Arabian Journal of Chemistry (2014) 7, 775–780

King Saud University

Arabian Journal of Chemistry

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ORIGINAL ARTICLE

Synthesis and antibacterial activity of some novel thieno[2,3-c]pyridazines using 3-amino-5-phenyl-2-ethoxycarbonylthieno[2,3-c]pyridazine as a starting material

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Received 24 September 2010; accepted 15 December 2010
Available online 24 December 2010

KEYWORDS

Pyridazine;
Thienopyridazines;
Pyrimidothienopyridazines;
Antibacterial activity

Abstract 3-Amino-5-phenyl-2-ethoxycarbonylthieno[2,3-c]pyridazine (**6**) was prepared by reaction of 4-cyano-6-phenylpyridazine-3(2*H*)-thione (**4**) with ethyl chloroacetate in the presence of sodium ethoxide. Hydrazinolysis of compound **6** yielded the corresponding carbohydrazide, (**9**) which on treatment with acetylacetone and ethyl acetoacetate produced the novel thieno[2,3-c]pyridazines (**10** and **11**). Treatment of compound **9** with nitrous acid yielded the corresponding carboazide (**13**), which upon boiling in toluene furnished imidazo[4′,5′:4,5]thieno[2,3-c]pyridazine (**15**). Pyrimidothienopyridazines (**16**–**18**) were achieved by cyclocondensation of compound **9** with some reagents, namely acetic anhydride, formic acid, and triethyl orthoformate. The newly synthesized compounds were confirmed by elemental analyses and spectral data. The antibacterial activities of the new compounds were also evaluated.

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1. Introduction

Several thienopyridazines are known to possess a broad spectrum of biological activities. Some of them, for example, have been evaluated pharmacologically and used for potent and selective phosphodiesterase IV inhibitor (Dal Piaz et al., 1997, 1998), immunosuppressants (Bantick et al., 1999), antitumor (Dumas et al., 2001), modules of protein tyrosine phosphatases (PTPases) (Andersen et al., 1999), antimicrobials (Somoza et al., 1998), blood platelet aggregation inhibitors (Iwase et al., 1993), antibacterial (Abbady and Radwan, 1994) and antiviral

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Peer review under responsibility of King Saud University.

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http://dx.doi.org/10.1016/j.arabjc.2010.12.020
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activity (Bundy et al., 2002). In view of the above observations and as a continuation of our ongoing program directed to the synthesis of heterocyclic systems containing thienopyridazine moiety (Al-Kamali, 2009; Al-Kamali et al., 2009; Kamal El-Dean and Al-Kamali, 2009), we report herein, the synthesis of some new thieno[2,3-c]pyridazines, imidazothienopyridazine and pyrimidothienopyridazines and their evaluation regarding antibacterial activity by using 4-cyano-6-phenylpyridazine-3(2*H*)-thione (**4**) as a starting material.

2. Experimental

2.1. Materials and methods

Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. The reactions were monitored by thin layer chromatography (TLC) on a silica coated aluminum sheet. The eluent was a mixture of dichloromethane and methanol in different proportions. IR spectra were recorded on a Shimadzu 470 IR spectrophotometer using KBr pellets. ^{1}H NMR spectra were measured on a Varian 300 MHz NMR spectrometer using TMS as the internal standard (δ in ppm). The mass spectra were recorded on a Jeol-JMS-600 apparatus. The UV spectrum was recorded on a Shimadzu mini-1240 Spectrophotometer. Elemental analyses were performed on a Perkin-Elmer 240 C microanalyzer.

2.2. Synthesis of 4-cyano-6-phenylpyridazine-3(2H)-thione (4)

A solution of compound **3** (0.01 mol) and thiourea (0.012 mol) in ethanol (20 mL) was heated under reflux for 4 h, the precipitate was boiled with 10% sodium hydroxide (5 mL) for 1 h. The solid product was dissolved in water and acidified with 2 N hydrochloric acid. The solid product was filtered off and recrystallized from ethanol to afford compound **4** as brown crystals in 89% yield; m.p. 206 °C. IR: ν = 3470 cm^{-1} (NH), 2222 cm^{-1} (C≡N), 1230 cm^{-1} (C=S); UV 324 nm (C=S); ^{1}H NMR (DMSO-d_6): δ 7.4–8.7 (m, 6H, Ar–H and pyridazine–H), 11.10 (broad, 1H, NH). *Anal.* Calcd. for $C_{11}H_7N_3S$ (213.26): C, 61.95; H, 3.31; N, 19.70; S, 15.03. Found: C, 61.99; H, 3.27; N, 19.73; S, 15.01%.

2.3. Synthesis of 4-cyano-3-ethoxycarbonylmethylthio-6-phenylpyridazine (5)

A mixture of compound **4** (0.01 mol), fused sodium acetate (0.012 mol) and ethyl chloroacetate (0.01 mol) in ethanol (50 mL) was stirred for 2 h. The solid product was filtered off and recrystallized from ethanol to give compound **5** as white crystals in 67% yield; m.p. 140 °C. IR: ν = 2220 cm^{-1} (C≡N), 1720 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.3 (t, 3H, CH_3), 4.2–4.3 (m, 4H, SCH_2 and OCH_2), 7.5–8.0 (m, 6H, Ar–H and pyridazine–H). *Anal.* Calcd. for $C_{15}H_{13}N_3O_2S$ (299.35): C, 60.19; H, 4.38; N, 14.04; S, 10.71. Found: C, 60.10; H, 4.35; N, 14.11; S, 10.80%.

2.4. Synthesis of 3-amino-5-phenyl-2-ethoxycarbonylthieno[2,3-c]pyridazine (6)

2.4.1. Method A

A mixture of compound **3** or **4** (0.01 mol) and ethylthioglycolate/sodium carbonate or ethyl chloroacetate (0.01 mol) in ethanol (50 mL) containing sodium ethoxide (0.012 mol) was refluxed for 3 h. After cooling the solid product was collected and recrystallized from ethanol–chloroform (9:1) to afford compound **6** as yellow crystals in 93% yield: m.p. 225 °C. IR: ν = 3430, 3300 cm^{-1} (NH_2), 1670 cm^{-1} (C=O); ^{1}H NMR (DMSO-d_6): δ 1.3 (t, 3H, CH_3), 4.3 (q, 2H, OCH_2), 7.4–8.2 (m, 6H, Ar–H and pyridazine–H), 9.0 (s, 2H, NH_2); MS: *m*/*z* 299 (M^+, 100%), 271 (7.61%), 253 (69.80%), 226 (6.00%), 77 (15.83%), 51 (13.65%). *Anal.* Calcd. for $C_{15}H_{13}N_3O_2S$ (299.35): C, 60.19; H, 4.38; N, 14.04; S, 10.71. Found: C, 59.90; H, 4.50; N, 14.25; S, 10.67%.

2.4.2. Method B

A mixture of compound **5** (0.01 mol), substituted anilines (0.01 mol) and sodium ethoxide (0.01 mol) in ethanol (50 mL) was heated under reflux for 2 h. The solid product was collected and recrystallized from ethanol–chloroform (9:1) to give compound **6** as yellow crystals in 93% yield: m.p. 225 °C. The product was identical with that reported in method A.

2.5. Synthesis of 4-cyano-6-phenyl(pyridazin-3-yl-thio)acetichydrazide (8)

A mixture of compound **5** (0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (20 mL) was stirred for 3 h. The solid precipitate was collected by filtration and recrystallized from ethanol–chloroform (9:1) to give compound **8** as yellow crystals in 91% yield: m.p. 242 °C. IR: ν = 3400, 3290, 3200 cm^{-1} (NH, NH_2), 2230 cm^{-1} (C≡N), 1680 cm^{-1} (C=O); ^{1}H NMR (DMSO-d_6): δ 4.1 (s, 2H, SCH_2), 4.5 (s, 2H, NH_2), 7.4–8.1 (m, 6H, Ar–H and pyridazine–H), 9.0 (s, 1H, NH). *Anal.* Calcd. for $C_{13}H_{11}N_5OS$ (285.32): C, 54.73; H, 3.89; N, 24.55; S, 11.24. Found: C, 54.68; H, 3.82; N, 24.62; S, 11.28%.

2.6. Synthesis of 3-amino-5-phenylthieno[2,3-c]pyridazine-2-carbohydrazide (9)

2.6.1. Method A

A mixture of compound **5** or **6** (0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (50 mL) was refluxed for 3 h, and then allowed to cool. The solid product was collected and recrystallized from ethanol to give compound **9** as yellow crystals in 93% yield: m.p. 298 °C. IR: ν = 3400, 3290, 3180 cm^{-1} (NH, NH_2), 1600 cm^{-1} (C=O); MS: *m*/*z* 285 ($M^{+\cdot}$, 62.59%), 270 (2.36%), 254 (100%), 77 (15.83%), 51 (13.65%). *Anal.* Calcd. for $C_{13}H_{11}N_5OS$ (285.32): C, 54.73; H, 3.89; N, 24.55; S, 11.24. Found: C, 54.77; H, 3.93; N, 24.48; S, 11.15%.

2.6.2. Method B

A mixture of compound **8** (0.01 mol) and anhydrous potassium carbonate (0.012 mol) in ethanol (30 mL) was heated under reflux for 4 h. The solid product was collected and recrystallized from ethanol to give compound **9** as yellow crystals in 93% yield: m.p. 298 °C.

2.7. Synthesis of 5-amino-3-phenyl-thieno[2,3-c]pyridazin-6-yl-(3,5-dimethyl-pyrazol-1-yl)-ketone (10)

A mixture of carbohydrazide (**9**) (0.01 mol) and acetylacetone (0.01 mol) in ethanol (10 mL) was heated under reflux for about 4 h. The precipitate was filtered off and recrystallized

from ethanol to give compound **10** as orange crystals in 86% yield: m.p. 288 °C. IR: ν = 3420, 3280 cm^{-1} (NH_2), 1680 cm^{-1} (C═O); ^1H NMR (DMSO-d_6): δ 2.3, 2.6 (2s, 6H, $2CH_3$), 6.2 (s, 1H, pyrazole–H), 7.4–8.1 (m, 6H, Ar–H and pyridazine–H), 9.0 (s, 2H, NH_2); MS: m/z 349 ($M^{+\cdot}$, 92.70), 253 (100%), 95 (12.39%). *Anal*. Calcd. for $C_{18}H_{15}N_5OS$ (349.41): C, 61.88; H, 4.33; N, 20.04; S, 9.18. Found: C, 61.88; H, 4.30; N, 20.01; S, 9.14%.

*2.8. Synthesis of 5-amino-3-phenyl-6-ethylacetoacetatecarbohydrazone-thieno[2,3-c]pyridazine (**11**)*

A mixture of compound **9** (0.01 mol) and ethyl acetoacetate (0.01 mol) in ethanol (10 mL) was heated under reflux for 3 h. The solid product was collected and recrystallized from ethanol to give compound **11** as yellow crystals in 82% yield: m.p. 265 °C. IR: ν = 3410, 3290 cm^{-1} (NH_2), 3190 cm^{-1} (NH), 1720 cm^{-1} (C═O, ester), 1680 cm^{-1} (C═O); ^1H NMR (DMSO-d_6): δ 1.2 (t, 3H, CH_3 of ester), 2.0 (s, 3H, CH_3), 3.4 (s, 2H, CH_2), 4.1 (q, 2H, OCH_2), 6.1 (s, 2H, NH_2), 7.5–8.3 (m, 6H, Ar–H and pyridazine–H), 9.1 (s, 1H, NH). *Anal*. Calcd. for $C_{19}H_{19}N_5O_3S$ (397.45): C, 57.42; H, 4.82; N, 17.62; S, 12.08. Found: C, 57.48; H, 4.85; N, 17.57; S, 12.06%.

*2.9. Synthesis of 3-amino-5-phenylthieno[2,3-c]pyridazine-2-carboazide (**13**)*

A sample of carbohydrazide (**9**) (0.01 mol) in glacial acetic acid (10 mL), solution of sodium nitrite (0.015 mol in 3 mL H_2O) was added dropwise, then allowed to stand for 2 h. The solid product was collected to give compound **13** as orange crystals in 71% yield: m.p. 195 °C (dec.). IR: ν = 3400, 3280 cm^{-1} (NH_2), 2120 cm^{-1} (N_3), 1620 cm^{-1} (C═O); MS: m/z 296 ($M^{+\cdot}$, 20.19%), 268 (30.67%), 253 (7.84%), 77 (38.98%), 51 (73.02%), 40 (100%). *Anal*. Calcd. for $C_{13}H_8N_6OS$ (296.31): C, 52.70; H, 2.72; N, 28.36; S, 10.82. Found: C, 52.60; H, 2.74; N, 28.42; S, 10.91%.

*2.10. Synthesis of 5-phenyl-1,3-dihydroimidazo[4′,5′:4,5]thieno-[2,3-c]pyridazine-2-one (**15**)*

Compound of carboazide (**13**) (0.01 mol) in dry toluene (10 mL) was heated under reflux for 6 h, and then allowed to cool. The solid product was collected and recrystallized from ethanol to give compound **15** as light brown crystals in 70% yield: m.p. > 300 °C. IR: ν = 3200 cm^{-1} (–NH–CO–NH–), 1704 cm^{-1} (C═O). *Anal*. Calcd. for $C_{13}H_8N_4OS$ (268.29): C, 58.20; H, 3.01; N, 20.88; S, 11.95. Found: C, 58.27; H, 3.03; N, 20.90; S, 11.90%.

*2.11. Synthesis of 7-acetylamino-6-methyl-3-phenylpyrimido[4′,5′:4,5]thieno[2,3-c]pyridazin-8-one (**16**)*

A mixture of compound **9** (0.01 mol) in acetic anhydride (10 mL) was heated under reflux for 3 h, then allowed to cool, and poured into water (50 mL).The solid product was collected and recrystallized from ethanol to give compound **16** as white crystals in 74% yield: m.p. 198 °C. IR: ν = 3300 cm^{-1} (NH), 1710 cm^{-1} (C═O, acetyl), 1675 cm^{-1} (C═O, pyrimidinone); ^1H NMR (DMSO-d_6): δ 2.16 (s, 3H, $COCH_3$), 2.5 (s, 3H, CH_3), 7.4–8.3 (m, 6H, Ar–H and pyridazine–H), 11.3 (s, 1H, NH). *Anal*. Calcd. for $C_{17}H_{13}N_5O_2S$ (351.38): C, 58.11; H, 3.73; N, 19.93; S, 9.12. Found: C, 58.06; H, 3.82; N, 19.91; S, 9.09%.

*2.12. Synthesis of 7-formylamino-3-phenylpyrimido[4′,5′:4,5]-thieno[2,3-c]pyridazin-8-one (**17**)*

A mixture of carbohydrazide (**9**) (0.01 mol) and formic acid (10 mL) was heated under reflux for 3 h, then allowed to cool and poured into water (50 mL). The formed product was collected and recrystallized from ethanol to give compound **17** as white crystals in 63% yield: m.p. 182 °C. IR: ν = 3270 cm^{-1} (NH), at 1710 cm^{-1} (C═O, formyl), 1650 cm^{-1} (C═O); ^1H NMR (DMSO-d_6): δ 7.4–8.4 (m, 6H, Ar–H and pyridazine–H), 8.6 (s, 1H, CHO), 8.8 (s, 1H, NH), 8.9 (s, 1H, pyrimidine–H). *Anal*. Calcd. for $C_{15}H_9N_5O_2S$ (323.33): C, 55.72; H, 2.81; N, 21.66; S, 9.92. Found: C, 55.76; H, 2.75; N, 21.70; S, 9.94%.

*2.13. Synthesis of 7-ethoxymethyleneamino-3-phenylpyrimido-[4′,5′:4,5]thieno[2,3-c]pyridazin-8-one (**18**)*

A mixture of carbohydrazide (**9**) (0.01 mol) and triethyl orthoformate (3 mL) in acetic anhydride (10 mL) was refluxed for 3 h. The solid product was collected and recrystallized from ethanol to give compound **18** as white crystals in 74% yield: m.p. 230 °C. IR: ν = 1660 cm^{-1} (C═O, pyrimidinone), 1630 cm^{-1} (C═N); ^1H NMR (DMSO-d_6): δ 1.4 (t, 3H, CH_3), 4.2 (q, 2H, OCH_2), 7.3–8.4 (m, 7H, Ar–H, pyridazine–H and pyrimidine–H), 9.1 (s, 1H, CH═N). *Anal*. Calcd. for $C_{17}H_{13}N_5O_2S$ (351.38): C, 58.11; H, 3.73; N, 19.93; S, 9.12. Found: C, 58.06; H, 3.81; N, 19.90; S, 9.07%.

2.14. Antibacterial activity

The compounds **4**–**6**, **8**–**11**, **16,** and **17** were screened for their antibacterial activity against the bacteria *Staphylococcus xylosus*, *Bacillus megaterium* (Gram-positive bacteria), and *Salmonella typhii* (Gram-negative bacteria) following the filter paper disc technique. Ciprofloxacin was used as the standard antibacterial agent. The synthesized compounds and Ciprofloxacin were dissolved in DMSO at 25, 50, and 100 μg/disc concentrations in nutrient agar media. Antibacterial activity was determined by measuring the diameter of the inhibition zone after an incubation for 24 h at 37 °C and the activity of each compound was compared with Ciprofloxacin as a positive control. The results are listed in Table 1. The antibacterial activity showed that all compounds were active against microorganisms. All compounds were less active in comparison to Ciprofloxacin, which was taken as a standard drug. Further, investigation on the biological activity of these compounds will be considered in the progress.

3. Results and discussion

The synthesis of the starting compound 4-cyano-6-phenylpyridazine-3(2*H*)-thione (**4**) was performed from 4-carbethoxy-6-phenylpyridazinone (**1**) by successive ammonolysis in methanol to give 4-carboxamide-6-phenylpyridazine-3(2*H*)-one (**2**). Treatment of the latter compound with phosphorous oxychloride ensured both the dehydration of the carboxamide

Table 1 Antibacterial screening results of the compounds **4–6**, **8–11**, **16**, and **17**.

Compound. No.	Concentration (μg/disc)	*S. xylosus*	*B. megaterium*	*S. typhii*
4	25	–	–	–
	50	–	–	–
	100	–	+	–
5	25	–	+	–
	50	–	+	–
	100	+	+	–
6	25	–	–	–
	50	+	–	–
	100	+ +	+	–
8	25	+	–	–
	50	+	+	–
	100	+	+	–
9	25	–	+	+
	50	–	+	+
	100	–	+	+
10	25	–	–	–
	50	+	+	–
	100	+	+	–
11	25	–	+	–
	50	–	+	–
	100	+	+	+ +
16	25	–	+	–
	50	–	+	–
	100	+	+	–
17	25	–	+	–
	50	–	+	–
	100	–	+	–
Ciprofloxacin		+ + +	+ + +	+ + +

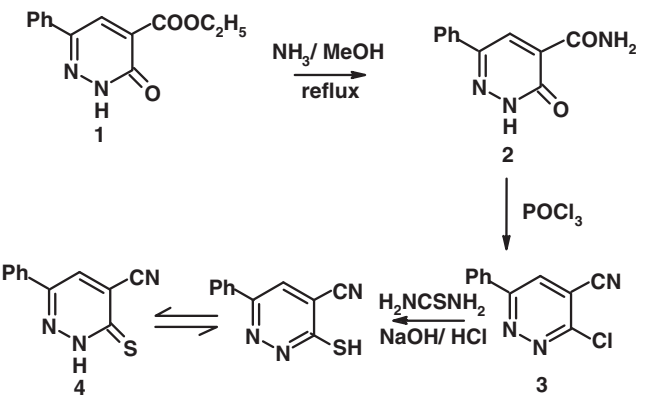
Highly active = + + + (inhibition zone > 27.9 mm).
Moderately active = + + (inhibition zone 18.7–27.9 mm).
Slightly active = + (inhibition zone 9.4–18.6 mm).
Inactive = – (inhibition zone < 9.3 mm).

function and the conversion of pyridazinone into 3-chloro-4-cyano-6-phenylpyridazine (**3**). Compound **3** was subjected to an addition–elimination reaction with thiourea in ethanol under reflux for about 4 h, to afford compound **4** (Scheme 1).

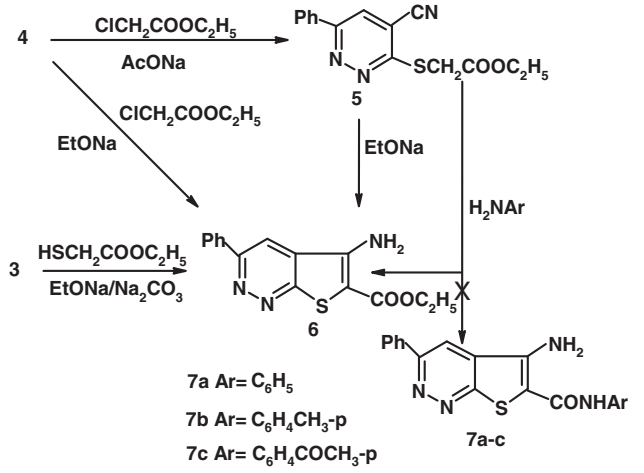
Compounds **1–3** were obtained according to the reported method (Wermuth et al., 1989) and the structures are in agreement with the reported data. The structure of the new compound **4** was established on the basis of elemental analysis and spectral data. The IR spectrum of compound **4** showed absorption bands at 3470, 2220 and 1230 cm^{-1} due to imino, cyano and thiocarbonyl groups, respectively. ^1H NMR spectrum (DMSO-d_6) of compound **4** showed a broad singlet at δ 11.1 ppm assigned to the NH and a multiplet at δ 7.4–8.7 ppm assigned to the phenyl protons and pyridazine proton.

The reaction of compound **4** with ethyl chloroacetate in refluxing ethanol, in the presence of sodium acetate, yielded 3-ethoxycarbonylmethylthiopyridazine derivative (**5**). Thieno[2,3-c]pyridazine derivative (**6**) was achieved either by the reaction of compound **3** with ethyl thioglycolate/sodium carbonate, or by the interaction of compound **4** with ethyl chloroacetate in ethanol in the presence of sodium ethoxide. The structure of compound **6** was established by another synthetic route *via* cyclization of compound **5** with substituted anilines in the presence of sodium ethoxide, instead, of the expected compounds **7a–c** (Scheme 2). The structure of compounds **5** and **6** was established by elemental analyses and spectral data. The IR spectrum of compound **5** showed absorption bands at 2220 and 1720 cm^{-1} could be attributed to cyano and ester groups whilst, that the compound **6** displayed the disappearance of cyano group and presence of the absorption bands at 3430, 3300 and 1670 cm^{-1} due to amino and carbonyl groups, respectively. The ^1H NMR spectrum of compound **6** in (DMSO-d_6) showed a triplet at δ 1.3 ppm, a quartet at δ 4.3 ppm assigned to ethoxycarbonyl moiety in addition to the aromatic and amino protons. Also, the structure of compound **6** was confirmed by the mass spectrum, which showed that the molecular ion peak (base peak) at $m/z = 299$ (100%), which is in agreement with its molecular formula ($C_{15}H_{13}N_3O_2S$).

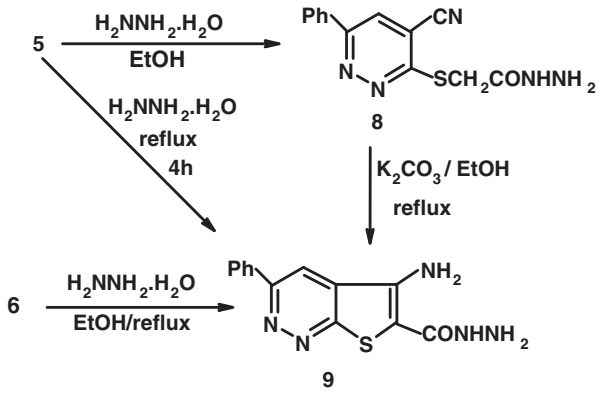
Treatment of compound **5** with hydrazine hydrate in ethanol at room temperature for 3 h, afforded the corresponding 3-methylthiocarbohydrazidepyridazine (**8**). However, carrying the reaction under reflux gave the novel 2-carbohydrazidethieno[2,3-c]pyridazine derivative (**9**). Also, the latter compound was obtained by refluxing compound **5** or **6** with hydrazine



Scheme 1



Scheme 2



Scheme 3

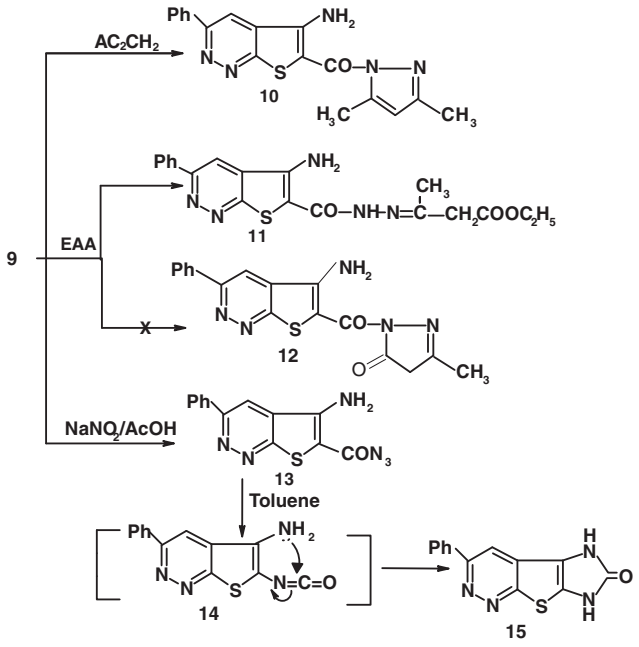
hydrate, or by compound **8** with potassium carbonate in ethanol (Scheme 3). The product compound **9** formed by the three routes is identical in all respects (m.p., m.m.p., T.L.C., and IR). The structure of the new compounds **8** and **9** was established on the basis of their elemental analyses and spectral data. The IR spectrum of compound **8** showed absorption bands at 3420, 3280, 3190, 2240, and 1620 cm^{-1} due to NH, amino, cyano, and carbonyl groups, respectively. Meanwhile, the IR spectrum of compound **9** showed the disappearance of cyano group and presence of absorption bands at 3410, 3300 and 3200 cm^{-1} for (NH_2), (NH, NH_2) groups and at 1600 cm^{-1} for (CO). Also, the structure of compound **9** was supported by its mass spectrum which, showed a molecular ion peak at m/z = 285, (62.59%) which is in agreement with its molecular formula ($C_{13}H_{11}N_5OS$).

2-Carbohydrazide derivative (**9**) was used as a precursor for synthesizing other new thienopyridazines and pyrimidothienopyridazines. Thus, refluxing of compound **9** with acetylacetone in ethanol yielded a novel pyrazolyl derivative (**10**). Also, compound **9** was reacted with ethyl acetoacetate in ethanol under reflux to produce the thienopyridazine derivative (**11**) instead, of the pyrazolone derivative (**12**). Treatment of compound **9** with nitrous acid at room temperature produced the carboazide derivative of compound **13**, which underwent *Curtius rearrangement* followed by intramolecular cyclization upon refluxing in dry toluene to furnish imidazo[4′,5′:4,5]thieno[2,3-c]pyridazine (**15**) *via* the isocyanate intermediate (**14**) (Scheme 4).

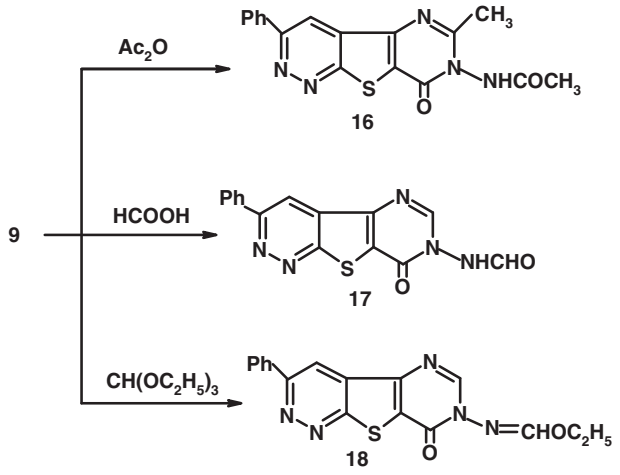
The structure of the new compounds **10, 11, 13** and **15** was confirmed on the basis of their elemental analyses and spectral data. The IR spectra of compounds **10** and **11** revealed absorption bands at 3420–3400, 3290–3280 for amino group, and at 1680 cm^{-1} due to carbonyl groups, respectively. The IR spectrum of compound **13** showed the characteristic band at 2120 cm^{-1} due to the azido group, which disappeared in the IR spectrum of compound **15**.

The ^1H NMR spectrum of compound **10** in (DMSO-d_6) showed two singlets at δ 2.3, 2.6 ppm characteristic for two methyls of pyrazole in addition to the expected signals attributed to amino, pyrazolo and aromatic protons. Also, the structure of compound **10** was supported by mass spectrum, which showed a molecular ion peak at m/z = 349 (92.7%) that is in agreement with its molecular formula ($C_{18}H_{15}N_5OS$).

Furthermore, the interaction of compound **9** with some reagents, namely acetic anhydride, formic acid, and triethyl



Scheme 4



Scheme 5

orthoformate produced the corresponding pyrimido[4′,5′:4,5]-thieno[2,3-c]pyridazine derivatives (**16–18**), respectively (Scheme 5). The structure of compounds **16–18** were confirmed based on elemental analyses and spectral data. The IR spectra of compounds **16** and **17** showed absorption bands at 3300, 3270 for NH, at 1710 for carbonyl of acetyl, formyl and at 1675, 1660 cm^{-1} for carbonyl of pyrimidinones, respectively. Also, the IR spectrum of compound **18** showed an absorption band at 1660 cm^{-1} for the (CO, pyrimidinone).

4. Conclusion

In the present work, the synthesis of novel pyridazines (**4**, **5, 8**), thienopyridazines (**6**, **9–11, 13**, **15**), and pyrimidothienopyridazines (**16–18**) is reported.. All spectroscopic analyses confirmed the proposed structures of these compounds. Antibacterial

activity data have shown that the synthesized compounds have a significant antibacterial activity against the tested microorganisms.

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