Sulfenylation of Heterocyclic 1,3-Dicarbonyl Systems: 4-Hydroxy-2-pyrones, 6-Hydroxy-4-pyrimidones, 4-Hydroxy-2-pyridones, 4-Hydroxy-6-pyridazinones, and 5-Hydroxy-3-pyrazolones

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Dedicated to the memory of Professor Raymond N. Castle

Anions of enolized heteroaromatic 1,3-dicarbonyl systems, such as the title compounds **1, 9, 14,** and **19**, react in dimethylformamide in the presence of potassium carbonate with diaryl disulfides **2** to yield arylsulfenyl derivatives (**3, 10, 15, 20**). The arylthiolate anions **4** formed in this reaction can be oxidized by air to yield the starting disulfides **2** again. Tetraalkylthiuram disulfides **7** react in the same manner to yield dialkylaminothiocarbonylthio derivatives (**8, 13, 18**) of the title compounds. Oxidation of the arylsulfenyl derivatives with hydrogen peroxide in sodium hydroxide solution usually leads to sulfoxides (**5, 11, 16**), whereas oxidation with peracetic acid affords sulfones (**6, 12, 17**).

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The direct sulfenylation of aryl compounds is an important subject in synthetic organic chemistry [1,2]. Disulfides behave as electrophiles, and non-activated aromatic compounds can be sulfenylated using Lewis acid catalysis (for instance $SbCl_5/AgSbF_6$) [3]. Sulfenylchlorides (RSCl) [4] can be used in the same way as well as sulfenyltosylates (RS-SO_2-*p*-tolyl) [5]. However, the latter reaction proceeds best with phenolic substrates under basic conditions [5]. Some 3-alkylthio-4-hydroxy-2-pyrones are effective HIV-protease inhibitors [6,7,8], and condensed 5-alkyl- and 5-arylthio-6-hydroxy-4-pyrimidones show some antiinflammatory activity [5]. This and the known fungicidal and antiseptic activity of thiram (tetramethylthiuram disulfide, **7a**) [9] and of disulfiram (antabuse, tetraethylthiuram disulfide, **7b**) [10] prompted our research in this field. Preliminary results concerning the sulfenylation of alicyclic and heterocyclic 1,3-dicarbonyl systems have been published as a lecture abstract [11]. More recently we have described the sulfidation of heterocycles such as 4-hydroxy-2-quinolones and 4-hydroxy-coumarins [12]. With barbituric acids it was shown that the direct introduction of the dialkylaminothiocarbonylthio group into the 5-position with tetraalkylthiuram disulfides **7a,b** is more effective than reactions *via* the 5-chloro derivative or 5-phenyliodonium ylids [13].

In the present paper we describe the reactions of the title compounds with a number of aromatic disulfides (**2a-f**) and tetraalkylthiuram disulfides (**7a,b**). Performing the reactions of compounds **1** on a 10 mmol scale in an open Erlenmeyer flask with one equivalent of diphenyl disulfide **2** overnight at 95° in dimethylformamide in the presence of potassium carbonate with magnetic stirring produced the desired sulfides **3** in good yields, however about 50% of the starting disulfide **2** could be recovered. Obviously, the thiophenolate anion **4** was oxidized by oxygen back to the disulfide **2**. Therefore, for preparations on a larger scale we reduced the employed disulfide by nearly 50% and bubbled air through the reaction mixture. The thioethers **3a-p** were obtained by this simple procedure in good yields (see Table 1). Aliphatic thioethers of this type cannot be obtained by this method! Apparently, aliphatic disulfides are not electrophilic enough. However, aliphatic thioethers of type **3** are available by the reaction of 3-chloro-4-hydroxy-2-pyridones or their 3-phenyliodoinum ylids [11,13,14,15]. On the other hand, tetraalkylthiuram disulfides **7a,b** are sufficiently electrophilic and produce good yields of 3-dialkylaminothiocarbonylthio-4-hydroxy-2-pyrons and 2-pyridones (**8a-f**). However, here equimolar amounts of reagent **7** are needed; oxidation of the dialkylaminodithiocarbamate anions is not possible under the reaction conditions.

As already mentioned, the dialkylaminothiocarbonylthio derivatives of type **8** can be obtained by two alternative routes. The starting compounds **1** are converted to their 3-chloro derivatives (usually by a two-step procedure) or their 3-phenyliodonium ylids, which is the safest way since chlorination of type **1** compounds usually leads to complex mixtures [16]. The arylthioethers **3** can be obtained in a similar fashion by using thiophenolate anions [11,14]. However these methods cannot compete with the simplicity of the preparations presented here. Most of the aromatic disulfides **2** used in this study are commercially available; if not (or too expensive), they can quantitatively be obtained by oxidizing alkaline solutions of the corresponding thiophenols with hydrogen peroxide. The thiuram disulfides **7** are commercially available, or can be easily obtained by oxidizing solutions prepared from secondary amine, sodium hydroxide, and carbon disulfide with hydrogen peroxide.

4-Hydroxy-6(1*H*)-pyridazones represent an interesting class of heterocyclic 1,3-dicarbonyl systems [17]. Some derivatives show herbicidal activity. The 3-phenyl-derivative **9a** as well as its 1-methyl derivative **9b** can readily be obtained on a large scale from an intermediate

Table 1

Experimental, Physical and Analytical Data of Compounds **3**

No.	X	R^1	R^2	R^3	Yield (%)	Mp (°C) (Solvent)	Formula (F.W.)	Analysis (%) Calcd./Found C	H	N
3a	O	H	H	H	37	158-161	$C_{12}H_{10}O_3S$	61.52	4.30	--
						toluene	234.30	61.85	4.33	--
3b	O	Cl	H	H	85	169-172	$C_{12}H_9ClO_3S$	53.63	3.38	--
						toluene	268.70	53.61	3.63	--
3c	O	NO_2	H	H	46	269-270	$C_{12}H_9NO_5S$	51.61	3.25	5.02
						acetic acid	279.30	51.21	3.41	4.82
3d	O	H	NO_2	H	44	215-216	$C_{12}H_9NO_5$	S51.61	3.25	5.02
						acetic acid	279.30	51.31	3.42	4.93
3e	O	H	COOH	H	48	246-250	$C_{13}H_{10}O_5S$	56.11	3.62	--
						acetic acid	278.30	55.77	3.86	--
3f	NH	H	H	H	55	237-239	$C_{12}H_{11}NO_2S$	61.78	4.75	6.00
						ethanol	233.30	61.82	4.74	5.96
3g	NH	Cl	H	H	72	255-257	$C_{12}H_{10}ClNO_2S$	53.83	3.76	5.23
						toluene	267.70	54.03	3.88	5.24
3h	NH	H	COOH	H	54	290-294	$C_{13}H_{11}NO_4S$	56.31	4.00	5.05
						aetic acid	277.30	55.94	4.06	4.89
3i	NH	H	NO_2	H	50	280-281	$C_{12}H_{10}N_2O_4S$	51.79	3.62	10.07
						acetic acid	278.30	51.82	3.76	10.04
3j	NH	Cl	Cl	Cl	70	310-311[a]	$C_{12}H_8C_3NO_2S$	42.80	2.38	4.16
						DMF	336.50	43.16	2.68	4.36
3k	NCH_3	H	H	H	51	208-211	$C_{13}H_{13}NO_2S$	63.13	5.30	5.66
						ethanol	247.3	62.86	5.37	5.60
3l	NCH_3	Cl	H	H	77	244-248	$C_{13}H_{12}ClNO_2S$	55.41	4.29	4.97
						ethanol	281.8	55.79	4.43	4.92
3m	NCH_3	NO_2	H	H	48	280[a]	$C_{13}H_{12}N_2O_4S$	53.41	4.14	9.59
						acetic acid	292.3	53.21	4.25	9.23
3n	NCH_3	H	NO_2	H	41	264-266	$C_{13}H_{12}N_2O_4S$	53.42	4.14	9.58
						DMF/H_2O	292.3	53.20	4.28	9.41
3o	NCH_3	H	COOH	H	65	271-274	$C_{14}H_{13}NO_4S$	57.72	4.50	4.81
						ethanol	291.3	57.64	4.61	4.76
3p	NCH_3	Cl	Cl	Cl	64	272-275[a]	$C_{13}H_{10}Cl_3NO_2S$	44.53	2.87	3.99
						1-butanol	350.65	44.62	2.73	3.93

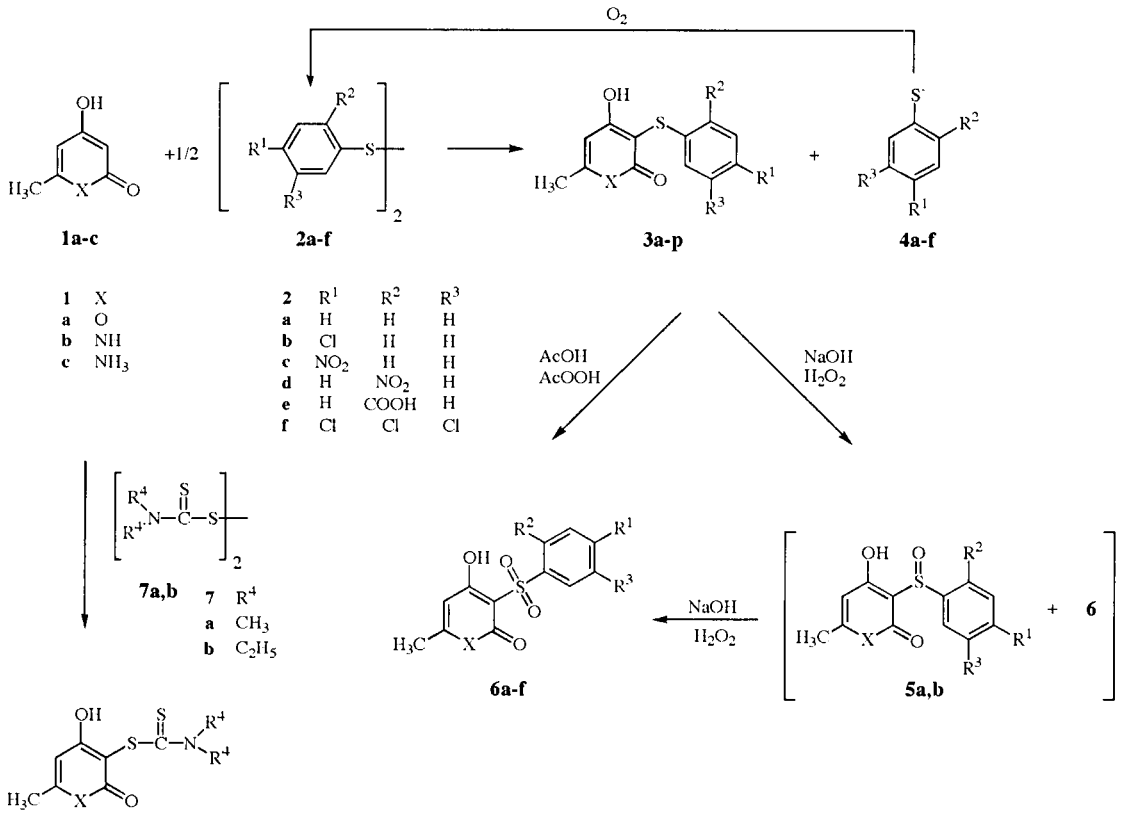
[a] decomposition

Table 2

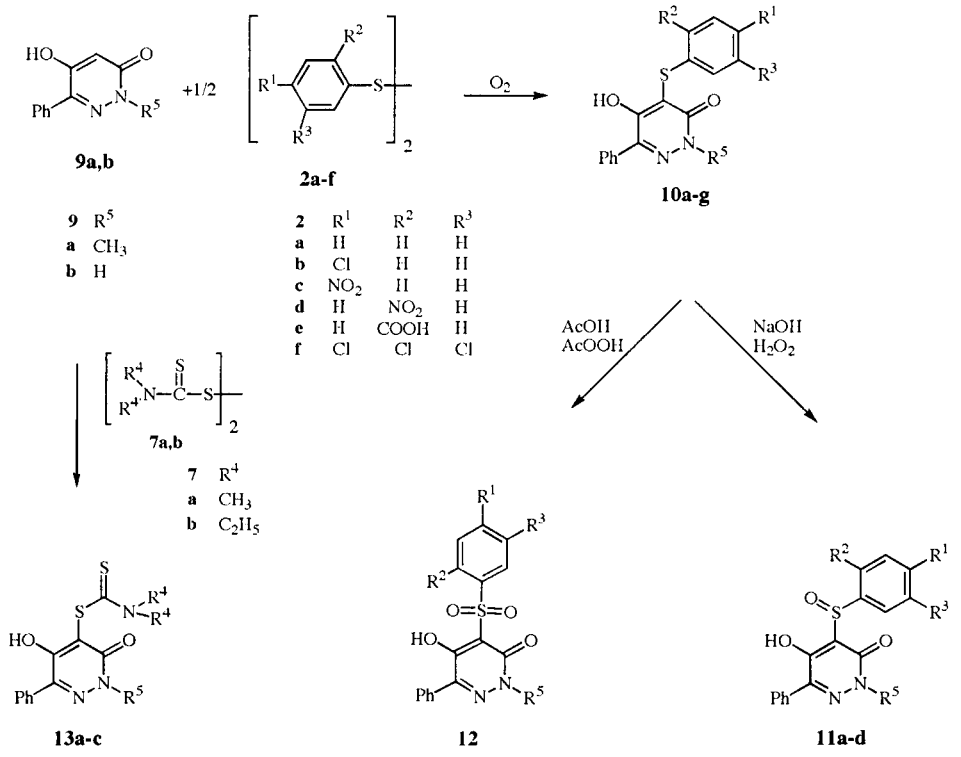
Spectroscopic Data of Compounds **3**

No.	IR (Potassium bromide cm^{-1})	1H nmr (δ, ppm)
3a	3380-2780 mb, 1725 w, 1650 s, 1550s.	2.27 (s, 3 H, CH_3), 6.20 (s, 1 H, 5-H), 7.06-7.32 (m, 5 H, Aryl-H).
3b	3260-2200 mb, 1630 s, 1540 s, 1478 m, 1450 s.	2.26 (s, 3 H, CH_3), 6.22 (s, 1 H, 5-H), 7.10 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H); 7.34 (d, J = 8 Hz, 2 H, Phenyl 2-H, 6-H).
3c	3240-2500 mb, 1670 m, 1635 s, 1560 m, 1510 s.	2.29 (s, 3 H, CH_3), 6.26 (s, 1 H, 5-H), 7.30 (d, J = 10 Hz, 2 H, Phenyl 3-H, 5-H), 8.12 (d, J = 10 Hz, 2 H, Phenyl 2-H, 6-H).
3f	3400-2400 mb, 1645 s, 1540 w, 1460 m	2.17 (s, 3 H, CH_3), 5.89 (s, 1 H, 5-H), 6.99-7.28 (m, 5 H, Aryl-H), 10.90 (s, 1 H, NH), 11.45 (s, 1H, OH).
3k	3350-2720 mb, 2680 w, 1630 s, 1565 s, 1470 s.	2.39 (s, 3 H, CH_3), 3.40 (s, 3 H, NCH_3), 6.02 (s, 1H, 5 -H), 7.00-7.32 (m, 5 H, Aryl-H).
3l	3630-2310 mb, 1630 m, 1555 s, 1475 m, 1405 s.	2.35 (s, 3 H, CH_3), 3.35 (s, 3 H, NCH_3), 6.00 (s, 1 H, 5-H), 7.00 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H), 7.28 (d, J = 8 Hz, 2 H, Phenyl 2-H, 6-H), 11.00 (s, 1 H, OH).
3m	3160-2300 mb, 1640 s, 1575-15550 sb, 1500 s.	2.40 (s, 3 H, CH_3), 3.42 (s, 3 H, NCH_3), 6.08 (s, 1 H, 5-H), 7.20 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H), 8.10 (d, J = 8 Hz, 2 H, Phenyl 2-H, 6-H), 11.30 (s, 1 H, OH).
3o	3300-2300 mb, 1675 s, 1625 s, 1560 s.	2.38 (s, 3 H, CH_3), 3.35 (3 H, NCH_3), 6.02 (s, 1 H, 5-H), 6.78 (d, J = 8 Hz, 1 H, Aryl-H), 7.13 (t, J = 8 Hz, 1 H, Aryl-H), 7.32 (t, J = 8 Hz, 1 H, Aryl-H), 7.90 (dd, J = 7 and 1.5 Hz, 1 H, Aryl-H).

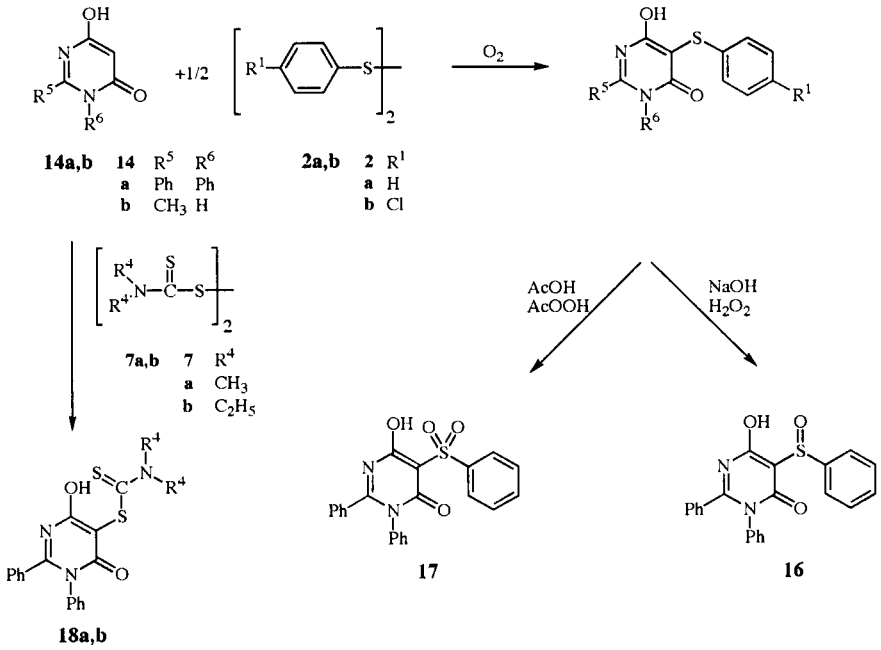
Scheme 1



Scheme 2



Scheme 3



Scheme 4

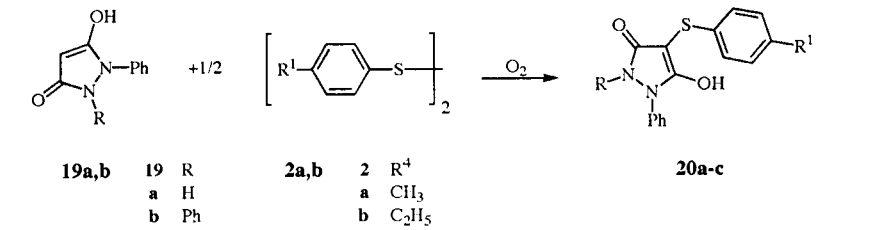


Table 3

Experimental, Physical and Analytical Data of Compounds **10**

No.	R^5	R^1	R^2	R^3	Yield (%)	Mp (°C) (Solvent)	Formula (F.W.)	Analysis (%) Calcd./Found C	H	N
10a	CH_3	H	H	H	80	141-143	$C_{17}H_{14}N_2O_2S$	65.78	4.55	9.03
						ethanol	310.40	65.80	4.63	9.10
10b	CH_3	Cl	H	H	78	185-186	$C_{17}H_{13}ClN_2O_2S$	59.21	3.80	8.13
						toluene	344.80	59.39	3.98	8.07
10c	CH_3	H	NO_2	H	78	250-255	$C_{17}H_{13}N_3O_4S$	57.46	3.69	11.82
						acetic acid	355.30	57.69	3.86	11.84
10d	CH_3	H	COOH	H	57	249-250	$C_{18}H_{14}N_2O_4S$	61.00	3.98	7.91
						ethanol	354.40	60.61	3.92	7.86
10e	H	H	H	H	55	253-254	$C_{16}H_{12}N_2O_2S$	64.84	4.08	9.46
						ethanol	296.40	65.01	4.14	9.43
10f	H	Cl	H	H	74	224-225	$C_{16}H_{11}ClN_2O_2S$	58.09	3.35	8.47
						ethanol	330.80	58.02	3.46	8.42
10g	H	Cl	Cl	Cl	62	237-239	$C_{16}H_9Cl_3N_2O_2S$	48.08	2.27	7.01
						toluene	399.69	48.48	2.24	6.80

of the industrial synthesis of PYRIDATE® [17]. The reaction of **9a,b** with aromatic disulfides **2a-f** proceeds in the same manner as described for compounds **1** leading to the thioethers **10a-g** (Scheme 2; Table 3). Similarily, the 5-dialkylaminothiocarbonylthio derivatives **13a-c** were obtained from **9a,b** and **7a,b**.

Two 6-hydroxy-4(3*H*)-pyrimidones (**14a,b**) served also as good substrates for the syntheses described

Table 4

Spectroscopic Data of Compounds **10**

No.	IR (Potassium bromide cm^{-1})	1H nmr (δ, ppm)
10a	3260-2600 mb, 1625 s, 1580 w, 1505 m.	3.70 (s, 3 H, NCH_3), 7.19-7.37 (m, 5 H, Aryl-H), 7.45-7.52 (m, 3 H, Aryl-H), 7.68-7.75 (m, 2 H, Aryl-H).
10b	3100-2700 wb, 1620 s, 1600 w, 1555 m.	3.70 (s, 3 H, NCH_3), 7.24-7.54 (m, 7 H, Aryl-H). 7.68-7.75 (m, 2 H, Aryl-H).
10c	3240-2500 wb, 1615 s, 1595 m, 1520 s.	3.73 (s, 3 H, NCH_3), 7.23 (dd, J = 7 and 1.5 Hz, 1 H, Aryl-H), 7.40-7.78 (m, 7 H, Aryl-H), 8.30 (dd, J = 7 and 1.5 Hz, 1 H, Aryl-H).
10d	3480-2320 mb, 1700 s, 1620 s, 1600 m, 1590 w.	3.72 (s, 3 H, NCH_3), 7.00 (d, J = 8 Hz, 1 H, Aryl-H), 7.27 (t, J = 8 Hz, 1 H, Aryl-H), 7.39-7.52 (m, 4 H, Aryl-H), 7.69-7.77 (m, 2 H, Aryl-H), 8.00 (dd, J = 7 and 1.5 Hz, 1 H, Aryl-H).
10e	3320-2500 mb, 1625 s, 1582 m, 1560 m, 1480 m.	7.14-7.53 (m, 8 H, Aryl-H), 7.65-7.73 (m, 2 H, Aryl-H).
10f	3300-2600 mb, 1630 s, 1585 m, 1570 m.	7.21-7.50 (m, 7 H, Aryl-H), 7.64-7.72 (m, 2 H, Aryl-H).
10g	3340-2700 mb, 1640 s, 1580 s	7.18-7.49 (m, 5 H, Aryl-H), 7.64-7.70 (m, 2 H, Aryl-H).

before. Thus sulfides **15a-b**, their oxidation products **16** and **17**, and the dialkylaminothiocarbonylthio derivatives **18a-b** were readily obtained.

In order to test further the generality of these reactions two 5-hydroxy-pyrazol-3(2*H*)-ones (**19a,b**, usually described as pyrazolidin-3,5-diones) were selected as examples of 5-membered heterocyclic ß-diketo compounds. With **2a,b** the thioethers **20a-c** were obtained in 58-66% yield.

In Schemes 1-3 the oxidation of the thioethers **3**, **10**, and **15** are also depicted. Usually, oxidation of this type of compounds with hydrogen peroxide in alkaline medium leads to sulfoxides while oxidation in acidic medium yields sulfones [11,12,18]. The preparation of sulfoxides was a main object of this research project since these sulfoxides are heteroanalogs of the so-called heterocyclic tricarbonylmethane systems [SO instead of CO]. Recently some aroyl derivatives of alicyclic and heterocyclic ß-dicarbonyl systems have found interest as herbicides [19,20]. Oxidation of sulfides **3**, **10**, and **15** to sulfoxides **5**, **11**, and **16** can be achieved with hydrogen peroxide under well defined conditions (only one compound, **11b**, was also obtained with peracetic acid). In the pyridone series (Scheme 1) sulfoxides **5** were contaminated with sulfones **6** even under mild reaction conditions. Only **5a,b** were obtained in a pure state. Further oxidation of mixtures of **5** and **6** with excess of hydrogen peroxide and longer reaction times lead to sulfones **6a-f**. Generally, oxidation of sulfides **3**, **10**, and **15** in acidic medium, preferable in acetic acid with peracetic acid, leads to sulfones **6**, **12**, and **17**.

EXPERIMENTAL

Melting points were obtained on a Gallenkamp melting point apparatus, Model MFB-595 in open capillary tubes. The ^1H nmr spectra (200 MHz) were obtained on a Varian Gemini 200 instrument. Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ-units. The solvent for ^1H nmr was hexadeuteriodimethyl sulfoxide unless otherwise stated. Microanalyses were performed on a Carlo Erba 1106 Elemental analyzer. Infrared spectra were taken on a Perkin-Elmer 298 spectrophotometer in potassium bromide pellets. Common reagent-grade chemicals are either commerically available and were used without further purification or prepared by standard literature procedures.

All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel F-254 (Merck) plates using uv light (254 and 366 nm) for detection.

General procedure for the synthesis of 4-Hydroxy-6-methyl-3-phenylthio-2-pyrones (**3a-e**), 4-Hydroxy-6-methyl-3-phenylthio-2(1*H*)-pyridones (**3f-j**), 4-Hydroxy-1,6-dimethyl-3-phenylthio-2(1*H*)-pyridones (**3k-p**), 4-Hydroxy-1-methyl-3-phenyl-5-phenylthio-6(1*H*)-pyridazones (**10a-d**) and 4-Hydroxy-3-phenyl-5-phenylthio-6(1*H*)-pyridazones (**10e-g**).

A mixture of 4-hydroxy-6-methyl-2-pyrone **1a**, 4-hydroxy-6-methyl-2(1*H*)-pyridone **1b**, 4-hydoxy-1,6-dimethyl-2(1*H*)-pyridone **1c**, 4-hydroxy-1-methyl-3-phenyl-6(1*H*)-pyridazone **9a** or 4-hydroxy-3-phenyl-6(1*H*)-pyridazone **9b** (20 mmol) the corresponding disulfide **2a-f** (10.5 mmol), and potassium carbonate (30 mmol) was heated in dimethyl formamide (DMF) (50 ml) for 5 hours at 90-95° bath temperature while air was bubbled through the mixture. After cooling water (40 ml) was added and the mixture was stirred for 15 minutes. After filtration, the product was precipitated by acidification with diluted hydrochloric acid, filtered by

suction, dried, and recrystallized from an appropriate solvent. Experimental data for compounds **3a-p**: Table 1; spectroscopic data for compounds **3a-p**: Table 2. Experimental data for compounds **10a-g**: Table 3; spectroscopic data for compounds **10a-g**: Table 4.

4-Hydroxy-6-methyl-3-phenylsulfinyl-2(1*H*)-pyridone (**5a**).

To a solution of **3f** (1.16 g, 5 mmol) in 2 *N* sodium hydroxide (20 ml), 6 ml of hydrogen peroxide (30%) were added. After standing for 2 hours at room temperature the product was precipitated by acidification with 2 *N* hydrochloric acid. The yield was 1.17 g (94%), mp 169-171° (toluene); ir: ν 3300-2400 mb, 1640 s , 1620 s, 1580 m, 1560 m, 1080 m, cm^{-1} ; ^1H nmr: δ 2.13 (s, 3 H, CH_3); 5.76 (s, 1 H, 5-H), 7.54-7.78 (m, 5 H, Aryl-H); 11.60 (s, 1 H, OH).

Anal. Calcd. for $C_{12}H_{11}NO_3S$ (249.30): C, 57.82; H, 4.45; N, 5.62; S, 12.86. Found: C, 57.84; H, 4.50; N, 5.54; S, 12.61.

3-(4-Chlorophenylsulfinyl)-4-hydroxy-6-methyl-2(1*H*)-pyridone (**5b**).

Compound **5b** was obtained from **3g** (1.33 g, 5 mmol) according to the preparation of **5a**. After standing for 3 hours the yield was 1.26 g (89%), mp 212-217° (dec.) (toluene); ir: ν 3200-2500 mb, 1645 s , 1620 s, 1560 m, 1110 m, cm^{-1} ; ^1H nmr: δ 2.13 (s, 3 H, CH_3); 5.78 (s, 1 H, 5-H), 7.60 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H), 7.85 (d, J = 8 Hz, 2 H, Phenyl 2-H, 6-H).

Anal. Calcd. for $C_{12}H_{10}ClNO_3S$ (283.52): C, 50.79; H, 3.53; N, 4.94. Found: 50.44; H, 3.76; N, 5.22.

4-Hydroxy-6-methyl-3-phenylsulfonyl-2-pyrone (**6a**).

To a mixture of **3a** (1.20 g, 5 mmol) and sodium carbonate solution (1.0 g sodium carbonate in 20 ml of water), 2 *N* sodium hydroxide was added until a clear solution was formed. Then 14 ml of hydrogen peroxide (30%) were added, and after standing overnight the product was precipitated by acidification with 2 *N* hydrochloric acid . The yield was 0.90 g (66%), mp 126-129° (toluene); ir: ν 3100 m, 3070 m, 1730 s, 1700 s, 1640 s, 1550 s, 1320 s, 1135 s, cm^{-1}; ^1H nmr: δ 2.20 (s, 3 H, CH_3), 6.12 (s, 1 H, 5-H), 7.50-7.72 (m, 3 H, Aryl-H); 7.95 (dd, J= 7 and 1.5 Hz, 2 H, Aryl-H).

Anal. Calcd. for $C_{12}H_{10}O_5S$ (266.30): C, 54.13; H, 3.97. Found: C, 53.73; H, 3.97.

3-(4-Chlorophenylsulfonyl)-4-hydroxy-6-methyl-2-pyrone (**6b**).

To a solution of **3b** (1.34 g, 5 mmol) in 20 ml acetic acid, 3 ml of peracetic acid (40%) were added. After standing for 2 hours at 50° the product was precipitated by acidification with 2 *N* hydrochloric acid. The yield was 1.08 g (72%), mp 174-176° (toluene); ir: ν 3260-2900 m, 1740 s, 1645 s, 1550 s, 1315 s, 1160 s, cm^{-1} ; ^1H nmr: δ 2.20 (s, 3 H, CH_3), 6.10 (s, 1 H, 5-H), 7.68 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H), 7.95 (d, J = 8 Hz, 2 H, Phenyl 2-H, 6-H).

Anal. Calcd. for $C_{12}H_9ClO_5S$ (300.70): C, 47.93; H, 3.02. Found: C, 47.86; H, 3.17.

4-Hydroxy-6-methyl-3-phenylsulfonyl-2(1*H*)-pyridone (**6c**).

Compound **6c** was obtained from **3f** (1.16 g, 5 mmol) according to the preparation of **6b**.

The yield was 1.09 g (82%), mp 232-234° (toluene); ir: ν 3300-2500 mb, 1680 s, 1650 s, 1475 m, 1315 s, 1120 s, cm^{-1}; ^1H nmr: δ 2.11 (s, 3 H, CH_3), 5.80 (s, 1 H, 5-H), 7.52-7.75 (m, 5 H, Aryl-H).

Anal. Calcd. for $C_{12}H_{11}NO_4S$ (265.10): C, 54.33; H, 4.15; N, 5.28. Found: C, 53.99; H, 4.17; N, 5.46.

3-(4-Chlorophenylsulfonyl)-4-hydroxy-6-methyl-2(1*H*)-pyridone (**6d**).

Compound **6d** was obtained from **3g** (1.33 g, 5 mmol) according to the preparation of **6b**. The yield was 1.29 g (86%), mp 311-312° (ethanol); ir: ν 3280 m, 3110 m, 1660 s, 1630 s, 1460 s, 1310 s, 1135 s, cm^{-1} ; ^1H nmr: δ 2.11 (s, 3 H, CH_3), 5.84 (s, 1 H, 5-H); 7.66 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H), 7.95 (d, J= 8 Hz, 2 H, Phenyl 2-H, 6-H).

Anal. Calcd. for $C_{12}H_{10}ClNO_4S$ (299.70): C, 48.09; H, 3.36; N, 4.67; S, 10.70. Found: C, 47.73; H, 3.41; N, 4.57; S, 10.68.

4-Hydroxy-1,6-dimethyl-3-phenylsulfonyl-2(1*H*)-pyridone (**6e**).

Method a: Oxidation with Hydrogen Peroxide.

Compound **6e** was obtained from **3k** (1.23 g, 5 mmol) according to the preparation of **6a**. The yield was 1.04 g (75%).

Method b: Oxidation with Peracetic Acid.

Compound **6e** was obtained from **3k** (1.23 g, 5 mmol) according to the preparation of **6b**. The yield was 1.10 g (78%), mp169-171° (ethanol); ir: ν 3300-2900 mb, 1655 s, 1605 s, 1555 m, 1320 s, 1120 s, cm^{-1}; ^1H nmr: δ 2.33 (s, 3 H, CH_3), 3.24 (s, 3 H, NCH_3), 6.07 (s, 1 H, 5-H), 7.54-7.72 (m, 3 H, Aryl-H), 8.00 (dd, J = 7 and 1.5 Hz, 2 H, Aryl-H).

Anal. Calcd. for $C_{13}H_{13}NO_4S$ (279.3): C, 55.90; H, 4.69; N, 5.01. Found: C, 55.92; H, 4.68; N, 4.98.

3-(4-Chlorophenylsulfonyl)-4-hydroxy-1,6-dimethyl-2(1*H*)-pyridone (**6f**).

Compound **6f** was obtained from **3l** (1.40 g, 5 mmol) according to the preparation of **6b**.

The yield was 1.27 g (81%), mp 205-207° (toluene); ir: ν 3260-3000 mb, 1650 s, 1630 s, 1570 m, 1315 s, 1130 s, cm^{-1}; ^1H nmr: δ 2.34 (s, 3 H, CH_3), 3.25 (s, 3 H, NCH_3), 6.07 (s, 1 H, 5-H), 7.69 (d, J = 8 Hz, 2 H, Phenyl 3-H, 5-H), 8.00 (d, J = 8 Hz, 2 H, Phenyl 2-H, 6-H).

Anal. Calcd. for $C_{13}H_{12}ClNO_4S$ (313.80): C, 49.76; H, 3.86; N, 4.46; s, 10.22.. Found: C, 49.62; H, 3.96; N, 3.33; S, 10.10.

3-Dimethylaminothiocarbonylthio-4-hydroxy-6-methyl-2-pyrone (**8a**).

A mixture of **1a** (1.26 g, 10 mmol), **7a** (2.65 g, 11 mmol,), potassium carbonate (2.76 g , 20 mmol) and DMF (30 ml) was heated under stirring for 4 hours at 90°. After removing half of the solvent *in vacuo*, the solution was poured into ice-water. After standing for 3 hours it was filtered and the filtrate was slowly acidified with diluted hydrochloric acid. The resulting precipitate was filtered by suction. The yield was 1.45 g (59%), mp 196-198° (toluene); ir: ν 3600-2800 mb, 1700 s, 1570 s, 1480 m, cm^{-1}; ^1H nmr: δ 2.23 (s, 3 H, CH_3), 3.28-3.45 (m, 6 H, 2 CH_3), 6.14(s, 1 H, 5-H), 12.05 (s, 1 H, OH).

Anal. Calcd. for $C_9H_{11}NO_3S_2$ (245.30): C, 44.06; H, 4.52; N, 5.71. Found: C, 44.08; H, 4.66; N, 5.69.

3-Diethylaminothiocarbonylthio-4-hydroxy-6-methyl-2-pyrone (**8b**).

Compound **8b** was obtained from **1a** (1.26 g, 10 mmol) and **7b** (3.26 g, 11 mmol) according to the preparation of **8a**. The yield was 1.30 g (48%), mp 183-185° (toluene); ir: ν 3500-2700

mb, 1640 s, 1560 s, 1490 w, cm^{-1}; ^1H nmr: δ 1.18 (t, J = 7 Hz, 3 H, CH_3), 1.32 (t, J = 7 Hz, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 3.78-3.96 (m, 4 H, 2 CH_2), 6.20 (s, 1 H, 5-H).

Anal. Calcd. for $C_{11}H_{15}NO_3S_2$ (273.13): C, 48.33; H, 5.49; N, 5.13. Found: C, 47.93; H, 5.51; N, 5.03.

3-Dimethylaminothiocarbonylthio-4-hydroxy-6-methyl-2(1*H*)-pyridone (**8c**).

Compound **8c** was obtained from **1b** (1.25g , 10 mmol) and **7a** (2.65 g, 11 mmol) according to the preparation of **8a**. The yield was 1.25 g (51%), mp >320° (dec.) (ethanol); ir: ν 3500-2500 mb, 1630 s, 1550 w, 1450 w, cm^{-1}; ^1H nmr: δ 2.21 (s, 3 H, CH_3), 3.25-3.49 (m, 6 H, 2 CH_3), 6.02 (s, 1 H, 5-H), 10.87 (s, 1 H, NH), 11.98 (s, 1 H, OH).

Anal. Calcd. for $C_9H_{12}N_2O_2S_2$ (244.30): C, 44.24; H, 4.95; N, 11.47. Found: C, 43.85; H, 4.55; N, 11.85.

3-Diethylaminothiocarbonylthio-4-hydroxy-6-methyl-2(1*H*)-pyridone (**8d**).

Compound **8d** was obtained from **1b** (1.25 g, 10 mmol) and **7b** (3.26 g, 11 mmol) according to the preparation of **8a**. The yield was 1.25 g (46%), mp 185-186° (ethanol). ir: ν 3600-2400 mb, 1630 s, 1540 w, 1455 m, cm^{-1}; ^1H nmr: δ 1.16 (t, J = 7 Hz, 3 H, CH_3), 1.28 (t, J = 7 Hz, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 3.72-3.85 (m, 4 H, 2 CH_2), 5.90 (s, 1 H, 5-H).

Anal. Calcd. for $C_{11}H_{16}N_2O_2S_2$ (272.40): C, 48.50; H, 5.92; N, 10.28. Found: C, 48.85; H, 5.52; N, 9.92.

3-Dimethylaminothiocarbonylthio-4-hydroxy-1,6-dimethyl-2(1*H*)-pyridone (**8e**).

Compound **8e** was obtained from **1c** (1.39 g, 10 mmol) and **7a** (2.65 g, 11 mmol) according to the preparation of **8a**. The yield was 1.31 g (51%), mp 223-225° (ethanol); ir: ν 3600-2500 mb, 1630 s, 1560 s, cm^{-1}; ^1H nmr: δ 2.29 (s, 3 H, CH_3), 3.25-3.52 (m, 9 H, 2 CH_3, NCH_3), 6.04 (s, 1 H, 5-H).

Anal. Calcd. for $C_{10}H_{14}N_2O_2S_2$ (258.36): C, 46.49; H, 5.46; N, 10.85. Found: C, 46.17; H, 5.50; N, 10.61.

3-Diethylaminothiocarbonylthio-4-hydroxy-1,6-dimethyl-2(1*H*)-pyridone (**8f**).

Compound **8f** was obtained from **1c** (1.39 g, 10 mmol) and **7b** (3.26 g, 11 mmol) according to the preparation of **8a.** The yield was 1.50 g (52%), mp 216-217° (ethanol); ir: ν 3640-2470 mb, 1640 s, 1555 s, cm^{-1}; ^1H nmr: δ 1.18 (t, J = 7 Hz, 3 H, CH_3), 2.26 (t, J = 7 Hz, 3 H, CH_3), 2.16 (s, 3 H, CH_3), 3.45 (NCH_3), 3.72-3.84 (m, 4 H, 2 CH_2), 5.96 (s, 1 H, 5-H).

Anal. Calcd. for $C_{12}H_{18}N_2O_2S_2$ (286.40): C, 50.32; H, 6.33; N, 9.78. Found: C, 50.72; H, 6.11; N, 9.43.

4-Hydroxy-1-methyl-3-phenyl-5-phenylsulfinyl-6(1*H*)-pyridazone (**11a**).

Compound **11a** was obtained from **10a** (1.55 g, 10 mmol) and hydrogen peroxide (14 ml) according to the preparation of **5a**. After standing overnight the yield was 1.50 g (92%), mp 124-127° (ethanol); ir: ν 3060 w, 1635 s, 1580 m, 1500 m, 1010 m cm^{-1}; ^1H nmr: δ 3.62 (s, 3 H, NCH_3), 7.42-7.53 (m, 3 H, Aryl H), 7.62-7.78 (m, 5 H, Aryl-H), 7.98-8.14 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{17}H_{14}N_2O_3S$ (326.40): C, 62.56; H, 4.32; N, 8.58. Found: C, 62.29; H, 4.48; N, 8.56.

5-(4-Chlorophenylsulfinyl)-4-hydroxy-1-methyl-3-phenyl-6(1*H*)-pyridazone (**11b**)

Method a: Oxidation with Hydrogen Peroxide.

Compound **11b** was obtained from **10b** (1.72 g, 10 mmol) and hydrogen peroxide (12 ml) according to the preparation of **5a**. After standing for 12 hours the yield was 1.48 g (82%).

Method b: Oxidation with Peracetic Acid.

To a solution of **10b** (1.72 g, 5 mmol) in 30 ml acetic acid, 3 ml of peracetic acid (40%) were added. After stirring for 40 minutes at 50° the product was precipitated after cooling with water. The yield was 1.60 g (89%), mp 125-127° (ethanol); ir: ν 3170-2860 wb, 1640 s, 1590 w, 1570 m, 1085 s cm^{-1}; ^1H nmr: δ 3.68 (s, 3 H, NCH_3), 4.42 (s, br, OH-H_2O-association), 7.42 (m, 3 H, Aryl-H), 7.67-7.78 (m, 4 H, Aryl-H), 7.98-8.14 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{17}H_{13}ClN_2O_3S$ (376.80): C, 56.59; H, 3.63; N, 7.76. Found: C, 56.17; H, 3.58; N, 7.42.

4-Hydroxy-3-phenyl-5-phenylsulfinyl-6(1*H*)-pyridazone (**11c**).

Compound **11c** was obtained from **10e** (1.56 g, 5 mmol) according to the preparation of **6a**. The yield was 1.30 g (83%), mp 192-193°° (ethanol); ir: ν 3220-2750 wb, 1630 s, 1585 m, 1560 m, 1040 m, cm^{-1}; ^1H nmr: δ 7.10-7.42 (m, 8 H, Aryl-H), 7.52-7.63 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{16}H_{12}N_2O_3S$ (312.35): C, 61.52; H, 3.87; N, 8.97. Found: C, 61.24; H, 4.10; N, 8.86.

5-(4-Chlorophenylsulfinyl)-4-hydroxy-3-phenyl-6(1*H*)-pyridazone (**11d**).

Compound **11d** was obtained from **10f** (1.65 g, 5 mmol) according to the preparation of **6a**. The yield was 1.58 g (91%), mp 202-203° (ethanol); ir: ν 3300-2680 mb, 1640 s, 1585 m, 1560 m, 1010 m, cm^{-1}; ^1H nmr: δ 7.20-7.50 (m, 7 H, Aryl-H), 7.62-7.70 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{16}H_{11}ClN_2O_3S$ (346.79): C, 55.41; H, 3.20; N, 8.08. Found: C, 55.30; H, 3.25; N, 8.13.

4-Hydroxy-3-phenyl-5-(2,4,5-trichlorophenylsulfonyl)-6(1*H*)-pyridazone (**12**).

To a solution of **10g** (2.00 g, 5 mmol) in acetic acid (40 ml) peracetic acid (5 ml , 40%) were added. After stirring for 2 hours at 80° and standing overnight the product was precipitated with water. The yield was 1.60 g (74%), mp 232-234° (dec.) (ethanol), ir: ν 3320-2600 mb, 1650 s, 1585 m, 1435-1335 m, 1170 s, cm^{-1}; ^1H nmr: δ 7.20-7.40 (m, 6 H, Aryl-H), 7.56-7.69 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{16}H_9Cl_3N_2O_4S$ (431.68): C, 44.52; H, 2.10; N, 6.49. Found: C, 44.73; H, 1.94, N, 6.38.

5-Dimethylaminothiocarbonylthio-4-hydroxy-1-methyl-3-phenyl-6(1*H*)-pyridazone (**13a**).

Compound **13a** was obtained from **9a** (2.02 g, 10 mmol) and **7a** (2.65 g, 11 mmol) after 6 hours according to the preparation of **8a**. The yield was 2.75 g (86%), mp. 184-187° (ethanol). ir: ν 3600-2600 mb, 1630 s, 1580 w, 1550 m, 1490 m, cm^{-1}; ^1H nmr: δ 3.46 (s, 3 H, CH_3), 3.51 (s, 3 H, CH_3), 3.68 (s, 3 H, NCH_3), 7.42-7.46 (m, 3 H, Aryl-H), 7.64-7.69 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{14}H_{15}N_3O_2S_2$ (321.40): C, 52.32; H, 4.70; N, 13.07. Found: C, 52.34; H, 4.75; N, 13.09.

5-Dimethylaminothiocarbonylthio-4-hydroxy-3-phenyl-6(1*H*)-pyridazone (**13b**).

Compound **13b** was obtained from **9b** (1.88 g, 10 mmol) and **7a** (2.65 g, 11 mmol) after 14 hours according to the preparation of **8a**. The yield was 2.18 g (71%), mp 187-189° (ethanol); ir: ν 3400-2600 mb, 1645 s, 1550 m, cm^{-1}; ^1H nmr: δ 3.49 (s, 3 H, CH_3), 3.59 (s, 3 H, CH_3), 7.38-7.44 (m, 3 H, Aryl-H), 7.56-7.62 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{13}H_{13}N_3O_2S_2$ (307.40): C, 50.79; H, 4.26; N, 13.67. Found: C, 49.38; H, 4.22; N, 13.13.

5-Diethylaminothiocarbonylthio-4-hydroxy-3-phenyl-6(1*H*)-pyridazone (**13c**).

Compound **13c** was obtained from **9b** (1.88 g, 10 mmol) and **7b** (3.26 g, 11 mmol) after 14 hours according to the preparation of **8a**. The yield was 2.34 g (70%), mp 168-169° (ethanol); ir: ν 3350-2500 mb, 1650 s, 1585 m, cm^{-1}; ^1H nmr: δ 1.16 (t, J = 7 Hz, 3 H, CH_3), 1.26 (t, J = 7 Hz, 3 H, CH_3), 3.78-3.88 (m, 4 H, 2 CH_2), 7.38-7.44 (m, 3 H, Aryl-H), 7.49-7.56 (m, 2 H, Aryl-H).

Anal. Calcd. for $C_{15}H_{17}N_3O_2S_2$ (335.44): C, 53.71; H, 5.11; N, 12.53. Found: C,53.49; H, 5.01; N, 12.50.

6-Hydroxy-2,3-diphenyl-5-phenylthio-4(3*H*)-pyrimidone (**15a**).

Compound **15a** was obtained from **14a** (5.28 g, 20 mmol) and **2a** (2.30 g, 10.5 mmol) according to the preparation of **3**. The yield was 5.00 g (67%); mp 214-217° (ethanol). ir: ν 3050 w, 1680 s, 1625 s, 1595 w, 1545 m, cm^{-1}; ^1H nmr: δ 7.10-7.52 (m, 15 H, Aryl-H).

Anal. Calcd. for $C_{22}H_{16}N_2O_2S$ (372.40): C, 70.94; H, 4.33; N, 7.52. Found: C, 70.93; H, 4.43; N, 7.47.

5-(4-Chlorophenylthio)-6-hydroxy-2,3-diphenyl-4(3*H*)-pyrimidone (**15b**).

Compound **15b** was obtained from **14a** (5.28 g, 20 mmol) and **2b** (3.00 g, 10.5 mmol) according to the preparation of **3**. The yield was 5.30 g (65%); mp 214-218° (toluene). ir: ν 3680-3080 mb, 1650 s, 1630 s, 1595 w, 1530 m, cm^{-1}; ^1H nmr: δ 7.20-7.48 (m, 14 H, Aryl-H).

Anal. Calcd. for $C_{22}H_{15}ClN_2O_2S$ (406.90): C, 64.94; H, 3.72; N, 6.89. Found: 65.87; H, 4.10; N, 6.58.

6-Hydroxy-2-methyl-5-phenylthio-4(3*H*)-pyrimidone (**15c**).

Compound **15c** was obtained from **14b** (2.50 g, 20 mmol) and **2a** (2.30 g, 10.5 mmol) at 120-125° according to the preparation of **3.** The yield was 3.30 g (70%); mp 300° (dec.) (ethanol); ir: ν 3120-2150 mb, 1620 s, 1555 s, 1455 s, cm^{-1}; ^1H nmr: δ 2.32 (s, 3 H, CH_3), 6.96-7.23 (m, 5 H, Aryl-H).

Anal. Calcd. for $C_{11}H_{10}N_2O_2S$ (234.30): C, 56.39; H, 4.30; N, 11.96. Found: C, 55.81; H, 4.56; N, 11.98.

6-Hydroxy-2,3-diphenyl-5-phenylsulfinyl-4(3*H*)-pyrimidone (**16**).

Compound **16** was obtained from **15a** (1.86 g, 5 mmol) and hydrogen peroxide (12 ml) after 6 hours according to the preparation of **5a.** The yield was 1.42 g (73%), mp 215-218° (ethanol); ir: ν 3660-3200 wb, 3100-2500 wb, 1715 w, 1695 m, 1640 s, 1545 s, 1035 m, cm^{-1}; ^1H nmr: δ 7.21-7.71 (m, 15 H, Aryl-H).

Anal. Calcd. for $C_{22}H_{16}N_2O_3S$ (388.40): C; 68.02; H, 4.15; N, 7.21. Found: C, 67.65; H, 4.20; N, 7.12.

6-Hydroxy-2,3-diphenyl-5-phenylsulfonyl-4(3*H*)-pyrimidone (**17**).

Compound **17** was obtained from **15a** (1.86 g, 5 mmol) and peracetic acid (3 ml, 40%) in acetic acid (30 ml) after stirring for 30 minutes at 60°. The product was fitered by suction to yield 1.57 g (78%), mp 282-283° (ethanol); ir: ν 3180-2900 wb, 1715 s, 1670 s, 1320 s, 1145 s, cm^{-1}; ^1H nmr: δ 7.21-7.64 (m, 13 H, Aryl-H), 8.00 (dd, J = 7 and 1.5 Hz, 2 H, Aryl-H).

Anal. Calcd. for $C_{22}H_{16}N_2O_4S$ (404.40): C, 65.33; H, 3.99; N, 6.93; S, 7.93. Found: C, 64.90; H, 4.03; N, 6.83; S, 8.12.

5-Dimethylaminothiocarbonylthio-6-hydroxy-2,3-diphenyl-4(3*H*)-pyrimidone (**18a**).

Compound **18a** was obtained from **14a** (1.26 g, 10 mmol) and **7a** (2.65 g, 11 mmol) after 5 hours according to the preparation of **8a**. The yield was 2.60 g (68%), mp 232-233° (ethanol); ir: ν 3600-3200 wb, 3200-2600 mb, 1700 m, 1660 s, 1610 w, 1550 m, cm^{-1}; ^1H nmr: δ 3.44 (s, 6 H, 2 CH_3), 7.20-7.34 (m, 10 H, Aryl-H).

Anal. Calcd. for $C_{19}H_{17}N_3O_2S_2$(383.13): C, 59.50; H, 4.43; N, 10.96. Found: C, 59.56; H, 4.44; N, 10.94.

5-Diethylaminothiocarbonylthio-6-hydroxy-2,3-diphenyl-4(3*H*)-pyrimidone (**18b**).

Compound **18b** was obtained from **14a** (1.26 g, 10 mmol) and **7b** (3.26 g, 11 mmol) after 6 hours according to the preparation of **8a**. The yield was 2.70 g (66%), mp 207-209° (ethanol); ir: ν 3200-2500 mb, 1660 s, 1600 w, 1545 m, 1490 m, cm^{-1}; ^1H nmr: δ 1.19 (t, J = 7 Hz, 3 H,CH_3), 1.32 (t, J = 7 Hz, 3 H, CH_3), 3.82-3.98 (m, 4 H, 2 CH_2), 7.18-7.44 (m, 10 H, Aryl-H).

Anal. Calcd. for $C_{21}H_{21}N_3O_2S_2$ (411.50): C, 62.29; H, 5.14; N, 10.21; S, 15.58. Found: C, 61.11; H, 5.09; N, 10.13; S, 15.73.

5-Hydroxy-1-phenyl-4-(phenylthio)pyrazol-3(2*H*)-one (**20a**).

Compound **20a** was obtained from **19a** (3.50 g, 20 mmol) and **2a** (2.30 g, 10.5 mmol) according to the preparation of **3**. The yield was 3.70 g (65%), mp 188-191° (toluene); ir: ν 3300-2660 mb, 1600 s, 1515 s, 1480 s, cm^{-1}; ^1H nmr: δ 7.04-7.48 (m, 8 H, Aryl-H), 7.68 (d, J = 8 Hz, 2 H, Aryl-H).

Anal. Calcd. for $C_{15}H_{12}N_2O_2S$ (284.30): C, 63.36; H, 4.26; N, 9.85. Found: C, 63.15; H, 4.37; N, 9.97.

5-Hydroxy-1,2-diphenyl-4-(phenylthio)pyrazol-3(2*H*)-one (**20b**).

Compound **20b** was obtained from **19b** (5.04 g, 20 mmol) and **2a** (2.30 g, 10.5 mmol) according to the preparation of **3**. The yield was 4.20 g (58%), mp 189-192° (ethanol); ir: ν 3650-3250 mb, 3050 w, 1595 s, 1495 s, cm^{-1}; ^1H nmr: δ 7.10-7.58 (m, 15 H, Aryl-H), 10.42 (s, 1 H, OH).

Anal. Calcd. for $C_{21}H_{16}N_2O_2S$ (360.40): C, 69.97; H, 4.48; N, 7.77. Found: C, 69.60; H, 4.53; N, 7.69.

4-(4-Chlorophenylthio)-5-hydroxy-1,2-diphenyl-pyrazol-3(2*H*)-one (**20c**).

Compound **20c** was obtained from **19b** (5.05 g, 20 mmol) and **2b** (3.00 g, 10.5 mmol) according to the preparation of **3**. The yield was 5.20 g (66%), mp 225-230° (acetic acid); ir: ν 1640 w, 1600 s, 1485 s, 1475 s cm^{-1}; ^1H nmr: δ 4.50 (s, OH–H_2O–Assoziation), 7.12-7.46 (m, 14 H, Aryl-H).

Anal. Calcd. for $C_{21}H_{15}ClN_2O_2S$ (394.90): C, 63.87; H,3.83; N ,7.10. Found: C, 63.80; H, 4.12; N, 7.00.

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