

A Novel Synthesis of Some New Pyrimidine, Thiazolopyrimidine and Pyrazole Derivatives Using Diarylepoxopropanones as Precursors

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Abstract: 3-Aryl-1-(2-naphthyl)-2, 3-epoxypropanones (**2**) reacted with thiourea to give 4-arylhexahydro-6-(2-naphthyl)-2-thioxopyrimidin-5-ones (**3**). Reaction of **3** with each of arenediazonium chlorides, chloroacetic acid and 3-bromopropanoic acid produced 6-arylhydrazonohexahydropyrimidinone, tetrahydrothiazolo[3,2-a]pyrimidine-3,6-diones and tetrahydropyrimido[2,1-b]-1,3-thiazine-4,7-diones, respectively. Compound **2** reacted with hydrazines to yield different 3-(2-naphthyl) pyrazoles, depending on the reaction conditions. Newly synthesized compounds were tested for their biological activity.

Key words: Epoxypropanones · Thioxopyrimidinones · Thiazolo [3, 2-a] pyrimidinediones and pyrazoles

INTRODUCTION

Oxiranes (epoxides) are extremely reactive precursors that can be used to synthesize several types of organic compounds [1-5]. They have carcinogenic [6] and mutagenic effects [7] and also are important in biosynthesis of marine organisms [8] and toxin for some species of fungi. In previous work Buchi *et al.* [9] the reaction of aryl methylenecycloalkanones pyrimidinethiones and thiazolones was studied [10-13] and some derivatives were found to possess anticancer activity [11, 13]. In this article, we would like to report the use of 1, 3-diaryl-2, 3-epoxypropan-1-ones (**2**) for the synthesis of some new heterocyclic compounds and their biological evaluation as antimicrobial activity.

RESULTS AND DISCUSSION

3-Aryl-1-(2-naphthyl) prop-2-en-1-ones (**1**) [14] reacted with hydrogen peroxide in alkaline medium to produce 1-(2-naphthyl)-[3-phenyl-oxiranyl] methanone (**2a**), 1-(2-naphthyl)-[3(*p*-bromophenyl)oxiranyl]-methanone (**2b**) and 1-(2-naphthyl)-[3(*p*-methoxy phenyl oxiranyl) methanone (**2c**), respectively which have been utilized as key starting materials in the synthesis of many interesting heterocyclic compounds (Scheme 1). Analytical and spectral data of compounds **2** are in total agreement with the proposed structure (c.f. Experimental section). Compounds **2** as a typical epoxides, reacted with thiourea in alcoholic potassium hydroxide solution to

produce 6-(2-naphthyl)-4-(phenyl)-2-thioxo-hexahydro pyrimidin-5-one (**3a**), 4-(*p*-bromophenyl)-6-(2-naphthyl) 2-thioxo-hexahydro pyrimidin-5-one (**3b**) and 4-(*p*-methoxyphenyl)-6-(2-naphthyl)-2-thioxo-hexahydro pyrimidin-5-one (**3c**), respectively (scheme 1). The reaction possible takes places *via* the following (Figure 1).

Compounds **3a-c** showed correct values in elemental analyses as well as compatible IR spectral data. ¹H-NMR spectrum (DMSO-*d*₆) of compound **3a** as an example, showed the expected signals corresponding to the aromatic protons and two types of exchangeable protons corresponding to two NH groups. Besides, two doublets appeared at (3.20 and 3.70 ppm, each corresponds to a pyrimidine proton. ¹³C-NMR spectrum of compound **3a** showed the expected signals for C=O, C=S and aromatic carbons, as well as two signals in the sp³ carbon region at (43.0 and 71.7 ppm. The appearance of the latter signals in ¹³C-NMR spectrum and the two signals at (3.20 and 3.70 ppm in ¹H-NMR spectrum of compound **3a** suggests that the produced pyrimidine ring is in fact alicyclic, not aromatic and prefers to be in twist boat form, in which the oxirane nucleus undergoes hetero ring opening by thiourea at carbon followed by 1,2-hydride shift and proton transfer affording the fleeting intermediate (A). The latter undergoes ring closure to give the desired products **3**. The two protons at C-4 and C-6 can undergo long range coupling and they both appear as doublets. Compounds **3a-c** are colourless (this ruled out thioquinone structure).

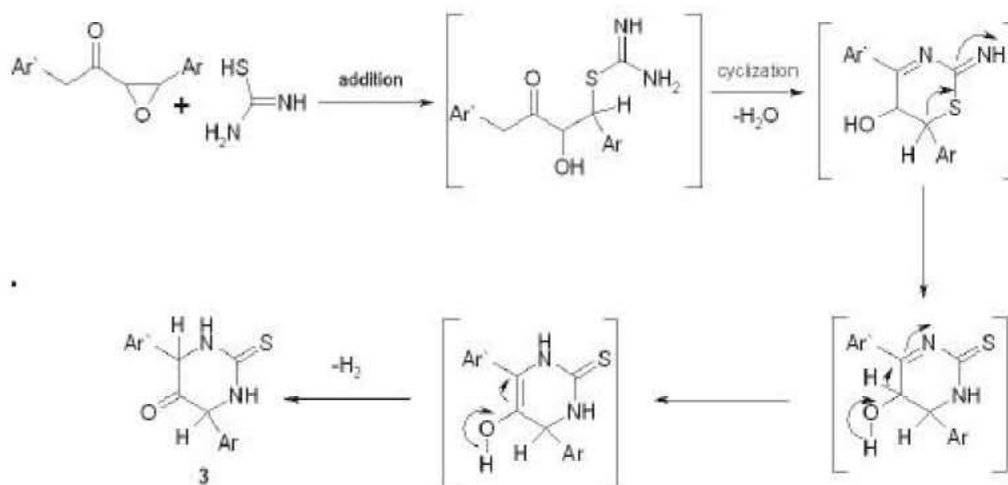
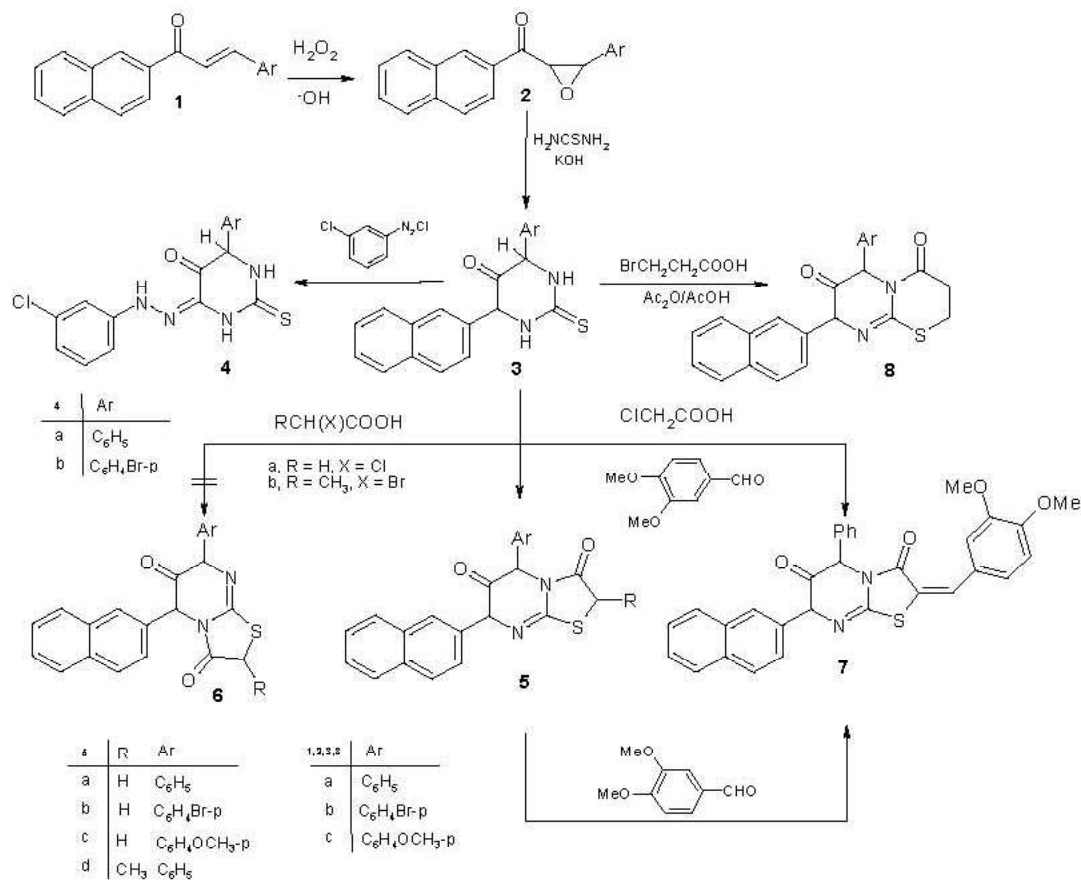


Fig. 1: Mechanism of formation of compound 3



Scheme 1

Scheme 1:

In the twist boat, the observed Raman spectrum of 1,4-cyclohexanedione showed seven bands, all which showed coincidences in the infrared (Figure 2) [15]. That

so many coincidences are highly coincidences are highly improbable to be accidental, but it rather suggests that the compound has the twist boat and not the chair.

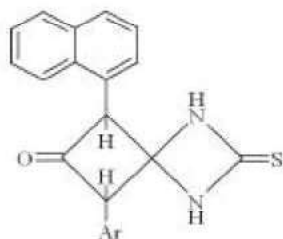


Fig. 2: Twist boat form of compounds 3

Compounds **3a, c** underwent reaction with chlorobenzenediazonium chloride where coupling took place with the elimination of naphthyl group (Japp-klingeman reaction) to yield the 4-aryl-6-(3-chlorophenylhydrazono)-2-thioxotetrahydro pyrimidin-5-ones (**4a, b**), respectively; (Scheme 1). Compound **4** gave correct values in elemental analysis as well as compatible spectroscopic data (Experimental).

Heating under reflux compounds **3** with chloroacetic acid in acetic acid/ Acetic anhydride mixture, in the presence of anhydrous sodium acetate, produces 5-aryl-7-(2-naphthyl-2,3,5,6-tetrahydro-7H-thiazolo[3,2-a]pyrimidine-3,6-dione (**5a-c**), rather than their isomeric structure **6**; compounds **5** gave correct values in elemental analyses besides displaying the expected carbonyl absorption bands in IR (Experimental). Preferring structure **5** over **6** was mainly based on $^1\text{H-NMR}$ spectra. Thus $^1\text{H-NMR}$ spectrum of **5a**, as an example showed two doublets signals at δ 3.70 and 3.95 ppm, corresponding to two pyrimidine protons, among other signals (Experimental). By comparing δ values of pyrimidine protons in **5a** with the corresponding protons in (**3a**) it is clear that one proton did not change its δ value (3.70 ppm, representing the methylnaphthalene-like proton), while the other proton absorbing at δ 3.20 ppm in **3a** (toluene-like proton) suffered from a down-field shift and appeared at δ 3.95 in **5a**. It was reported in literature that ring closure involving a certain nitrogen atom affects the δ value of a proton on the adjacent carbon atom. According, Sherif *et al.* [16] it is concluded that the nitrogen atom neighboring to the toluene like proton (C-4 proton) is the one involved in thiazole ring formation and consequently, structure (**5**) is inferred as the reaction product. The two protons at C-2 are clearly diastereotopic, hence they are magnetically non-equivalent and they suffer from geminal coupling, resulting in the appearance of two doublets at 4.04 and δ 4.70 ppm ($J = 3$ Hz).

Compound **3a** reacted similarly with 2-bromopropionic acid, under the same reaction conditions to produce 2-methyl-7-(2-naphthyl)-5-phenyl-2,3,5,6-

tetrahydro-7H-thiazolo [3, 2-a] pyrimidine-3,6-dione (**5d**). Elemental analyses, as well as its spectral data are compatible with the proposed structure (Experimental).

The presence of an activated methylene group in **5a-c** could be confirmed by condensation of compound (**5a**) with 3,4-dimethoxy-benzaldehyde in acetic acid/ acetic anhydride mixture, in presence of anhydrous sodium acetate to produce 2-(3,4-dimethoxyphenylmethylene)-7-(2-naphthyl)-5-phenyl-2,3,5,6-tetrahydro-7H-thiazolo [3,2-a] pyrimidine-3,6-dione (**7**). Compounds **7** gave agreeable data in elemental analyses and spectral data (Experimental).

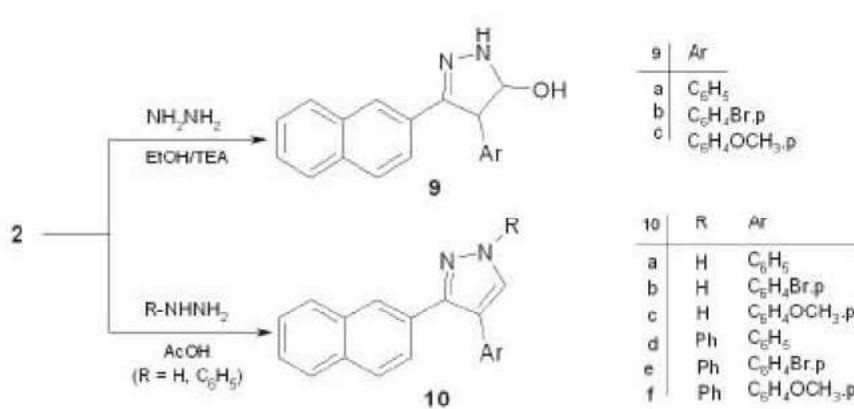
Compounds **7** could be directly prepared from **3a** in one step. Thus heating **3a** with chloroacetic acid and 3, 4-dimethoxybenzaldehyde in acetic acid/ acetic anhydride mixture, in the presence of anhydrous sodium acetate gave product identical with **7** in all aspects (m.p., mixed m.p. and IR). On the other hand, compounds **3a-c** reacted with 3-bromopropionic acid under similar reaction conditions to produce 6-aryl-8-(2-naphthyl)-2,3,6,8-tetrahydro-4H-pyrimido-[2,1-b]-1,3-thiazine4,7-diones (**8a-c**); Scheme 1. Elemental analyses of compounds **8a-c** as well as their spectral data agreed with the proposed structure (Experimental).

Additionally, behavior of the epoxides **2** towards hydrazine hydrate depended on the reaction conditions. Thus, when compounds **2a-c** reacted with hydrazine hydrate in ethanol containing triethylamine, the product could be formulated as 4-aryl-5-hydroxy-3-(2-naphthyl)-4,5-dihydro-1H, pyrazoles (**9a-c**); (Scheme 2). Structure of compounds (**9**) was verified by elemental analyses, IR, $^1\text{H-NMR}$ and mass spectroscopic data (Experimental). On the other hand, treatment of compounds **2a-c** with hydrazine hydrate or phenyl hydrazine in glacial acetic acid yielded 5-aryl-3-(2-naphthyl)-1H-pyrazoles (**10a-c**) and 5-aryl-3-(2-naphthyl)-1-phenyl derivatives (**10d-f**) (Scheme 2).

Reaction products were assigned structures **10** based on correct values in elemental analyses, as well as compatible spectral data (Experimental).

Biological Evaluation

Antimicrobial Activity: The antimicrobial activity of the compounds considered was tested on 1) *Escherichia coli*, 2) *Pseudomonas putide*, 3) *Bacillus subtilis*, 4) *Streptococcus lactis*, 5) *Aspergillus niger*, 6) *Penicillium sp.* and 7) *Candida albicans*. The biological activity was determined according to the filter paper disc-diffusion method [17]. The sensitivity of microorganisms to the compounds is identified in the following manner.



Scheme 2:

Table 1: *In vitro* antimicrobial activity of some newly synthesized heterocyclic compounds

Compound	Inhibition zone (mm)						
	Microorganism						
	Bacteria						
	Gram-negative		Gram-positive		Fungi		Yeast
	<i>Escherichia coli</i>	<i>Pseudomonas putide</i>	<i>Bacillus subtilis</i>	<i>Streptococcus lactis</i>	<i>Aspergillus niger</i>	<i>Penicillium Sp.</i>	<i>Candida albicans</i>
1a	16	16	16	16	0	0	0
2c	0	0	0	0	0	0	0
3b	14	12	10	10	0	0	8
4b	18	16	18	18	18	12	14
5b	0	0	0	0	0	0	0
5d	18	15	18	18	0	0	12
7a	12	13	16	16	0	0	8
9b	0	0	0	0	0	0	0
9c	0	0	0	0	0	0	0
10f	0	0	17	17	18	0	0

Highly sensitive = 15-20 mm, moderately sensitive = 10-15 mm, slightly sensitive = 5-10 mm

Not sensitive = 0 mm

It could be mentioned that the most determined effect is brought about by compounds (1a, 4b, 5d), (1a, 4b, 5d, 7a, 10f) and (4b, 10f) showed high activity against (*E. coli* and *P. putide*), (*B. subtilis* and *S. lactis*) and (*A. niger*), respectively. The test of compounds number (3b, 7a), (3b), (4b) and (4b, 5d) showed moderate activity towards (*E. coli* and *P. putide*), (*B. subtilis* and *S. lactis*), (*P. sp.*) and (*C. albicans*), respectively. The test compounds number (3b and 7a) showed slight activity against (*C. albicans*). Compounds number 2c, 5b, 9b and 9c showed no activity towards all the tested microorganisms.

Experimental: All melting points are uncorrected. IR spectra were recorded (KBr) on Pye Unicam SP-1000 spectrophotometer. ¹H- and ¹³C-NMR spectra were

obtained with a Varian ¹H-Gemini 200 spectrometer with chemical shifts expressed in δ ppm using TMS as the internal reference. Mass spectra were obtained on GC-MSQP 1000 EX mass spectrometer operating at 70 eV. The elementary analyses were performed by the microanalytical unit, National Research Center, Cairo, Egypt.

Compound 1 was prepared according to method reported by Coffen *et al.* [14].

Synthesis of 3-aryl-1-(2-naphthyl)-2,3-epoxypropanones (2a-c): Hydrogen peroxide (5 ml, 30%) was added portion-wise to a mixture of 3-aryl-1-(naphthyl)prop-2-en-1-ones (1a-c, 0.01 mole) in acetone (50 ml) and methanol (15 ml) containing NaOH (1 g), at 20-25°C with stirring. The reaction mixture was left overnight. Cold water was added

Table 2: Characterization Data for the Newly Synthesized Compounds

Compd No.	Mol. Form. (M.Wt.)	Yield %	M.P. °C (Solvent)	Analysis		IR (KBr) cm ⁻¹	¹ H-NMR and ¹³ C-NMR (DMSO-d ₆) δ ppm	MS (m/z) M ⁺ (%)
				Calc. %C %H %N %S %Br %Cl	Found %C %H %N %S %Br %Cl			
2a	C ₁₉ H ₁₄ O ₂ (274)	75	120 (methanol)	83.21 5.11 ----- ----- ----- -----	83.10 5.20 ----- ----- ----- -----	1680 (CO)	¹ H-NMR: 4.20 (s, 1H, epoxy-H), 5.00 (s, 1H, epoxy-H) and 7.25-8.90 (m, 12H, ArH)	274 (17%)
2b	C ₁₉ H ₁₃ BrO ₂ (353)	70	125 (methanol)	64.59 3.68 ----- ----- 22.66 -----	64.50 3.80 ----- ----- 22.30 -----	1685 (CO)	¹ H-NMR: 4.20 (s, 1H, epoxy-H), 5.10 (s, 1H, epoxy-H) and 7.40-8.90 (m, 11H, ArH)	353 (17.5%)
2c	C ₂₀ H ₁₆ O ₃ (304)	72	128 (methanol)	78.95 5.26 ----- ----- ----- -----	78.60 5.70 ----- ----- ----- -----	1680 (CO)	¹ H-NMR: 3.75 (s, 3H, OCH ₃), 4.20 (s, 1H, epoxy-H), 5.00 (s, 1H, epoxy-H), 6.90 (d, 2H, ArH), 7.10 (d, 2H, ArH) and 7.60-8.30 (m, 7H, ArH)	304 (15.9%)
3a	C ₂₀ H ₁₆ N ₂ OS (332)	70	250 (acetic acid)	72.29 4.82 8.43 9.64 ----- -----	72.50 4.60 8.50 9.70 ----- -----	3340-3180 (2NH), 1725 (CO)	¹ H-NMR: 3.20 (d, 1H, pyrimidine H-4), 3.70 (d, 1H, pyrimidine H-6), 7.20-8.20 (m, 12H, ArH), 10.90 (s, 1H, NH, D ₂ O exchangeable) and 11.70 (s, 1H, NH, D ₂ O exchangeable): ¹³ C-NMR (DMSO-d ₆): δ 43.0 ppm (sp ³ carbon), 71.70 (sp ³ carbon), 125.60-137.70 (14 signals, sp ² carbons), 175.80 (CS) and 181.50 (CO).	332 (100%)
3b	C ₂₀ H ₁₃ BrN ₂ OS (411)	72	252 (acetic acid)	58.39 3.65 6.81 7.78 19.46 ----- -----	58.30 3.60 6.60 7.80 19.30 ----- -----	3338-3185 (2NH), 1730 (CO)	¹ H-NMR: 3.25 (d, 1H, pyrimidine H-4), 3.75 (d, 1H, pyrimidine H-6), 7.20-8.20 (m, 11H, ArH), 10.92 (s, 1H, NH, D ₂ O exchangeable) and 11.70 (s, 1H, NH, D ₂ O exchangeable)	411 (100%)
3c	C ₂₁ H ₁₈ N ₂ O ₂ S (362)	70	255 (acetic acid)	69.61 4.97 7.73 8.84 ----- -----	69.10 4.80 7.90 8.80 ----- -----	3340-3200 (2NH), 1725 (CO)	¹ H-NMR: 3.20 (d, 1H, pyrimidine H-4), 3.70 (d, 1H, pyrimidine H-6), 3.80 (s, 3H, OCH ₃), 7.20 (d, 2H, ArH), 7.35 (d, 2H, ArH), 7.55-8.25 (m, 7H, ArH), 10.50 (s, 1H, NH, D ₂ O exchangeable) and 11.70 (s, 1H, NH, D ₂ O exchangeable)	362 (100%)
4a	C ₁₆ H ₁₁ ClN ₄ OS (342.5)	35	210	56.06 3.21 16.35 9.34 ----- 10.36	56.00 3.00 16.50 9.30 ----- 10.20	3472-3322 (2NH), 1720 (CO)	¹ H-NMR: 1.25 (s, 1H, NH, D ₂ O exchangeable), 1.56 (s, 1H, NH, D ₂ O exchangeable) and 7.18-7.46 (m, 9H, ArH)	
4b	C ₁₇ H ₁₃ ClN ₄ O ₂ S (372.5)	40	220	54.77 3.49 15.03 8.59 ----- 9.53	54.60 3.60 15.00 8.50 ----- 9.30	3475-3330 (2NH), 1720 (CO)	¹ H-NMR: 1.30 (s, 1H, NH, D ₂ O exchange-able), 1.58 (s, 1H, NH, D ₂ O ex-changeable), 3.75 (s, 3H, OCH ₃) and 7.18-7.46 (m, 8H, ArH)	

Table 2: Continued

5a	$C_{22}H_{16}N_2O_2S$ (372)	60	190 (acetic acid)	70.97 4.30 7.53 8.60 ----- -----	70.80 4.10 7.50 8.50 ----- -----	1720, 1740 (2CO)	1H -NMR: 3.70 (d, 1H, pyrimidine H-7), 3.95 (d, 1H, pyrimidine H-5), 4.40 (d, 1H, thiazole H), 4.70 (d, 1H, thiazole H) and 7.10-8.20 (m, 12H, ArH)	372 (100%)
5b	$C_{22}H_{15}BrN_2O_2S$ (451)	55	220 (acetic acid)	58.54 3.33 6.21 7.10 17.73 ----- -----	58.50 3.40 6.20 7.20 17.60 ----- -----	1715, 1745 (2CO)	1H -NMR: 3.75 (d, 1H, pyrimidine H-7), 4.00 (d, 1H, pyrimidine H-5), 4.50 (d, 1H, thiazole H) 4.75 (d, 1H, thiazole H) and 7.10-8.25 (m, 11H, ArH)	451 (100%)
5c	$C_{23}H_{18}N_2O_3S$ (402)	57	210 (acetic acid)	68.66 4.48 6.97 7.96 ----- -----	68.60 4.50 6.90 7.90 ----- -----	1720, 1740 (2CO)	1H -NMR: 3.70 (d, 1H, pyrimidine H-7), 3.80 (s, 1H, OCH_3), 3.95 (d, 1H, pyrimidine H-5), 4.41 (d, 1H, thiazole H) 4.70 (d, 1H, thiazole H), 6.85 (d, 2H, ArH), 7.10 (d, 2H, ArH) and 7.60-8.30 (m, 7H, ArH)	402 (100%)
5d	$C_{23}H_{18}N_2O_2S$ (386)	55	210 (acetic acid/ methanol)	71.50 4.66 7.25 8.29 ----- -----	71.40 4.60 7.40 8.20 ----- -----	1748, 1725 (2CO)	1H -NMR: 1.20 (d, 3H, CH_3), 3.70 (d, 1H, pyrimidine H-7), 3.95 (d, 1H, pyrimidine H-5), 4.82 (q, 1H, thiazole H) and 7.00-8.20 (m, 12H, ArH)	386 (100%)
7	$C_{31}H_{24}N_2O_4S$ (520)	65	260 (dioxane)	71.54 4.62 5.38 6.15 ----- -----	71.50 4.70 5.40 6.10 ----- -----	1715, 1755 (2CO)	1H -NMR: 3.70 (d, 1H, pyrimidine H-7), 3.90 (s, 6H, $2OCH_3$), 4.10 (d, 1H, pyrimidine H-5) and 7.20-8.10 (m, 15H, ArH)	520 (0.35%)
8a	$C_{31}H_{18}N_2O_2S$ (386)	55	200 (acetic acid)	71.50 4.66 7.25 8.29 ----- -----	71.60 4.60 7.30 8.10 ----- -----	1725, 1740 (2CO)	1H -NMR: 2.35 (m, 2H, CH_2), 3.80 (m, 2H, CH_2), 3.85 (d, 1H, pyrimidine H-8), 4.05 (d, 1H, pyrimidine H-6) and 7.00-7.20 (m, 12H, ArH)	386 (100%)
8b	$C_{23}H_{17}BrN_2O_2S$ (465)	50	225 (dioxane)	59.35 3.66 6.02 6.88 17.20 ----- -----	59.60 3.60 6.20 6.80 17.10 ----- -----	1730, 1745 (2CO)	1H -NMR: 2.40 (m, 2H, CH_2), 3.85 (m, 2H, CH_2), 3.90 (d, 1H, pyrimidine H-8), 4.15 (d, 1H, pyrimidine H-6) and 6.95-7.20 (m, 11H, ArH)	465 (100%)
8c	$C_{24}H_{20}N_2O_3S$ (416)	55	220 (dioxane)	69.23 4.81 6.73 7.69 ----- -----	69.50 4.60 6.70 7.90 ----- -----	1725, 1740 (2CO)	1H -NMR: 2.35 (m, 2H, CH_2), 3.75 (s, 3H, OCH_3), 3.80 (m, 2H, CH_2), 3.87 (d, 1H, pyrimidine H-8), 4.05 (d, 1H, pyrimidine H-6), 6.77 (d, 2H, ArH), 6.85 (d, 2H, ArH) and 7.50-8.10 (m, 7H, ArH)	416 (100%)
9a	$C_{19}H_{16}N_2O$ (288)	55	189 (ethanol)	79.17 5.56 9.72 ----- ----- -----	79.40 5.50 9.70 ----- ----- -----	3000-2600 (OH), 3250 (NH)	1H -NMR: 4.50 (d, 1H, pyrazole H-4), 5.05 (t, 1H, pyrazole H-5), 6.25 (d, 1H, pyrazole NH, D_2O exchangeable) and 7.20-8.20 (m, 13H, 12 ArH + OH, D_2O exchangeable)	288 (70%)
9b	$C_{19}H_{15}BrN_2O_2$ (367)	52	205 (ethanol)	62.13 4.09 7.63 ----- 21.79 -----	62.30 4.20 7.70 ----- 21.80 -----	3100-2800 (OH), 3330 (NH)	1H -NMR: 4.52 (d, 1H, pyrazole H-4), 5.10 (t, 1H, pyrazole H-5), 6.26 (d, 1H, pyrazole NH, D_2O exchangeable) and 7.25-8.28 (m, 12H, 11 ArH + OH, D_2O exchangeable)	

Table 2: Continued

9c	C ₂₀ H ₁₈ N ₂ O ₂ (318)	55	190 (ethanol)	75.47	75.50	3000-2700 (OH),	¹ H-NMR: 3.75 (s, 3H, OCH ₃), 4.51 (d, 1H, pyrazole H-4), 5.05 (t, 1H, pyrazole H-5), 6.25 (d, 1H, pyrazole NH, D ₂ O exchangeable), 6.92 (d, 2H, ArH), 7.30 (d, 2H, ArH) and 7.55-8.21 (m, 8H, 7 ArH + OH, D ₂ O exchangeable)	318 (70%)
				5.66	5.60	3300 (NH)		
				8.81	8.70			
				-----	-----			
				-----	-----			
				-----	-----			
10a	C ₁₉ H ₁₄ N ₂ (270)	57	190 (acetic acid)	84.44	84.50	3250 (NH)	¹ H-NMR: 7.15-8.46 (m, 13H, 12ArH+ pyrazole H-4) and 13.32 (s, 1H, NH, D ₂ O exchangeable)	270 (100%)
				5.19	5.30			
				10.37	10.50			
				-----	-----			
				-----	-----			
				-----	-----			
10b	C ₁₉ H ₁₃ Br N ₂ (349)	55	230 (dioxane)	65.33	65.23	3350 (NH)	¹ H-NMR: 7.30-8.50 (m, 12H, 11ArH+ pyrazole H-4) and 13.52 (s, 1H, NH, D ₂ O exchangeable)	349 (100%)
				3.72	3.80			
				8.02	8.10			
				-----	-----			
				22.92	22.90			
				-----	-----			
10c	C ₂₀ H ₁₆ N ₂ O (300)	60	220 (dioxane)	80.00	80.20	3300 (NH)	¹ H-NMR: 3.80 (s, 3H, OCH ₃), 7.05-8.45 (m, 12H, 11 ArH pyrazole H-4) and 13.30 (s, 1H, NH, D ₂ O exchangeable)	300 (100%)
				5.33	5.30			
				9.33	9.50			
				-----	-----			
				-----	-----			
				-----	-----			
10d	C ₂₅ H ₁₈ N ₂ (346)	60	165 (ethanol)	86.71	86.60	3100 (CH aromatic),	¹ H-NMR: 7.15-8.50 (m, 18H, 17ArH + pyrazole H-4)	346 (39%)
				5.20	5.40	2800 (CH aliphatic),		
				8.09	8.10	1620 (C=N)		
				-----	-----			
				-----	-----			
				-----	-----			
10e	C ₂₅ H ₁₇ Br N ₂ (425)	60	105 (methanol)	70.59	70.70	3150 (CH aromatic),	¹ H-NMR: 7.16-8.52 (m, 17H, 16ArH + pyrazole H-4)	425 (35.5%)
				4.00	4.10	2800 (CH aliphatic),		
				6.59	6.70	1620 (C=N)		
				-----	-----			
				18.82	18.90			
				-----	-----			
10f	C ₂₆ H ₂₀ N ₂ O (376)	55	130 (ethanol)	82.98	83.20	3100 (CH aromatic),	¹ H-NMR: 3.75 (s, 3H, OCH ₃), 6.85-8.39 (m, 17H, 16 ArH + pyrazole H-4)	376 (29%)
				5.32	5.20	2800 (CH aliphatic),		
				7.45	7.60	1620 (C=N)		
				-----	-----			
				-----	-----			
				-----	-----			

and the precipitated solid was filtered off, washed with cold water and crystallized from methanol to give compounds **2a-c** (Table 2).

Synthesis of 4-arylhexahydro-6-(2-naphthyl)-2-thioxopyrimidin-5-ones (**3a-c**)

A mixture of compounds **2a-c** (0.01 mole) and thiourea (0.01 mole) in alcoholic potassium hydroxide (100 ml, 2 g KOH in 100 ml ethanol) was refluxed for 4 hrs. The alcohol was evaporated and the obtained solid was washed with acidified cold water several times, crystallized from acetic acid to give compounds **3a-c** (Table 2).

Synthesis of 4-aryl-6-(3-chlorophenylhydrazone)-2-thioxotetrahydro-pyridin-5-ones (**4a, b**)

3-Chloroaniline (1.27 g, 0.01 mole) was dissolved in concentrated hydrochloric acid (3 ml), cooled to -5°C and treated with sodium nitrite solution (0.7 g, 0.11 mole in 2 ml of water). The diazonium salt was cooled for 15 min. and then added gradually with stirring to a cooled solution of compounds **3a, c** (0.01 mole) in pyridine (10 ml). The reaction mixture was cooled for 30 min. and poured onto cold water. The formed solid was collected and purified by silica gel column eluted with benzene to afford pure samples of **4a, b** (Table 2).

Synthesis of 5-aryl-7-(2-naphthyl)-2,3,5,6-tetrahydro-7H-thiazolo [3,2-a]-pyrimidine-3, 6-diones (5a-c): A mixture of compounds **3a-c** (0.01 mole) with chloroacetic acid (0.95 g, 0.01 mole) and fused sodium acetate (2 g) in glacial acetic acid (30 ml) and acetic anhydride (15 ml) was refluxed for 3 hrs, left to cool, then poured gradually onto cold water. The formed solid was filtered off, washed with water and crystallized from acetic acid to give compounds **5a-c** (Table 2).

Synthesis of 2-methyl-7-(2-naphthyl)-5-phenyl-2,3,5,6-tetrahydro-7H-thiazolo[3,2-a]pyrimidine-3,6-dione(5d): A similar method to that used for preparation of **5a-c** was applied, using 2-bromopropanoic (0.01 mole) acid instead of chloroacetic acid. The obtained solid was crystallized from acetic acid / methanol to give compound **5d** (Table 2).

Synthesis of 2-(3,4-dimethoxyphenylmethylene)-7-(2-naphthyl)-5-phenyl-2,3,5,6-tetrahydro-7H-thiazolo [3,2-a]pyrimidine-3, 6-dione (7)

Method A: A mixture of compound **5a** (0.01 mole), an equimolar amount of 3,4- dimethoxy-benzaldehyde in acetic anhydride (30 ml) was refluxed for 3 hrs, left to cool, then poured onto cold water. The formed solid was collected and crystallized from dioxane to give compound **7** (Table 2).

Method B: A mixture of compound **3a** (0.01 mole), chloroacetic acid (0.95 g, 0.01 mole), fused sodium acetate (2 g) and an equimolar amount of 3,4-dimethoxybenzaldehyde in glacial acetic acid (30 ml) and acetic anhydride (15 ml) was refluxed for 3 hrs. The reaction mixture was left to cool and poured onto cold water. The formed solid was collected and crystallized from dioxane to give a compound identical in all aspects with **7** (m.p., mixed m.p and IR)

Synthesis of 6-aryl-8-(2-naphthyl)-2,3,6,8-tetrahydro-4H-pyrimido[2,1-b]-1,3-thiazine-4,7-diones (8a-c): A similar method to that used for preparation of **5a-c** was applied, using 3-bromo-propanoic acid (0.01 mole) instead of chloroacetic acid. The obtained solid was crystallized from the proper solvent to give compound **8a-c** (Table 2).

Synthesis of 4-aryl-5-hydroxy-3-(2-naphthyl)-4,5-dihydro-1H-pyrazoles (9a-c): A solution of compounds **2a-c** and hydrazine hydrate (0.01 mole, 99%) in absolute ethanol (30 ml) and drops of triethylamine was heated under reflux for 4 hrs, left to cool and then poured onto acidified ice-cold water. The obtained solid was filtered

off, washed several times with water and crystallized from ethanol to give compounds **9a-c** (Table 2).

Synthesis of 4-aryl-3-(2-naphthyl)-1H-pyrazoles (10a-c): A solution of compounds **2a-c** (0.01 mole) and hydrazine hydrate (0.01 mole, 99%) in glacial acetic acid (30 ml) was refluxed for 3 hrs, left to cool and then poured onto ice-cold water. The produced solid was filtered off, washed with water and crystallized from the proper solvent to give compounds **10a-c** (Table 2).

Synthesis of 4-aryl-3-(2-naphthyl)-1-phenyl-1H-pyrazoles (10d-f): A similar method to that used for preparation of **10a-c** was applied, using phenyl hydrazine (0.01 mole) instead of hydrazine hydrate. The obtained solid was crystallized from the proper solvent to give compound **10d-f** (Table 2).

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