Articles

Synthesis of a New Diels-Alder Quinone Adduct and Its Use in Preparing Thiazolo- and Oxazoloquinolines†

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Syn (or *anti*) cinnamaldehydeoxime (**1a, b**) undergoes Diels-Alder addition to tetrabromo-*p*-benzoquinone (**2**) in dry xylene in 1 : 1 and 2 : 1 molar ratios to give the mono- and diadducts **3** and **4a, b** respectively. The reaction of **3** with thioamides in ethanol gave thiazoloquinoline diones **6a-d**, whereas with acid amides in ethylene glycol, it gave oxazoloquinolinediones **12a-f**.

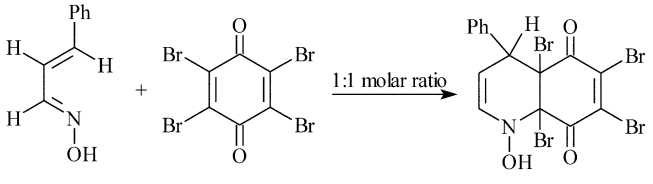
Key Words : Cinnamaldehydeoxime, Bromanil, Monoadduct, Thiazoloquinolines, Oxazoloquinolines

Introduction

Many reports ascribe interesting biological activities to quinones and their derivatives, especially those containing fused heterocyclic rings.[1-3] Thus, among quinones, naphthoquinones have been found to possess good fungicidal[4,5] as well as antimalarial activities.[6] On the other hand, quinones fused to oxazole or thiazole nuclei have been endowed with good bactericidal activity.[7,8] These interesting properties have encouraged the present studies to prepare previously unreported thiazoloquinolinediones and oxazoloquinolinediones, some or all of which may be associated with interesting biological properties.

Diels-Alder reaction of *syn* (or *anti*) cinnamaldehydeoxime **1a** (or **1b**) with bromanil (**2**) in a 1 : 1 molar ratio in boiling dry xylene for 30 hours afforded the monoadduct **3**.

The chemical structure of compound **3** is based on both elemental and spectral analyses. Its mass spectrum of electron impact did not show a molecular ion peak, but showed peaks corresponding to cinnamaldehydeoxime (**1**) and bromanil (**2**), indicating that a *retro Diels-Alder* reaction[9] has occurred to **3**. Five peaks corresponding to the molecular ion of bromanil appeared in the mass spectrum at m/z 419.5 (0.1%), 421.5 (17.29%), 423.6 (66.72%), 425.5 (100%) and 427.6 (62%). These fit with the 5 possible ratios of isotopic ^{79}Br and ^{81}Br, namely 0 : 4, 1 : 3, 2 : 2, 3 : 1 and 4 : 0, respectively.



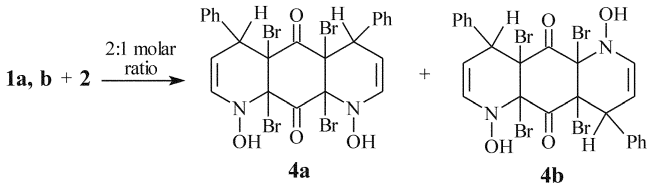
1a,b **2** **3**

Scheme 1

Repeating the mass spectra of the monoadduct **3** under FAB conditions showed peaks corresponding to fragment ions resulting from *retro Diels-Alder* reaction.[9]

Repeating the reaction of the diene **1** with bromanil (**2**) in 2 : 1 molar ratio also preceded readily giving two products. One was dark brown and precipitated during reflux with a melting point above 360 °C; the other was light brown and was separated by concentrating the mother liquor and melts at 183 °C. The two products showed identical elemental analysis that correspond to a diadduct resulting from a (4−2) *Diels-Alder* addition of 2 moles of the diene to one mole of bromanil, retaining the four bromine atoms. From the theoretical point of view, the structure of the two resulting isomeric products can be represented by **4a** and **4b**. However, which of the two products has the higher melting point and which has the lower melting point cannot be deduced on chemical and spectral bases. Nevertheless, on the basis of observations of *syn* and *anti* isomeric compounds (e.g. *syn* and *anti* cinnamaldehydeoximes), we can unequivocally suggest that the *anti*-isomer (**4a**) is the lower-melting point compound (Scheme 2).

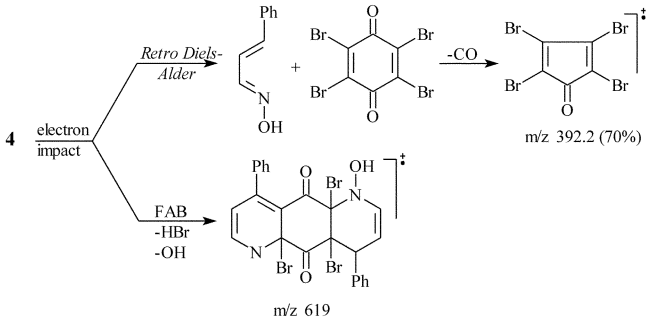
Similar to the monoadduct **3**, the mass spectrum of the diadduct **4**, did not show the molecular ion peak but showed ions corresponding to fragments resulting from *retro Diels-Alder* reaction, at m/z 147 (cinnamaldehydeoxime) and m/z 425.6 (bromanil). However, with the repeat of the mass



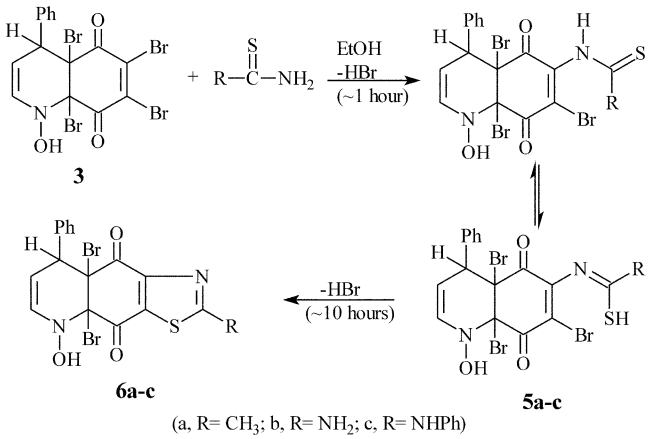
4a **4b**

Scheme 2

†Presented at the 18th International Congress of Heterocyclic Chemistry, July 29-August 3, 2001, Yokohama, Japan.



Scheme 3

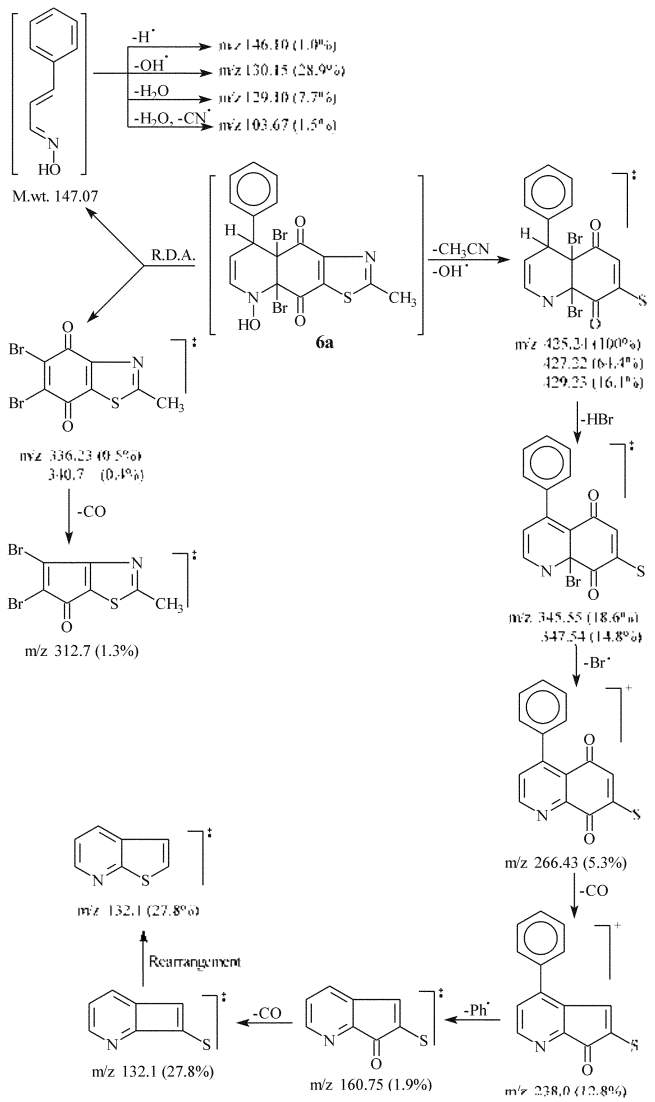


Scheme 4

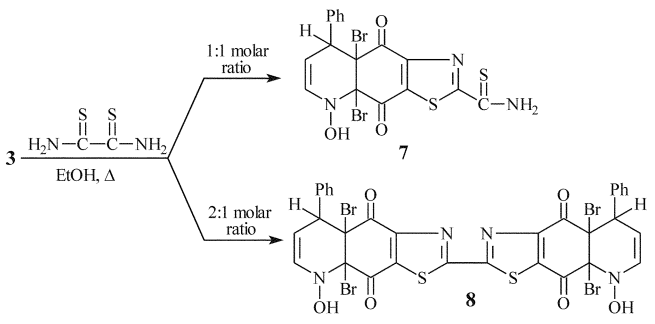
spectra of **4** under FAB conditions, a parent ion peak at m/z 619 corresponding to the molecular ion that lost an OH group and a hydrogen bromide molecule appeared (Scheme 3).

Following our reported procedure,[10] the reaction of the monoadduct **3** with thioamides in absolute ethanol resulted in dark colored solids within 9-11 hours after the reaction commenced, with 50-75% yield. The solids were identified as dibromotetrahydroquinolino[2,3-*d*]thiazolediones **6a-c** on basis of elemental and spectral analyses. Carrying the reaction of **3** with thioacetamide as an example for a short period (~1 hour) gave the product **5a**, which could be separately transformed into **6a** by refluxing in ethanol for a prolonged period (~10 hours). Therefore, **5a** can be suggested to exist as an intermediate during formation of **6a** (Scheme 4).

The mass spectra of compounds **6a-c** were of special interest, since they fragmented in two ways. **6a** (R=CH_3), as an example, fragmented under electron impact in two manners: in one of them it underwent *retro Diels-Alder* reaction as indicated by the presence of fragment ions at m/z 146.1 (1%), m/z 130.15 (28.9%), m/z 129.1 (7.7%) and m/z 103.67 (1.5%), corresponding to the cinnamaldehydeoxime that had lost a hydrogen atom, an OH group, H_2O molecule or H_2O and a cyano group, respectively, in addition to the complementary fragment ion corresponding to the dibromobenzothiazoledione at m/z 336.23 (0.5%). In another way, **6a** (R=CH_3) fragmented by loss of CH_3CN and OH groups to



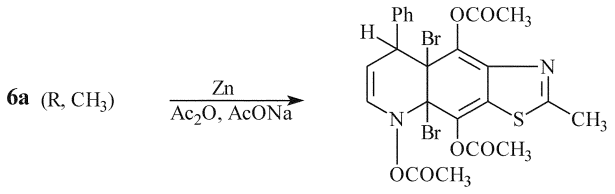
Scheme 5. Fragmentation pattern of compound **6a**.



Scheme 6

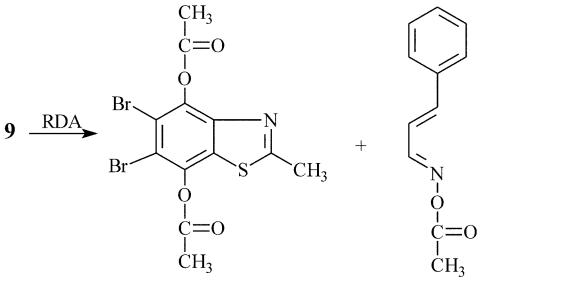
give three fragment ions at m/z 425.24 (100%), m/z 427.22 (64.4%) and m/z 429.23 (16.1%), containing different ratios of isotopic bromine. These successively lost HBr, Br, CO, C_6H_5 and CO to give the relatively stable fragment corresponding to pyridothiophene at m/z 132.1 (27.8%) (Scheme 5).

Dithioxamide, having two thioamido groups, also reacted



9

Scheme 7



10 **11**

m/z 427.1 (1.9%) m/z 189.66 (19.3%)

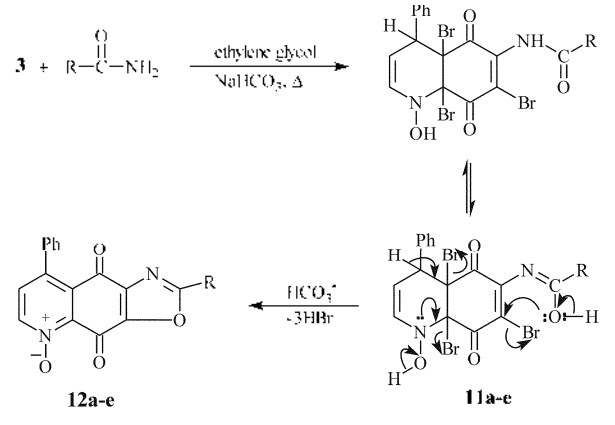
Scheme 8

readily with the monoadduct **3** in a 1 : 1 molar ratio to give **7**, and in a 1 : 2 molar ratio to give **8** (Scheme 6).

Reductive acetylation of **6a** (R=CH_3), using zinc dust-acetic anhydride-fused sodium acetate mixture, gave the triacetate derivative **9**, whose mass spectrum showed molecular ion peaks at m/z 614.01 (0.8%) and m/z 616.05 (4.3%), corresponding to intact molecules containing different ratios of isotopic bromine: one containing 1 ^{79}Br and 1 ^{81}Br and the other containing 2 ^{81}Br (Scheme 7).

Another indication of the occurrence of a *retro Diels-Alder* reaction of the triacetate under electron impact was obtained by observing the fragment ions at m/z 427.1 (1.9%) and m/z 189.66 (19.3%), which correspond to structures **10** and **11**, respectively (Scheme 8).

The appearance of the molecular ion peak of **9** is an indication of the relative stability of the triacetate derivative as compared with the parent compound **6a**, which is possibly



(a, R= H; b, R= CH_3; c, R= Ph; d, R= CH_2Ph; e, R= NH_2)

Scheme 9

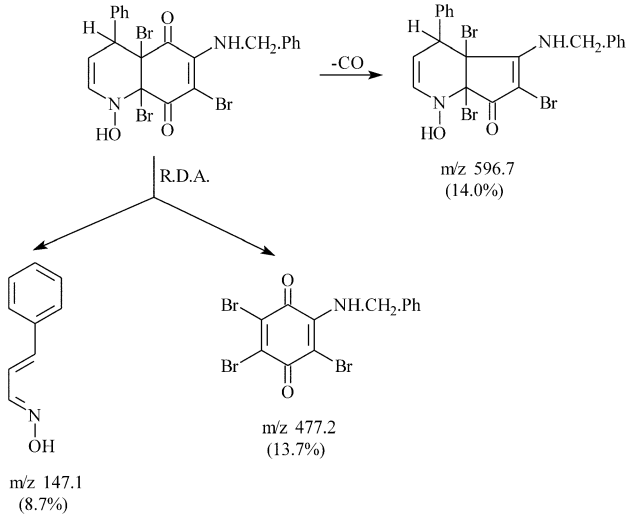
due to the partial aromatization of the quinonoid ring.

Oxazoloquinolinediones **12a-e** were prepared by interaction of **3** with acid amides in boiling ethylene glycol in the presence of bicarbonate. Following this established method of ours,[11] dark brown crystalline products **12a-e** resulted in good yields after 8-10 hours reflux.

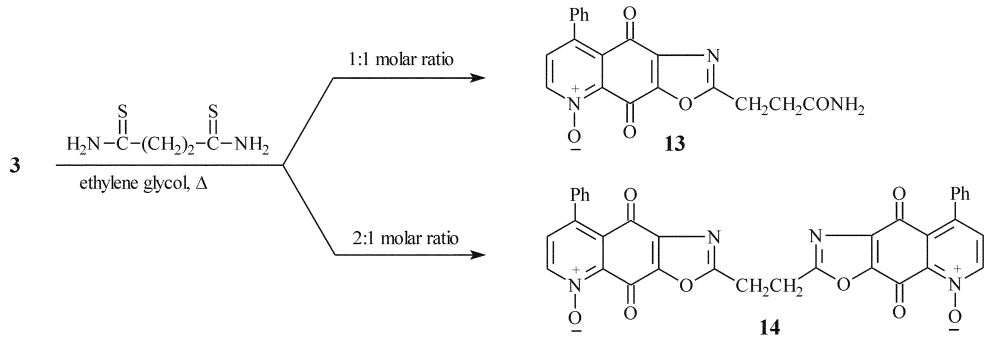
The structure of compounds **12a-e** was determined by elemental and spectral analyses. Elemental analysis showed the absence of halogen, the IR spectra showed bands at 1650 cm^{-1}, 1600 cm^{-1} and 1550 cm^{-1} characteristic of an oxazole system, in addition to bands at 1670 cm^{-1}, 1100 cm^{-1} and 755-675 cm^{-1} characteristic of νC=O conjugated with C=C, νN-O in aromatic ring and ν5adj Ar-H, respectively. Also, the mass spectrum of compound **12d** (R=CH_2Ph), as an example, showed a peak at m/z 385 corresponding to M+2.

The mechanism of formation of compounds **12a-e** is suggested to proceed according to Scheme 9 in which the amide undergoes a nucleophilic attack at position 2 of the adduct **3** to give an intermediate **11a-e**, which undergoes dehydrobromination most likely under the influence of the basic effect of the bicarbonate and the high energy of the reaction medium to give a final mesoionic product **12a-e** (Scheme 9).

An experimental proof to the involvement of **11a-e** as intermediate during formation of the oxazoloquinolinedione **12a-e** was approached from the separation of **11d** as a minor product on dilution (with water) of the mother liquor of the reaction, together with its formation in quantitative yield on repeating the reaction between phenylacetamide and the adduct **3** for 30 minutes only, in the absence of bicarbonate. Moreover, heating **11d** in ethylene glycol for ~7 hours in the presence of HCO_3^- transformed it into the oxazoloquinolinedione **12d** in good yield. The structure of the intermediate **11d**, R=CH_2Ph is based on elemental, IR and mass spectral analyses. The latter did not show a molecular ion peak at m/z 624.7 but showed a peak corresponding to M-CO at m/z 596.7 (14.0%). The mass spectrum revealed also that the compound undergoes *retro Diels-Alder* reaction



Scheme 10



Scheme 11

Table 1. Antibacterial screening of some selected thiazoloquinolinediones (diameter of inhibition zones)

Bacterial species / Compound	*Staph. aureus*	*Staph albus*	*Salmonella*	*Klebsiella*
	Diameter of zone of inhibition (in mm)			
Garamycin	17	6	14	6
3	12	0	13	7
6a	10	0	16	7
6b	9	0	10	8
6c	10	0	10	7
7	8	8	6	7

under electron impact as indicated by the appearance of the two complementary fragments at m/z 147.1 (8.7%) and m/z 477.2 (13.7%), corresponding to the cinnamaldehydeoxime and 2-benzylamino-3,5,6-tribromo-*p*-benzoquinone (Scheme 10).

The reaction of succinamide, with the monoadduct **3** could be made to give the products **13** and **14**, depending on the molar ratios of the reactants used (Scheme 11).

Antimicrobial Screening. Some of the prepared compounds possessing fair solubility in ethylene glycol were selected, and their *in vitro* antimicrobial activities against four strains of bacteria were determined using the filter paper disc method.[12,13] These strains included *Staphylococcus aureus* and *Staphylococcus albus* as gram-positive bacteria and *Salmonella* and *Klebsiella* as gram-negative. The results obtained are included in Table 1.

These data show that with exception of *Staphylococcus albus*, which was lightly resistant to the majority of tested compounds, all other bacteria strains were sensitive. The sensitivity however, varied with change of both type of nucleus or substituent.

From the limited data of biological screening that we obtained, working out a correlation between structure and activity is rather difficult.

However, we have concluded that the results obtained are satisfactory and encourage further synthetic studies in this field.

Experimental Section

All melting points are uncorrected and determined on a Gallenkamp apparatus with a digital thermometer type MFB-595-010M. The IR spectra were measured on an IR-470 Spectrophotometer [SHIMADZU], using the KBr Wafer technique. The mass spectra were run on a JEOL JMS$_{600}$ apparatus at Assiut University. Preparation of bromanil **2** (m.p. 298-300 °C), *syn* cinnamaldehydeoxime (m.p. 138 °C) and *anti* cinnamaldehydeoxime (m.p. 64 °C) was carried out by known procedure.

Preparation of Diels-Alder monoadduct 3. Bromanil **2** (4.24 g, 0.01 mol) was dissolved in dry *p*-xylene (20 mL) and the solution treated with 1.47 g (0.01 mol) of the high-melting point cinnamaldehydeoxime dissolved also in dry *p*-xylene (20 mL). The reaction mixture was refluxed on a sand bath (at 130-145 °C) for about 20 hours, until the color of the reaction mixture changed from reddish orange to dark reddish brown, then it was cooled and filtered from any tetrabromohydroquinone formed. Concentration of the filtrate followed by cooling and the addition of few mls of petroleum ether (40-60 °C) precipitated a dark brown crystalline product that was collected and recrystallized from EtOH as deep brown fine crystals of 5α,6,7,8α-tetrabromo-1,4,5α,8α-tetrahydro-1-hydroxy-4-phenyl-5,8-quinolinedione (**3**), m.p. 217 °C (yield 40%). Anal. Calc. for $C_{15}H_8Br_4NO_3$: C, 31.56; H, 1.58; N, 2.45; Br, 55.9. Found. C, 31.4; H, 1.34; N, 2.41; Br, 55.67.

The previous reaction was repeated under the same conditions, using low melting-point cinnamaldehydeoxime instead of the high-melting one. The product obtained was identical in all respects with that obtained from high melting-point cinnamaldehydeoxime, m.p. and mixed m.p. 247 °C.

Acetylation of the monoadduct **3**, using acetic anhydride-fused sodium acetate, gave a yellow-brown acetate crystallized from ethanol. m.p. 134 °C. Anal. Calc. for $C_{17}H_{11}Br_4NO_4$: N, 2.28; Br, 52.14. Found: N, 2.43; Br, 51.83.

Preparation of diadducts 4a, b.

Reaction of bromanil (2) with the high melting-point cinnamaldehyeoxime (1a) in 2 : 1 molar ratios: A mixture of bromanil **2** (4.24 g, 0.01 mol) and high melting-point cinnamaldehyeoxime **1a** (2.24 g, 0.02 mol) in dry *p*-xylene (50 mL) was refluxed on a sand bath (at 120-140 °C) for about 30 hours, with the color of the reaction mixture changing from red to dark reddish brown and a dark crystalline product separated out, which was collected by

Table 2. Reaction products from monoadduct 3 and thioamides

Compd.	Thioamide or amide used	Colour (time, h)	Solvent	m.p. °C (% yield)	Formula	Calculated / Found				
						%C	%H	%N	%Br	%S
3a	Thioacetamide	reddish-brown (9)	ethanol	191 (78)	$C_{17}H_{12}Br_2N_2O_3S$	42.21 42.10	2.49 2.45	5.78 5.70	33.0 33.2	6.6 6.4
3b	Thiourea	dusty-brown (10)	acetone	202 (63)	$C_{16}H_{11}Br_2N_3O_3S$	39.61 39.5	2.28 2.22	8.66 8.80	32.94 33.00	6.59 6.95
3c	Phenylthiourea	light-brown (11)	methanol	226 (35)	$C_{22}H_{15}Br_2N_3O_3S$	47.08 46.99	2.69 2.70	7.48 7.20	28.47 28.31	5.71 5.78
7	Dithioxamide * (1 : 1)	brownish-red (10)	ethanolbenzene	169 (58)	$C_{17}H_{11}Br_2N_3O_3S_2$	38.58 38.36	2.09 2.13	7.94 7.76	30.20 30.47	
8	Dithioxamide * (1 : 2)	dark-brown (11)	ethanolbenzene	290 (50)	$C_{32}H_{18}Br_4N_4O_6S_2$	40.97 40.66	1.93 2.06	5.97 5.79	34.06 34.40	6.82 6.88

* Ratio of monoadduct to acid amide.

filtration. The product was insoluble in all available organic solvents (benzene, ethanol, chloroform and acetic acid) and was only partially soluble in dimethyl sulphoxide. This product was purified by exhaustive boiling with benzene leaving a residual dark brown solid, which was dried and analyzed as **4a**, m.p. >360 °C. Anal. Calc. for $C_{24}H_{18}Br_4N_2O_4$: C, 40.09; H, 2.57; N, 3.98; Br, 44.51. Found: C, 40.1; H, 2.7; N, 4.07; Br, 44.88.

The dark colored mother liquor of the reaction was concentrated and cooled: a light brown product precipitated, which was collected and recrystallized from benzene-petroleum ether (40-60 °C) as reddish brown micro crystals **4b**, m.p. 183 °C (yield 34%). Anal. Calc. for $C_{24}H_{18}Br_4N_2O_4$: C, 40.09; H, 2.57; N, 3.98; Br, 44.51. Found: C, 39.88; H, 2.7; N, 3.92; Br, 44.87.

Reaction of monoadduct 3 with thioamides.

General procedure: The monoadduct **3** (0.57 g, 0.001 mol) was dissolved in (30 mL) of absolute EtOH and treated with 0.001 mol of the appropriate thioamide dissolved in the minimum amount of ethanol (~10 mL). The mixture was gently refluxed on a water bath or a sand bath for varying periods (~9-12 hours), depending on the thioamide used, with the light red colored solution turning to dark red or brown. The reaction was followed using TLC spot tests on small purchased thin layer plates prepared from silica gel, using methanol/petroleum ether (40-60 °C) in 1 : 3 ratio as eluant. The reaction mixture was then concentrated to about one third of its volume and cooled, with light to dark brown crystalline solids precipitating, which were collected by filtration and recrystallized from the appropriate solvents to give **6a-c**. The products obtained and their characteristics are included in Table 2.

Using one mole of dithiooxamide with one mole of **3** gave 4α,8α-dibromo-8-hydroxy-4α,5,8,8α-tetrahydro-4,9-dioxy-5-phenylthioquinolino[2,3-*d*]thiazole-2-carboxamide (**7**) (Table 2).

Using one mole of dithiooxamide with two moles of **3** gave 2,2'-bis(4α,8α-dibromo-8-hydroxy-4α,5,9,8α-tetrahydro-5-phenylquinolino[2,3-*d*]thiazole-4,9-dione) (**8**) (Table 2).

Preparation of *N*-(3,4α,8α-tribromo-5-hydroxy-4α,5,8,8α-tetrahydro-1,4-dioxo-8-phenyl-2-quinolinylthioacetamide (5a). A mixture of **3** (0.57 g, 0.001 mol) and thioacetamide (0.075 g, 0.001 mol) dissolved in (20 mL) absolute EtOH was refluxed for about one hour, with the reactants going into solution, giving a light brown solution. The latter on dilution with water precipitated off a light greenish brown solid that was recrystallized from ethanol as a yellowish brown micro crystals of **5a**, m.p. 208 °C (yield 78%). Anal. Calc. for $C_{17}H_{13}Br_3N_2O_3S$: C, 36.13; H, 2.31; N, 4.95; Br, 42.42. Found: C, 36.2; H, 2.4; N, 4.9; Br, 42.7; S, 5.8.

Transformation of *N*-(3,4α,8α-tribromo-5-hydroxy-4α,5,8,8α-tetrahydro-1,4-dioxo-8-phenyl-2-quinolinyl)thioacetamide (5a) into the cyclized form (6a). Compound **5a** (0.5 g) in absolute ethanol (30 mL) was refluxed for about 10 hours, and the color changed from light brown to dark reddish brown. Concentration and cooling of the reaction mixture precipitated a deep brown crystalline product that was collected and recrystallized from ethanol as reddish brown crystals of **6a**, m.p. 192 °C (yield 75%). Anal. Calc. for $C_{17}H_{12}Br_2N_2O_3S$: C, 42.21; H, 2.49; N, 5.78; Br, 33.0; S, 6.6. Found: C, 42.17; H, 2.56; N, 5.83; Br, 33.2; S, 6.52.

Reductive acetylation of 4α,8α-dibromo-8-hydroxy-4α,5,8,8α-tetrahydro-2-methyl-5-phenylquinolino[2,3-*d*]-thiazole-4,9-dione (9). Compound **6a** (0.5 g) was dissolved in acetic anhydride (15 mL), giving a deep brownish red solution. To this solution was added 2-3 g of zinc dust (or granules), 3 g of fused sodium acetate and ~3 mL of glacial acetic acid. The mixture was refluxed for ~2 hours. Its color faded gradually to pale yellow. The reaction mixture was then filtered while hot. The filtrate was cooled and diluted with ice cold water and stirred. A yellow to light brown solid separated out, which was filtered, washed with excess water, air dried and recrystallized from EtOH to give **9**, m.p. 103 °C. Anal. Calc. for $C_{23}H_{20}Br_2N_2O_6S$: C, 45.12; H, 3.29; N, 4.57. Found: C, 45.62; H, 3.47; N, 4.2.

Reaction of the monoadduct 3 with acid amides.

Description of general procedure: A mixture of the monoadduct **3** (0.57 g, 0.001 mol) and the appropriate acid amide (0.001 mol) was dissolved in about (30 mL) ethylene glycol, and the solution was refluxed gently for about 2 hours. The dark colored solution was then treated with 2-3

Table 3. Reaction products from monoadduct 3 and amides

Compd.	Thioamide or amide used	Colour (time, h)	Solvent	m.p. °C (% yield)	Formula	Calculated / Found			
						%C	%H	%N	%Br
12a, R=H	Formamide	dark-brown (8)	insoluble	> 360 (80)	$C_{16}H_8N_2O_4$	65.75 65.30	2.75 2.95	9.58 9.46	0.00 0.00
12b, R=CH_3	Acetamide	dark-brown (10)	insoluble	> 360 (51)	$C_{17}H_{10}N_2O_4$	66.66 66.33	3.29 3.46	9.14 9.26	0.00 0.00
12c, R=Ph	Benzamide	light-brown (9)	insoluble	> 360 (55)	$C_{22}H_{12}N_2O_4$	71.63 71.57	3.28 3.50	7.60 7.29	0.00 0.00
12d, R=CH_2Ph	Phenyl acetamide	brown (8)	insoluble	> 360 (53)	$C_{23}H_{14}N_2O_4$	72.24 71.97	3.69 3.39	7.32 7.11	0.00 0.00
12e, R=NH_2	Urea	yellowishbrown (9)	insoluble	> 360 (40)	$C_{16}H_9N_3O_4$	62.54 62.40	5.95 3.05	13.67 13.90	0.00 0.00
13	Succinamide * (1:1)	yellowishbrown (8)	insoluble	> 360 (51)	$C_{19}H_{13}N_3O_5$	62.81 63.00	3.60 3.79	11.56 11.32	0.00 0.00
14	Succinamide * (2:1)	brownishviolet (10)	insoluble	> 360 (52)	$C_{34}H_{18}N_4O_8$	66.80 66.43	2.97 2.83	9.17 9.11	0.00 0.00

*Ratio of monoadduct to acid amide.

mL of 10% aqueous solution of sodium bicarbonate and reflux continued for a further 6-8 hours during which dark fine crystalline solids of the corresponding oxazoloquinolinedione precipitated. These were filtered from the hot reaction mixture, washed with water and finally with ethanol (yield 40-80%). All compounds prepared were characterized by sparing solubility in most organic solvents, hence they were purified by exhaustive extraction of the impurities with suitable organic solvents, leaving analytically pure crystalline solids. Dilution of the mother liquors of the original reaction precipitated light colored products that were filtered off, recrystallized from the appropriate solvent, and identified as *N*-substituted amide derivatives of tetrahydroquinolinedione.

The results obtained from the various acid amides used are listed in Table 3.

Using one mole of succinamide with one mole of **3** gave 8-oxy-5-phenylquinolino[2.3-*d*]oxazole-4.9-dione-2-carbosuccinamide (**13**) (Table 3).

Using one mole of succinamide with two moles of **3** gave 1,2-bis[8-oxy-5-phenylquinolino[2.3-*d*]oxazole-4.9-dione]-ethane (**14**) (Table 3).

Preparation of *N*-(3,4α,8α-tribromo-5-hydroxy-4α,5,8,8α-tetrahydro-1,4-dioxo-8-phenyl-2-quinolinyl)acetamide (11b): A mixture of **3** (0.57 g, 0.001 mol) and acetamide (0.059 g, 0.0011 mol) dissolved in ethylene glycol (30 mL) was refluxed gently for about 30 minutes, with the reactants going into solution, giving a reddish brown liquor. The latter on dilution with water precipitated a light brown solid that was recrystallized from EtOH as brown micro crystals of **11b**, m.p. 320 °C (dec) (yield 83%). Anal. Calc. for $C_{17}H_{13}Br_3N_2O_3$: N, 5.10; Br, 43.66. Found: N, 5.45; Br, 43.4.

Preparation of *N*-(3,4α,8α-tribromo-5-hydroxy-4α,5,8,8α-tetrahydro-1,4-dioxo-8-phenyl-2-quinolinyl)phenyl acetamide (11d): A mixture of **3** (0.57 g, 0.001 mol) and phenyl acetamide (0.135 g, 0.0011 mol), dissolved in about (30 mL) ethylene glycol was refluxed gently for about 30 minutes, and the reactants went into solution, giving a deep reddish brown liquor. Dilution of the reaction mixture with water precipitated a reddish brown solid that was recrystallized from EtOH as light brown micro crystals of **11d**, m.p. 125 °C (yield 76%). Anal. Calc. for $C_{23}H_{17}Br_3N_2O_4$: C, 44.19; H, 2.74; N, 4.48; Br, 38.34. Found: C, 44.03; H, 2.4; N, 4.23; Br, 37.91.

Transformation of 11b into 12b. Compound **11b** (0.5 g) was dissolved in about 30 mL of ethylene glycol and the solution treated with 3 mL of 10% aqueous sodium bicarbonate. The reaction mixture was refluxed for about 8 hours, and a dark brown solid precipitated completely. The product was collected and washed with water then with hot ethanol and air dried. The compound was identified as 2-methyl-8-oxy-5-phenylquinolino[2.3-*d*]oxazole-4.9-dione, m.p. >360 °C (yield 64%).

Antimicrobial Screening. Bacterial species were firstly grown for 24 hours on nutrient broth of the following composition: peptone (10 g), beef extract (3 g), NaCl (5 g) and 1 liter distilled water. Then 1 mL of the broth culture was placed in a sterile plate; next, 10 mL of nutrient agar medium was poured just before solidification and mixed thoroughly with bacterial inoculum. After solidification of the media in plates, filter paper discs (Whatman No. 3) of 5 mm diameter, which were previously immersed in a solution of the tested chemical compounds, were placed on the surface of the agar medium. Plates were incubated at 37 °C for 24 hours and the clear zones around the discs were measured.

Solvent of samples : ethylene glycol
Concentration : 100 μg/disc
Standard antibiotic (disc) : garamycin
Incubation time : 24 hours
Agar medium : nutrient agar
Bacterial strains used : *Staphylococcus aureus*, *Staphylococcus albus*, *Salmonella* and *Klebsiella*

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