Interaction of quinone diimides of the 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide series with sodium *p*-toluenesulfinate in acetic acid and hydrogen chloride

Anatoliy V. Vakulenko*[a] and Kostyantyn S. Burmistrov[b]

[a] Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, FL 32611-7200

[b] *Ukrainian State University of Chemical Technology, Boulevard Gagarina 8, Dnepropetrovsk, 49005 Ukraine*

E-mail: anatoliy@ufl.edu

(received 28 Oct 05; accepted 16 Dec 05; published on the web 25 Dec 05)

Abstract

Treatment of quinone diimides of the 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide series with sodium *p*-toluenesulfinate in acetic acid and hydrogen chloride affords addition products in moderate to good yields. The chloride anion regioselectively attacks position 1 of the unsubstituted quinone diimide ring and the *p*-toluenesulfonyl group enters positions 1 and 4 giving a mixture of two isomers in 5 and 42% yield, respectively. The hydrochlorination of a quinone diimide, where positions 1 and 4 are blocked, proceeds at position 2 with *1*,*4*-orientation (for designation of addition orientation see numbering in italic description at structure **2** as shown in Scheme 1). The same addition reaction using sodium *p*-toluenesulfinate, however, gives the benzene sulfinic acid adduct with *6*,*1*-orientation.

Keywords: Heterocyclic quinone diimides, 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide, sodium *p*-toluenesulfinate, hydrogen chloride

Introduction

Benzoquinone imides are a well-known class of organic compounds with a multiplicity of useful properties. They are specific analytical reagents,[1] selective dehydrogenation agents,[2] rubber additives,[3] pesticides,[4] drugs[5] and useful reagents for the selective chemical cleavage of proteins.[6] Interest in these compounds has increased during the last 25 years due to the significant biological properties of many naturally occurring heterocyclic quinone imides isolated from marine sponges, tunicates, and mollusks.[7-9]

The regioselective addition of HCl to unsubstituted unsymmetrical benzoquinone diimines was first reported by Adams, who observed that *1*,*4*-addition of chloride anion occurs at the ring

position meta to the most basic nitrogen.[10] Later this rule for the orientation of the chloride anion was revised to take account of the comparative stability of the isomeric quinonoid intermediates based on the oxidation-reduction potentials of *p*-benzoquinone monoimides with analogous substituents at nitrogen.[11] Addition reactions of benzoquinone diimides with sodium arenesulfinates were also reported[12] but the reactivity of heterocyclic quinone diimides has not been studied thoroughly.[13,14]

Quinone diimides based on the 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide skeleton are heterocyclic analogues of bis-arenesulfonyl *p*-quinone diimides in which direct connection of the substituent at one imide nitrogen of the quinone ring has been realized. Syntheses of the quinone diimide **2** and its derivatives were first reported by our group.[15,16] Later we measured the oxidation-reduction potentials for some derivatives of this class[17] and studied the reactivity of quinone monoimides of the 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide series towards sodium *p*-toluenesulfinate[18,19] and hydrogen chloride.[20]

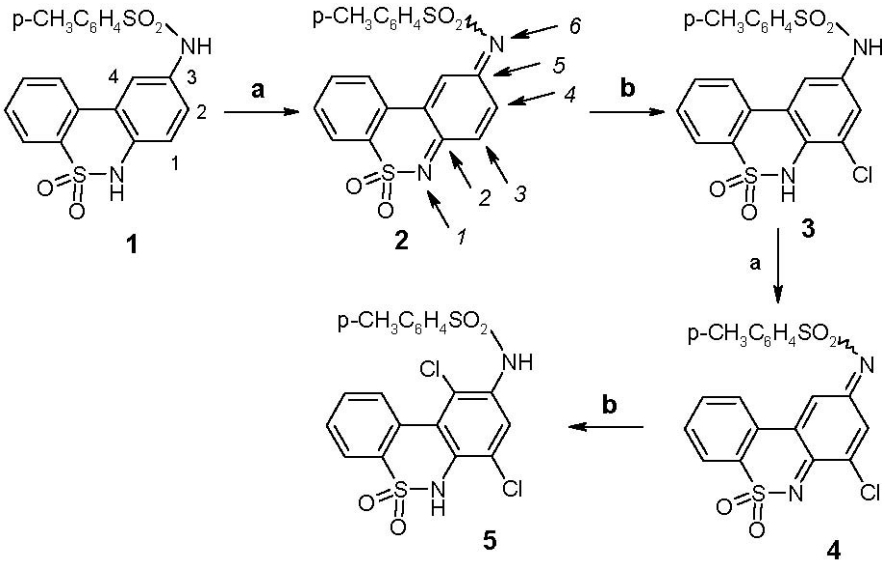
In the present work we have investigated the influence of a substituent in the quinone diimide ring of *N*-[9,9-dioxo-9*H*-9λ^6-thia-10-aza-phenanthren-3-ylidene]-4-methyl-benzenesulfonamides on regioselective addition reactions with sodium *p*-toluenesulfinate and hydrogen chloride.

Results and Discussion

Quinone diimide **2** and its 1-methyl derivative **6** were selected for investigation of the addition reaction. The use of the 4-methylbenzenesulfonyl moiety in quinone diimides **2**, **6** and **14** simplified interpretation of the NMR spectra of reaction products by location of signals of the arenesulfonyl fragments at low field compared to signals for the 1,4-diarenesulfonyl- substituted ring. The choice of sodium *p*-toluenesulfinate and hydrogen chloride as reagents was made on the basis of the different nucleophilicity of the respective anions which results in a change of position for the addition reaction.[21,22]

Intermediate quinone diimides were obtained by oxidation of the corresponding adducts with lead tetraacetate in acetic acid.[15] The structures of the addition products were determined by NMR and confirmed by CHN analysis. The IR spectra of adducts **1, 3, 5, 7, 8, 11-13, 16-19** contain bands for the NH group at 3165-3310 $cm^{-1}$and for the SO_2 group at 1155-1185 cm^{-1} and 1315-1335 cm^{-1}. The IR spectra of quinone diimides **2, 4, 6, 9-10, 14-15** do not show absorption bands for NH bonds but absorptions in the regions of 1150-1175, 1310-1340 and 1555-1575 cm^{-1} are visible, characteristic of SO_2 and C=N bonds in *N*-arenesulfonyl subtituted quinone imides.

Addition of hydrogen chloride. The reaction of quinone diimides with hydrogen chloride was carried out by bubbling dry HCl through a solution of the starting material in a solvent mixture of benzene and acetone (50/50). Addition of the first chloride anion to the unsubstituted quinone ring of **2** proceeds regioselectively at position 1 as indicated by the ^{1}H NMR spectrum of **3**, which contains two doublets with J = 2.7 Hz, characteristic of 1,3 protons in an aromatic ring (Scheme 1).

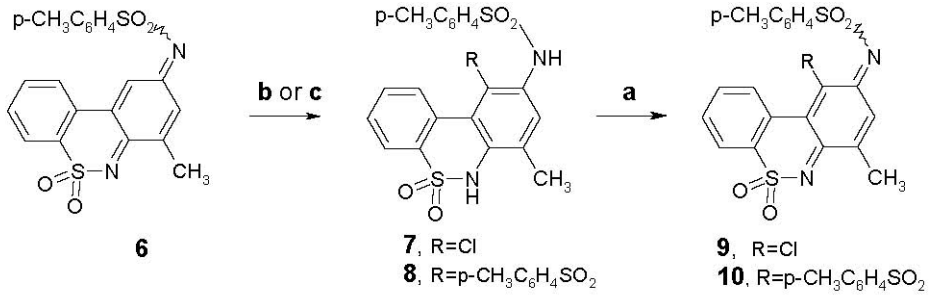


a, $Pb(OAc)_4$, AcOH, 50-60 °C, 1 h; **b**, HCl, benzene-acetone, 25 °C, 1-3 h

Scheme 1

Hydrochlorination of 1-chloro- substituted quinone diimide **4**, obtained by oxidation of intermediate **3** with lead tetraacetate, forms analogue **5** with the second chloride at position 4 (Scheme 1). The structure of **5** was also confirmed by comparison of its ^{1}H NMR spectrum with those of compounds **1** and **3**. The characteristic multiplets for the ABX aromatic system of **1** allowed assignment of the chemical shifts for H-1, H-2 and H-4 protons respectively as follows: 7.09 (d, J = 8.4 Hz, H-1), 7.18 (dd, J = 8.4, 2.4 Hz, H-2), 7.80 (d, J = 2.4 Hz, H-4). Further comparative analysis of the ^{1}H NMR spectrum of **1** and **3** shows that introduction of chlorine at position 1 of the 1,4-diarenesulfonylamido- substituted ring lowers the chemical shift of proton 2 by 0.12 ppm. The chemical shift for H-2 of **5** was also shifted to lower field by 0.16 ppm [7.46 (s, H-2)], which confirms structure **5**.

Hydrochlorination of the 1-methyl substituted quinone diimide **6** provided further proof for the position of chlorination since sulfonamide **7** was formed followed by oxidation to the diimide **9** in which ^4J between the protons of the C-1 methyl group and H-2 was 1.8 Hz. This confirms that chlorination occurred at C-4 of the quinone moiety (Scheme 2).



6

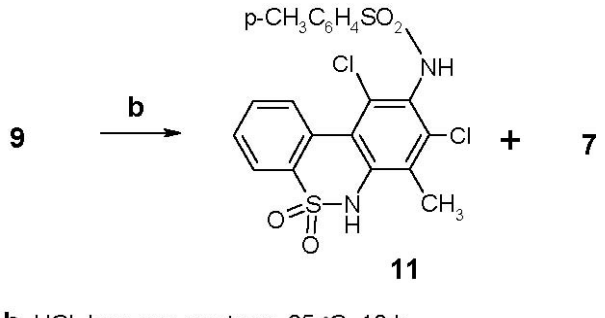
7, R=Cl
8, R=p-$CH_3C_6H_4SO_2$

9, R=Cl
10, R=p-$CH_3C_6H_4SO_2$

a, $Pb(OAc)_4$, AcOH, 50-60 °C, 1 h; **b**, HCl, benzene-acetone, 25 °C, 1-3 h; **c**, p-$CH_3C_6H_4SO_2Na$, AcOH, 25 °C, 14 h.

Scheme 2

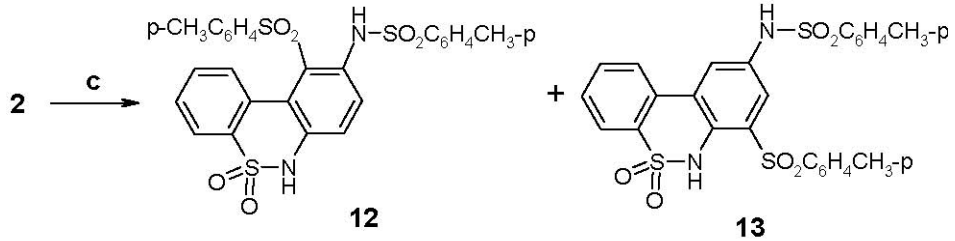
Chlorination at C-2 is also observed when the positions 1 and 4 of the quinone diimide ring are blocked. Thus, sulfonamide **9** reacts slowly with hydrogen chloride to give **7** (35%) and 2,4-dichlorobenzenesulfonamide **11** (51%) (Scheme 3).



b, HCl, benzene-acetone, 25 °C, 10 h

Scheme 3

Addition of sodium *p*-toluenesulfinate. Reaction of quinone diimides with sodium *p*-toluenesulfinate was carried out in glacial acetic acid at room temperature over 14 h. In the case of quinone diimide **2**, the *p*-toluenesulfonyl group enters positions 1 and 4, giving a mixture of isomers in 5% and 42% yields respectively (Scheme 4). The structures of **12** and **13** were confirmed by ^{1}H NMR, in which the protons of the 1,4-diarenesulfonylamido- substituted ring appear as two doublets with J = 9.0 Hz for **12** together with two doublets (J = 2.7 Hz) for **13**.



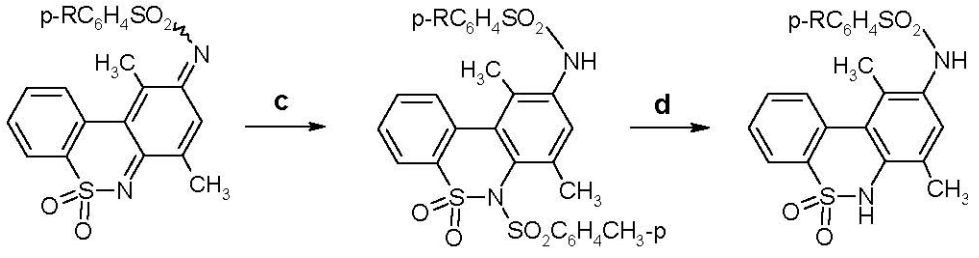
c, p-$CH_3C_6H_4SO_2Na$, AcOH, 25°C, 14 h

Scheme 4

Regioselective introduction of the *p*-toluenesulfonyl group into position 4 was successful for the quinone diimide **6** with position 1 blocked. The choice of a methyl group as the blocking substituent allowed significant simplification and hence confirmation of structures **8** and **10** (Scheme 2).

In contrast to the reaction of hydrogen chloride with **9**, the addition of sodium *p*-toluenesulfinate to compounds **14** and **15** occurred at the endocyclic nitrogen giving *6,1*-addition products **16** (82%) and **17** (60%) whose structures were determined by comparison of the chemical shifts of the aryl hydrogens of the *p*-toluenesulfonyl group attached to endo- and exocyclic nitrogen (Scheme 5). Thus the aryl hydrogens of the *p*-toluenesulfonyl group attached

to the exocyclic nitrogen were observed at 7.34 and 7.57 ppm identical to that of an authentic sample of **18**.[17] The chemical shifts of this moiety in the spectrum of **16** are almost the same at 7.43 and 7.71 ppm. However the presence of an additional AA′BB′ spin system at 7.01 and 7.18 ppm confirms the position of the second *p*-toluenesulfonyl group.



14 R=CH_3
15 R=Cl

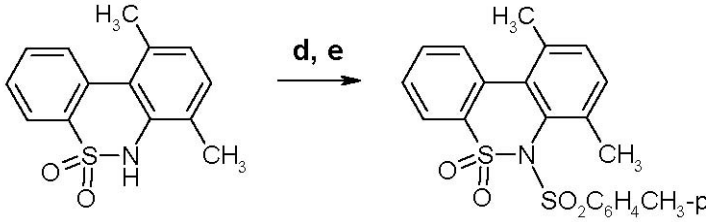
16, R=CH_3
17, R=Cl

18, R=CH_3
19, R=Cl

c, p-$CH_3C_6H_4SO_2Na$, AcOH, 25 °C, 14 h; **d**, aq. NaOH, reflux, 2 h

Scheme 5

In order to afford further structural evidence, sulfonamide **21** with a *p*-toluenesulfonyl group attached to the endocyclic nitrogen atom was synthesized as shown in Scheme 6. The location of signals of the AA′BB′ spin system of **21** at 7.02 and 7.22 ppm is in agreement with our previous observations. Furthermore, the base-catalyzed hydrolysis of sulfonamide **17** with two different arenesulfonyl substituents at the nitrogen atoms led to benzenesulfonamide **19** rather than to a mixture of the two possible 9-arenesulfonylamido derivatives **18** and **19** (Scheme 5). This result also confirms the *6,1*-addition of *p*-toluenesulfinate at endocyclic nitrogen.



20 **21**

d, aq. NaOH, 25 °C, 0.5 h; **e**, p-$CH_3C_6H_4SO_2Cl$, DMF, 25 °C, 24 h.

Scheme 6

In summary, we have investigated the addition reactions of heterocyclic quinone diimides of the 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide series with sodium *p*-toluenesulfinate in acetic acid and hydrogen chloride and have concluded that the products depend on the nucleophilic properties of the reagent. Furthermore, the reactivity of the heterocyclic quinone diimides is not

analogous to the corresponding reaction in the acyclic arenesulfonamide series.

Experimental Section

General Procedures. Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were recorded on a Varian VXR-300 spectrometer in $CDCl_3$ (for **2**, **4**, **6**, **9**, **10**, **14**, **15**) or DMSO-D_6 (for **1**, **3**, **5**, **7**, **8, 11-13**, **16-21**) with TMS as the internal standard for ^1H (300 MHz). Infrared spectra were recorded on a Specord 75IR spectrophotometer. Samples were analyzed as KBr discs. MS spectra were recorded on a Finnigan Mat.Incos-50 spectrometer. Micro elemental analyses were performed on a Carlo Erba EA-1108 elemental analyzer.

Materials. Following compounds were synthesized according to the previously published procedures:[15,17] **(2) -** (84%), mp 215-217 °C (lit.[15] mp 215-217 °C); **(4)** - (79%), mp 211-212 °C (lit.[17] mp 211-212 °C); **(6)** - (85%), mp 200-202 °C (lit.[17] mp 200-202 °C; **(14)** - (96 %), mp 224–226 °C (lit.[17] mp 224-226 °C); **(20)** - (51 %), mp 210-212 (lit.[17] mp 210-212 °C).

***N*-(9,9-Dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-4-methyl-benzenesulfonamide (1).** White microcrystals from 2-propanol (86 %), mp 199–200 °C; ^1H NMR δ 11.24 (br s, 1H), 10.28 (br s, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.84 (t, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, H-1), 7.18 (dd, *J* = 8.4, 2.4 Hz, H-2), 7.80 (d, *J* = 2.4 Hz, H-4), 2.32 (s, 3H); IR, ν, cm^{-1}: 3213 (NH), 1323, 1160 (SO_2); m/z 400; Anal. Calcd for $C_{19}H_{16}N_2O_4S_2$: C, 56.98; H, 4.03; N, 6.99. Found: C, 56.72; H, 4.14; N, 6.58.

***N*-[4-Chloro-1-methyl-9,9-dioxo-9*H*-9λ^6-thia-10-aza-phenanthren-3-ylidene]-4-methyl-benzenesulfonamide (9).** Orange needles from benzene (82 %), mp 164–166 °C (dec.); ^{1}NMR δ 8.42–8.36 (m, 1H), 8.19–8.13 (m, 1H), 8.00 (d, *J* = 1.8 Hz, H-2), 7.74–7.69 (m, 2H), 7.94 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 2.48 (s, 3H), 2.37 (d, *J* = 1.8 Hz, 3H); IR, ν, cm^{-1}: 1575 (C=N), 1337, 1175, 1154 (SO_2); Anal. Calcd for $C_{20}H_{15}ClN_2O_4S_2$: C, 53.75; H, 3.38; N, 6.27. Found: C, 53.56; H, 3.12; N, 6.09.

4-Methyl-*N*-[1-methyl-9,9-dioxo-4-(toluene-4-sulfonyl)-9*H*-9λ^6-thia-10-aza-phenanthren-3-ylidene]-benzenesulfonamide (10). Orange microcrystals from benzene (64 %), mp 209–210 °C (dec.); ^{1}NMR δ 8.17 (d, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.76 (d, *J* = 1.8 Hz, H-2), 7.21 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 2.57 (s, 3H), 2.33 (s, 3H), 2.30 (d, *J* = 1.8 Hz, 3H); IR, ν, cm^{-1}: 1570, 1555 (C=N), 1340, 1324, 1172, 1153 (SO_2); Anal. Calcd for $C_{27}H_{22}N_2O_6S_3$: C, 57.23; H, 3.91; N, 4.94. Found: C, 57.56; H, 3.66; N, 5.10.

4-Chloro-*N*-[1,4-dimethyl-9,9-dioxo-9*H*-9λ6-thia-10–aza-phenanthren-3-ylidene] benzenesulfonamide (15). Orange microcrystals from benzene (84 %), mp 175–177 °C (dec.);

^{1}NMR δ 8.25–8.13 (m, 4H); 7.96-7.91 (m, 1H); 7.81-7.76 (m, 1H); 7.54 (d, *J* = 8.4 Hz, 2H); 7.44 (d, *J* = 1.8 Hz, 1H); 2.28 (d, *J* = 1.8 Hz, 3H); 2.11 (s, 3H); Anal. Calcd for $C_{20}H_{15}ClN_2O_4S_2$: C, 53.75; H, 3.38; N, 6.27. Found: C, 53.83; H, 3.66; N, 5.89.

1,4-Dimethyl-10-(toluene-4-sulfonyl)-10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide (21). 10*H*-9-thia-10-aza-phenanthrene 9,9-dioxide (**20**) (2.77 g, 10.7 mmol) was added to solution of sodium hydroxide (0.4 g, 10 mmol) at room temperature and the suspension was stirred for 0.5 h. The reaction mixture was filtered and the water was evaporated under reduced pressure. The residue was dried under vacuum for 12 h and then was dissolved in DMF (25 mL). *p*-Toluenesulfonyl chloride (2.1 g, 11 mmol) was added to resultant solution at room temperature and the mixture was stirred for 24 h. Then water (75 mL) was added to reaction mixture. The precipitated solid was collected by filtration and recrystallized from acetic acid to give the addition product as white prisms (3 g, 69 %), mp 190-192; ^{1}NMR δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 2.53 (s, 3H), 2.52 (s, 3H), 2.29 (s, 3H); IR, ν, cm^{-1}: 1390, 1378, 1198, 1175 (SO_2); m/z=413; Anal. Calcd for $C_{21}H_{19}NO_4S_2$: C, 61.00; H, 4.63; N, 3.39. Found: C, 61.22; H, 4.67; N, 3.23.

General procedure for the addition of hydrogen chloride to the quinone diimides (2, 4, 6, 9)

Dry hydrogen chloride was bubbled into the solution of quinone diimine (2 mmol) in a mixture of benzene (20 mL) and acetone (20 mL) at room temperature during which time the reaction mixture becomes colorless. The solvent was evaporated under reduced pressure and the residue was recrystallized from acetic acid to give corresponding addition product.

***N*-(1-Chloro-9,9-dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-4-methyl-benzenesulfonamide (3).** White microcrystals from acetic acid (70 %), mp 210–212 °C (lit.[17] mp 209–211 °C); ^{1}NMR δ 10.85 (br s, 1H), 10.62 (br s, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.87 (t, *J* = 7.8 Hz, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 2.7 Hz, H-4), 7.30 (d, *J* = 2.7 Hz, H-2), 2.33 (s, 3H); IR, ν, cm^{-1}: 3295, 3235 (NH), 1315, 1160 (SO_2); Anal. Calcd for $C_{19}H_{15}ClN_2O_4S_2$: C, 52.47; H, 3.48; N, 6.44. Found: C, 52.58; H, 3.14; N, 6.35.

***N*-(1,4-Dichloro-9,9-dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-4-methyl-benzenesulfonamide (5).** White microcrystals from acetic acid (54 %), mp 240–242 °C; ^{1}NMR δ 8.26–8.20 (m, 1H), 8.00–7.94 (m, 1H), 7.84–7.70 (m, 2H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.46 (s, H-2), 7.39 (d, *J* = 7.8 Hz, 2H), 2.38 (s, 3H); IR, ν, cm^{-1}: 3295, 3235 (NH), 1315, 1160 (SO_2); Anal. Calcd for $C_{19}H_{14}Cl_2N_2O_4S_2$: C, 48.62; H, 3.01; N, 5.97. Found: C, 48.51; H, 3.18; N, 6.02.

***N*-(4-Chloro-1-methyl-9,9-dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-4-methyl-benzenesulfonamide (7).** White powder from acetic acid (61 %), mp 262–264 °C; ^{1}NMR δ 10.75 (br s, 1H), 10.05 (br s, 1H), 8.17 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 1H), 7.75 (t, *J* = 7.2 Hz, 1H), 7.70 (t, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.27 (s, H-2), 2.38 (s, 3H), 2.28 (s, 3H); IR, ν, cm^{-1}: 3270, 3222 (NH), 1336, 1182, 1160 (SO_2); m/z 448; Anal. Calcd for $C_{20}H_{17}ClN_2O_4S_2$: C, 53.51; H, 3.82; N, 6.24. Found: C, 53.58; H, 3.56; N, 6.32.

***N*-(2,4-Dichloro-1-methyl-9,9-dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-4-methyl-benzenesulfonamide (11).** White microcrystals from acetic acid (51 %), mp 214–215 ^{o}C (dec.); ^{1}NMR δ 11.16 (br s, 1H), 10.21 (br s, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.83–7.72 (m, 2H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H); IR, ν, cm^{-1}: 3240, 3165 (NH), 1325, 1172, 1155 (SO_2); Anal. Calcd for $C_{20}H_{16}Cl_2N_2O_4S_2$: C, 49.69; H, 3.34; N, 5.80. Found: C, 49.58; H, 3.56; N, 5.47.

General procedure for the addition of sodium *p*-toluenesulfinate to the quinone diimides (2, 6, 14, 15)

Sodium *p*-toluenesulfinate (1.7 mmol) was added to the suspension of quinone diimides (1 mmol) in acetic acid (5 mL) at room temperature. The mixture was stirred overnight. Then water (20 mL) was added to reaction mixture. The precipitated solid was collected by filtration and recrystallized from acetic acid to give the corresponding addition product.

4-Methyl-*N*-[1-methyl-9,9-dioxo-4-(toluene-4-sulfonyl)-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl]-benzenesulfonamide (8). White powder from acetic acid (93 %), mp 199–201 ^{o}C; ^{1}NMR δ 11.62 (br s, 1H), 9.76 (br s, 1H), 8.16-8.08 (m, 2H), 7.89-7.80 (m, 2H), 7.34 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.31-7.25 (m, 4H), 2.41 (s, 3H), 2.36 (s, 3H), 2.29 (s, 3H); IR, ν, cm^{-1}: 3267 (NH), 1330, 1185, 1165 (SO_2); m/z 568; Anal. Calcd for $C_{27}H_{24}N_2O_6S_3$: C, 57.03; H, 4.25; N, 4.93. Found: C, 56.81; H, 4.06; N, 4.78.

***N*-[9,9-Dioxo-4-(toluene-4-sulfonyl)-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl]-4-methyl-benzenesulfonamide (12).** White microcrystals from acetic acid (42 %), mp 152–154 ^{o}C (dec.); ^{1}NMR δ 11.73 (br s, 1H), 9.59 (br s, 1H), 7.95–7.87 (m, 2H), 7.79–7.70 (m, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.33–7.30 (m, 3H), 7.25 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 9 Hz, 1H), 2.38 (s, 3H), 2.33 (s, 3H); IR, ν, cm^{-1}: 3310, 3245 (NH), 1330, 1177, 1163 (SO_2); Anal. Calcd for $C_{26}H_{22}N_2O_6S_3$: C, 56.30; H, 4.00; N, 5.05. Found: C, 56.01; H, 4.06; N, 4.99.

***N*-[9,9-Dioxo-1-(toluene-4-sulfonyl)-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl]-4-methyl-benzenesulfonamide (13).** White microcrystals from acetic acid (5 %), mp 193–195 ^{o}C; ^{1}NMR δ 11.21 (br s, 1H), 9.39 (br s, 1H), 8.03 (d, *J* = 2.7 Hz, 1H), 7.92 (d, *J* = 2.7 Hz, 1H), 7.89–7.81 (m, 3H), 7.75–7.68 (m, 5H), 7.41–7.22 (m, 4H), 2.39 (s, 3H), 2.37 (s, 3H); IR, ν, cm^{-1}: 3310, 3240 (NH), 1330, 1170 (SO_2); Anal. Calcd for $C_{26}H_{22}N_2O_6S_3$: C, 56.30; H, 4.00; N, 5.05. Found: C, 56.12; H, 3.86; N, 4.86.

***N*-[1,4-Dimethyl-9,9-dioxo-10-(toluene-4-sulfonyl)-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl]-4-methyl-benzenesulfonamide (16).**White microcrystals from acetic acid (82 %), mp 223–225 ^{o}C; ^{1}NMR δ 9.97 (br s, 1H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.13 (s, H-2), 7.01 (d, *J* = 8.4 Hz, 2H), 2.42 (s, 3H), 2.40 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H); IR, ν, cm^{-1}: 3252 (NH), 1380, 1365, 1190, 1170 (SO_2); Anal. Calcd for $C_{28}H_{26}N_2O_6S_3$: C, 57.71; H, 4.50; N, 4.81. Found: C, 57.60; H, 4.36; N, 4.85.

4-Chloro-*N*-[1,4-dimethyl-9,9-dioxo-10-(toluene-4-sulfonyl)-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl]-benzenesulfonamide (17).White microcrystals from acetic acid (60 %), mp

234–236 °C (dec.); ^{1}NMR δ 10.15 (br s, 1H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 2H), 7.12 (s, H-2), 7.02 (d, *J* = 8.7 Hz, 2H), 2.43 (s, 3H), 2.29 (s, 3H), 2.23 (s, 3H); IR, ν, cm^{-1}: 3290 (NH), 1365, 1345, 1170, 1150 (SO_2); Anal. Calcd for $C_{27}H_{23}ClN_2O_6S_3$: C, 53.77; H, 3.84; N, 4.64. Found: C, 53.60; H, 3.67; N, 4.23.

Hydrolysis of compounds (16 and 17) with sodium hydroxide. A suspension of compound (**16** or **17**) (0.5 mmol) in a solution of sodium hydroxide (2 w/w %, 20 mL) was refluxed for 2 h. The reaction mixture was filtered, and the filtrate was acidified with hydrochloric acid (5 w/w %). The precipitated solid was collected by filtration, washed with water and recrystallized from acetic acid to give corresponding hydrolysis product **18** or **19**.

***N*-(1,4-Dimethyl-9,9-dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-4-methyl-benzenesulfonamide (18).** White microcrystals from acetic acid (67 %), mp 266–267 °C (lit.[17] mp 266-267 °C); ^{1}NMR δ 10.31 (br s, 1H), 9.63 (br s, 1H), 7.89-7.59 (m, 4H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 6.84 (s, 1H), 2.35 (s, 3H), 2.28 (s, 3H), 2.15 (s, 3H); Anal. Calcd for $C_{21}H_{20}N_2O_4S_2$: C, 58.86; H, 4.70; N, 6.54. Found: C, 58.60; H, 4.67; N, 6.29.

4-Chloro-*N*-(1,4-dimethyl-9,9-dioxo-9,10-dihydro-9λ^6-thia-10-aza-phenanthren-3-yl)-benzenesulfonamide (19). White microcrystals from acetic acid (62 %), mp 260–262 °C; ^{1}NMR δ 10.35 (br s, 1H), 9.84 (br s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.75-7.63 (m, 3H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 6.84 (s, 1H), 2.37 (s, 3H), 2.19 (s, 3H); Anal. Calcd for $C_{20}H_{17}ClN_2O_4S_2$: C, 53.51; H, 3.82; N, 6.24. Found: C, 53.68; H, 3.67; N, 5.99.

Acknowledgments

The authors are indebted to Dr. Dennis Hall (University of Florida) for help and useful discussions during the preparation of this manuscript.

References

1. Titov, E. A.; Avdeenko, A. P.; Rudchenko, V. F.; Velichko, V. V. USSR Pat. 428274, 1974; *Chem. Abstr*. **1975**, *82*, 25465.
2. Sheikman, A. K.; Chmilenko, T. S.; Vdovlina, G. G.; Chernishov, A. I. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1985**, 671.
3. Titov, E. A.; Kalinichenko, V. H.; Grischenko, A. S., Blokh, G. A. *Voprosi Khim. Khim. Tekhnol*. *(Russ. Ed.)* **1952**, 30.
4. Petersen, S.; Gauss, W.; Urbschaft, E. *Angew. Chem.* **1955**, *67*, 217.
5. Blower, P. E.; Yang, C.; Fligner, M. A.; Verducci, J. S.; Yu, L.; Richman, S.; Weinstein, J. N. *The Pharmacogenomics J.* **2002**, 259.

6. Holmes, T. J.; Lawton, R. G. *J. Org. Chem.* **1983**, *48*, 3146.
7. Molinski, T. F. *Chem. Rev.* **1993**, *93*, 1825.
8. Gupta, S. P. *Chem. Rev.* **1994**, *94*, 1507.
9. Aubart, K. M.; Heathcock, C. H. *J. Org. Chem.* **1999**, *64*, 16.
10. Adams, R.; Reifschneider, W. *Bull. Soc. Chim. Fr.* **1958**, 23.
11. Burmistrov, K. S.; Yurchenko, A. G. *Rus. J. Org. Chem. (Engl. Transl.)* **1990**, *26*, 1722.
12. Adams, R.; Nair, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 177.
13. Zjawiony, J. K.; Srivastava, A. R.; Hufford, C. D.; Clark, A. M. *Heterocycles* **1994**, *39*, 779.
14. Koller, A.; Rudi, A.; Gravalos, M. G.; Kashman, Y. *Molecules*, **2001**, *6*, 300.
15. Burmistrov, K. S.; Burmistrov, S. I.; Malinovski, M. S. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1977**, *13*, 1201.
16. Burmistrov, K. S.; Vakulenko, A. V.; Burmistrov, S. I. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1985**, 282.
17. Vakulenko, A. V.; Dunovsky, S. A.; Burmistrov, S. I; Burmistrov, K. S. *Ukr. Khim. Zn. (Russ. Ed.)* **1987,** *53*, 1203; *Chem. Abstr*. **1988**, *109*, 230914.
18. Burmistrov, K. S.; Vakulenko, A. V.; Starovoytova, V. I. *Voprosi Khim. Khim. Tekhnol. (Russ. Ed.)* **2000**, 11.
19. Burmistrov, K. S.; Toropin, N. V.; Vakulenko, A. V.; Yurchenko, A. G.; Markov, V. I. *Voprosi Khim. Khim. Tekhnol. (Russ. Ed.)* **2000,** 30.
20. Avdeenko, A. P.; Konovalova, S. A.; Burmistrov, K. S.; Toropin, N. V.; Vakulenko, A. V. *Rus. J. Org. Chem. (Engl. Transl.)* **2004**, *40*, 962.
21. Adams, R.; Looker, J. H. *Am. Chem. Soc.* **1951**, *73*, 1145.
22. Adams, R.; Whitaker, L. *Am. Chem. Soc.* **1956**, *78*, 658.