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Sulfenylation of Heterocyclic 1,3-Dicarbonyl Compounds

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Summary. Anions of heteroaromatic 1,3-dicarbonyl compounds, such as 4-hydoxy-2-quinolones and 4-hydroxy-coumarins, react in *DMF* in the presence of potassium carbonate with diaryl disulfides to yield 3-arylsulfenyl derivatives. The arylthiolate anions formed in this reaction can be oxidized by air to yield the starting diaryl disulfides again. Tetraalkylthiuram disulfides react in the same manner to yield 3-dialkylaminothiocarbonylthio derivatives of the title compounds. Oxidation of the arylthioderivatives with hydrogen peroxide in sodium hydroxide solution usually leads to sulfoxides, whereas oxidation with peracetic acid affords sulfones.

Keywords. 3-Arylthio-4-hydroxy-2(1*H*)-quinolones; 3-Arylthio-4-hydroxy-coumarins; 3-Dialkylaminothiocarbonylthio-2(1*H*)-quinolones; 3-Dialkylaminothiocarbonylthio-4-hydroxy-coumarins; Sulfoxides; Sulfones.

Sulfenylierung heterocyclischer 1,3-Dicarbonylverbindungen

Zusammenfassung. Anionen von heteroaromatischen 1,3-Dicarbonylverbindungen, wie etwa von 4-Hydroxy-2(1*H*)-chinolonen und 4-Hydroxy-cumarinen, reagieren mit Diaryldisulfiden in *DMF* in Anwesenheit von Kaliumcarbonat zu 3-Arylthioderivaten. Die bei dieser Reaktion anfallenden Thiophenolatanionen können durch Oxidation mit Luft in die Diaryldisulfide zurückgeführt werden und erneut in die Reaktion eingreifen. Tetraalkylthiuramdisulfide reagieren in ähnlicher Weise mit den Titelverbindungen unter Ausbildung von 3-Dialkylaminthiocarbonylthio-4-hydroxy-2(1*H*)-chinolonen und -cumarinen. Oxidation der 3-Arylthio-4-hydroxy-2-chinolone und -cumarine mit Wasserstoffperoxid in Natronlauge führt im allgemeinen zu Sulfoxiden, während die Oxidation mit Peressigsäure die entsprechenden Sulfone liefert.

Introduction

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 (*R*SCl) [4] can be used in the same way as well as *R*-thio-*p*-toluene-sulfonates (*p*-tolyl-SO_2-S*R*) [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

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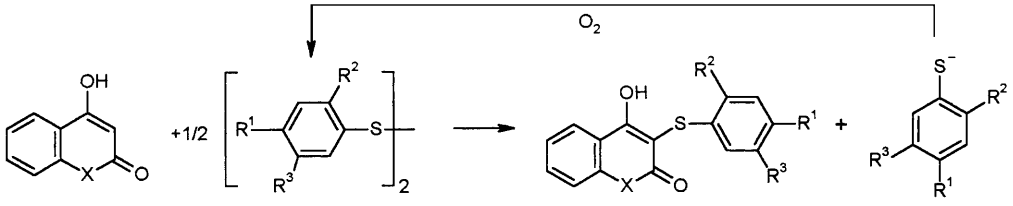
other 3-alkylthio-4-hydoxy-2-pyrimidone derivatives show antiinflammatory activity [5]. This and the known fungicidal and antiseptic activity of disulfiram (Antabus, **4a**) [9] and thiuram (tetramethythiuram disulfide, *TMTD*, **4b**) [10] prompted our research in this field. Preliminary results have been published as a lecture abstract [11].

Results and Discussion

The results of a preliminary experiment by stirring one equivalent of 4-hydroxy-l-methyl-(1*H*)-quinolone (**1a**) with one equivalent of diphenlyldisulfide (**2a**) overnight at 95°C in *DMF* in an open *Erlenmeyer* flask were as follows: quenching with water resulted in a voluminous precipitate of the starting disulfide, suggesting that the anticipated reaction did not work, at least not with an appreciable yield. Surprisingly, acidification of the remaining solution produced again a precipitate which proved to be the desired compound **3a**. Obviously, the thiophenolate anion resulting from the reaction of **1** with diphenyldisulfide **2** was oxidized by oxygen back to the disulfide **2**. Therefore, for preparations on a larger scale we reduced the



1a-e

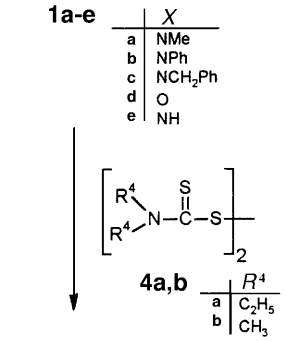
	X
a	NMe
b	NPh
c	NCH_2Ph
d	O
e	NH

2a-g

	R^1	R^2	R^3
a	H	H	H
b	Cl	H	H
c	H	NO_2	H
d	H	COOH	H
e	Cl	Cl	Cl
f	NO_2	H	COOH
g	NO_2	H	H

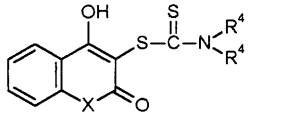
3a-q

	X	R^1	R^2	R^3
a	NMe	H	H	H
b	NMe	Cl	H	H
c	NMe	H	NO_2	H
d	NMe	H	COOH	H
e	NMe	Cl	Cl	Cl
f	NMe	NO_2	H	COOH
g	O	H	H	H
h	O	Cl	H	H
i	O	H	NO_2	H
j	O	H	COOH	H
k	NPh	H	H	H
l	NPh	Cl	H	H
m	NPh	H	NO_2	H
n	NPh	Cl	Cl	Cl
o	N-CH_2-Ph	Cl	H	Cl
p	NH	Cl	Cl	



4a,b

	R^4
a	C_2H_5
b	CH_3



5a-d

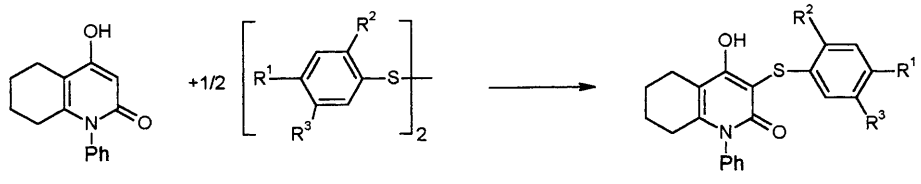
	X	R^4
a	NCH_3	C_2H_5
b	O	CH_3
c	NPh	C_2H_5
d	NPh	CH_3

Scheme 1

employed disulfide nearly by 50% and bubbled air through the reaction mixture. The thioethers **3a**–**p** were obtained by this simple procedure in good to excellent yields. Aliphatic thioethers of this type cannot be obtained by this method. Obviously, the corresponding aliphatic disulfides are not electrophilic enough. However, aliphatic thioethers are available by the reaction of 3-chloro-4-hydroxy-2-quinolones or 3-chloro-4-hydroxy-cumarins or from their corresponding iodonium ylides [11–13]. On the other hand, tetraalkylthiuram disulfides (**4a**,**b**) are sufficiently electrophilic and produce good yields of 3-dialkylaminothiocarbonylthio-4-hydroxy-2-quinolones (**5a**,**c**,**d**) and 4-hydroxy-coumarins (**5b**) in the reaction system *DMF*/K_2CO_3. However, equimolar amounts of the reagents **4** are required; oxidation of the dialkylaminothiocarbamate anions is not possible under these reaction conditions.

As already mentioned, the dialkylaminothiocarbonylthio derivatives of type **5** can be obtained by two alternative routes: the starting materials **1** are converted to their 3-chloro derivatives (usually a two-step procedure) or their 3-phenyliodonium ylides. Both species react with sodium dialkylaminodithiocarbamates to compounds **5**. The thioethers **3** can be obtained in a similar fashion by using thiophenolate anions [11, 12]. 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, they can quantitatively be obtained by oxidizing alkaline solutions of the corresponding thiophenolates with hydrogen peroxide. The thiuram disulfides **4** can be obtained by oxidizing solutions prepared from the secondary amine, sodium hydroxide, and carbon disulfide with hydrogen peroxide.

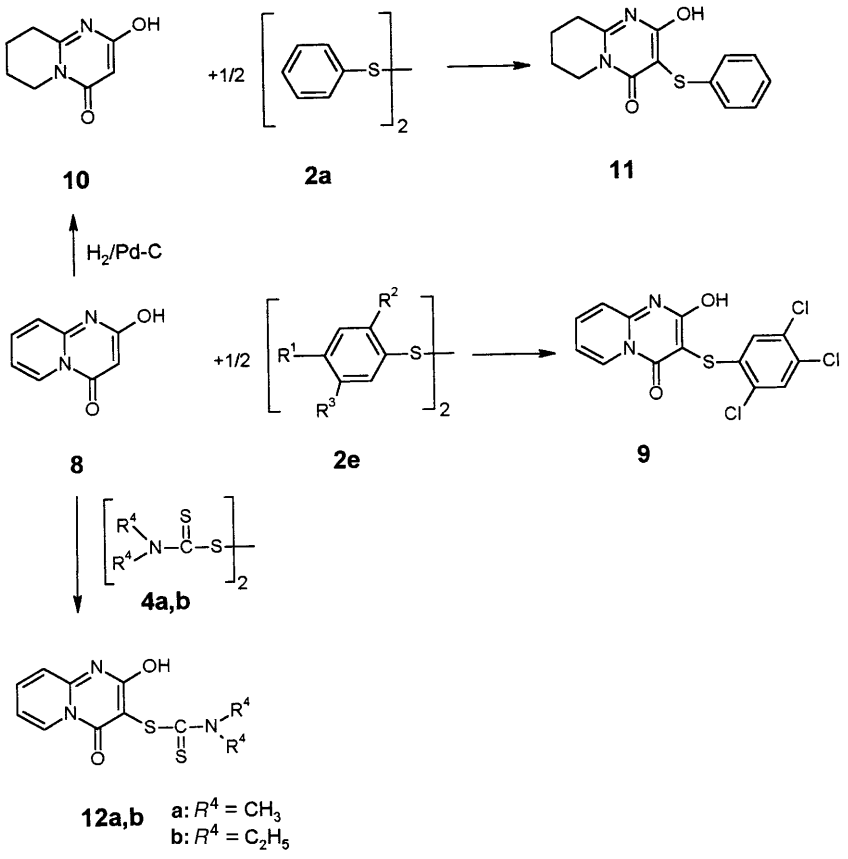
4-Hydroxy-1-phenyl-tetrahydro-2-quinolone (**6**) can readily and on a large scale be prepared from cyclohexanoneanil and malonic acid derivatives [14, 15]. It served also as a good substrate for the reaction with diaryldisulfides **2** yielding 3-arylthioethers **7a**–**c**. *Tschitschibabin*'s malonyl-α-aminopyridine [16] (**8**) is one of the best studied enolized aromatic 1,3-dicarbonyl compounds. It exists in the solid state and in aqueous solution in a tautomeric betaine structure [17, 18]. We studied its reaction with **2e** leading to the sulfide **9** in 85% yield. With thiuram disulfides **4** thiolation to the dithioamides **12a**,**b** was achieved. The catalytic hydrogenation of



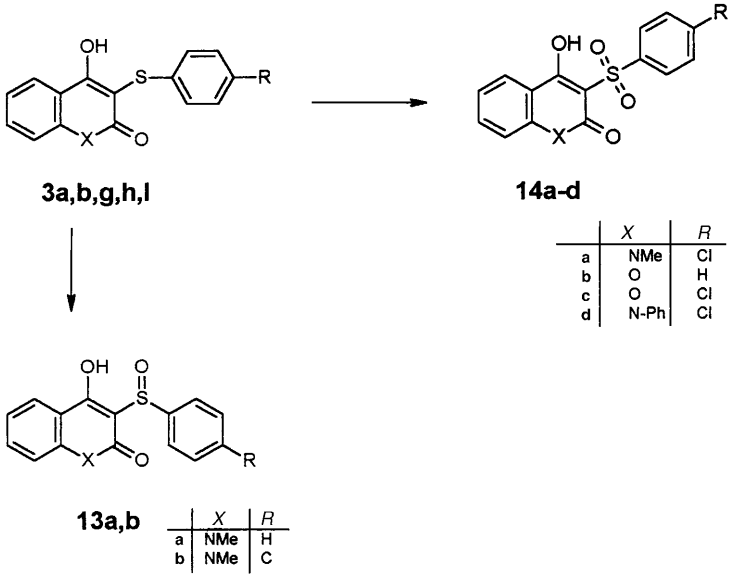
6 **2a-c,e,g** **7a-e**

	R^1	R^2	R^3
a	H	H	H
b	Cl	H	H
c	NO_2	H	H
d	H	NO_2	H
e	Cl	Cl	Cl

Scheme 2



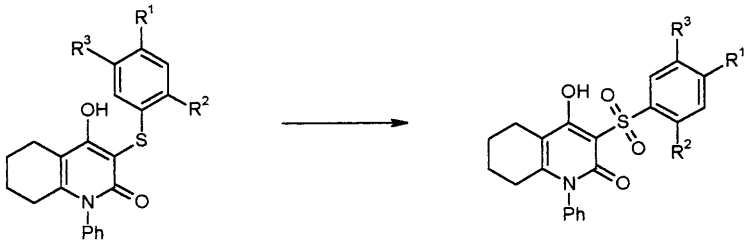
Scheme 3



	X	R
a	NMe	Cl
b	O	H
c	O	Cl
d	N-Ph	Cl

	X	R
a	NMe	H
b	NMe	C

Scheme 4



7a,b,e **15a-c**

	R^1	R^2	R^3
a	H	H	H
b	Cl	H	H
c	Cl	Cl	Cl

Scheme 5

8 to the bicyclic hydroxy-pyrimidon **10** has recently been described [19]. Treatment of this compound with diphenyldisulfide (**2a**) under the usual condition gives **11** in 93% yield.

Some oxidation reactions of 3-arylthioethers of 4-hydroxy-2-quinolones and coumarins are summarized in Schemes 4 and 5. Careful reduction of thioethers **3** with hydrogen peroxide in sodium hydroxide solution leads to sulfoxides as *e.g.* **13a**,**b**, whereas oxidation with peracetic acid in acetic acid gives sulfones **14a–d** without complication. Attempts to obtain sulfoxides from tetrahydroquinolones **7** failed; even under mild conditions (room temperature, no excess of hydrogen peroxide) the sulfones **15** are formed.

Experimental

Melting points were obtained on a Gallenkamp melting point apparatus, Mod. MFB-595 (open capillary tubes); IR spectra were recorded on a Perkin-Elmer 298 (KBr-pellets), ^{1}H NMR spectra on a Varian Gemini 200 instrument (*TMS* as internal standard, δ-values in ppm, *DMSO*-d_6 as solvent unless otherwise stated). Elemental analyses were performed on a C,H,N-Automat Carlo Erba 1106; they agreed favourably with the calculated values ($\pm$0.4%).

General procedure for the synthesis of 4-hydroxy-3-phenylthio-2(1H)-quinolones and -coumarins **3a–p**,*4-hydroxy-3-phenylthio-1-phenyl-5,6,7,8-tetrahydro-2(1H)-quinolones* **7a–e**, *and 2-hydroxy-3-phenylthio-6,7,8,9-tetrahydro-pyrido[1,2-a]pyrimidin-4-one* **11**

A mixture of 4-hydroxy-2(1*H*)-quinolones **1a–c**, 4-hydroxycoumarin **1d** or 4-hydroxy-1-phenyl-5,6,7,8-tetrahydro-2(1*H*)-quinolone **6** (20 mmol), the corresponding disulfide **2a–f** (10.5 mmol), and potassium carbonate (30 mmol) was heated in *DMF* (50 cm^3 for 5 h at 90–95°C bath temperature while air was bubbled through the mixture. After cooling water (40 cm^3) 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.

4-Hydroxy-1-methyl-3-phenylthio-2(1H)-quinolone (**3a**, $C_{16}H_{13}NO_2S$)

Prepared from **1a** and **2a** in 75% yield; m.p.: 230–232°C (ethanol); IR: $\nu = 3280$–2700 wb, 1610 s, 1585 m, 1550 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.62 (s, 3H, NCH_3), 7.08–7.38 (m, 6H,

aryl-H), 7.58 (d, $J = 8$ Hz, 1H, aryl-H), 7.68–7.80 (t, $J = 8$ Hz, 1H, aryl-H), 8.05 (dd, $J = 7$ and 1.5 Hz, 1H, 5-H), 11.20 (s, 1H, OH) ppm.

3-(4-Chlorophenylthio)-4-hydroxy-1-methyl-2(1H)-quinolone (**3b**; $C_{16}H_{12}ClNO_2S$)

Prepared from **1a** and **2b** in 74% yield; m.p.: 205–208°C (ethanol); IR: $\nu = 3300$–2700 mb, 1615 s, 1585 s, 1555 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.62 (s, 3H, NCH_3), 7.17 (d, $J = 8$ Hz, 2H, aryl-H), 7.32 (m, 3H, aryl-H), 7.57 (d, $J = 8$ Hz, 1H, aryl-H), 7.68–7.78 (m, 1H, aryl-H), 8.08 (dd, $J = 7$ and 1.5 Hz, 1H, 5-H) ppm.

4-Hydroxy-1-methyl-3-(2-nitrophenylthio)-2(1H)-quinolone (**3c**; $C_{16}H_{12}N_2O_4S$)

Prepared from **1a** and **2c** in 64% yield; m.p.: 250°C with dec. (acetic acid); IR: $\nu = 3300$–2800 mb, 1620 s, 1585 m, 1570 m, 1514 s cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.64 (s, 3H, NCH_3), 7.09 (dd, $J = 7$ and 1.5 Hz, 1H, aryl-H), 7.30–7.42 (m, 2H, aryl-H), 7.50–7.62 (m, 2H, aryl-H), 7.72–7.82 (m, 1H, aryl-H), 8.08 (dd, $J = 7$ and 1.5 Hz, 1H, aryl-H), 8.28 (dd, $J = 7$ and 1.5 Hz, 1H, aryl-H) ppm.

3-(2-Carboxyphenylthio)-4-hydroxy-1-methyl-2(1H)-quinolone (**3d**; $C_{17}H_{13}NO_4S$)

Prepared from **1a** and **2d** in 87% yield; m.p.: 274–276°C (toluene); IR: $\nu = 3290$ m, 3060–2800 wb, 1700 s, 1600 s, 1575 s cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.62 (s, 3H, NCH_3), 6.85 (d, $J = 8$ Hz, 1H, aryl-H), 7.13–7.40 (m, 3H,aryl-H), 7.57 (d, $J = 8$ Hz, 1H, aryl-H), 7.69–7.79 (t, $J = 8$ Hz, 1H, aryl-H), 7.92–8.08 (m, 2H, aryl-H),11.12 (s, 1H, OH) ppm.

4-Hydroxy-1-methyl-3-(2,4,5-trichlorophenylthio)-2(1H)-quinolone (**3e**; $C_{16}H_{10}Cl_3NO_2S$)

Prepared from **1a** and **2e** in 82% yield; m.p.: 304–306°C (*DMF*); IR: $\nu = 3300$–2500 wb, 1610 s, 1580 s, 1545 w, 1500 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.68 (s, 3H, NCH_3), 6.88 (s, 1H, aryl-H), 7.37 (t, $J = 8$ Hz, 1H, aryl-H), 7.60 (d, $J = 8$ Hz, 1H, aryl-H), 7.72–7.82 (m, 1H, aryl-H), 7.91 (s, 1H, aryl-H), 8.09 (d, $J = 8$ Hz, 1H, aryl-H) ppm.

3-(3-Carboxy-4-nitrophenylthio)-4-hydroxy-1-methyl-2(1H)-quinolone (**3f**; $C_{17}H_{12}N_2O_6S$)

Prepared from **1a** and **2f** in 86% yield; m.p.: 301–304°C (methanol); IR: $\nu = 3300$–2500 wb, 1625 s, 1615 s, 1575 w, 1545 m, 1490 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.65 (s, 3H, NCH_3), 7.28–7.40 (m, 2H, aryl-H), 7.46 (s, 1H, aryl-H), 7.59 (d, $J = 8.5$ Hz, 1H, aryl-H), 7.72–7.82 (m, 1H, aryl-H), 7.93 (d, $J = 8.5$ Hz 1H, aryl-H), 8.10 (d, $J = 8$ Hz, 1H, aryl-H) ppm.

4-Hydroxy-3-phenylthio-coumarin (**3g**; $C_{15}H_{10}O_3S$)

Prepared from **1d** and **2a** in 75% yield; m.p.: 188–189°C (ethanol); IR: $\nu = 3320$–2700 wb, 1678 s, 1605 s, 1545 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 7.12–7.49 (m, 7H, aryl-H), 7.68–7.78 (m, 1H, aryl-H), 7.98 (d, $J = 8$ Hz, 5-H) ppm.

3-(4-Chlorophenylthio)-4-hydroxy-coumarin (**3h**; $C_{15}H_9ClO_3S$)

Prepared from **1d** and **2b** in 77% yield; m.p.: 192–195°C (toluene); IR: $\nu = 3320$–2940 mb, 1695 s, 1605 s, 1540 s cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 7.20–7.48 (m, 6H, aryl-H), 7.70–7.80 (m, 1H, aryl-H), 7.99 (dd $J = 7$ and 1.5 Hz, 1H, 5-H) ppm.

4-Hydroxy-3-(2-nitrophenylthio)-coumarin (**3i**; $C_{15}H_9NO_5S$)

Prepared from **1d** and **2c** in 57% yield; m.p.: 260°C with dec. (acetic acid).

3-(2-Carboxyphenylthio)-4-hydroxy-coumarin (**3j**; $C_{16}H_{10}O_5S$)

Prepared from **1d** and **2d** in 91% yield; m.p.: 237–240°C (toluene); IR: $\nu = 3360$–2700 wb, 1685 s, 1605 s, 1530 s cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 7.06 (d, $J = 8$ Hz, 1H, aryl-H), 7.22 (t, $J = 8$ Hz, 1H, aryl-H), 7.35–7.51 (m, 3H, aryl-H), 7.69–7.80 (m, 1H, aryl-H), 7.92–8.03 (d, $J = 8$ Hz, 2H, aryl-H) ppm.

4-Hydroxy-1-phenyl-3-phenylthio-2(1H)-quinolone (**3k**; $C_{21}H_{15}NO_2S$)

Prepared from **1b** and **2a** in 49% yield; m.p.: 180–183°C (toluene); IR: $\nu = 3330$ m, 3050 w, 1655 s, 1615 s, 1590 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 6.68 (d, $J = 8$ Hz, 1H, aryl-H), 7.12–7.39 (m, 8H, aryl-H), 7.49–7.69 (m, 4H, aryl-H), 8.12 (dd, $J = 7$ and 1.5 Hz, 1H, 5-H) ppm.

3-(4-Chlorophenylthio)-4-hydroxy-1-phenyl-2(1H)-quinoione (**3l**; $C_{21}H_{14}ClNO_2S$)

Prepared from **1b** and **2b** in 41% yield; m.p.: 207–210°C (toluene); IR: $\nu = 3360$–2800 mb, 1630 s, 1610 s, 1590 s, 1550 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 6.56 (d, $J = 8$ Hz, 1H, aryl-H), 7.18–7.38 (m, 7H, aryl-H), 7.48–7.68 (m, 4H, aryl-H), 8.10 (dd, $J = 7$ and 1.5 Hz, 1H, 5-H) ppm.

4-Hydroxy-3-(2-nitrophenylthio)-1-phenyl-2(1H)-quinolone (**3m**; $C_{21}H_{14}N_2O_4S$)

Prepared from **1b** and **2c** in 70% yield; m.p.: 265–268°C (acetic acid); IR: $\nu = 3300$–2700 mb, 1620 s, 1590 w, 1570 m, 1510 s cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 6.62 (dd, $J = 8$ and 2 Hz, 1H, aryl-H), 7.29–7.72 (m, 10H, aryl-H), 8.07 (dd, $J = 7$ and 1.5 Hz, 1H, aryl-H), 8.29 (dd, $J = 7$ and 1.5 Hz, 1H, aryl-H) ppm.

4-Hydroxy-1-phenyl-3(2,4,5-trichlorophenylthio)-2(1H)-quinolone (**3n**; $C_{21}H_{12}Cl_3NO_2S$)

Prepared from **1b** and **2e** in 82% yield; m.p.: 232–234°C (acetic acid); IR: $\nu = 3300$–2700 wb, 1625 s, 1615 s, 1575 w, 1545 m, 1490 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 6.60 (d, $J = 7.5$ Hz, 1H, aryl-H), 7.10 (s, 1H, aryl-H), 7.28–7.40 (m, 3H, aryl-H), 7.48–7.68 (m, 4H, aryl-H), 7.90 (s, 1H, aryl-H), 8.12 (d, $J = 7$ Hz, 1H, aryl-H) ppm.

1-Benzyl-3-(4-chlorophenylthio)-4-hydroxy-2(1H)-quinolone (**3o**; $C_{22}H_{16}ClNO_2S$)

Prepared from **1c** and **2b** in 50% yield; m.p.: 166–170°C (toluene).

4-Hydroxy-3-(2,4,5-trichlorophenylthio)-2(1H)-quinolone (**3p**; $C_{15}H_8Cl_3NO_2S$)

Prepared from **1e** and **2e** in 75% yield; m.p.: 316–317°C (*DMF*); IR: $\nu = 3300$–2500 wb, 1640 s, 1600 s, 1580 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 6.83 (s, 1H, aryl-H), 7.20–7.40 (m, 3H, aryl-H), 7.58–7.70 (m, 1H, aryl-H), 7.98 (dd, $J = 7.5$ and 1 Hz, 1H, 5-H), 11.72 (sb, 1H, NH) ppm.

4-Hydroxy-1-phenyl-3-phenylthio-5,6,7,8-tetrahydro-2(1H)-quinolone (**7a**; $C_{21}H_{19}NO_2S$)

Prepared from **6** and **2a** in 72% yield; m.p.: 163–165°C (toluene/cyclohexane); IR: $\nu = 3380$–2600 mb, 1630 s, 1600 w, 1585 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 1.62 (s, 4H, 6-H, 7-H), 2.08 (s, 2H, 8-H), 2.50 (s, 2H, 5-H), 7.100–7.58 (m, 10H, aryl-H), 10.38 (s, 1H, OH) ppm.

3-(4-Chlorophenylthio)-4-hydroxy-1-phenyl-5,6,7,8-tetrahydro-2(1H)-quinolone (**7b**; $C_{21}H_{18}ClNO_2S$)

Prepared from **6** and **2b** in 54% yield; m.p.: 227–228°C (toluene); IR: $\nu = 3320$–3120 mb, 2939 m, 1642 s, 1540 s, 1470 s cm^{-1}; ^1H NMR (200 MHz, δ,*DMSO*-d_6): 1.61 (s, 4H, 6-H, 7-H), 2.05 (s, 2H, 8-H), 2.47 (s, 2H, 5-H), 7.12 (d, $J = 8$ Hz, 2H, phenyl-3-H, 5-H), 7.22 (dd, $J = 7$ and 1.5 Hz, 2H, aryl-H), 7.33 (d, $J = 8$ Hz, 2H, phenyl-2-H, 6-H), 7.41–7.53 (m, 3H, aryl-H), 10.48 (s, 1H, OH) ppm.

4-Hydroxy-3-(4-nitrophenylthio)-1-phenyl-5,6,7,8-tetrahydro-2(1H)-quinolone (**7c**; $C_{21}H_{18}N_2O_4S$)

Prepared from **6** and **2g** in 51% yield; m.p.: 251–255°C (toluene); IR: $\nu = 3080$–2800 wb, 1635 s, 1580 w, 1540 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 1.62 (s, 4H, 6-H, 7-H), 2.06 (s, 2H, 8-H), 2.42 (s, 2H, 5-H), 7.15–7.32 (m, 5H aryl-H), 7.42–7.58 (m, 3H, aryl-H), 8.13 (d, $J = 8$ Hz, 1H, aryl-H) ppm.

4-Hydroxy-3-(2-nitrophenylthio)-1-phenyl-5,6,7,8-tetrahydro-2(1H)-quinolone (**7d**; $C_{21}H_{18}N_2O_4S$)

Prepared from **6** and **2c** in 63% yield; m.p.: 247–249°C (toluene); IR: $\nu = 3140$–2805 wb, 1645 s, 1605 w, 1580 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 1.64 (s, 4H, 6-H, 7-H), 2.10 (s, 2H, 8-H), 2.48 (s, 2H, 5-H), 7.12–7.68 (m, 8H, aryl-H), 8.25 (d, $J = 8$ Hz, 1H, aryl-H), 10.70 (s, 1H, OH) ppm.

4-Hydroxy-1-phenyl-3-(2,4,5-trichlorophenylthio)-5,6,7,8-tetrahydro-2(1H)-quinolone (**7e**; $C_{21}H_{16}Cl_3NO_2S$)

Prepared from **6** and **2e** in 68% yield; m.p.: 211–214°C (toluene); IR: $\nu = 3100$–2800 wb, 1645 s, 1620 s, 1590 w, 1565 m cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 1.60 (s, 4H, 6-H, 7-H), 2.05 (s, 2H, 8-H), 2.42 (s, 2H, 5-H), 6.40–6.64 (m, 2H, aryl-H), 7.83–7.93 (m, 2H, aryl-H), 8.16–8.23 (m, 2H, aryl-H), 8.38 (s, 1H, aryl-H) ppm.

2-Hydroxy-3-(2,4,5-trichlorophenylthio)-pyrido[1,2-a]pyrimidin-4-one (**9**; $C_{14}H_7Cl_3N_2O_3S$)

Prepared from **8** and **2e** in 85% yield; m.p.: 296–297°C (methanol).

2-Hydroxy-3-phenylthio-6,7,8,9-tetrahydro-pyrido[1,2-a]pyrimidin-4-one (**11**; $C_{14}H_{14}N_2O_2S$)

Prepared from **10** and **2a** in 93% yield; m.p.: 271–275°C (toluene); IR: $\nu = 3300$–2650 mb, 1685 s, 1595 w, 1535 s cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 1.72–1.95 (m, 4H, 7-H, 8-H), 2.86 (t, $J = 7$ Hz, 2H, 9-H), 3.75 (t, $J = 7$ Hz, 2H, 6-H), 7.00–7.28 (m, 5H aryl-H), 12.40 (s, 1H, OH) ppm.

3-Diethylaminothiocarbonylthio-4-hydroxy-1-methyl-2(1H)-quinolone (**5a**; $C_{15}H_{18}N_2O_2S_2$)

A mixture of 1.75 g **1a** (10 mmol), 3.26 g tetraethylthiuram disulfide (**4a**, 11 mmol), 2.76 g potassium carbonate (20 mmol), and 30 ml *DMF* was heated under stirring for 4 h at 90°C. After removing half of the solvent *in vacuo*, the solution was poured into ice-water. After standing for 3 h it was filtered and the filtrate slowly acidified with diluted hydrochloric acid. The resulting precipitate was filtered by suction.

Yield: 2.40 g (74%); m.p.: 148–152°C (ethanol); IR: $\nu = 3400$–2800 mb, 1630 s, 1600 s, 1550 s, 1500 w cm^{-1}; ^1H NMR (200 MHz, δ, *DMSO*-d_6): 1.20 (t, $J = 7$ Hz, 3H, CH_3), 1.40 (t, $J = 7$ Hz, 3H, CH_3), 3.59 (s, 3H, NCH_3), 3.86–4.02 (m, 4H, $2CH_2$), 7.30 (t, $J = 7$ Hz, 1H, aryl-H), 7.52 (d, $J = 8$ Hz, 1H, aryl-H), 7.72 (d, $J = 7$ Hz, 1H, aryl-H), 8.02 (dd, $J = 7$ and 1.5 Hz, 1H, 5-H) ppm.

3-Dimethylaminothiocarbonylthio-4-hydroxy-coumarin (**5b**; $C_{14}H_{11}NO_3S_2$)

From 1.62 g **1d** (10 mmol) and 2.65 g **4b** (11 mmol) according to the preparation of **5a**; yield: 2.10 g (68%); m.p.: 170–173°C (ethanol); IR: $\nu = 3360$–2700 wb, 1685 s, 1610 s, 1555 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.49 (s, 3H, CH_3), 3.52 (s, 3H, CH_3), 7.37–7.48 (m, 2H, aryl-H), 7.70–7.80 (m, 1H, aryl-H), 7.98 (dd, J = 7.5 and 1 Hz, 1H, aryl-H) ppm.

3-Diethylaminothiocarbonylthio-4-hydroxy-1-phenyl-2(1H)-quinolone (**5c**; $C_{20}H_{20}N_2O_2S_2$)

From 2.37 g **1b** (10 mmol) and 3.26 g **4a** (11 mmol) according to the preparation of **5a**; yield: 1.92 g (50%); m.p.: 166–169°C (ethanol).

3-Dimethylaminothiocarbonylthio-4-hydroxy-1-phenyl-2(1H)-quinolone (**5d**; $C_{18}H_{16}N_2O_2S_2$)

From 2.37 g **1b** (10 mmol) and 2.65 g **4b** (11 mmol) according to the preparation of **5a**; yield: 1.99 g (56%); m.p.: 171–173°C (toluene); IR: $\nu = 3000$–2500 wb, 1630 s, 1610 s, 1590 m, 1550 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.48 (s, 3H, CH_3), 3.52 (s, 3H, CH_3), 6.64 (d, $J = 8$ Hz, 1H, aryl-H), 7.19–7.31 (m, 3H, aryl-H) 7.45–7.68 (m, 4H, aryl-H) 8.08 (dd, $J = 7.5$ and 1 Hz, 1H, aryl-H) ppm.

3-Diethylaminothiocarbonylthio-2-hydroxy-pyrido-[1,2-a]pyrimidin-4-one (**12a**; $C_{13}H_{15}N_3O_2S_2$)

From 1.62 g **8** (10 mmol) and 3.26 g **4a** (11 mmol) accordieng to the preparation of **5a**; yield: 2.00 g (65%); m.p.: 250–252°C (ethanol).

3-Dimethylaminothiocarbonylthio-2-hydroxy-pyrido[1,2-a[pyrimidin-4-one (**12b**; $C_{11}H_{11}N_3O_2S_2$)

From 1.62 g **8** (10 mmol) and 2.65 g **4b** (11 mmol) according to the preparation of **5a**; yield: 1.95 g (70%); m.p.: 260–262°C (ethanol); IR: $\nu = 3000$–2200 wb, 1700 m, 1620 s, 1580 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.48 (s, 6H, 2xCH_3), 7.38–7.52 (m, 2H, aryl-H), 8.20–8.30 (m, 1H, aryl-H), 9.00 (d, $J = 7$ Hz, 1H, aryl-H), 12.60 (s, 1H, OH) ppm.

4-Hydroxy-1-methyl-3-phenylsulfinyl-2(1H)-quinolone (**13a**; $C_{16}H_{13}NO_3S$)

To a solution of 1.42 g **3a** (5 mmol) in 20 cm^3 of 2 *N* sodium of hydroxide, 8 cm^3 of hydrogen peroxide (30%) were added. After stirring overnight the product was precipitated by acidification with diluted hydrochloric acid.

Yield: 1.34 g (89%); m.p.: 175–176°C (ethanol); IR: $\nu = 1630$ s, 1595 w, 1565 m, 1080 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.52 (s, 3H, NCH_3), 7.32–7.43 (m, 1H, aryl-H), 7.52–7.84 (m, 5H, aryl-H), 7.92–8.00 (m, 2H, aryl-H), 8.10 (dd, $J = 7$ and 1.5 Hz, 1H, 5-H) ppm.

3-(4-Chlorophenylsulfinyl)-4-hydroxy-1-methyl-2(1H)-quinolone (**13b**; $C_{16}H_{12}ClNO_3S$)

From 1.59 g **3b** (5 mmol) according to the preparation of **13a**; yield: 1.57 g (94%); m.p.: 183–185°C (toluene); IR: $\nu = 1625$ s, 1590 w, 1570 m, 1500 m, 1090 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.51 (s, 3H, NCH_3), 7.28–7.42 (m, 1H, aryl-H), 7.57 (d, $J = 8$ Hz, 1H, aryl-H), 7.68–7.82 (m, 3H, aryl-H), 7.92–8.04 (m, 3H, aryl-H) ppm.

3-(4-Chlorophenylsulfonyl)-4-hydroxy-1-methyl-2(1H)-quinolone (**14a**; $C_{16}H_{12}ClNO_4S$)

To a solution of 1.59 g **3b** (5 mmol) in 20 cm^3 acetic acid, 3 cm^3 of peracetic acid (40%) were added. After stirring for 90 min at 50°C the product was precipitated by acidification with 2 *N* HCl.

Yield: 1.07 g (61%); m.p.: 214–218°C (toluene); IR: $\nu = 3280$–2860 mb, 1640 s, 1620 s, 1555 m, 1320 m, 1125 s cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 3.49 (s, 3H, NCH_3), 7.40 (t, $J = 7$ Hz, 1H, aryl-H), 7.58 (d, $J = 8$ Hz, 1H, aryl-H), 7.68–7.90 (m, 3H, aryl-H), 8.08–8.19 (m, 3H, aryl-H) ppm.

4-Hydroxy-3-phenylsulfonyl-coumarin (**14b**; $C_{15}H_{10}O_5S$)

From 1.35 g **3g** (5 mmol) according to the preparation of **14a**; yield: 1.24 g (82%); m.p.: 178–181°C (toluene); IR: $\nu = 3100$–2860 wb, 1725 s, 1615 s, 1605 s, 1550 s, 1330 m, 1130 s cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 4.92 (s, OH-H_2O-assoziation), 7.20–7.36 (m, 2H, aryl-H), 7.50–7.70 (m, 4H, aryl-H), 7.87–8.08 (m, 3H, aryl-H) ppm.

3-(4-Chlorophenylsulfonyl)4-hydroxy-coumarin (**14c**; $C_{15}H_9ClO_5S$)

A solution of 1.52 g **3h** (5 mmol) in 20 cm^3 acetic acid and 3 cm^3 of peracetic acid (40%) was stirred for 2 h at 50°C. After cooling to room temperature the formed precipitate was filtered by suction.

Yield: 1.30 g (77%); m.p.: 173–176°C (toluene); IR: $\nu = 3100$–2940 wb, 1715 s, 1615 s, 1602 s, 1545 s, 1335 s, 1135 s, cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 7.12–7.25 (m, 2H, aryl-H), 7.49–7.61 (m, 3H, aryl-H, phenyl 3-H, 5-H), 7.80 (dd, $J = 7$ and 1.5 Hz, 1H, aryl-H), 7.94 (d, $J = 8$ Hz, 2H, phenyl 2-H, 6-H) ppm.

3-(4-Chlorophenylsulfonyl)-4-hydroxy-1-phenyl-2(1H)-quinolone (**14d**; $C_{21}H_{14}ClNO_4S$)

To a solution of 1.90 g **3l** (5 mmol) in 20 cm^3 acetic acids, 3 cm^3 of peracetic acid (40%) were added. After stirring for 2 h at 50°C the product was precipitated by acidification with 2 *N* HCl.

Yield: 1.80 g (87%); m.p.: 235–237°C (toluene).

4-Hydroxy-1-phenyl-3-phenylsulfonyl-5,6,7,8-tetrahydro-2(1H)-quinolone (**15a**; $C_{21}H_{19}NO_4S$)

a) Oxidation with hydrogen peroxide

To a mixture of 1.75 g **7a** (5 mmol) and sodium carbonate solution (1.0 g Na_2CO_3 in 20 cm^3 of water), 2 *N* NaOH was added until a clear solution formed. Then, 12 cm^3 of H_2O_2 (30%) were added, and after standing overnight the product was precipitated by acidification with 2 *N* HCl.

Yield: 1.65 g (86%).

b) Oxidation with peracetic acid

To a solution of 1.75 g **7a** (5 mmol) in 25 cm^3 acetic acid, 3 cm^3 of peracetic acid (40%) were added. After stirring for 2 h at 50°C the product was precipitated by acidification with 2 *N* HCl.

Yield: 1.63 g (86%); m.p.: 189–192°C (ethanol); IR: $\nu = 3060$ w, 2940 w, 1650 s, 1550 s, 1330 m, 1125 m cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 1.59 (s, 4H, 6-H, 7-H), 2.02 (s, 2H, 8-H), 2.50 (s, 2H, 5-H), 7.10–7.58 (m, 10H, aryl-H) ppm.

3-(4-Chlorophenylsulfonyl)-4-hydroxy-1-phenyl-5,6,7,8-tetrahydro-2(1H)-quinolone (**15b**; $C_{21}H_{18}ClNO_4S$)

To a solution of 1.90 g **7b** (5 mmol) in 25 cm^3 acetic acid, 3 cm^3 of peracetic acid (40%) were added. After stirring for 90 min at 50°C the product was precipitated by acidification with 2 *N* HCl.

Yield: 1.40 g (66%); m.p.: 221–224°C (ethanol); IR: $\nu = 3100$ m, 2940 m, 1650 s, 1555 s, 1325 s, 1128 s cm^{-1}; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6): 1.60 (s, 4H, 6-H, 7-H), 2.05 (s, 2H, 8-H), 2.50 (s,

2H, 5-H), 7.12–7.20 (m, 2H, aryl-H), 7.44–7.51 (m, 3H, aryl-H), 7.68 (d, $J = 8$ Hz, 2H, phenyl 3-H, 5-H), 8.01 (d, $J = 8$ Hz, 2H, phenyl 2-H, 6-H) ppm.

4-Hydroxy-3-((2,4,5-trichlorophenylsulfonyl)-1-phenyl-5,6,7,8-tetrahydro-2(1H)-quinolone (**15c**; $C_{21}H_{16}Cl_3NO_4S$)

A solution of 1.13 g **7e** (2.5 mmol) in 20 cm^3 acetic acid and 2 cm^3 of peracetic acid (40%) was stirred for 2 h at 50°C. After standing overnight at room temperature, the solution was diluted with water and the formed precipitate was filtered by suction.

Yield: 0.86 g (71%); m.p.: 220–221°C (ethanol).

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