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SITE SELECTIVITY IN REACTION OF HYDRAZONOYL HALIDES WITH 6-AMINO-2-THIOXOPYRIMIDIN-4-ONE

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ABSTRACT

Reaction of hydrazonoyl halides **1** with 6-amino-2-thioxopyrimidin-4-one **6** was proved to be regio- and site-selective as they gave the respective 1,2,4-triazolo[4,3-*a*]pyrimidin-5-one derivatives **9**. The structures of the latter compounds were elucidated based on their spectral data, alternate synthesis and chemical reactions. The mechanism of the studied reactions is discussed.

Keywords: Site selectivity, enaminones, triazolopyrimidine and hydrazonyl halides.

INTRODUCTION

A survey of literature revealed that reactions of hydrazonoyl halides **1** with 2-thioxopyrimidin-4-one derivatives **2** led to the formation of the corresponding derivatives of 1,2,4-triazolo[4,3-*a*]pyrimidin-5-one **3** **[Shawali *et al.*, (2007); Shawali *et al.*, (2006); Shawali *et al.*, (2006) and Shawali & Edrees (2006)]** (Chart 1). Also, reactions of such hydrazonoyl halides **1** with endocyclic enaminones **4** afforded the respective fused pyrazoles **5** **[Shawali *et al.*, (2004)]** (Chart 1). In the light of these findings, it was thought interesting to study the reactions of **1** with 6-amino-2-thioxopyrimidin-4-one **6.** The interesting in the latter compound is due to the fact that it has both 2-thioxo-pyrimidine and endocyclic enaminone residues and thus its reactions with **1** can lead theoretically to compounds **9, 10** and/ or **11** (Scheme 1). Accordingly, the results of the reactions of **1** with **6** will shed some light on the site selectivity of the target reactions which have been investigated **[Hassaneen *et al.*, (1985); Mansour *et al.*, (1995); Abdelhadi *et al.*,**

(1999) and Hassaneen *et al.*, (2001)]. In addition, the target compounds are expected to have pharmacological interest as many derivatives of fused 1,2,4-triazolopyrimidine were reported **[Shawali *et al.*, (2006)]** to be useful calcium-channel blocking vasodilators and have antihypertensive **[Awal (1985)]**, cardiovascular **[Barthelemy *et al.*, (1985) and Bru-Magniez *et al.*, 1995)]** and anxioltic activities. **[Albright *et al.*, (1980)]**.

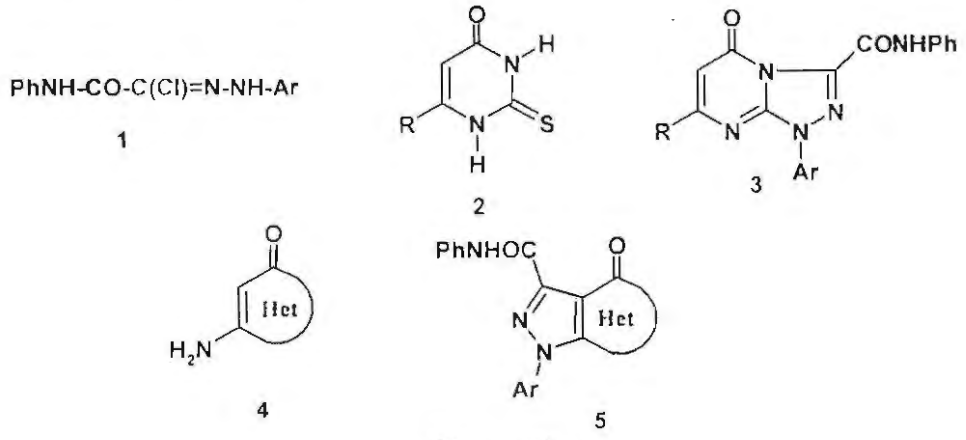


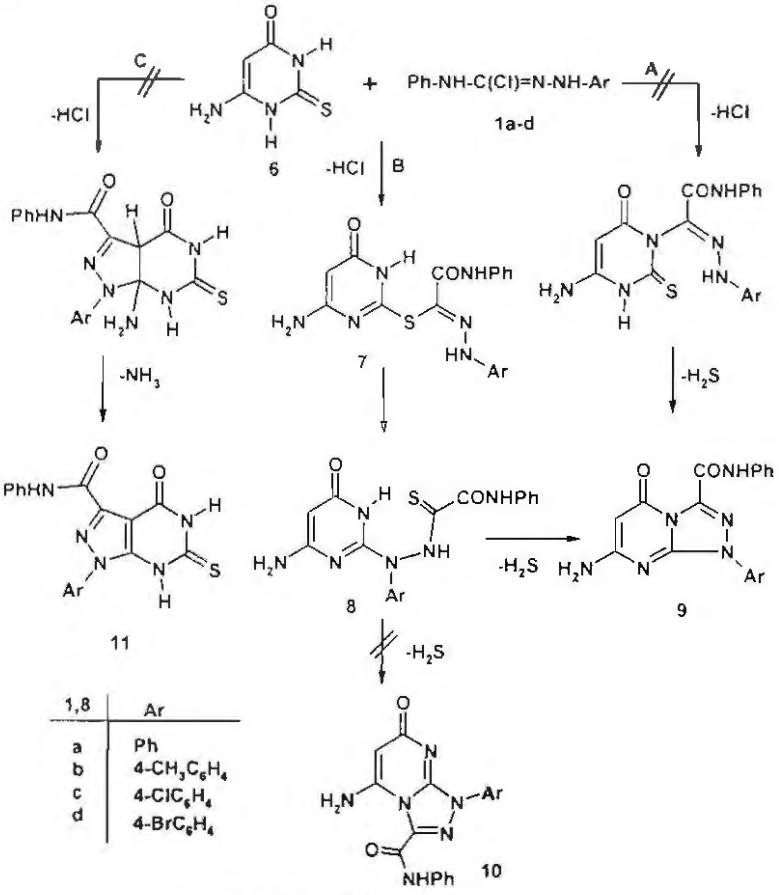
Chart (1)

RESULTS AND DISCUSSION

The required hydrazonoyl chlorides **1a-d [Bullow & King (1924)]** and 6-amino-2-thioxopyrimidin-4-one **6** [**Taylor (1960)]** were prepared as previously described. Reactions of **6** with each **1a-d** in refluxing dioxane in the presence of triethylamine as a base catalyst gave. in each case, one isolable product as evidenced by TLC analysis of the crude product. This finding indicates that the studied reactions are regio- and site-selective. On the basis of the spectral data and elemental analysis data (see the experimental section), the isolated products were assigned the structure of 1,2,4-triazolo[4,3-*a*]pyrimidin-5(1H)-one **9** rather than the structure of **10** and **11** (Scheme 1). For example, the ^{13}C-NMR spectrum of **9a,** taken as a typical example of the series prepared, showed two carbonyl carbon signals at δ 165 and 156 assignable for the cyclic and the anilide CO groups, respectively. The δ value of 165 for the cyclic CO carbon is similar to that reported for fused 1,2,4-triazolo[4,3-*a*]pyrimidin-5(1H)-ones (δ 161-165) and different from that of the

isomeric 1,2,4-triazolo[3,4-*b*]pyrimidin-5(1H)-ones (δ 170-175) [**Shawali *et al.*, (2001)**]. By analogy to literature (Ms, IR, ^{1}H, and ^{13}C-NMR) which showed all of the expected signals as well as reports, the formation of **9** could be accounted for by either one of two routes A and B depicted in Scheme 1.

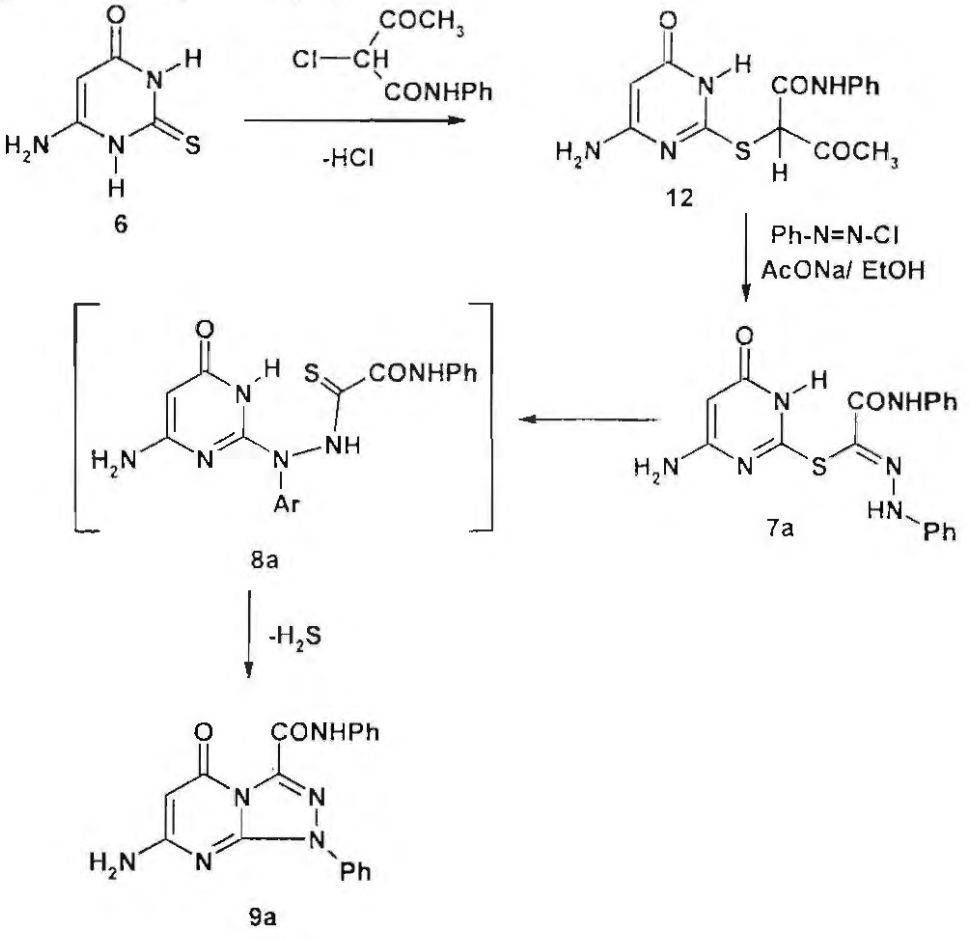
To distinguish between these two possible routes and to provide further evidence for assigned structure **9**. compound **9a** was prepared by alternate route (Scheme 2). Thus, treatment of **6** with 3-oxo-2-chloro-*N*-phenylbutanamide in ethanol in the presence of sodium ethoxide afforded the substitution product **12**. Coupling of the latter **12** with diazotized aniline in ethanol in the presence of sodium acetate yielded the thiohydrazonate **7a** (Scheme 2). Treatment of the latter with sodium ethoxide in refluxing ethanol gave **9a** directly *via* tandem rearrangement of **7a** to give the



1,8	Ar
a	Ph
b	4-$CH_3C_6H_4$
c	4-ClC_6H_4
d	4-BrC_6H_4

Scheme (1)

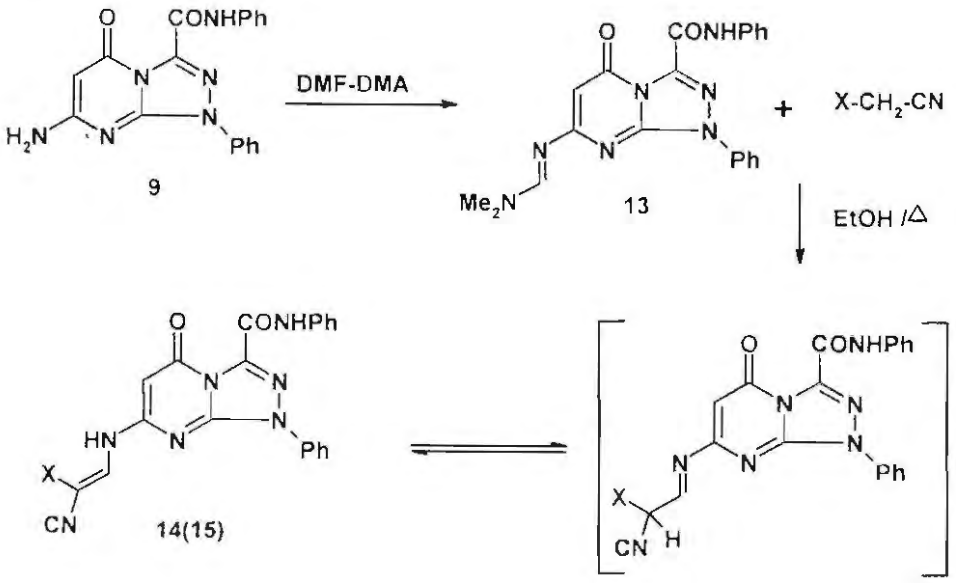
thiohydrazide **8a** and cyclization of the latter to give **9a** as end product which proved identical in all respects (mp, mixed mp, and spectral data) with that one obtained above from reaction of **1a** with **6** (Scheme 1). This finding indicates that reactions of **1** with **6** proceeds through route B (Scheme 1) which involves the initial formation of the thiohydrazonate ester **7** as an intermediate that undergoes in *situ* rearrangement, under the reaction conditions employed, to give the respective thiohydrazide **8**. The latter intermediate in turn cyclizes *via* elimination of hydrogen sulfide to give **9** as end product (Scheme 1).



Scheme (2)

Furthermore, to provide extra evidence for structure **9** assigned for the products of the studied reactions, their conversion into the respective imino derivatives was examined. Thus, treatment of each of the products **9a-d** with dimethylformamide dimethylacetal (DMF-DMA) afforded the respective *N*-dimethylaminomethine derivatives **13a-d** (Scheme 3). Reaction of the latter each with malononitrile and ethyl cyanoacetate in ethanol afforded the corresponding substitution products **14** and **15** respectively (Scheme 3). The structures of the products **14** and **15** were established by spectral and elemental analyses (see Experimental).

It is worthy to mention herein that all attempts to cyclize the latter products **14 (15)**, as it was reported for 1,3-diphenyl-1,2,4-triazolo[3,4-*d*]pyrimidinyl-*N,N*-dimethyl-formamidine analogs **[Hassneen & abdallah (2003)]**, were failed.



14	Ar/ X
a	Ph / CN
b	4-$CH_3C_6H_4$ / CN
c	4-ClC_6H_4 / CN
d	4-BrC_6H_4 / CN

15	Ar / X
a	Ph / COOEt
b	4-$CH_3C_6H_4$ / COOEt
c	4-ClC_6H_4 / COOEt
d	4-BrC_6H_4 / COOEt

Scheme (3)

EXPERIMENTAL

Melting points were determined on a Gallenkamp electrothermal apparatus and are uncorrected. IR spectra (KBr) were recorded on a Pye Unicam SP-300 IR spectrophotometer and Testscan Shimadzu FT-IR 8000 series. ^{1}H NMR were recorded on a Varian Gemini 200 and Varian EM 390 spectrometers for solution in dimethyl sulfoxide-d_6 using TMS as internal standard. Mass spectra were recorded on a GCMS-QP 1000-EX Shimadzu, Japan. Elemental analyses were carried out at the microanalytical center, University of Cairo, Giza, Egypt. *N*-aryl-2-oxo-2-phenylaminoethane hydrazonoyl chlorides **1a-d [Bullow & King (1924)]** 6-Amino-2-thioxopyrimidin-4-one **6 [Taylor & Cheng (1960)]** were prepared as previously described.

Synthesis of 7-amino-1,5-dihydro-5-oxo-*N*-phenyl-1-aryl[1,2,4] triazolo[4,3-*a*]-pyrimidin-3-carboxamide 9a-d:

Method A

To a stirred solution of *N*-aryl-2-oxo-2-phenylaminoethane hydrazonoyl chloride **1a-d** (5 mmoles) and 6-amino-2-thioxopyrimidine-4-one **6** (1.1 gm, 5 mmoles) in dioxane (30 mL) was added triethylamine (0.7 mL, 5 mmoles) at room temperature. The reaction mixture was refluxed till the hydrazonoyl chloride disappeared (4-6h) as indicated by TLC analysis. The solvent was evaporated under reduced pressure and the residue was treated with methanol (10 ml). The solid formed was collected and crystallized from dimethylformamide to give the corresponding compounds **9a-d**, respectively.

Method B

To an ethanolic sodium ethoxide solution [prepared by dissolving sodium metal (0.11 gm, 5 mmole) in ethanol (20 mL)], compound **7a.** (1.9 gm, 5 mmole) was added. The reaction mixture was refluxed for 6h then the excess solvent was evaporated under reduced pressure and the residue was treated with methanol (10 mL). The solid was collected and crystallized from dimethylformamide to give the corresponding product which identical in all respects (mp, mixed mp, and spectral data) with **9a** obtained by method **A**

7-amino-1,5-dihydro-5-oxo-*N*,1-diphenyl[1,2,4]triazolo[4,3-*a*]pyrimidin-3-carbo-xamide 9a has mp. 230°C; 85% yield; IR (KBr) ν 3385, 3323, 3230 (NH, NH_2), 1694, 1654 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.12 (s, 1H-pyrimidine), 7.18-8.13 (m, 12H), 13.01(s, 1H) ppm; ^{13}C NMR (DMSO-d_6) δ 77.77, 119.57, 120.70, 121.25, 124.38, 127.45, 129.14, 136.23, 137.90, 139.37, 148.37, 152.64, 156.52, 165.01; MS, m/z (%) 346(M^+, 28.6), 226(18.2), 159(23.4), 110(37.3), 77(100), 65(64.9), 51(57.1).
Anal. Calcd for $C_{18}H_{14}N_6O_2$(M wt 346.35): C, 62.42; H, 4.07; N, 24.27: Found: C, 62.32, H, 4.11; N, 24.34%.

7-amino-1,5-dihydro-5-oxo-*N*-phenyl-1-(4-methylphenyl)[1,2,4]triazolo[4,3-*a*]pyrimidin-3-carbox-amide 9b has mp. 235°C; 86% yield; IR (KBr) ν 3473, 3311, 3217 (NH, NH_2), 1697, 1654 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.51 (s, 3H), 5.20 (s, 1H-pyrimidine), 5.68 (s, 2H), 7.19-8.10 (m, 9H), 13.16(s, 1H) ppm; MS, m/z (%) 360(M^+, 36.4), 132(57.6), 91(100), 77(97). Anal. Calcd for $C_{19}H_{16}N_6O_2$(M wt 360.38): C, 63.32; H, 4.48; N, 23.32. Found: C, 63.29, H, 4.40; N, 23.40%.

7-amino-1,5-dihydro-5-oxo-*N*-phenyl-1-(4-chlorophenyl)[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carbox-amide 9c has mp. 253°C; 80% yield; IR (KBr) ν 3481, 3311, 3212 (NH, NH_2), 1695, 1664 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.10 (s, 1H-pyrimidine), 7.19-8.19 (m, 11H), 12.97(s, 1H) ppm; MS, m/z (%) 382(M+2, 12), 381(M+1, 7.5), 380(M^+, 17), 253(12), 152(17.5), 110(46.5), 68(100). Anal. Calcd for $C_{18}H_{13}$ Cl N_6O_2 (M wt 380.80): C, 56.78; H, 3.44; Cl, 9.31; N, 22.07. Found: C, 56.72, H, 3.36; Cl, 9.21; N, 22.13%.

7-amino-1,5-dihydro-5-oxo-N-phenyl-1-(4-bromophenyl)[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carbox-amide 9d has mp. 328°C; 75% yield; IR (KBr) ν 3480, 3309, 3213 (NH, NH_2), 1695, 1673 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.08 (s, 1H-pyrimidine), 7.15-8.11 (m, 11H), 12.94(s, 1H) ppm; ^{13}C NMR (DMSO-d_6) δ 77.88, 119.15, 119.18, 120.19, 122.13, 124.15, 129.12, 132.13, 135.16, 137.19,148.13, 152.15, 156.15, 164.15; MS, m/z (%) 426(M+2, 28.9), 425(M+1, 10.5),424(M^+, 29), 381(14), 306(10.8), 253(25), 198(22), 110(70), 68(100). Anal. Calcd for $C_{18}H_{13}BrN_6O_2$(M wt 425.25): C, 50.84; H, 3.08; N, 19.76. Found: C, 50.66, H, 2.98; N, 19.70%.

Synthesis of 2-(4-amino-1,6-dihydro-6-oxo-pyrimidin-2-ylthio)-3-oxo-*N*-phenyl-butanamide 12

To a mixture of equimolar quantities of 6-amino-2,3-dihydro-2-thioxo-pyrimidin-4(1H)-one **6** (1.43 gm, 10 mmoles) and α-chloroacetoacetanilide (2.1 gm, 10 mmoles) in absolute ethanol (30 mL) was added triethylamine (1.4 ml, 10 mmoles). The mixture was stirred at room temperature for 24 h, then the solvent was distilled under reduced pressure and the residue was collected and crystallized from ethanol to give compound **12**, has mp.190°C; 85% yield; IR (KBr) ν 3444, 3354, 3188 (NH), 1700, 1696 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.31 (s, 3H), 2.61 (s, 1H), 5.58 (s, 1H-pyrimidine), 6.56-7.60 (m, 7H), 10.14 (s, 1H), 10.39 (s, 1H) ppm; MS, m/z (%) 318(M^+,1.3), 225(19.3), 110(55.3), 92(12.0), 93(100.0), 267(16.3), 68(41.2), 65(30.6).
Anal. Calcd for $C_{14}H_{14}N_4O_3S$ (M wt 318.36): C, 52.82; H, 4.43; N, 17.60; S, 10.07. Found: C, 52.71, H, 4.39; N, 17.99; S, 9.96%.

Synthesis of thiohydrazonate ester 7a

To a stirred solution of **12** (3.18 gm, 10 mmoles) in ethanol (50 mL), sodium acetate trihydrate (1.3 gm, 10 mmoles) was added. After stirring for 15 min, the mixture was cooled at 0°C and treated with a cooled solution of benzene diazonium chloride [Prepared from aniline (0.93 gm, 10 mmoles) in hydrochloric acid (6 M, 6 mL) with sodium nitrite (1 M, 10 mL)]. The whole mixture was then left in a refrigerator overnight. The precipitated solid was collected, washed with water and finally crystallized from dimethylformamide to give compound **7a**, has mp.>320°C; 65% yield; IR (KBr) ν 3193, 3445 (broad NH), 1671 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.41 (s, 1H-pyrimidine), 6.72-8.00 (m, 15H) ppm; MS, m/z (%) 380(M^+, 3.8), 160(12.5), 128(26.1), 119(68.2), 93(72.7),77(43.2), 64(100.0), 51(48.9). Anal. Calcd for $C_{18}H_{16}N_6O_2S$(M wt 380.43): C, 56.83; H, 4.24; N, 22.09; S, 8.43. Found: C, 56.71, H, 4.19; N, 22.19; S, 8.48%.

Synthesis of 7-*Z*-(dimethylformamido)-1,5-dihydro-5-oxo-*N*-phenyl-1-aryl[1,2,4]-triazolo[4,3-*a*]pyrimidine-3-carboxamide 13a-d:

7-Amino-1,2,4-triazolo[4,3-a]pyrimidine-5-one **9a-d** (5 mmoles) was refluxed with DMF DMA (0.6 gm, 5 mmoles) for 3h. The product that precipitated on cooling was collected by filtration and crystallized from dimethylformamide to give the corresponding compounds **13a-d**, respectively.

7-*Z*-(Dimethylformamido)-1,5-dihydro-5-oxo-*N*,1-diphenyl[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 13a has mp. 265°C; 82% yield; IR (KBr) ν 3212(NH), 1698 and 1662 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.06 (s, 3H), 3.11 (s, 3H), 5.47 (s, 1H-pyrimidine), 7.16-8.18 (m, 10H), 8.61 (s, 1H, CH=N), 12.47 (s, 1H) ppm; MS, m/z (%) 401(M^+,14), 237(2.3), 123(9.5), 118(5.2), 98(22.7), 77(100). Anal. Calcd for $C_{21}H_{19}N_7O_2$(M wt, 401.42): C, 62.83; H, 4.77; N, 24.42. Found: C, 62.75, H, 4.71; N, 24.49%.

7-*Z*-(Dimethylformamido)-1,5-dihydro-5-oxo-*N*-phenyl-1-(4-methylphenyl)[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 13b has mp. 270°C; 80% yield; IR (KBr) ν 3217(NH), 1679 and 1669 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.51 (s, 3H), 3.07 (s, 3H), 3.20 (s, 3H) 5.46 (s, 1H-pyrimidine), 7.19-8.05 (m, 9H), 8.61 (s, 1H, CH=N), 12.46 (s, 1H) ppm; MS, m/z (%) 415(M^+, 65.7), 386(3.6), 225(10), 165(18.5), 123(28.7), 91(100). Anal. Calcd for $C_{22}H_{21}N_7O_2$(M wt, 415.46): C, 63.60; H, 5.09; N, 23.60. Found: C, 63.75, H, 4.91; N, 23.79%.

7-*Z*-(Dimethylformamido)-1,5-dihydro-5-oxo-*N*-phenyl-1-(4-chlorophenyl)[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 13c has mp. 281°C; 79% yield; IR (KBr) ν 3220(NH), 1701 and 1668 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.06 (s, 3H), 3.20 (s, 3H) 5.46 (s, 1H-pyrimidine), 7.19-8.23 (m, 9H), 8.62 (s, 1H, CH=N), 12.45 (s, 1H) ppm; MS, m/z (%) 437(M+2, 9.7), 436(M+1, 9.7), 435(M^+, 30.9), 391(11.5), 259(6), 165(21.7), 99(100), 77(72). Anal. Calcd for $C_{21}H_{18}ClN_7O_2$(M wt, 435.87): C, 57.87; H, 4.16; Cl, 8.13; N, 22.49 Found: C, 57.80, H, 4.11; Cl.8.15; N, 22.57%.

7-*Z*-(Dimethylformamido)-1,5-dihydro-5-oxo-*N*-phenyl-1-(4-bromophenyl)[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 13d has mp. 278°C; 77% yield; IR (KBr) ν3219(NH), 1699 and 1675 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.11 (s, 3H), 3.25 (s, 3H), 5.50 (s, 1H-pyrimidine), 7.25-8.66 (m, 9H), 8.66 (s, 1H, CH=N), 12.56 (s, 1H) ppm; MS, m/z (%) 482(M+2, 20.3), 481 (M+1, 62.9), 480(M^+, 54.5), 210(13.4), 165(41.3), 99(100), 57(33.8). Anal. Calcd for $C_{21}H_{18}BrN_7O_2$(M wt, 480.33): C, 52.51; H, 3.78; N, 20.41. Found: C, 52.65, H, 3.83; N, 20.52%.

Synthesis of 7-(2,2-dicyanoethylideneamino)-1,5-dihydro-5-oxo-1-aryl-*N*-phenyl[1,2,-4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 14a-d:

A solution of malononitrile (0.33 gm, 5 mmoles) and the enaminone **13a-d** (5 mmoles) in ethanol (30 mL) was refluxed for 3h. The solvent was evaporated under reduced pressure and the residue was triturated with methanol (10 mL) where it is solidified. The crude product was collected and crystallized from dimethylformamide to afford the corresponding compounds **14a-d**, respectively.

7-(2,2-dicyanoethylideneamino)-1,5-dihydro-5-oxo-*N*,1-diphenyl[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 14a has mp. 330°C; 79% yield; IR (KBr) ν 3201(NH), 2217(CN), 1708, 1665(CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.07 (s, 1H-pyrimidine), 7.26-8.25 (m, 10H), 8.77 (s, 1H), 11.58 (s, 1H), 11.81 (s, 1H) ppm; MS, m/z (%) 422(M^+, 24.4), 377(18.3), 302(17.1), 144(33.1), 118(52.8), 77(100). Anal. Calcd for $C_{22}H_{14}N_8O_2$(M wt, 422.40): C, 62.56; H, 3.34; N. 26.53 Found: C, 62.49, H, 3.27; N, 26.57%.

7-(2,2-dicyanoethylideneamino)-1,5-dihydro-5-oxo-*N*-phenyl-1-(4-methylphenyl)[1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 14b has mp. 322°C; 72% yield; IR (KBr) ν 3170(NH), 2224(CN), 1700, 1690(CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.43(s, 3H), 5.99 (s, 1H-pyrimidine), 7.21-8.00 (m, 9H), 8.64 (s, 1H), 11.57 (s, 1H), 11.76 (s, 1H) ppm; MS, m/z (%) 436(M^+,100), 391(80.2), 316(43.7), 251(13.8), 186 (12.3), 132(75.5), 91 (89.6). Anal. Calcd for $C_{23}H_{16}N_8O_2$(M wt, 436.43): C, 63.30; H, 3.70; N, 25.68 Found: C, 63.39, H, 3.64; N, 25.61%.

7-(2,2-dicyanoethylideneamino)-1,5-dihydro 5-oxo-*N*-phenyl-1-(4-chlorophenyl)[1,2,-4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 14c has mp. 330°C; 72% yield; IR (KBr) ν 3280, 3213 (NH), 2226 (CN), 1711, 1697(CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.07 (s, 1H-pyrimidine), 7.26-8.77 (m, 10H), 8.74 (s, 1H), 11.58 (s, 1H), 11.80 (s, 1H) ppm; MS, m/z (%) 458(M+2,14.0), 457 (M+1;15.3), 456(M^+,40), 411(41.9), 336(29.9), 247 (11.4), 186 (18.9), 152(100), 65(82.6). Anal. Calcd for $C_{22}H_{13}ClN_8O_2$(M wt, 456.84): C, 57.84; H, 2.87; Cl, 7.76; N, 24.53 Found: C, 57.89, H, 2.81; Cl, 7.69; N, 24.47%.

7-(2,2-dicyanoethylideneamino)-1,5-dihydro 5-oxo-*N*-phenyl-1-(4-bromophenyl)[1,2,-4]triazolo[4,3-*a*]pyrimidine-3-carboxamide 14d has mp. 340°C; 70% yield; IR (KBr) ν 3279, 3213, (NH), 2227 (CN), 1711 and 1691 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.08 (s, 1H-pyrimidine), 7.27-8.19 (m, 9H), 8.76 (s, 1H), 11.58 (s, 1H), 11.81 (s, 1H) ppm; MS, m/z (%) 503(M+2, 7.3), 502 (M+1, 6.3), 501(M^+,28.8), 457(25.6.2), 382(19.0), 196 (53.4), 119(100). Anal. Calcd for $C_{22}H_{13}N_8O_2Br$(M wt, 501.30): C, 52.71; H, 2.61; N, 22.35 Found: C, 52.69, H, 2.69; N, 22.29%.

Synthesis of ethyl 3-[3-(phenylcarbamoyl)-1,5-dihydro-5-oxo-1-aryl[1,2,4]triazolo-[4,3-*a*]pyrimidin-7-ylimino-]2-cyanopropenoate 15a-d

These compounds were prepared by thesame procedure described for the preparation of **14a-d** using ethyl cyanoacetate in place of malononitrile.

Ethyl 3-(3-phenylcarbamoyl)-1,5-dihydro-5-oxo-1-phenyl[1,2,4]triazolo-[4,3-*a*]-pyrimidin-7-ylimino]-2-cyanopropenoate 15a has mp. 215°C; 78% yield; IR (KBr) ν 3213 (NH), 2227 (CN), 1701 and 1668 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.29 (t, J=7Hz, 3H), 4.23 (q, J= 7Hz, 2H), 5.09 (s, 1H-pyrimidine), 7.19-8.18 (m, 10H), 8.95 (s, 1H), 11.74 (s, 1H), 13.08 (s, 1H) ppm; MS, m/z (%) 469(M^+,10), 374(18.6), 302(18.1), 226(20.1), 187 (18.1), 118(42.8), 77(100). Anal. Calcd for $C_{24}H_{19}N_7O_4$(M wt, 469.46): C, 61.40; H, 4.08; N, 20.89 Found: C, 61.46, H, 4.11; N, 20.85%.

Ethyl 3-[(3-phenylcarbamoyl)-1,5-dihydro-5-oxo-1-(4-methylphenyl)[1,-2,4]triazolo-[4,3-*a*]pyrimidin-7-ylimino-]2-cyanopropenoate 15b has mp. 288°C; 77% yield; IR (KBr) ν 3178 (NH), 2227 (CN), 1701 and 1668 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.29 (t, J=7Hz, 3H), 2.42 (s, 3H), 4.23 (q, J= 7Hz), 5.99 (s, 1H-pyrimidine), 7.17-7.98 (m, 9H), 8.91 (s, 1H), 11.48 (s, 1H), 11.78 (s, 1H) ppm; MS, m/z (%) 483(M^+, 80.5), 438(26.2), 291(26.1), 251(20.7), 132 (56.6), 91(100). Anal. Calcd for $C_{25}H_{21}N_7O_4$(M wt, 483.48): C, 62.11; H, 4.38; N, 20.28 Found: C, 62.08, H, 4.41; N, 20.25%.

Ethyl 3-[(3-phenylcarbamoyl)-1,5-dihydro-5-oxo-1-(4-chlorophenyl)[1,2-,4]triazolo-[4,3-*a*]pyrimidin-7-ylimino-]2-cyanopropenoate 15c has mp. 310°C; 73% yield; IR (KBr) ν 3206 (NH), 2227 (CN), 1701 and 1668 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.29 (t, J=7Hz, 3H), 4.26 (q, J=

7Hz, 2H), 6.01 (s, 1H-pyrimidine), 7.22-8.17 (m, 9H), 8.91 (s, 1H), 11.51 (s, 1H), 11.96 (s, 1H) ppm; MS, m/z (%) 505(M+2, 24.8), 504 (M+1, 22.4), 503(M^+, 64.7), 458(29.6), 311(29.3), 210(14.6), 163 (35.7),125(74.2), 68(100). Anal. Calcd for $C_{24}H_{18}ClN_7O_4$(M wt, 503.90): C, 57.21; H, 3.60; Cl, 7.04; N, 19.46 Found: C, 57.18, H, Cl, 7.12; 3.63; N, 19.39%.

Ethyl 3-[3-(phenylcarbamoyl)-1,5-dihydro-5-oxo-1-(4-bromophenyl)[1,-2,4]triazolo-[4,3-*a*]pyrimidin-7-ylimino-]2-cyanopropenoate 15d has mp.340°C; 73% yield; IR (KBr) ν 3213 (NH), 2227 (CN), 1701 and 1668 (CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.27 (t, J=7Hz, 3H), 4.22 (q, J= 7Hz,2H), 5.99 (s, 1H-pyrimidine), 7.25-8.20 (m, 9H), 11.54 (s, 1H), 11.97 (s, 1H) ppm; MS, m/z (%) 550(M+2,1.7), 549 (M+1,3.8), 452 (52.1), 409(27.6), 306(17.9), 267(16.3), 198(28.0), 119(31.0), 68(100.0). Anal. Calcd for $C_{24}H_{18}BrN_7O_4$(M wt, 548.35): C, 52.57; H, 3.31; N, 17.88 Found: C, 52.51, H, 3.39; N, 17.99%.

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الاختيارية الانتقالية فى تفاعل هيدرازونيل الهاليدات مع ٦-أمينو-٢-ثيوكسوبير ميديين-٤-اوان

هيام عبد الحميد عبد الهادى

تفاعل احدى مشتقات هاليدات الهيدرازونويل 1 مع 6-امينو-2- ثيوكسوبيريمدين-4-اون(6-امينو-2-ثيويوراسيل) 6 قد اثبت اللانتقائية الاختيارية والمكانية ليعطى فى خطوة واحدة مشتقات 1و2و4-تريازولو[4-a, 3] بيريمدين-5-اون9. وتم تفاعل المركبات الناتجة مع داى ميثيلفور ماميد-دايميثيلاسيتال ليعطى مشتقات N -دايميثيلامينوميثين 13. بتفاعل النواتج الاخيره مع ملونونيتريل وايثيل سيانواسيتات فى ايثانول مغلى اعطى النواتج المستبدلة 14و15.

وتم التاكد من تركيب المركبات الجديدة عن طريق التحاليل العنصرية واليفية المختلفة (الاشعة تحت الحمراء والرنين النووى المغناطيسى وطيف الكتلة) وكذلك بطريقة كيميائية مقابلة.