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Note

Synthesis of some new 2-(pyrazol-1-yl)-4-(pyrimidin-5-yl)thiazoles

V K Ahluwalia*, Pooja Sharma & Bindu Goyal
Department of Chemistry, University of Delhi, Delhi 110 007
and
Renu Aggarwal
Gargi College, Siri Fort Road, New Delhi 110 049, India
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The reaction of 1, 3-diaryl-5-chloroacetyl-4, 6-dioxo-2-thioxohexahydropyrimidines **2a-h** with thiosemicarbazide gives 2-hydrazino-4-[1, 3-diaryl-4, 6-dioxo-2-thioxohexahydropyrimidin-5-yl]thiazoles **3a-h**, which on condensation with acetyl acetone yield 4-[1, 3-diaryl-4, 6-dioxo-2-thioxohexahydropyrimidin-5-yl]-2-[3, 5-dimethyl-1*H*-pyrazol-1-yl]thiazoles **4a-h.**

A wide spectrum of biological activities viz. anti-inflammatory[1], analgesic[1], antibacterial[2], anti-tubercular[3], antihypertensive[4], and hypothermic activities[5] etc. are found to be associated with compounds having pyrazole, pyrimidine and thiazole moieties. Thus, a system incorporating these moieties may result in the formation of some interesting bioactive compounds. Keeping this in view, the synthesis of the title compounds has been carried out.

1,3-Bis(4-methylphenyl)-4, 6-dioxo-2-thioxo-hexahydropyrimidine **1a** on reaction with chloroacetyl chloride gave 5-chloroacetyl-1, 3-bis(4-methylphenyl)-4, 6-dioxo-2-thioxohexahydropyrimidine[6] **2a** which on condensation with thiosemicarbazide in methanol afforded a yellow compound in 89% yield. Its IR spectrum showed absorption bands at 3500 (NH); 3300, 3200(NH_2); 1710, 1640(C=O) and 1600 cm^{-1} (C=N). The ^1H NMR (DMSO-d_6) spectrum showed two singlets at δ 2.3 and 4.5 for 6 protons (2×CH_3) and 2 protons (NH_2) respectively, a multiplet at δ 6.7-7.2 for 10 protons (8 Ar-H, 2×CH_3) and a broad singlet at δ 6.7–7.2 for 10 protons (8 Ar-H, 2×CH) and a broad singlet at δ 13.6 for 1 proton (NH, D_2O exchangeable) and the mass spectrum showed the molecular ion peak at m/z 437. On the basis of the above spectral data the product was assigned the structure 2-hydrazino-4-[1, 3-bis(4-methylphenyl)-4, 6-dioxo-2-thioxo-hexahydropyrimidin-5-yl]thiazole **3a**. In a similar manner compounds **3b-h** were synthesized.

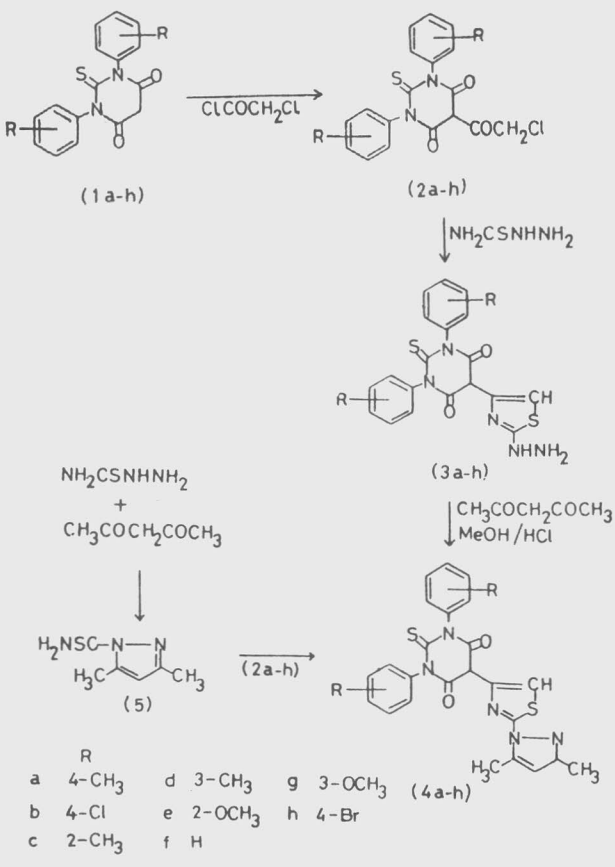
Further, the reaction of **3a** with acetyl acetone in methanol containing a catalytic amount of conc. hydrochloric acid afforded a yellow crystalline compound in 84% yield. The IR spectrum of the compound exhibited absorptions at 1680, 1640 (C=O) and 1600 cm^{-1} (C=N). Its ^1H NMR($CDCl_3$+TFA) spectrum showed a multiplet at δ 2.2-2.5 for 12 protons (4×CH_3), a singlet at δ 4.8 for 1 proton (C_4-H) and a multiplet at δ 7.1-7.4 for 10 protons (8 Ar-H, 2×CH). In the mass spectrum, the molecular ion peak was observed at m/z 501. Based on these spectral data the structure of the product was established as 4-[1, 3-bis(4-methylphenyl)-4, 6-dioxo-2-thioxohexahydropyrimidin-5-yl]-2-[3, 5-dimethyl-1*H*-pyrazol-1-yl]thiazole **4a**. Other members of the series **4b-h** were similarly prepared. (Scheme I)

Alternatively, compounds **4b-h** were also prepared by the condensation of **2a-h** with 3, 5-dimethyl-1-thioamido-1*H*-pyrazole **5** in the presence of methanol. The compounds obtained by the two methods were identical in all respects (m.m.p., TLC and superimposable IR).

Experimental Section

Melting points were uncorrected. IR spectra were recorded on a Shimadzu Infrared Spectrophotometer IR-435; ^1H NMR spectra on a Perkin Elmer R-32 (90 Mhz) spectrometer using. TMS as an internal standard and mass spectra on a JEOL-300 (EI/CI) instrument. Compounds **1a-h** and **5** were prepared by well-known methods.

2-Hydrazino-4-[1, 3-bis(4-methylphenyl)-4, 6-dioxo-2-thioxohexahydropyrimidin-5-yl]thiazole 3a. A mixture of **2a** (0.01 mole) and thiosemicarbazide (0.01 mole) in methanol (10 mL) was refluxed for 30 min. The separated solid was filtered, washed with methanol and recrystallised from methanol to give **3a**, m.p. 200-201° C (d),



Scheme I

yield 89% (Found: C, 59.82; H, 4.13; N, 6.90 $C_{20}H_{17}O_3N_2ClS$ requires C, 59.93; H, 4.21; N, 6.94%).

Compounds **3b-h** were prepared similarly and their characterization data are given in Table I.

4-[1, 3-Bis(4-methylphenyl)-4, 6-dioxo-2-thioxohexahydropyrimidin - 5 - yl] - 2 - [3, 5 - dimethyl-1*H*-pyrazol-1-yl]thiazole 4a; Method-A

A mixture of **3a** (0.01 mole) and acetyl acetone (0.01 mole) in methanol in the presence of conc. hydrochloric acid (5 drops) was refluxed for 3 hr. The reaction mixure was concentrated and cooled. The resulting solid was filtered, washed with methanol and recrystallised from methanol to give **4a**, m.p. 121-22°C, yield 84% (Found C, 62.60; H, 4.46; N, 13.85. $C_{26}H_{23}N_5S_2O_3$ requires C, 62.28; H, 4.59; N, 13.97%).

Compounds **4b-h** were prepared similarly and their characterization data are given in Table I.

Method-B. A mixture of **2a** (0.01 mole) and **5** (0.01 mole) was refluxed in methanol (10 mL) for 3 hr. The reaction mixture was concentrated and cooled. The separated solid was filtered, washed with methanol and recrystallised from methanol to give **4a**.

Table I—Characterization data of compounds **3b-h** and **4b-h**

Compd	Yield (%)	m.p. °C	Mol. formula	Found % (Calc.) C	H	N	^{1}H NMR (δ, /ppm)
3b*	86	>295	$C_{19}H_{13}N_5S_2O_2Cl_2$	47.77 (47.70	2.90 2.72	14.29 14.64)	13.6(brs, 1H, NH, D_2O exchangeable), 7.1-7.7(m 10H, 8Ar-H, 2×CH), 5.0(S, 2H, NH_2)
3c*	88	>295	$C_{21}H_{19}N_5S_2O_2$	57.50 (57.67	4.27 4.35	16.16 16.02)	13.6(brs, 1H, NH, D_2O exchangeable), 7.1-7.5(m 9H, 8Ar-H, CH), 6.9(s, 1H, CH), 4.8(s, 2H, NH_2), 2.2(s, 6H, 2×CH_3)
3d*	85	250-51(d)	$C_{21}H_{19}N_5S_2O_2$	57.51 (57.67	4.21 4.35	16.29 16.02)	13.6(brs, 1H, NH, D_2O exchangeable), 6.9-7.6(m, 10H, 8Ar-H, 2×CH), 4.7 (s, 2H, NH_2) 2.2(s, 6H, 2×CH_3)
3e*	89	295-96(d)	$C_{21}H_{19}N_5S_2O_4$	53.92 (53.73	4.10 4.05	14.80 14.92)	13.6(brs, 1H, NH, D_2O exchangeable), 6.9-7.6(m, 10H, 8Ar-H, 2×CH), 4.7(s, 2H, NH_2), 3.8(s, 6H, 2×OCH_3)
3f*	86	>295	$C_{21}H_{19}N_5S_2O_4$	53.62 (53.73	4.23 4.05	14.76 14.92)	13.6(brs, 1H, NH, D_2O exchangeable), 7.1-7.6(m, 12H, 10Ar-H, 2×CH), 4.9(s, 2H, NH_2)

Table I—Characterization data of compounds **3b-h** and **4b-h**

Compd	Yield (%)	m.p. °C	Mol. formula	Found % (Calc.) C	H	N	^{1}H NMR (δ, /ppm)
3g*	88	>295	$C_{19}H_{15}N_5S_2O_2$	55.99 (55.75	3.54 3.67	17.25 17.12)	13.6(brs, 1H, NH, D_2O exchangeable), 7.0-7.8(m, 10H, 8Ar-H, 2×CH), 5.0(s, 2H, NH_2), 3.7(s, 6H, 2×OCH_3)
3h*	87	>295	$C_{19}H_{15}N_5S_2O_2Br_2$	40.21 (40.01	2.45 2.29	12.44 12.30)	13.6(brs, 1H, NH, D_2O exchangeable), 7.0-7.8((m, 10H, 8Ar-H, 2×CH), 4.9(s, 2H, NH_2)
4b**	85	235-36(d)	$C_{24}H_{17}N_5S_2O_2Cl_2$	53.08 (53.14	3.21 3.14	12.98 12.92	7.6-7.1(m, 10H, 8Ar-H, 2×CH), 4.2(s, 1H, C_4-H), 2.7(s, 3H C_5-CH_3), 2.6(s, 3H, C_3-CH_3
4c**	85	165-66	$C_{26}H_{23}N_5S_2O_2$	62.54 (62.28	4.23 4.59	13.81 13.97)	7.4-7.1(m, 10H, 8Ar-H, 2×CH), 4.2(s, 1H, C_5-CH_3), 2.6(S, 3H, C_3-CH_3), 2.6(s, 3H, C_3-CH_3),.4(s, 6H, 2×CH_3)
4d**	82	163-63	$C_{26}H_{23}N_5S_2O_2$	62.45 (62.28	4.27 4.59	13.84 13.97)	7.5-7.0(m, 10H, 8Ar-H, 2×CH), 4.8(s, 1H, C_4-H), 2.5-2.3(m, 12H, 4×CH)
4e**	84	159-60	$C_{26}H_{23}N_5S_2O_4$	58.82 (58.84	4.49 4.32	13.19 13.13)	7.5-6.9(m, 10H, 8Ar-H, 2×CH), 4.2(s, 1H, C_4-H), 3.8(s, 6H, 2×OCH_3), 2.7(s, 3H, C_5-CH_3), 2.6(s, 3H, C_3-CH_3)
4f**	83	>260	$C_{26}H_{23}N_5S_2O_4$	58.41 (58.54	4.40 4.32	13.21 13.13	7.8-7.0(m, 10H, 8Ar-H, 2×CH), 4.7(s, 1H, C_4-H), 2.8-2.5(m, 6H, 2×CH_3)
4g**	81	119-20	$C_{24}H_{19}N_5S_2O_4$	60.74 (60.89	4.02 4.01	14.91 14.80)	7.4-6.7(m, 10H, 8Ar-H, 2×CH), 4.2(s, 1H, C_4-H), 3.8(s, 6H, 2×OCH_3), 2.7(s, 3H, C_5-CH_3)
4h**	81	220-21(d)	$C_{24}H_{17}N_5S_2O_2Br_2$	49.95 45.50	2.74 2.69	11.23 11.06	7.6-7.0(m, 10H, 8Ar-H, 2×CH), 4.2(s, 1H, C_4-H), 2.7(s, 3H, C_5-CH_3), 2.6(s, 3H, C_3-CH_3)

*^{1}H NMR were taken in DMSO-d_6; **^{1}H NMR were taken in $CDCl_3$+TFA

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