A novel one-pot three-components reaction: synthesis of indeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'',1''-*c*]triazole-5,7-dione. A new ring system

Huwaida M. E. Hassaneen

Chemistry Department, Faculty of Science, Cairo University, Giza, A. R. Egypt
E-mail: huwaidah@hotmail.com

Abstract

6-Amino-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one **1** reacted with a mixture of formaldehyde and indane-1,3-dione **7** in one-pot synthesis to yield the tetracyclic system **11a**. On the other hand, the dihydro derivatives **10b-f** were isolated when a mixture of **1** and **7** reacted with aromatic aldehydes. Compounds **11** reacted with hydrazonoyl chlorides **5** to yield the title compounds **12**. The proposed structures of the newly synthesized compounds are based on spectral data and are confirmed by alternative method.

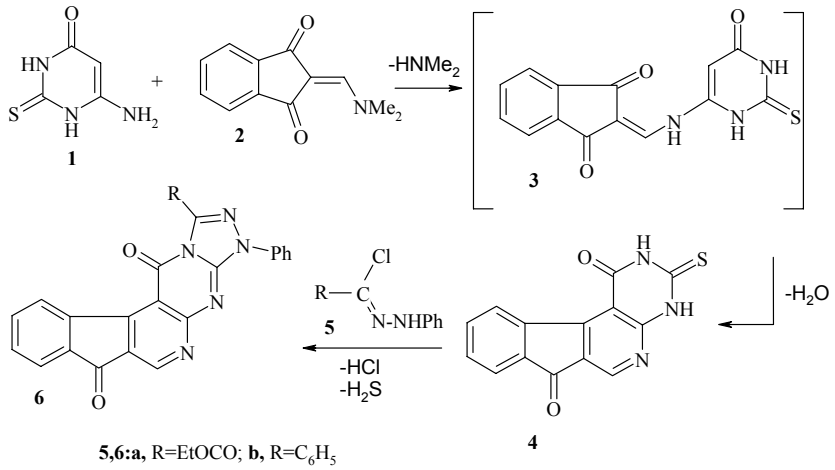
Keywords: Indane-1,3-dione, X-ray, hydrazonoyl chloride, 6-amino-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one

Introduction

Multicomponent condensation reactions (MCRs) have recently been discovered to be a powerful method for the synthesis of organic compounds, since the products are formed in a single step and diversity can be achieved by simply varying each component.[1-3] Due to biological activity of a significant number of compounds containing condensed pyrimidines (for example, they have been used as effective antitumor agents[4], as herbicide antidotes[5], antibacterials[6], diuretics[7] or antivirals[8]) and our interest in MCRs we wish to report the synthesis of tetra- and penta-heterocycles such as azinopyrimidine ring systems by a one-pot three-components condensation of aldehydes and indane-1,3-dione **7** in presence of 6-amino-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one **1** and 7-amino-1-phenyl-3-substituted-1,2,4-triazolo[4,3-a]pyrimidin-5-one **17**, respectively.

Results and Discussion

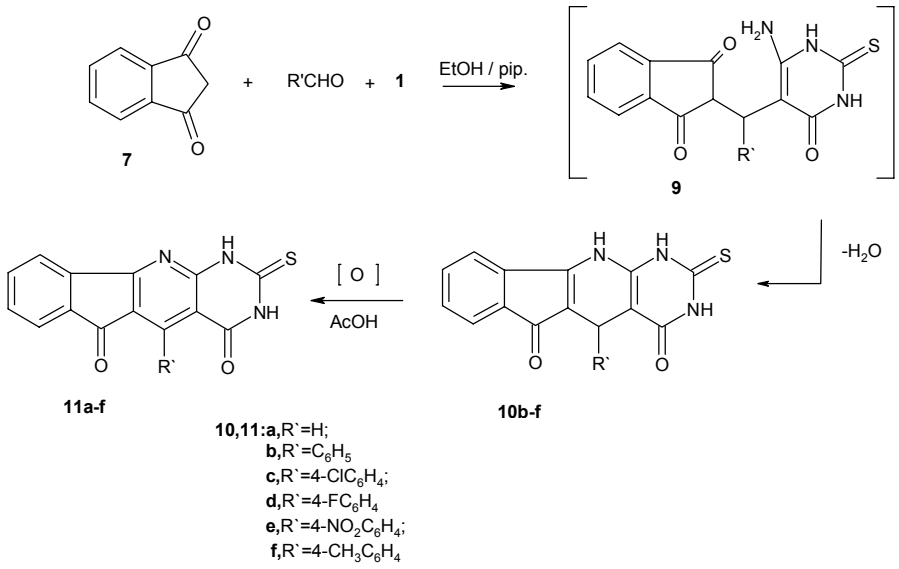
In previous work[9] from our laboratories we have reported that **1** reacted with **2** in acetic acid to yield the tetracyclic product **4**. The latter product reacted with hydrazonoyl chlorides **5a,b** in chloroform in presence of triethylamine to yield the pentacyclic product **6** (Scheme 1).



Scheme 1

In continuation to this work, it seemed possible to us to synthesize compound **4** *via* reaction of aldehydes, indane-1,3-dione **7** and **1** followed by oxidation of the formed dihydro-derivatives **10**. However, we have found that the reaction of **7** with formaldehyde (R' = H) and **1** gave a product isomeric to **4**. It was thus concluded that this product is **11a** which formed *via* the non-isolable intermediates **9** and **10** (R' = H) (cf. Scheme 2). On the other hand, when a mixture of **7** and **1** reacted with aromatic aldehyde in ethanol in presence of piperidine the dihydro-derivatives **10b-f**; (R' = Ar) could be isolated. The stability of **10** despite the fact that it is not aromatic may be rationalized for by the fact that the planar aromatic **11** should suffer plenty of intramolecular steric repulsion.

The assigned structure for products **11** was based on elemental and spectral analyses (see Experimental Section). Structure **11d**, taken as a typical example, was further proved based on X-ray crystal analysis. X-ray crystal analysis of structure **11d** indicates that the 4-fluoro-phenyl function group rotation around the single bond is hindered and thus, the aryl group is forced in a position almost perpendicular to the plane of the ring[10], to fit steric requirements.



Scheme 2

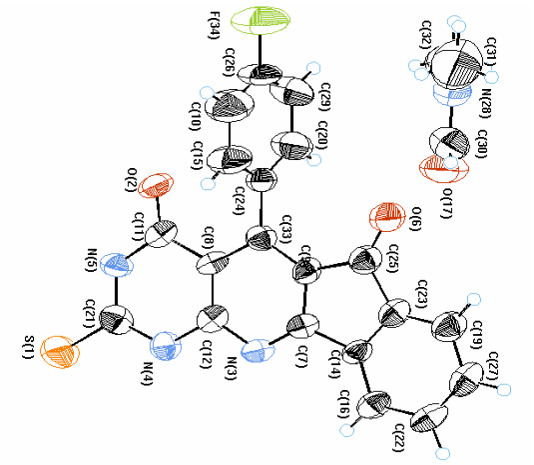
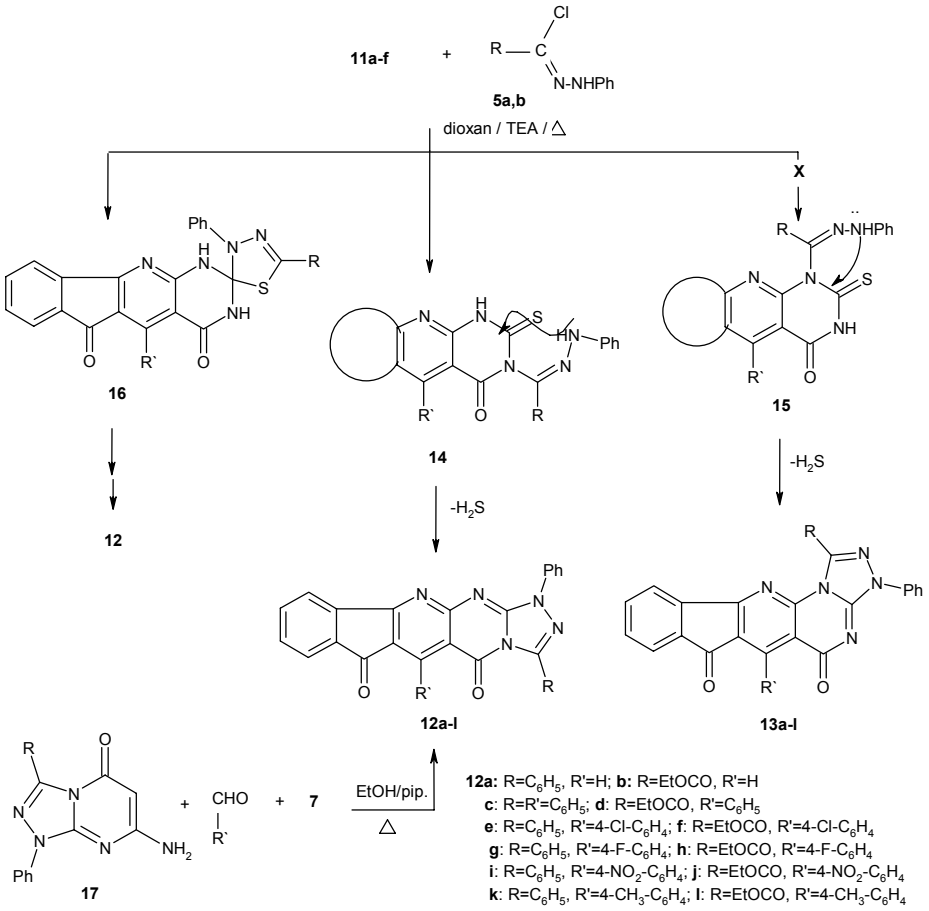


Figure 1. X-ray crystal structure for compound **11d**.

Compounds **11a-f** reacted with hydrazonoyl chlorides **5a,b** to yield products that may be formulated as **12** or **13**. These can result either from initial formation of **14** or isomeric **15** and followed by cyclization *via* elimination of hydrogen sulphide. However, a possible initial [3+2] cycloaddition at the thiocarbonyl group and subsequent rearrangement afforded products **12** following well accepted mechanism initially suggested by Hassaneen *et al*[11-15] (Scheme 3). The assigned structure for compounds **12** was further confirmed by chemical transformation. Thus, reaction of 7-amino-1-phenyl-3-substituted-1,2,4-triazolo[4,3-*a*]pyrimidin-5-one[13,14] **17** with aromatic aldehydes and **7** in absolute ethanol in presence of piperidine led to formation of products which are identical in all respects (mp, mixed mp and IR) with products **12**.

In conclusion, we have developed a novel one-pot three-components condensation reaction of aldehyde derivatives and indane-1,3-dione **7** in presence of **1** or **17** which is an efficient approach for the synthesis of **11** and **12**, respectively.



Scheme 3

Experimental Section

General Procedures. All melting points were determined on GallenKamp electrothermal apparatus and are uncorrected. IR spectra were recorded as KBr pellets with a Pye Unicam SP 3000 infrared spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in deuterated dimethylsulfoxide DMSO-d_6 at 300 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane (TMS) as internal reference and the results are expressed as δ values. Mass spectra were performed on a Shimadzu GCMS-QP 1000 Ex mass spectrometer at 70 eV. Elemental analyses were carried out at the Micro-analytical Centre of Cairo University. Crystal structure was performed using Envaf Nonius 591 Kappa CCD single crystal diffraction. Due to

the limited solubility of compounds **10b-f, 11b-f** and **12a-l** in common ^{13}C NMR solvents, the ^{13}C NMR spectra were unrecorded with the exception of compound **11a**.

General procedure for preparation of 2-thioxo-2,3,5,11-tetrahydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione derivatives (10b-f)

To a mixture of **1** (1.43 g, 10 mmol), aldehyde derivatives (10 mmol) and indane-1,3-dione (1.46 g, 10 mmol) in absolute ethanol (30 mL) was added a catalytic amount of piperidine (0.85 g, 10 mmol). The reaction mixture was heated under reflux for 30 min; after cooling to room temperature the solid product formed, which was collected and crystallized from dimethylsulfoxide to give compounds **10b-f**.

5-Phenyl-2-thioxo-2,3,5,11-tetrahydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (10b). This compound was obtained as yellow needles, (2.15 g, 60 %), mp 333-334ºC; *Anal*. Calcd. $C_{20}H_{13}N_3O_2S$ (359.41): C, 66.84; H, 3.65; N, 11.69; S, 8.90. Found C, 66.52; H, 3.44; N, 11.35; S, 8.75. IR (KBr, cm^{-1}) 1663 (CO), 1690 (CO), 2923 (aliphatic CH), 3100 (NH), 3230 (NH), 3442 (NH); ^1H NMR (300 MHz, DMSO-d_6) δ 4.69 (s, 1H, H-5), 7.12-7.51 (m, 9H, Ar-H), 9.88 (br, 1H, NH), 11.72 (br, 1H, NH), 12.34 (s, 1H, NH).

5-(4-Chlorophenyl)-2-thioxo-2,3,5,11-tetrahydro-1*H*-indeno[2',1':5,6]pyrido[2,3-*d*] pyrimidine-4,6-dione (10c). This compound was obtained as yellow needles, (2.60 g, 66 %), mp 352-353ºC; *Anal*. Calcd. $C_{20}H_{12}ClN_3O_2S$ (393.85): C, 60.99; H, 3.07; N, 10.67; S, 8.14. Found: C, 60.78; H, 2.85; N, 10.52; S, 8.02. IR (KBr, cm^{-1}) 1660 (CO), 1693 (CO), 2932 (aliphatic CH), 3112 (NH), 3227 (NH), 3440 (NH); ^1H NMR (300 MHz, DMSO-d_6) δ 4.91 (s, 1H. H-5), 7.20-7.62 (m, 8H, Ar-H), 7.85 (br, 1H, NH), 11.30 (br, 1H, NH), 12.40 (s, 1H, NH).

5-(4-Fluorophenyl)-2-thioxo-2,3,5,11-tetrahydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*] pyrimidine-4,6-dione (10d). This compound was obtained as orange needles, (2.64 g, 70%), mp 355-356ºC; *Anal*. Calcd. $C_{20}H_{12}FN_3O_2S$ (377.40): C, 63.65; H, 3.20; N, 11.13; S, 8.50. Found: C, 63.55; H, 3.12; N, 11.06; S, 8.36. IR (KBr, cm^{-1}) 1665 (CO), 1699 (CO), 2939 (aliphatic CH), 3122 (NH), 3239 (NH), 3427 (NH); ^1H NMR (300 MHz, DMSO-d_6) δ 4.95 (s, 1H, H-5), 7.26-7.71 (m, 8H, Ar-H), 7.64 (br, 1H, NH), 10.92 (br, 1H, NH), 11.49 (s, 1H, NH).

5-(4-Nitrophenyl)-2-thioxo-2,3,5,11-tetrahydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*] pyrimidine-4,6-dione (10e). This compound was obtained as red needles, (2.79 g, 69%), mp 320-321ºC; *Anal*. Calcd. $C_{20}H_{12}N_4O_4S$ (404.41): C, 59.40; H, 2.99; N, 13.85; S, 7.93. Found: C, 59.22; H, 2.68; N, 13.72; S, 7.85. IR (KBr, cm^{-1}) 1333, 1554 (NO_2), 1665 (CO), 1689 (CO), 2935 (aliphatic CH), 3100 (NH), 3232 (NH), 3420 (NH); ^1H NMR (300 MHz, DMSO-d_6) δ 5.09 (s, 1H, H-5) 7.05 (s, 1H, NH), 7.21-7.98 (m, 8H, Ar-H), 10.06 (s, 1H, NH), 11.45 (br, 1H, NH).

5-(4-Methylphenyl)-2-thioxo-2,3,5,11-tetrahydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*] pyrimidine-4,6-dione (10f). This compound was obtained as yellow needles, (2.20 g, 59 %), mp 315-316ºC; *Anal*. Calcd. $C_{21}H_{15}N_3O_2S$ (373.44): C, 67.54; H, 4.05; N, 11.25; S, 8.59. Found: C, 67.46; H, 3.88; N, 11.12; S, 8.46. IR (KBr, cm^{-1}) 1659 (CO), 1689 (CO), 2962 (aliphatic CH), 3089 (NH), 3333 (NH), 3405 (NH); ^1H NMR (300 MHz, DMSO-d_6) δ 1.32 (s, 3H, CH_3), 4.64 (s, 1H, H-5) 7.11-7.58 (m, 8H, Ar-H), 7.75 (br, 1H, NH),10.96 (s, 1H, NH), 11.25 (br, 1H, NH).

General procedure for preparation of 2-thioxo-2,3-dihydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione derivatives (11a-f)

A mixture of **1** (1.43 g, 10 mmol), aldehyde derivatives (10 mmol) and indane-1,3-dione (1.46 g, 10 mmol) in acetic acid (30 mL) was heated under reflux for 3 h. After cooling at room temperature the solid product formed, which was collected by filtration and crystallized from dimethylsulfoxide to give compounds **11a-f** (except compound **11d** was crystallized from dimethylformamide).

2-Thioxo-2,3-dihydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (11a). This compound was obtained as dark yellow needles, (2.25 g, 80%), mp 250-251ºC; *Anal*. Calcd. $C_{14}H_7N_3O_2S$ (281.287): C, 59.78; H, 2.51; N, 14.94; S, 11.40. Found: C, 59.59; H, 2.43; N, 14.80; S, 10.95. IR (KBr, cm^{-1}) 1660 (CO), 1686 (CO), 3396 (NH), 3235 (NH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.78 (br, 1H, NH), 7.42-7.95 (m, 4H, Ar-H), 8.45 (s, 1H, H-5), 12.05 (br, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6) δ 112.33, 122.79, 124.93, 131.96, 134.14, 136.88, 141.93, 153.85, 160.51, 163.34, 164.45, 170.14, 173.71, 189.75; MS (EI) m/z 281 (M^+, 100%), 223 (43), 157 (30), 139 (12), 91 (3), 70 (6), 53 (7).

5-Phenyl-2-thioxo-2,3-dihydro-1*H*-indeno[2`,1`:5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (11b). This compound was obtained as pale orange needles, (2.96 g, 83%), mp 352-354ºC; *Anal*. Calcd. $C_{20}H_{11}N_3O_2S$ (357.385): C, 67.22; H, 3.10; N, 11.76; S, 8.97. Found: C, 67.15; H, 2.95; N, 11.56; S, 8.62. IR (KBr, cm^{-1}) 1664 (CO), 1690 (CO), 3232 (NH), 3440 (NH); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.05 (br, 1H, NH), 7.25-7.27 (m, 2H, Ar-H), 7.75-7.78 (m, 1H, Ar-H), 7.35-7.43 (m, 3H, Ar-H), 7.5-7.65 (m, 2H, Ar-H), 7.85-7.87 (m, 1H, Ar-H),12.47 (br, 1H, NH); MS (EI) m/z 357 (M^+, 37), 299 (18), 233 (24), 143 (17), 91 (24), 50 (10).

5-(4-Chlorophenyl)-2-thioxo-2,3-dihydro-1*H*-indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (11c). This compound was obtained as dark yellow needles, (3.33 g, 85%), mp > 360ºC; *Anal*. Calcd. $C_{20}H_{10}ClN_3O_2S$ (391.83): C, 61.31; H, 2.57; N, 10.72; S, 8.18. Found: C, 61.20; H, 2.33; N, 10.67; S, 8.09. IR (KBr, cm^{-1}) 1665 (CO), 1697 (CO), 3237 (NH), 3449 (NH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.28-7.84 (m, 8H, Ar-H), 7.90 (s, 1H, NH), 11.49 (s, 1H, NH); MS (EI) m/z 391 (M^+, 100%), 333 (25), 282 (40), 250 (10), 214 (24), 130 (16), 51 (24).

5-(4-Fluorophenyl)-2-thioxo-2,3-dihydro-1*H*-indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (11d). This compound was obtained as dark orange needles, (3.90 g, 87%), mp > 360ºC; *Anal*. Calcd. $C_{23}H_{17}FN_4O_3S$ (448.48): C, 61.60; H, 3.82; N, 12.49; S, 7.15. Found: C, 61.48; H, 3.79; N, 12.35; S, 7.29. IR (KBr, cm^{-1}) 1665 (CO), 1689 (CO), 3232 (NH), 3417 (NH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.28-7.84 (m, 8H, Ar-H), 7.94 (s, 1H, NH), 11.49 (s, 1H, NH); MS (EI) m/z 375 (M^+, 100%), 317 (23), 288 (11), 232 (15), 109 (4), 51 (2).

5-(4-Nitrophenyl)-2-thioxo-2,3-dihydro-1*H*-indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (11e). This compound was obtained as brown needles, 3.26 g (81%), mp 325-326ºC; *Anal*. Calcd. $C_{20}H_{10}N_4O_4S$ (402.38): C, 59.70; H, 2.50; N, 13.92; S, 7.97. Found: C, 59.56; H, 2.33; N, 13.79; S, 7.81. IR (KBr, cm^{-1}) 1332, 1558 (NO_2), 1669 (CO), 1691 (CO), 3233 (NH), 3417 (NH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.82 (s, 1H, NH), 7.32-8.27 (m, 8H, Ar-H), 10.25 (s, 1H, NH); MS (EI) m/z 402 (M^+, 100%), 355 (20), 297 (12), 115 (21), 92 (5), 50 (16).

5-(4-Methylphenyl)-2-thioxo-2,3-dihydro-1*H*-indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine-4,6-dione (11f). This compound was obtained as dark yellow needles, (3.04 g, 82%), mp 335-337ºC; *Anal*. Calcd. $C_{21}H_{13}N_3O_2S$ (371.41): C, 67.91; H, 3.53; N, 11.31; S, 8.63. Found: C, 67.75; H, 3.33; N, 11.02; S, 8.54. IR (KBr, cm^{-1}) 1664 (CO), 1690 (CO), 3355 (NH), 3409 (NH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.39 (s, 3H, CH_3), 6.62 (s, 1H, NH), 7.12-7.89 (m, 8H, Ar-H), 11.15 (s, 1H, NH); MS (EI) m/z 371 (M^+, 100%), 354 (38), 284 (10), 228 (7), 91 (2), 56 (22).

General procedure for preparation of indeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'',1''-*c*]triazole-5,7-dione derivatives (12a-l)

Method A. To a stirred solution of the appropriate hydrazonoyl chloride **5a,b** (10 mmol) and **11a-f** (10 mmol) in dioxan (40 mL) was added triethylamine (1.4 mL, 10 mmol). The reaction mixture was refluxed until the hydrogen sulfide gas ceased to evolve (24 h). The solvent was evaporated under reduced pressure and the residue was treated with methanol (10 mL). The solid formed, was collected and crystallized from dimethylsulfoxide to give compounds **12a-l**.

Method B. To a solution of a mixture of **17** (10 mmol), aldehyde derivatives (10 mmol) and indane-1,3-dione (1.46 g, 10 mmoles) in absolute ethanol (30 ml) was added a catalytic amount of piperidine (0.85 g, 10 mmol). The reaction mixture was heated under reflux for 3h., and after cooling at room temperature; the solid product formed, was collected and crystallized from dimethylsulfoxide to give compounds **12a-l**.

1,3-Diphenylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'',1''-*c*]triazole-5,7-dione (12a). This compound was obtained as bright yellow needles, (3.30 g, 75%), mp > 360 ºC; *Anal*. Calcd. $C_{27}H_{15}N_5O_2$ (441.45): C, 73.46; H, 3.42; N, 15.86. Found: C, 73.24; H, 3.25; N, 15.66. IR (KBr, cm^{-1}) 1716 (CO), 1667 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.08-7.81 (m, 14H, Ar-H), 7.95 (s, 1H, H-11); MS (EI) m/z 441 (M^+, 100%), 324 (3), 195 (1), 102 (1), 91 (3), 51 (3).

3-Ethoxycarbonyl-1-phenylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'',1''-*c*]-triazole-5,7-dione (12b). This compound was obtained as yellow needles, (3.06 g, 70%), mp > 360ºC; *Anal*. Calcd. $C_{24}H_{15}N_5O_4$ (437.42): C, 65.90; H, 3.46; N, 16.01. Found: C, 65.76; H, 3.33; N, 15.80. IR (KBr, cm^{-1}) 1719 (CO), 1707 (CO), 1667 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.41 (t, J = 7.2 Hz, 3H, CH_3), 4.57 (q, J = 7.2 Hz, 2H, CH_2), 7.53 (m, 1H, Ar-H), 7.67-7.71 (m, 3H, Ar-H*)*, 7.80-7.83 (m, 2H), 8.06 (m, 1H, Ar-H), 8.14-8.16 (m, 2H, Ar-H), 8.57 (s, 1H, H-11); MS (EI) m/z 437 (M^+, 100%), 324 (29), 248 (8), 195 (7), 91 (8), 51 (7).

1,3,6-Triphenylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido-[2'',1''-*c*]triazole-5,7-dione (12c). This compound was obtained as dark yellow needles, (3.88 g, 75%), mp > 360ºC; *Anal*. Calcd. $C_{33}H_{19}N_5O_2$ (517.55): C, 76.59; H, 3.70; N, 13.53. Found: C, 76.35; H, 3.46; N, 13.35. IR (KBr, cm^{-1}) 1707 (CO), 1667 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.21-8.12 (m, 19H, Ar-H); MS (EI) m/z 517 (M^+, 100%), 422 (66), 260 (10), 1207 (14), 91 (73), 51 (13).

1,6-Diphenyl-3-ethoxycarbonylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'',1''-*c*]triazole-5,7-dione (12d). This compound was obtained as red needles, (3.75 g, 73 %), mp > 360ºC; *Anal*. Calcd. $C_{30}H_{19}N_5O_4$ (513.52): C, 70.17; H, 3.73; N, 13.64. Found: C, 70.02; H, 3.61; N, 13.54. IR (KBr, cm^{-1}) 1722 (CO), 1697 (CO), 1659 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.29 (t, J =

7.2 Hz, 3H, CH_3), 4.45 (q, *J* = 7.2 Hz, 2H, CH_2), 7.10-8.12 (m, 14H, Ar-H); MS (EI) m/z 514 (M^+, 5%), 472 (100), 400 (31), 358 (20), 125 (11), 55 (8).

6-(4-Chlorophenyl)-1,3-iphenylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'',1''-*c*]triazole-5,7-dione (12e). This compound was obtained as dark yellow needles, (4.14 g, 75 %), mp > 360ºC; *Anal*. Calcd. $C_{33}H_{18}ClN_5O_2$ (551.99): C, 71.81; H, 3.29; N, 12.69. Found: C, 71.75; H, 3.15; N, 12.55. IR (KBr, cm^{-1}) 1701 (CO), 1690 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.23-7.66 (m, 13H, Ar-H), 7.74 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.81 (m, 1H, Ar-H), 8.17 (d, *J* = 8.1 Hz, 2H, Ar-H); MS (EI) m/z 551 (M^+, 32%), 443 (30), 442 (100), 339 (2), 92 (8), 51 (3).

6-(4-Chlorophenyl)-3-ethoxycarbonyl-1-phenylindeno[2',1':5,6]pyrido[2,3:4'', 5'']pyrimido[2'',1''-*c*]triazole-5,7-dione (12f). This compound was obtained as yellow needles, (4.16 g, 76%), mp > 360ºC; *Anal*. Calcd. $C_{30}H_{18}ClN_5O_4$ (547.96): C, 65.76; H, 3.31; N, 12.78. Found: C, 65.66; H, 3.22; N, 12.60. IR (KBr, cm^{-1}) 1721 (CO), 1713 (CO), 1655 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.29 (t, *J* = 7.2 Hz, 3H, CH_3), 4.43 (q, *J* = 7.2 Hz, 2H, CH_2), 7.37 (d, *J* =8.1 Hz, 2H, Ar-H), 7.50-7.55 (m, 3H, Ar-H), 7.64-7.72 (m, 4H, Ar-H), 7.79-7.83 (m, 1H, Ar-H), 8.07 (m, 1H, Ar-H), 8.15 (d, *J* = 8.1 Hz, 2H, Ar-H); MS (EI) m/z 547 (M^+, 77%), 474 (28), 200 (13), 91 (100), 77 (52), 51 (19).

1,3-Diphenyl-6-(4-fluorophenyl)indeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido-[2'',1''-*c*] triazole-5,7-dione (12g). This compound was obtained as dark orange needles, (4.24 g, 76%), mp > 360ºC; *Anal*. Calcd. $C_{33}H_{18}FN_5O_2$ (535.54): C, 74.01; H, 3.39; N, 13.08. Found: C, 73.91; H, 3.30; N, 13.00. IR (KBr, cm^{-1}) 1686 (CO), 1660 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.97-7.66 (m, 13H, Ar-H), 7.75 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.81 (m, 1H, Ar-H), 8.18 (d, *J* = 8.1 Hz, 2H,Ar-H); MS (EI) m/z 535 (M^+, 50%), 442 (100), 339 (4), 194 (9), 91 (53), 51 (2).

3-Ethoxycarbonyl-6-(4-fluorophenyl)-1-phenylindeno[2',1':5,6]pyrido[2,3:4'',5''] pyrimido[2'',1''-*c*]triazole-5,7-dione (12h). This compound was obtained as orange needles, (3.94 g, 74%), mp > 360ºC; *Anal*. Calcd. $C_{30}H_{18}FN_5O_4$ (531.5): C, 67.79; H, 3.41; N, 13.18. Found: C, 67.62; H, 3.33; N, 13.06. IR (KBr, cm^{-1}) 1721 (CO), 1713 (CO), 1655 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.55 (t, *J* = 7.2 Hz, 3H, CH_3), 4.70 (q, *J* = 7.2 Hz, 2H, CH_2), 7.22-7.90 (m, 8H, Ar-H), 8.0 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.36 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.47 (m, 1H, Ar-H); MS (EI) m/z 531 (M^+, 9%), 434 (11), 210 (20), 114 (17), 91 (100), 77 (5), 51 (5).

1,3-Diphenyl-6-(4-nitrophenyl)indeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido-[2'',1''-*c*]triazole-5,7-dione (12i). This compound was obtained as pale orange needles, 3.93 g (70%), mp > 360 ºC; *Anal*. Calcd. $C_{33}H_{18}N_6O_4$ (562.54): C, 70.46; H, 3.23; N, 14.94. Found: C, 70.33; H, 3.20; N, 14.85. IR (KBr, cm^{-1}) 1342, 1558 (NO_2), 1705 (CO), 1689 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.23-7.83 (m, 13H, Ar-H), 8.06 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.17 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.26-8.33 (m, 1H); MS (EI) m/z 562 (M^+, 31%), 442 (24), 384 (42), 113 (33), 91 (100), 51 (5).

3-Ethoxycarbonyl-6-(4-nitrophenyl)-1-phenylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido [2'',1''-*c*]triazole-5,7-dione (12j). This compound was obtained as red needles, (4.07 g, 73%), mp > 360ºC; *Anal*. Calcd. $C_{30}H_{18}N_6O_6$ (558.50): C, 64.52; H, 3.25; N, 15.05. Found: C, 64.44; H, 3.16; N, 15.01. IR (KBr, cm^{-1}) 1350, 1542 (NO_2), 1720 (CO), 1710 (CO), 1660 (CO); ^{1}H

NMR (300 MHz, DMSO-d_6) δ 1.30 (t, *J* = 7.2 Hz, 3H, CH_3), 4.44 (q, *J* = 7.2 Hz, 2H, CH_2), 7.26-7.83 (m, 8H, Ar-H), 8.06 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.26 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.32-8.35 (m, 1H, Ar-H); MS (EI) m/z 558 (M^+, 28%), 384 (100), 356 (39), 91 (2), 55 (5).

1,3-Diphenyl-6-(4-methylphenyl)indeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido[2'', 1''-*c*] triazole-5,7-dione (12k). This compound was obtained as yellow needles, (4.04 g, 76%), mp > 360ºC; *Anal*. Calcd. $C_{34}H_{21}N_5O_2$ (531.57): C, 76.82; H, 3.98; N, 13.17. Found: C, 76.65; H, 3.94; N, 13.09. IR (KBr, cm^{-1}) 1712 (CO), 1660 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.09 (s, 3H, CH_3), 7.15-7.89 (m, 18H, Ar-H); MS (EI) m/z 531 (M^+, 66%), 430 (20), 214 (15), 91 (100), 51 (10).

3-Ethoxycarbonyl-6-(4-methylphenyl)-1-phenylindeno[2',1':5,6]pyrido[2,3:4'',5'']pyrimido [2'',1''-*c*]triazole-5,7-dione (12l). This compound was obtained as bright yellow needles, (3.95 g, 75%), mp > 360ºC; *Anal*. Calcd. $C_{31}H_{21}N_5O_4$ (527.53): C, 70.58; H, 4.01; N, 13.28. Found: C, 70.44; H, 3.88; N, 13.15. IR (KBr, cm^{-1}) 1720 (CO), 1712 (CO), 1655 (CO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.31 (t, *J* = 7.2 Hz, 3H, CH_3), 2.09 (s, 3H, CH_3), 4.38 (q, *J* = 7.2 Hz, 2H, CH_2), 7.17-7.25 (m, 4H, Ar-H), 7.49-7.55 (m, 1H, Ar-H), 7.61-7.72 (m, 3H, Ar-H), 7.79-7.83 (m, 1H, Ar-H), 8.08 (d, *J* = 8.1 Hz, 2H, Ar-H), 8.16 (d, *J* = 8.1 Hz, 2H, Ar-H); MS (EI) m/z 527 (M^+, 100%), 454 (33), 240 (16), 213 (13), 91 (68), 51 (15).

References

1. Dandia, A.; Arya, K.; Khaturia, S. *Arkivoc* **2005**, (*xiii)*, 80.
2. Domling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168.
3. J. Zhu; Bienayme, Eds. Eds., In *Multicomponent Reactions*; Wiley-VCH: Weinheim, 2005.
4. Akimoto, H.; Miwa, T.; Otsu, K. Japan Pat. 04, 1992, 235, 986; *Chem. Abstr.,* **1993**, *118*, 213101a.
5. Bratz, M.; Kober, R.; Seele, R.; Saupe, T.; Meyer, N.; Walker, N.; Landes, A.; Walter, H.; Canadian Pat. Appl; 2, 1993, 078, 4767; *Chem. Abstr*., **1994,** 120, 77293b
6. Hurlbert, B. S.; Valenti, B. F. *J. Med. Chem.* **1968**, *11*, 708.
7. Parish, H. A.; Gilliom, R. D.; Purcell, W. P.; Browne, R. K.; Spirk; R. F.; White, H. D. *J. Med. Chem*., **1982**, *25*, 98.
8. Bouzard, D.; In *Antibiotics and Antiviral Compounds*; Krohn, K.; Kirst, K. A.; Maag, M. Eds; Wiley-VCH: Weinheim, **1993**, *99*, pp186-203.
9. Hassaneen, H. M.; Abdallah, T. A.; Abdelhadi, H. A.; Hassaneen, H. M. E.; Pagni, R. M. *Heteroatom Chem*. **2003**,*14*, 491.
10. Crystal data of **11d** (ref. CCDC 611538) can be obtained on request from the director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.
11. Mansour, A.; Elwan, N. M.; Abdelhadi, H. A.; Abdallah, T. A.; Hassaneen, H. M. *Sulfur Letters* **1994**, *18*, 105.

12. Elwan, N. M.; Fahmy, A. A.; Abdallah, T. A.; Hassaneen H. M.; Algharib, M. S. *Sulfur Lett.* **1994**, *18*, 9.
13. Hassaneen, H. M.; Abdelhadi, H. A.; Abdallah, T. A. *Tetrahedron* **2001**, *57*, 10133.
14. Mosselhi, M. A. *Monatsh. Chem*. **2002**, *133*, 1297.
15. Abdallah, T. A.; Darwish, M. A.; Hassaneen, M. H. *Molecules* **2002**, *7*, 494.

