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Synthesis, Reactions and Antimicrobial Activity of Some 10,10-dimethyl-chromeno[4',3':4,5]thieno[2,3-*d*]pyrimidin-4-ones

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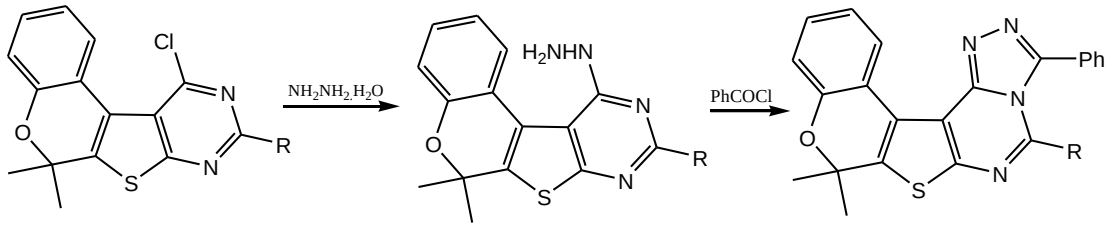
ABSTRACT

A variety of 10,10-dimethyl-3H,10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-ones (4a-c) were synthesized, in one pot reaction, via the reaction of 2-amino-4,4-dimethyl-4H-thieno[2,3-c]chromene-1-carbonitrile (3a,b) with various aliphatic acids in the existence of phosphorus oxychloride. Moreover, 8,8-dimethyl-8H-chromeno[4',3':4,5]thieno[3,2-e][1,3,4]triazolo[1,5-c]pyrimidines (7a-c) were prepared from the reaction of 4-hydrazino-10,10-dimethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-ones (6a-c) with benzoyl chloride. The newly synthesized chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-ones derivatives were proved by their Infra-red (IR), Proton Nuclear Magnetic Resonance (^{1}H-NMR), MS spectra and elemental analyses. The newly synthesized products (6a-c) and (7a-c) showed promising antimicrobial activity.



Keywords: Hindered chroman-4-one, Chromeno[4',3':4,5]thieno[2,3-*d*]pyrimidin-4-ones, Chromeno[4',3':4,5]thieno[3,2-*e*][1,3,4]triazolo[1,5-*c*]pyrimidines, Antimicrobial activity

INTRODUCTION

Chromanones are considered as one of the significant classes of naturally occurring substances [1-3] and have attracted the attention of many researchers because of their renowned features as Antihuman Immunodeficiency Virus (HIV-1) that gives rise to the Acquired Immune Deficiency Syndrome (AIDS) [4-6].

In addition, a number of thienopyrimidines have acquired intrinsic interest owing to their important biological and pharmacological activities [7-9]. These derivatives have also displayed analgesic [10,11], antimicrobial [12], anti-inflammatory effects [13], platelet aggregation inhibitory activity [14] and antagonism of α-adrenoceptor [15]. In addition 1,2,4-triazole model incorporating compounds have been known to possess considerable antitubercular [16] and anticancer activities [17].

MATERIALS AND METHODS

Melting points were taken on a digital melting point apparatus and they are uncorrected. Infrared spectra (KBr for solid or neat for liquid) were measured on a Bruker-Vector 22, Germany (Cairo university, Faculty of Science) and Mass spectra were measured on Hewlett-Packard 5988 A (1000 Hz) instrument, Shimadzu GCMS-QP-1000EX mass spectrometer at 70 ev (Cairo University, Faculty of Science). ^{1}H-NMR spectra were obtained by using a JEOL EX-500 MHz (National Research Center, Central Services Laboratory) spectrometers and ($CDCl_3$) with Tetramethylsilane (TMS) as internal standard. Chemical shifts were quoted in δ and were related to that of the solvents. Splitting patterns were designated as follow: s-Singlet; m-Multiplt.

Elemental analyses were operated using Mario Elementar apparatus, Organic Microanalysis Unit, National Research Center, Cairo, Egypt. All reactions were monitored by Thin Layer Chromatography (TLC). All microorganisms used were obtained from the culture collection of the Department of Natural and Microbial Products, National Research Centre, Dokki, Cairo, Egypt.

Chemistry

Synthesis of 2-(2,3-dihydro-2,2-dimethylchromen-4-ylidene)malononitrile (2)

A mixture of 17.6 g (0.1 mol) of 2,2-dimethylchroman-4-one (1) [18] and 8 g (0.12 mol) of malononitrile were dissolved in 100 ml $CHCl_3$, then 5 ml glacial AcOH and 2 g ammonium acetate were added. The mixture was refluxed for 6 h.

After the mixture was cooled, poured unto water. The organic layer was separated and dried over $CaCl_2$, after that the solvent was evaporated under reduced pressure. The residue was treated with petroleum ether 40-60 to give the solid, which was filtered and crystallized from petroleum ether 40-60; colorless crystals, yield 60%, mp. 85-87°C, ^{1}H-NMR: δ=1.57 (s, 6H, $2CH_3$), 4.90 (s, 2H, CH_2), 6.90-7.04 (m, 2H, ArH), 7.15-7.23 (m, 1H, ArH), 7.89 (dd, 1H, ArH). IR: *v* 2200 cm^{-1} (C≡N). MS: *m/z* (%), 224 (33) [M], 209 (100) [M–CH_3], 182 (10), 159 (5), 127 (6). Anal. Calcd. For $C_{14}H_{12}N_2O$ (224.152): C 75.01, H-5.35, N-12.49; Found: C-74.91, H-5.20, N-12.39.

Synthesis of 2-amino-4,4-dimethyl-4H-thieno[2,3-c]chromene-1-carbonitrile (3)

A mixture of 22.4 g (0.1 mol) of 2-(2,3-dihydro-2,2-dimethylchromen-4-ylidene)malononitrile (2), 3.5 g (0.11 mol) of sulfur, 100 ml absolute ethanol, and 3 ml TEA was refluxed for 6 h. The mixture was cooled, then the formed solid was filtered off and crystallized from ethanol; pale yellow crystals, yield 80%, mp. 190-191°C. ^{1}H-NMR: δ=1.25 (s, 6H, $2CH_3$), 4.57 (s, 2H, NH_2), 6.50-6.70 (m, 2H, ArH), 6.80-6.85 (m, 1H, ArH), 7.55 (dd, 1H, ArH). IR: *v* 3450 cm^{-1} (NH_2), 2200 cm^{-1} (C≡N). MS: *m/z* (%), 256 (55) [M], 241 (100) [M – CH_3], 211 (5), 170 (7), 127 (7), 115 (6). Anal. Calcd. For $C_{14}H_{12}N_2OS$ (256.217): C-65.62, H-4.68, N-10.93, S-12.51; Found: C-65.50, H-4.57, N-10.78, S-12.33.

General procedure for synthesis of chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-ones (4a-c) synthesis of 4a.

$POCl_3$ (0.2 ml) was added to a solution of 2-amino-4,4-dimethyl-4H-thieno[2,3-c]chromene-1-carbonitrile (3) (0.26 g, 1 mmol) in glacial acetic acid (3 ml). The reaction mixture was refluxed for 3 h. After cooling the mixture, a solution of K_2CO_3 was added to neutralize the acid. The formed solid was filtered, and washed with a small amount of ethanol, dried and crystallized from ethanol.

10,10-Dimethyl-3H,10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-one (4a)

Colorless crystals, yield 75%, mp. 258-260°C. ^{1}H NMR: δ=1.61 (s, 6H, 2 CH_3), 6.91 (d, 1H, ArH), 7.09 (t, 1H, ArH), 7.17 (t, 1H, ArH), 7.97 (s, 1H, CH pyramid.), 8.72 (d, 1H, ArH), 11.00 (s, 1H, NH). IR: *v* 3300 cm^{-1} (NH), 1704 cm^{-1} (C=O). MS: *m/z* (%), 284 (50) [M], 269 (100) [M–CH_3], 254 (25), 137 (7). Anal. Calcd. For $C_{15}H_{12}N_2O_2S$ (284.222): C-63.38, H-4.22, N-9.85, S-11.28; Found: C-63.20, H-4.11, N-9.70, S-11.08.

2,10,10-Trimethyl-3H,10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-one (4b)

Colorless crystals, yield 70%, mp. 270-273°C. ^{1}H-NMR: δ=1.61 (s, 6H, 2 CH_3), 2.31 (s, 3H, CH_3), 6.91 (d, 1H, ArH), 7.09 (t, 1H, ArH), 7.17 (t, 1H, ArH), 8.72 (d, 1H, ArH), 12.00 (s, 1H, NH). IR: *v* 3310 cm^{-1} (NH), 1708 cm^{-1} (C=O). MS: *m/z* (%), 298 (50) [M], 283 (100) [M–CH_3], 268 (34), 137 (10), 115 (8). Anal. Calcd. For $C_{16}H_{14}N_2O_2S$ (298.232): C-64.43, H-4.69, N-9.39, S-010.75; Found: C-64.25, H-4.60, N-9.19, S-10.58.

10,10-Dimethyl-2-ethyl-3H,10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-one (4c)

Colorless crystals, yield 70%, mp. 245-247°C. ^{1}H-NMR: δ=1.23 (t, 3H, CH_3), 1.61 (s, 6H, 2 CH_3), 2.75 (q, 2H, CH_2), 6.91 (d, 1H, ArH), 7.09 (t, 1H, ArH), 7.17 (t, 1H, ArH), 8.72 (d, 1H, ArH), 11.26 (s, 1H, NH). IR: *v* 3308 cm^{-1} (NH), 1705 cm^{-1} (C=O). MS: *m/z* (%), 312 (100) [M], 273 (65), 258 (34), 243 (10). Anal. Calcd. For $C_{17}H_{16}N_2O_2S$ (312.242): C-65.38, H-5.12, N-8.97, S-10.27; Found: C-65.19, H-5.01, N-8.96, S-10.09.

General procedure for preparation of chlorochromeno[4',3':4,5]thieno[2,3-d]pyrimidines 5a-c; preparation of 5a

A solution of 4a (2.8 g, 10 mmol) in dry dioxane (30 ml) was treated with phosphorus oxychloride (7 ml) and the mixture was stirred under reflux for 3 h. The reaction mixture was allowed to cool to room temperature and poured into ice water, the separated solid was filtered off and crystallized from petroleum ether.

4-Chloro-10,10-dimethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (5a)

Colorless crystals, yield 75%, mp. 201-203°C. ^{1}H-NMR: δ=1.61 (s, 6H, $2CH_3$), 6.91 (d, 1H, ArH), 7.09 (t, 1H, ArH), 7.17 (t, 1H, ArH), 7.97 (s, 1H, CH pyramid.), 8.72 (d, 1H, ArH). MS: *m/z* (%), 304 (15) [M, Cl^{37}], 302 (50) [M, Cl^{35}], 287 (100) [M–CH_3], 272 (25), 236(7). Anal. Calcd. For $C_{15}H_{11}ClN_2OS$ (302.672): C-59.52, H-3.63, Cl-11.71, N-9.25, S-10.59; Found: C-59.35, H-3.46, Cl-11.53, N-9.06, S-10.43.

4-Chloro-2,10,10-trimethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (5b)

From 4b: Colorless crystals, yield 70%, mp. 221-225°C. ^{1}H-NMR: δ=1.61 (s, 6H, $2CH_3$), 2.31 (s, 3H, CH_3), 6.91 (d, 1H, ArH), 7.09 (t, 1H, ArH), 7.17 (t, 1H, ArH), 8.72 (d, 1H, ArH). MS: *m/z* (%), 318 (9) [M, Cl^{37}], 316 (25) [M, Cl^{35}], 301(100) [M–CH_3], 286 (30), 271(5). Anal. Calcd. For $C_{15}H_{13}ClN_2OS$ (316.682): C-60.68, H-4.10, Cl-11.19, N-8.84, S-10.12; Found: C-60.45, H-3.98, Cl-10.95, N-8.61, S-9.91.

4-Chloro-10,10-dimethyl-2-ethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (5c)

From **4c**: Colorless crystals, yield 70%, mp. 198-201°C. ^{1}H-NMR: δ=1.25 (t, 3H, CH_3), 1.61 (s, 6H, $2CH_3$), 2.65 (q, 2H, CH_2), 6.91 (d, 1H, ArH), 7.09 (t, 1H, ArH), 7.17 (t, 1H, ArH), 8.72 (d, 1H, ArH). MS: *m/z* (%), 332 (7) [M, Cl^{37}], 330 (30) [M, Cl^{35}], 301(100) [M–CH_2CH_3], 286 (30), 271(5). Anal. Calcd. For $C_{16}H_{15}ClN_2OS$ (330.692): C-61.74, H-4.53, Cl-10.72, N-8.47, S-9.69; Found: C-61.58, H-4.31, Cl-10.51, N-8.29, S-9.39.

General procedure for preparation of hydrazinochromeno[4',3':4,5]thieno[2,3-d]pyrimidines (6a-c)

A mixture of compound 5a (3 g, 10 mmol) and hydrazine hydrate 99% (7 ml) in ethanol (50 ml) was heated under reflux for 3 h. The reaction mixture was allowed to cool to room temperature. The formed precipitate was filtered off and crystallized from dioxane.

4-Hydrazino-10,10-dimethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (**6a**)

Colorless crystals, yield 70%, mp. 261-263°C. ^{1}H-NMR: δ=1.59 (s, 6H, $2CH_3$), 4.61 (br s, 2H, NH_2, D_2Oexchangeable), 5.42 (br s, 1H, NH, D_2O exchangeable), 6.89 (d, 1H, ArH), 7.07 (t, 1H, ArH), 7.15 (t, 1H, ArH), 7.94 (s, 1H, CH pyramid), 8.71 (d, 1H, ArH). MS: *m/z* (%), 298 (100) [M^+], 283 (35) [M–CH_3], 268 (25), 266 (10), 236 (7). Anal. Calcd. For $C_{15}H_{14}N_4OS$ (298.332): C-60.38, H-4.72, N-18.78, S-10.75; Found: C-60.16, H-4.60, N-18.55, S-10.49.

4-Hydrazino-2,10,10-trimethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (**6b**)

From 5b: Colorless crystals, yield 80%, mp. 281-285°C. ^{1}H-NMR: δ=1.58 (s, 6H, $2CH_3$), 2.28 (s, 3H, CH_3), 4.59 (br s, 2H, NH_2, D_2O exchangeable), 5.41 (br s, 1H, NH, D_2O exchangeable), 6.90 (d, 1H, ArH), 7.08 (t, 1H, ArH), 7.17 (t, 1H, ArH), 8.72 (d, 1H, ArH). MS: *m/z* (%), 312 (100) [M^+], 297(54) [M–CH_3], 282 (30), 281 (7). Anal. $C_{16}H_{16}N_4OS$ (312.356): Calcd. C-61.52, H-5.16, N-17.93, S-10.26; Found: C-61.31, H-5.01, N-17.71, S-9.99.

4-Hydrazino-10,10-dimethyl-2-ethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (**6c**)

From 5c: Colorless crystals, yield 67%, mp. 258-261°C. ^{1}H-NMR: δ=1.22 (t, 3H, CH_3), 1.59 (s, 6H, $2CH_3$), 2.61 (q, 2H, CH_2), 4.57 (br s, 2H, NH_2, D_2Oexchangeable), 5.39 (br s, 1H, NH, D_2O exchangeable), 6.89 (d, 1H, ArH), 7.05 (t, 1H, ArH), 7.14(t, 1H, ArH), 8.72 (d, 1H, ArH). MS: *m/z* (%), 326 (1000) [M^+], 311(15) [M–CH_3], 297 (30), 296 (28), 294 (54). Anal. Calcd. For $C_{17}H_{18}N_4OS$ (326.362): C-62.56, H-5.55, N-17.17, S-9.82; Found: C-62.35, H-5.33, N-16.96, S-9.61.

General procedure for preparation of chromeno[4',3':4,5]thieno[3,2-e][1,3,4]triazolo[1,5-c]pyrimidines 7a-c; preparation of 7a

A mixture of 4-Hydrazino-10,10-dimethyl-10H-chromeno[4',3':4,5]thieno[2,3-d]pyrimidine (6a) (0.6 g, 2 mmol), benzoyl chloride (6 ml) was stirred under reflux for 7 h. The reaction mixture was allowed to cool to room temperature and poured into water (200 ml). The precipitate that was formed was collected by filtration, washed with ethanol (50 ml), dried and crystallized from Dioxane: Ethanol mixture (2:1).

8,8-dimethyl-3-phenyl-8H-chromeno[4',3':4,5]thieno[3,2-e][1,3,4]triazolo[1,5-c]pyrimidine (7a)

Colorless crystals, yield 65%, mp. 294-296°C. ^{1}H-NMR: δ=1.59 (s, 6H, $2CH_3$), 6.89 (d, 1H, ArH), 7.07 (t, 1H, ArH), 7.15 (t, 1H, ArH), 7.34-7.61 (m, 5H, ArH), 8.44 (s, 1H, CH pyramid.), 8.71 (d, 1H, ArH). MS: *m/z* (%), 384 (100) [M^+], 369 (50), 354 (35), 307 (10). Anal. Calcd. For $C_{22}H_{16}N_4OS$ (384.416): C-68.73, H-4.19, N-14.57, S-8.34; Found: C-68.46, H-4.00, N-11.29, S-8.19.

5,8,8-trimethyl-3-phenyl-8H-chromeno[4',3':4,5]thieno[3,2-e][1,3,4]triazolo[1,5-c]pyrimidine (7b)

From 6b: Colorless crystals, yield 60%, mp. 301-302°C. ^{1}H-NMR: δ=1.59 (s, 6H, CH_3), 2.30 (s, 3H, 2-CH_3), 6.89 (d, 1H, ArH), 7.07 (t, 1H, ArH), 7.15 (t, 1H, ArH), 7.44-7.71 (m, 5H, ArH), 8.71 (d, 1H, ArH). MS: *m/z* (%), 398 (65) [M^+], 383 (100), 368 (10), 321 (7). Anal. Calcd. For $C_{23}H_{18}N_4OS$ (398.44): C-69.33, H-4.55, N-14.06, S-8.05; Found: C-68.46, H-4.00, N-11.29, S-8.19.

8,8-Dimethyl-5-ethyl-3-phenyl-8H-chromeno[4',3':4,5]thieno[3,2-e][1,3,4]triazolo[1,5-c]pyrimidine(7c)

From 6c: Colorless crystals, yield 49%, mp 203-205°C. ^{1}H-NMR: δ=1.22 (t, 3H, CH_3), 1.58 (s, 6H, $2CH_3$), 2.63 (q, 2H, CH_2), 6.91 (d, 1H, ArH), 7.10 (t, 1H, ArH), 7.7 (t, 1H, ArH), 7.46-7.73 (m, 5H, ArH), 8.2 (d, 1H, ArH). MS: *m/z* (%), 412 (100) [M^+], 383 (10), 397 (5), 382 (6). Anal. Calcd. For $C_{24}H_{20}N_4OS$ (412.646): C-69.85, H-4.88, N-13.58, S 7.77; Found C-69.64, H-4.76, N-13.39, S-7.59.

Antimicrobial activity

The *in vitro* antimicrobial activity of the newly synthesized derivatives 6a-c and 7a-c were tested against several pathogenic representative Gram-negative bacteria, Gram-positive bacteria, fungi and yeast. All microorganisms used were obtained from the culture collection of the Department of Natural and Microbial Products, National Research Centre, Dokki, Cairo, Egypt.

Sterilization medium [19-21]

The cap-assay method containing (g/L): Peptone 6, yeast extract 3, meat extract 1.5, glucose 1 and agar 20 was used. The medium was sterilized and divided while hot (50-60°C) in 15 ml portions among sterile 9 cm diameter petri dishes. One ml of the spore suspension of each microorganism was spread all over the surface of the cold solid medium placed in the petri dish.

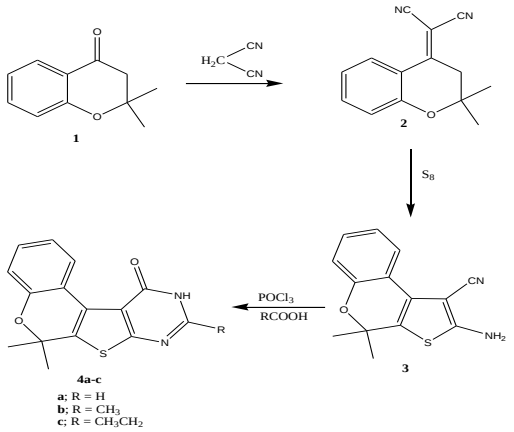
Method of analysis

0.0005 g of each of the tested compounds was dissolved in 5 ml of N, N-Dimethylformamide, an amount of 0.1 ml of test solution was placed on a 9 mm diameter Whatman paper disc and the solvent was left to evaporate. These saturated discs were placed carefully on the surface of the incubated solid medium; each petri dish contains at least 3 discs. The petri dishes were incubated at 5°C overnight and then examined. The results were then recorded by measuring the inhibition zone diameters.

RESULTS AND DISCUSSION

Chemistry

2-(2,3-dihydro-2,2-dimethylchromen-4-ylidene)malononitrile (2) was isolated, as a product of Knoevenagel-Cope condensation, from the reaction of 2,2-dimethylchroman-4-one (1) with malononitrile (Scheme 1) [22,23]. Compound 2 structures was affirmed by means of IR spectrum which showed the presence of band at 2200 cm^{-1} due to ν_{CN} in addition to its corresponding ^{1}H-NMR which displayed the signal of the CH_2 at δ=4.90 ppm in addition to the remaining expected signals.

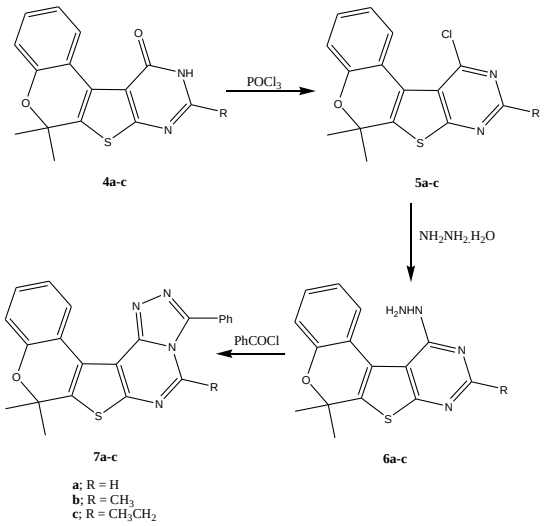


Scheme 1: Knoevenagel-cope condensation

The compound 2 was treated with sulfur in the existence of TEA to afford 2-amino-4,4-dimethyl-4H-thieno[2,3-c]chromene-1-carbonitrile (3) (Scheme 1) [24]. The structure of the thieno[2,3-c]chromene-1-carbonitrile derivative 3 was established by the presence of 2200 cm^{-1} due to νCN and the existence of 3450 cm^{-1} due to νNH_2 in IR. Additional it is also reinforced by the presence of a signal at δ=4.57 ppm as singlet in ^{1}H-NMR spectrum due to NH_2 group.

Chromeno[4',3':4,5]thieno[2,3-d]pyrimidin-4-ones 4a-c were prepared via the reaction of 2-amino-4,4-dimethyl-4H-thieno[2,3-c]chromene-1-carbonitrile (3) with formic acid, acetic acid, and propionic acid, respectively, in the presence of $POCl_3$ (Scheme 1). The structure of 4a, as an example, was achieved by the revealed absorptions of νC=o at 1704 and νNH at 3300 cm^{-1} in IR and a signal at δ=7.97 due to N=CH. And also a singlet at δ=11.00 for NH in the ^{1}H-NMR spectrum, beside with the other expected signals.

Chromeno[4',3':4,5]thieno[2,3-*d*]pyrimidin-4-ones (4a-c) were treated with phosphorous oxychloride in dry dioxane to afford corresponding 4-chloro derivatives 5a-c (Scheme 2) [25]. These derivatives were belayed by the absence of νC=O and νNH bands in IR. The ^{1}H-NMR spectrum of compound 5b, as an example, showed a signal at δ=2.31 due to 2-CH_3, along with the other expected signals.



Scheme 2: Chromeno[4',3':4,5]thieno[2,3-*d*]pyrimidin-4-ones

Meanwhile, hydrazino derivatives (6a-c) were prepared on treatment of 4-chloro derivatives 5a-c with hydrazine hydrate (Scheme 2) [25]. Formation of the products 6a, as an example, was confirmed by the ^{1}H-NMR spectrum. Which, showed D_2O exchangeable singlets at δ=4.61 and 5.42 due to amino groups and the C2−H of pyrimidine resonated at δ=7.94 as a singlet beside with other expected signals. The MS of derivative 6a showed the molecular ion peak as base peak (cf. experimental part).

On the other hand, hydrazino derivatives (6a-c) were treated with benzoyl chloride to afford the corresponding triazolothienopyrimidine derivatives (7a-c) (Scheme 2) [26]. The ^{1}H-NMR spectrum of compound 7a showed the C−H of pyrimidine resonated at δ=8.44 as a singlet along with other expected signals, also its MS displayed the M^+ peak at *m/z* 384 (100) (cf. experimental part).

***In vitro* antimicrobial activity**

The antimicrobial activity of the tested compounds (6a–c and 7a–c) was evaluated by measuring the zone diameters and their results were compared with those of well-known drugs as in Table 1. Triazolo[1,5-c]pyrimidine derivatives 7a–c showed good antimicrobial activity. However, Triazolo[1,5-c]pyrimidine derivative 7b validated inhibitory activity more than 7a and 7c.

Table 1: The antimicrobial activity of some newly synthesized compounds

Tested compounds and standards	Inhibition zone (mm)			
	Microorganism			
	Bacteria		Fungi	Yeast
	Gram-negative	Gram-positive		
	Escherichia coli	*Bacillus subtilis*	*Aspergillus niger*	*Candida albicans*
Streptomycin	+++	+++	+	+++
Fusidic acid	—	—	+++	+++
6a	—	—	—	+
6b	—	—	+	++
6c	—	—	—	+
7a	+	+	—	++
7b	+	+	—	+++
7c	+	+	—	++

+++Highly sensitive (21–25 mm); ++ Fairly sensitive (16–20 mm); + Slightly sensitive (15–10 mm); —Not sensitive

CONCLUSION

A variety of 10,10-Dimethyl-3*H*,10*H*-chromeno[4',3':4,5]thieno[2,3-*d*]pyrimidin-4-ones (4a-c) and 8,8-dimethyl-8*H*-chromeno[4',3':4,5]thieno[3,2-*e*][1,3,4]triazolo[1,5-*c*]pyrimidines (7a-c) were synthesized. The newly synthesized compounds were confirmed by IR, ^{1}H-NMR, MS and elemental analyses. Triazolo[1,5-c]pyrimidine derivatives 7a–c showed good antimicrobial activity. However, Triazolo[1,5-c]pyrimidine derivative 7b validated inhibitory activity more than 7a and 7c.

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REFERENCES

[1] M.A. Ponce, J.M. Scervino, R. Erra-Balsells, J.A. Ocampo, A.M. Godeas, *Phytochemistry.*, **2004**, 65, 3131-3134.
[2] F. Cottiglia, B. Dhanapal, O. Sticher, J. Heilmann, *J. Nat. Prod*., **2004**, 67, 537-541.
[3] J. Mutanyatta, B. Matapa, D.D. Shushu, B.M. Abegaz, *Phytochemistry.*, **2003**, 62, 797-804.
[4] J. Wu, X. Wang, Y. Yi, K. Lee, *Bioorg. Med. Chem. Lett*., **2003**, 13, 1813-1815.
[5] T. Ishikawa, Y. Oku, T. Tanaka, T. Kumamoto, *Tetrahedron Lett*., **1999**, 40, 3777-3780.
[6] Z.Q. Xu, R.W. Bucheit, T.L. Stup, M.T. Flavin, A. Khilevich, J.D. Rezzo, L. Lin, D.E. Zembower, *Bioorg. Med. Chem. Lett*., **1998**, 8, 2179-2184.
[7] B.V. Ashalatha, B. Narayana, K.K. Vijaya raj, S. Kumari, *Eur. J. Med. Chem*., **2007**, 42 719-728.
[8] J. Katada, K. Lijima, M. Muramatsu, M, Takami, E. Yasuda, M. Hayashi, M. Hattori, Y. Hayashi, *Bioorg. Med. Chem. Lett*., **1999**, 9, 797-802.
[9] K. Jain, J. Bariwal, M. Kathiravan, M, Phoujdar, R. Sahne, B. Chauhan, Shah, M. Yadav, *Bioorg. Med. Chem. Lett*., **2008**, 16, 4759-4800.
[10] C.G. Dave, P.R. Shah, K.C. Dave, V.J. Patel, *J. Indian Chem. Soc*., **1989**, 66, 48-50.
[11] E. Bousquet, G. Romero, F. Guerrera, A. Caruso, M. Roxas, *Farmaco. Ed. Sci*., **1985**, 40, 869-874.
[12] R.V. Chambhare, B.G. Khadse, A.S. Bobde, R.H. Bahekar, *Eur. J. Med. Chem*., 2003, **38**, 89-100.
[13] M. Modica, M. Santagati, A. Santagati, V. Cutuli, N. Mangano, A. Caruso, *Pharmazie.*, **2000**, 55, 500-502.
[14] S. Leistner, G. Wagner, M. Guetscharo, E. Glusa, *Pharmazie.*, **1986**, 41, 54-55.
[15] M.D. Meyer, R.J. Altenbach, F.Z. Basha, W.A. Carroll, S. Condon, S.W. Elmore, J.F. Kerwin, K.B. Sippy, K. Tietje, M. Wendt, *J. Med. Chem*., **2000**, 43, 1586-1603.
[16] C. Gill, G. Jadhav, M. Shaikh, R. Kale, A. Ghawalkar, *Bioorg. Med. Chem. Lett*., **2008**, 18, 6244-6247.
[17] A. Kamal, N. Shankaraiah, V. Devaiah, K.L. Reddy, A. Juvekar, *Bioorg. Med. Chem. Lett*., **2008**, 18, 1468-1473.
[18] C.D. Gabbutt, J.D. Hepworth, B.M. Heron, *Tetrahedron.*, **1994**, 50, 5245-5254.
[19] H.Z. Malina, *Acta Microbiol. Polon*., **1993**, 32, 405-407.
[20] A.A. Abou-Zeid, Y.M. Shehata, *Indian J. Pharm.*, **1969**, 31, 72-75.
[21] H. Ericsson, *Scand. J. Clin. Lab. Invest*., **1960**, 12, 414-422.
[22] R.W. Sabnis, *Sulfur Rep*., **1994**, 16, 1-17.
[23] I. Adachi, T. Yamamori, Y. Hiramatsu, K. Skakai, S.I. Mihara, M. Kawakami, M. Masui, O. Uno, M. Ueda, *Chem. Pharm. Bull*., **1988**, 36, 4389-4402.
[24] B. Naumann, R. Böhm, F. Fülöp, G. Bernáth, *Pharmazie.*, **1996**, 51, 4-6.
[25] A.E. Rashad, M.I. Hegab, R.E. Abdel-Megeid, M.M. Ali, F.M. Abdel-Megeid, *Phosphorus, Sulfur and Silicon.*, **2010**, 185, 74-83.
[26] S.L. Gaonkar, C. Ahn, Princia, N.S. Shetty, *J. Korea. Chem. Soc*., **2014**, 58, 388-392.