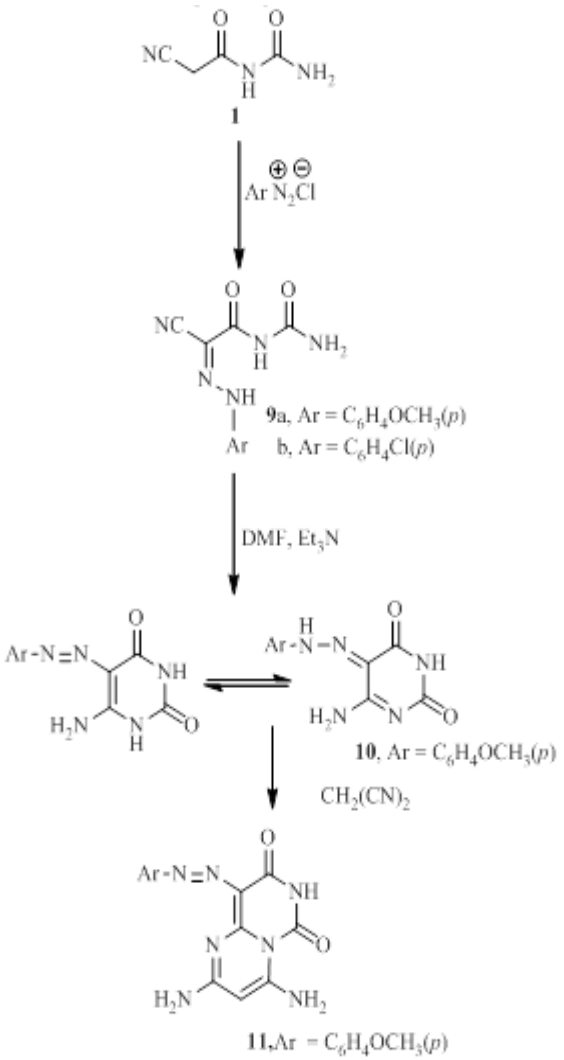
Reaction of an equimolecular amounts of *N*-(4-chlorophenyl)2-oxo- 2-ureidoacetohydrazono-yl cyanide **9**b and triethylorthoformate yielded a product with molecular formula $C_{13}H_{12}N_5O_3Cl$ (M^+ = 321). 2-(4-Chlorophenyl)-6-cyano-3-ethoxy-5-oxo-2,3-dihydro-1,2,4-triazine -4(5*H*)-carboxamide **13** was assigned for the reaction product (*c.f.* Scheme 4) .Compound **13** is assumed to be formed by the condensation of triethylorthoformate with **9**b to give the intermediate **12**.The latter was cyclised *via* ethanol elimination to give **13**.



Scheme 2. Preparation of 7-hydroxycoumarine 7

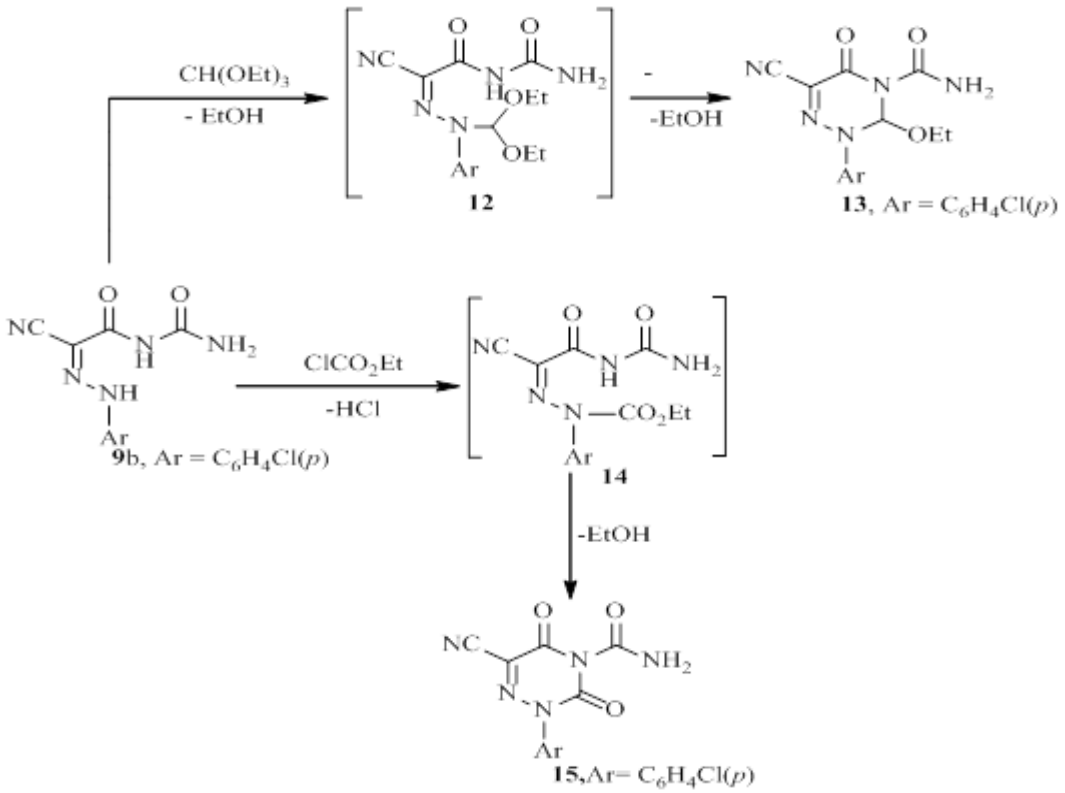
N-(4-chlorophenyl)-2-oxo- 2-ureidoacetohydrazonoyl cyanide **9**b also reacted with ethyl chloroformate in ethanol and in presence of triethylamine as catalyst to afford 2-(4-chlorophenyl)-6-cyano-3,5-dioxo-2,3-dihydro-1,2,4-triazine-4(5*H*)-carboxamide **15**. Analytical and spectral data is in good agreement with structure **15** (*c.f.* Experimental). Compound **15** is proposed to be obtained by first condensation of **9**b with ethyl chloroformate to give the intermediate **14** and then cyclised to **15**.

Again we have studied the reactivity of cyanoacetylurea **1** towards aryl hydrazones.For example,cyanoacetylurea **1** reacted with 3-(2-(4-chlorophenyl)hydrazono)pentane-2,4-dione **16** in boiling ethanol catalysed by piperidine to give a product for which 3-acetyl-1-(4-chlorophenyl)-4-methylpyrimido[4,5-*c*]pyridazine-5,7-(1*H*,6*H*)-dione **19** was established as a reaction product based on its spectral data.

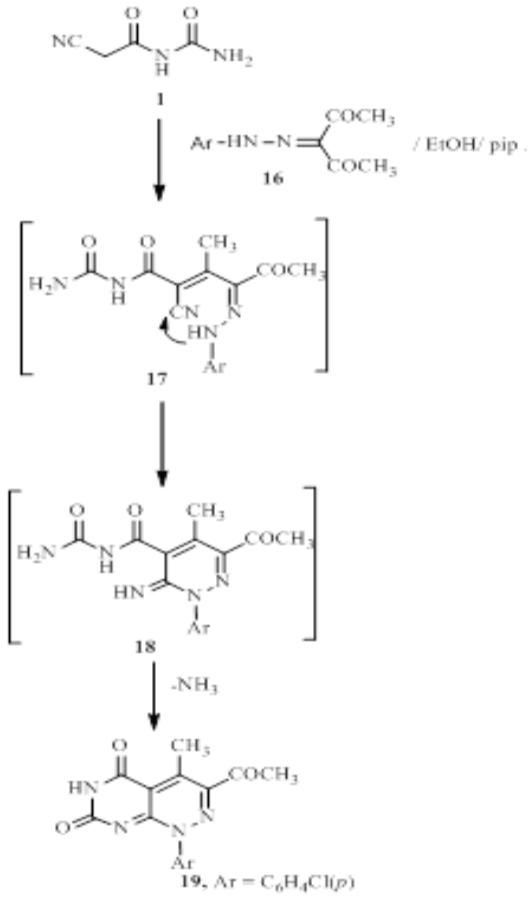


Scheme 3. Formation of pyrimidopyrimidine 11

Thus, IR spectrum revealed the presence of signals at *v*= 3421, 3317 cm^{-1} for NH, *v*= 1743, 1666, 1623 cm^{-1} for acetyl and amidic carbonyl functions. ^{1}H-NMR spectrum showed signals in addition to aromatic protons, signals at δ, ppm = 2.45 attributable to CH_3, signal at δ, ppm= 3.37 attributable to CH_3 and signal at δ, ppm= 13.86 attributable to NH function. Compound **19** is proposed to be obtained *via* the first condensation of the ketonic carbonyl group in **16** with the active methylene in **1**to give the intermediate **17** and then cyclised again through ammonia elimination to yield the final isolable product **19** (*c.f.* Scheme 5).



Scheme 4. Synthesis of 1,2,4-triazines 13, 15



Scheme 2. Preparation of Pyrimidopyridazine 17

6-Amino-5-(2-(4-methoxyphenyl) hydrazono-pyrimidine-2,4-(3*H*,5*H*)-dione **10**a as heterocyclic amidine cyclocondensed with malononitrile in refluxing ethanol/ dimethylforamide to give 2,4-diamino-9-(4-methoxyphenyl) diazenyl)-6*H*-pyrimido[1,6-*a*] pyrimidine -6,8(7*H*)-dione **11**. Structure **11** was supported from its analytical and spectral data. Thus, IR spectrum showed signals at ν = 3490, 3413, 3232cm^{-1} attributable to NH_2 and $_{NH}$), ν = 1724c m^{-1} and 1620 cm^{-1} for two carbonyl groups. ^{1}H-NMR spectrum showed signals in addition to aromatic protons, signals at δ, ppm = 3.78 attributable to OCH_3, signals at δ, ppm= 10.41, 10.85 attributable to NH, NH_2 respectively.

Conclusion

We conclude that, several new pyrimidine, coumarine, pyrimido pyrimidine,1,2,4-triazine and pyrimidopyridazine derivatives were prepared *via* reacting cyanoacetylurea with different reagents as readily obtainable starting components that can be useful for further chemical and biological studies.

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الملخص العربى

طرق جديدة وسهلة لتحضير مشتقات من البيريميدين، الكومارين، الترايازين، والبييريميدوبيريدازين

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في هذا البحث إتجهنا إلي تحضير مشتقات جديدة من البيريميدين والكومارين والترايازين والبيريميدوبيريدازين من تفاعل سيانوأسيتيل يوريا مع الكواشف المختلفة كمواد أولية. من المتوقع أن يكون للمواد الناتجة الجديدة نشاط بيولوجي . وتم إثبات التركيب البنائي للمواد الناتجة بإستخدام طرق التحليل الطيفي المختلفة وكذلك التحليل العنصري.