Synthesis of linear and angular anthraquinonoisothiazol-3-ones, their *S*-oxides, and *S*,*S*-dioxides

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2-Methyltetrahydroanthra[2,3-*d*]isothiazole-3,5,10-trione and 2-R-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-triones were synthesized by the reactions of 3-chloro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide and 1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide with alkanethiols followed by cyclization of the resulting alkylthioamides into isothiazolones under the action of SO_2Cl_2. The products were oxidized to give the corresponding *S*-oxides and *S*,*S*-dioxides.

Key words: 2-methyl-2,3,5,10-tetrahydroanthra[2,3-*d*]isothiazole-3,5,10-trione, 2-methyl-2,3,5,10-tetrahydroanthra[2,3-*d*]isothiazole-3,5,10-trione 1,1-dioxide, 2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-triones, 2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione 1-oxides.

It is known that many compounds containing an anthraquinone fragment possess antitumor activity. Among them are natural anthraquinone antibiotics, namely, anthracyclines[1,2] and some of their synthetic analogs.[3,4] Antitumor properties are also exhibited by some anthraquinones fused with thiazole.[5]

Unlike the synthesis of dioxoanthrathiazoles, which can be prepared by simple and well studied methods,[6—11] approaches to the synthesis of their isomers, dioxoanthraisothiazoles and -isothiazolones, are virtually lacking. Only one compound of this series has been synthesized.[12] Because annelated isothiazoles possess bactericidal activities,[13—16] it can be expected that a molecule combining the anthraquinone and isothiazole (isothiazolone) fragments will have new useful properties.

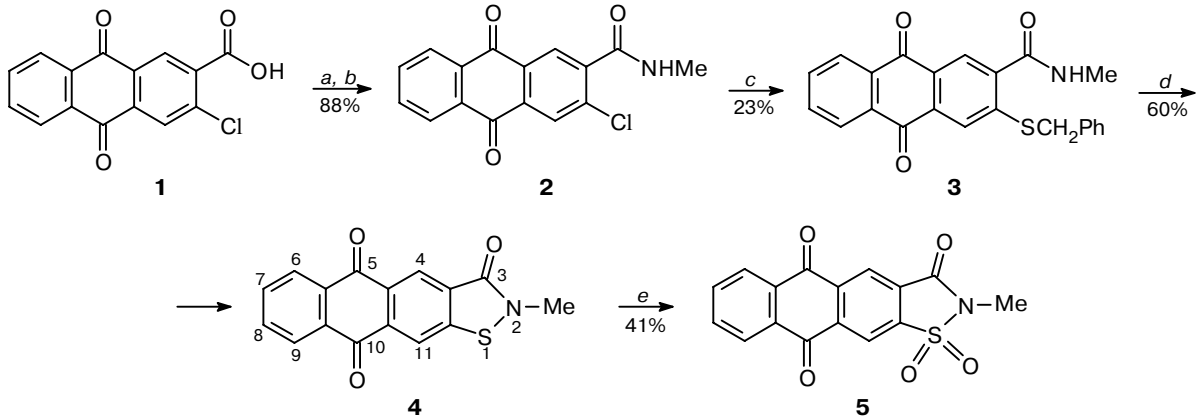
The goal of our work was to develop general approaches to the synthesis of trioxoanthraisothiazoles with linearly and angularly fused carbo- and heterocycles and study their chemical transformations.

These approaches were based on the substitution of the $PhCH_2S$ group for the nitro group in *ortho*-nitroarenecarboxamides[17] followed by heterocyclization under the action of a chlorinating agent.[18,19] Analogously, the halogen atom in the corresponding amide can be replaced.

Results and Discussion

Linear trioxoanthraisothiazole was synthesized from 3-chloro-9,10-dioxo-9,10-dihydroanthracene-2-carboxy-

Scheme 1



Reagents and conditions: *a*. $SOCl_2$, PhH, refluxing; *b*. $MeNH_2$, PhH/H_2O; *c*. $PhCH_2SH$, K_2CO_3 (1 equiv.), DMF; *d*. SO_2Cl_2, CH_2Cl_2, 20 °C; *e*. H_2O_2 (50%), AcOH.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 1580—1584, September, 2001.

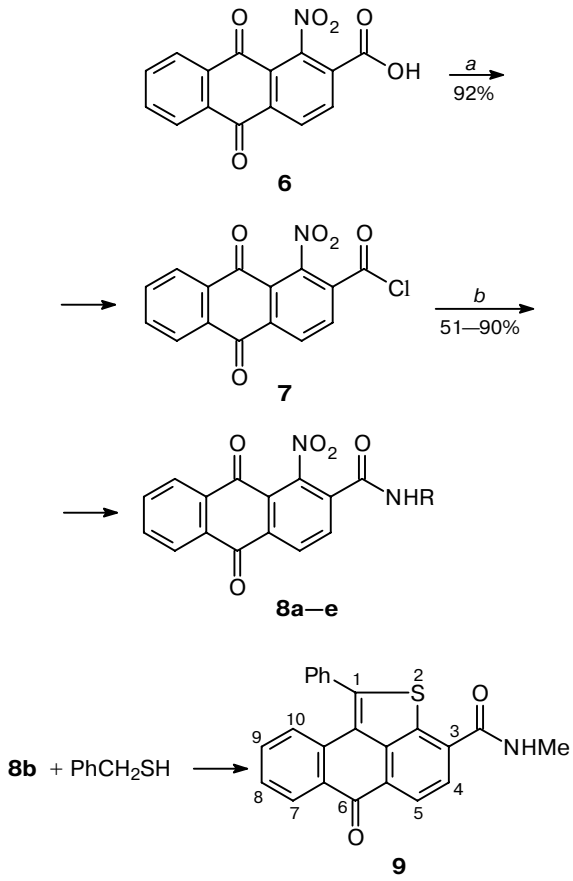
1066-5285/01/5009-1657 $25.00

lic acid[20] (**1**). The starting compound was converted into acid chloride by the reaction with $SOCl_2$ and then into amide (**2**) with aqueous $MeNH_2$, and the Cl atom was replaced by the $PhCH_2S$ group with subsequent cyclization (Scheme 1). The synthesis of benzylthio derivative **3** by this method requires prolonged heating of the reagents; the reaction is accompanied by side processes decreasing the yield of **3** to 23%. Apparently, this is due to a low reactivity of the halogen atom in position 3 of the anthraquinone fragment in S_NAr reactions.

Sulfuryl chloride was used to perform the cyclization of (benzylthio)amide **3** into the target trioxoanthraisothiazole **4**, which was then oxidized to *S*,*S*-dioxide **5** with hydrogen peroxide.

The angular trioxoanthraisothiazoles were synthesized by the treatment of 1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxylic acid[21] (**6**) with $SOCl_2$ followed by the reactions of acid chloride **7** with various amines (Scheme 2). Amide **8b** reacts with $PhCH_2SH$ to

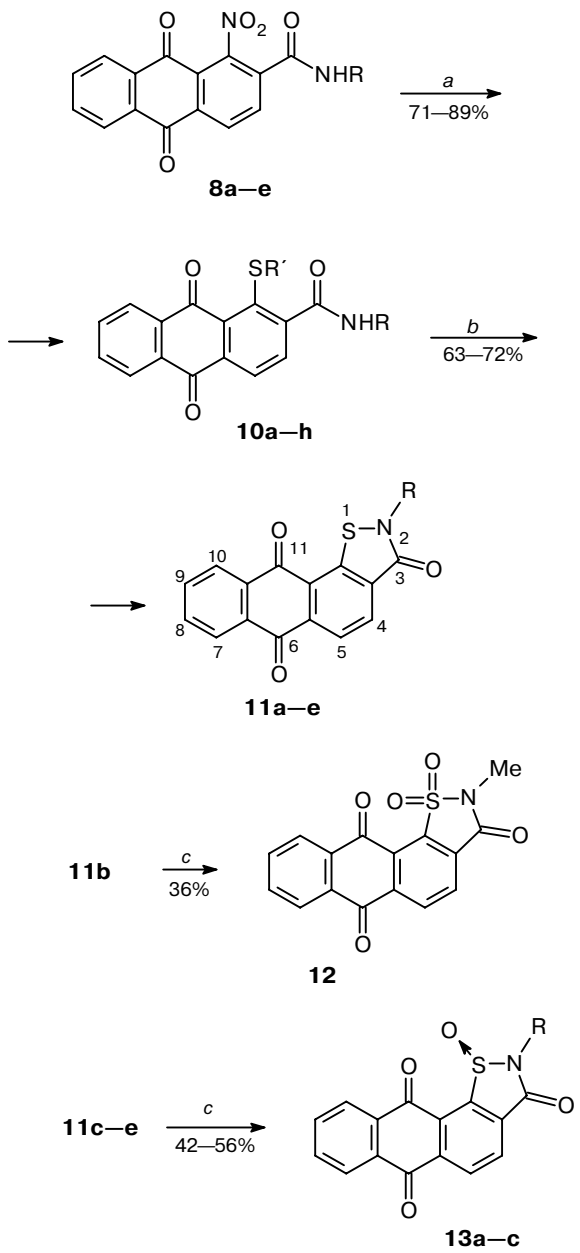
Scheme 2



R = H (**a**), Me (**b**), Ph (**c**), $PhCH_2$ (**d**), CH_2COOMe (**e**)

Reagents and conditions: *a*. $SOCl_2$, PhH, ~80 °C, 3 h; *b*. RNH_2, PhH, 15 °C.

Scheme 3



8, 11: R = H (**a**), Me (**b**), Ph (**c**), CH_2Ph (**d**), CH_2COOMe (**e**)

10	R	R′
a	H	Me
b	Me	Me
c	Ph	Me
d	CH_2Ph	Me
e	H	CH_2Me
f	Ph	CH_2Me
g	CH_2Ph	CH_2Me
h	CH_2COOMe	CH_2Me

Reagents and conditions: *a*. MeSNa (EtSNa), DMF, 20 °C; *b*. SO_2Cl_2, CH_2Cl_2, 20 °C; *c*. H_2O_2/AcOH, 50 °C.

give a complex mixture of products containing compound **9** (^{1}H NMR data).

Product **9** seems to result from an intramolecular condensation of the benzylthio group with the carbonyl group of the anthraquinone system, as it was suggested the transformation of 1-(carboxymethylthio)anthraquinone into a corresponding acid under alkaline conditions.[22,23]

This undesirable reaction did not take place when sodium methanethiolate or ethanethiolate were used instead of α-toluenethiol. Products **10a**—**h** were obtained in high yields (71—89%) (Scheme 3).

Amides **10a**—**h** were converted to the target trioxoanthraisothiazoles **11a**—**e** by the reactions with SO_2Cl_2; their high yields (63—72%) confirm the patent data[18,19] on the capability of *ortho*-(alkylthio)benzamides to undergo cyclization into benzo[*d*]isothiazol-3-one derivatives under the action of halogenating agents.

Trioxoanthraisothiazoles **11** were oxidized with hydrogen peroxide in acetic acid to the corresponding *S*-oxides and *S*,*S*-dioxides. The final oxidation state depends on the substituent R at the N atom. Thus compound **11b** was oxidized to dioxide **12**, while compounds **11c**—**e** afforded *S*-monoxides **13a**—**c**. This difference is probably due to steric hindrances for the approach of a second oxidant molecule to the S atom in compounds with bulky substituents R.

The structures of all new compounds were confirmed by ^{1}H NMR and elemental analysis data. In some cases, mass spectrometry was also used.

It is noteworthy that the diastereotopic methylene protons in *S*-monoxides **13b,c** are nonequivalent and give two doublets in their ^{1}H NMR spectra.

Experimental

^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 MHz) in DMSO-d_6. Chemical shifts were measured with reference to Me_4Si as the internal standard. Mass spectra were recorded on an MS-30 (Kratos) instrument (EI). TLC was carried out on Silpearl UV-250 silica gel.

Solvents were purified by standard methods. 3-Chloro-9,10-dioxo-9,10-dihydroanthracene-2-carboxylic acid[20] (**1**) and 1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxylic acid[21] (**6**) were prepared according to the known procedures.

***N*-Methyl-3-chloro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (2).** A mixture of compound **1** (0.3 g, 1.05 mmol), anhydrous benzene (10 mL), $SOCl_2$ (2 mL), and a catalytic amount of anhydrous DMF was refluxed for 3 h (calcium chloride tube). The resulting acid chloride gradually passed into solution. The solvent was removed *in vacuo*. The residue was dissolved in anhydrous benzene (8 mL), and the resulting solution was slowly added dropwise to a solution of methylamine (10 mL of 5% aqueous solution of CH_3NH_2) with vigorous stirring at 15 °C, the formation of a white precipitate of the amide being observed. The reaction mixture was stirred for 2 h. Then benzene was removed *in vacuo*, and the residue was acidified with HCl. The precipitate was filtered off, washed with water (3×10 mL), and recrystallized from THF—ethanol (2 : 1) to give amide **2**, yield 0.27 g (88%), m.p. 240—245 °C. Found (%): C, 64.21; H, 3.15; Cl, 11.75; N, 4.75 $C_{16}H_{10}ClNO_3$. Calculated (%): C, 64.12; H, 3.36; Cl, 11.83; N, 4.67. ^{1}H NMR, δ: 2.82 (d, 3 H, NMe, J = 3.3 Hz); 7.94—8.02 (m, 2 H, H-6, H-7); 8.15 (s, 1 H, H-1); 8.17 (s, 1 H, H-4); 8.20—8.32 (m, 2 H, H-5, H-8); 8.74 (br.s., 1 H, NH).

***N*-Methyl-3-benzylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (3).** A mixture of amide **2** (0.40 g, 1.34 mmol), anhydrous DMF (4 mL), α-toluenethiol (0.19 mL, 1.60 mmol), and finely ground calcined K_2CO_3 (0.22 g, 1.60 mmol) was stirred in an atmosphere of argon at 40 °C for 16 h. The reaction mixture was poured into 5% HCl (20 mL), and the precipitate that formed was filtered off, washed with water (3×10 mL), and chromatographed on silica gel L (40/100) in toluene and then in toluene—ethyl acetate (2 : 1) to isolate compound **3**. Recrystallization from toluene gave amide **3**, yield 0.12 g (23%), m.p. 226—229 °C. Found (%): C, 71.02; H, 4.11; N, 3.84; S, 8.58 $C_{23}H_{17}NO_3S$. Calculated (%): C, 71.30; H, 4.42; N, 3.62; S, 8.28. ^{1}H NMR, δ: 2.75 (d , 3 H, NMe, J = 3.3 Hz); 4.41 (s, 2 H, SC$\underline{H_2}$Ph); 7.22—7.38 (m, 3 H, (SC$H_2\underline{Ph}$) H_p, H_m); 7.49 (d, 2 H, (SC$H_2\underline{Ph}$) H_o, J = 5.5 Hz); 7.89—7.98 (m, 2 H, H-6, H-7); 8.11 (s, 1 H, H-1); 8.14 (s, 1 H, H-4); 8.16—8.22 (m, 2 H, H-5, H-8), 8.71 (br.s., 1 H, NH).

2-Methyl-2,3,5,10-tetrahydroanthra[2,3-*d*]isothiazole-3,5,10-trione (4). Sulfuryl chloride (0.03 mL, 0.37 mmol) was added with stirring to a solution of benzylthioamide **3** (0.10 g, 0.26 mmol) in 4 mL of anhydrous CH_2Cl_2. The solution was kept at 15 °C for 2 h and concentrated *in vacuo*. The residue was repeatedly washed with hot hexane to give compound **4**, yield 0.046 g (60%), m.p. 215—220 °C. Found (%): C, 65.33; H, 3.24; N, 4.44; S, 10.65 $C_{16}H_9NO_3S$. Calculated (%): C, 65.07; H, 3.07; N, 4.74; S, 10.86. ^{1}H NMR ($CDCl_3$), δ: 3.47 (s, 3 H, NMe); 7.84—7.94 (m, 2 H, H-7, H-8); 8.35—8.44 (m, 2 H, H-6, H-9); 8.85 (s, 1 H, H-4); 8.92 (s, 1 H, H-11).

2-Methyl-2,3,5,10-tetrahydroanthra[2,3-*d*]isothiazole-3,5,10-trione 1,1-dioxide (5). A mixture of isothiazolone **4** (46 mg, 0.16 mmol), AcOH (2.50 mL), and 50% H_2O_2 (0.13 mL) was kept at 50 °C for 14 h. The resulting solution was cooled and concentrated *in vacuo*, and the residue was recrystallized from THF—ethanol (2 : 1) to give dioxide **5**, yield 20 mg (41%), m.p. 305—310 °C. Found (%): C, 58.93; H, 2.55; N, 4.16; S, 9.71 $C_{16}H_9NO_5S$. Calculated (%): C, 58.71; H, 2.77; N, 4.28; S, 9.80. ^{1}H NMR, δ: 3.23 (s, 3 H, NMe); 7.96—8.06 (m, 2 H, H-7, H-8); 8.25—8.33 (m, 2 H, H-6, H-9); 8.64 (s, 1 H, H-4), 9.02 (s, 1 H, H-11).

MS (EI, 70 eV), m/z (I_{rel} (%)): 327 $[M]^+$ (100), 263 (58.3), 235 (19.7), 208 (20.4), 207 (40.9), 206 (37.1), 180 (17.2), 179 (31.1), 178 (49.7), 151 (21.5), 150 (86.6), 149 (18.1).

1-Nitro-9,10-dioxo-9,10-dihydroanthracene-2-carbonyl chloride (7). A mixture of acid **6** (2 g, 6.73 mmol), anhydrous benzene (20 mL), $SOCl_2$ (4 mL), and a catalytic amount of anhydrous DMF was refluxed (calcium chloride tube) for 3 h. The solvent was removed *in vacuo* to give acid chloride **7**, yield 1.95 g (92%), m.p. 243—244 °C (*cf.* Ref. 24: m.p. 243—244 °C).

1-Nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamides (8a—e) (general procedure). A 5% aqueous solution of NH_3 (or amines) (10 mL) was slowly added to a suspension of acid chloride **7** (0.30 g, 0.95 mmol) in 10 mL of benzene. The reaction mixture was vigorously stirred at 15 °C for 2 h. The benzene was removed *in vacuo*, and the residue was acidified with aqueous HCl. The precipitate that formed was filtered off, washed with water (3×10 mL), and recrystallized from THF—DMF (3 : 1) to give amides **8a**—**e**.

The yield of compound **8a** was 0.25 g (90%), m.p. 327—330 °C. Found (%): C, 61.03; H, 2.64; N, 9.67 $C_{15}H_8N_2O_5$. Calculated (%): C, 60.82; H, 2.72; N, 9.46. ^{1}H NMR, δ: 7.93—8.02 (m, 3 H, H-6, H-7, NH_2); 8.11—8.29 (m, 2 H, H-5, H-8); 8.19 (d, 1 H, H-4, J = 9.9 Hz); 8.44 (d, 1 H, H-3); 8.46 (s, 1 H, NH_2).

***N*-Methyl-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (8b).** Yield 85%, m.p. 279—281 °C. Found (%): C, 61.72; H, 3.18; N, 9.32 $C_{16}H_{10}N_2O_5$. Calculated (%): C, 61.94; H, 3.25; N, 9.03. ^{1}H NMR, δ: 2.78 (d, 3 H, NMe, J = 2.75 Hz); 7.90—7.98 (m, 2 H, H-6, H-7); 8.08—8.21 (m, 3 H, H-5, H-8, H-4); 8.43 (d, 1 H, H-3); 8.95 (br.s, 1 H, NH).

1-Nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxanilide (8c). Yield 84%, m.p. 281—283 °C (from THF—ethanol, 2 : 1). Found (%):C, 67.93; H, 3.14; N, 7.36 $C_{21}H_{12}N_2O_5$. Calculated (%): C, 67.74; H, 3.25; N, 7.52. ^{1}H NMR, δ: 7.17 (t, 1 H, (NHPh) H_p, J = 7.33 Hz); 7.40 (t, 2 H, (NHPh) H_m); 7.69 (d, 2 H, (NHPh) H_o); 7.94—8.02 (m, 2 H, H-6, H-7); 8.12—8.27 (m, 2 H, H-5, H-8); 8.37 (d, 1 H, H-4, J = 8.25 Hz); 8.52 (d, 1 H, H-1); 11.03 (s, 1 H, NH).

***N*-Benzyl-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (8d).** Yield 82%, m.p. 262—264 °C (THF—ethanol, 2 : 1). Found (%): C, 68.57; H, 3.43; N, 7.37 $C_{22}H_{14}N_2O_5$. Calculated (%): C, 68.39; H, 3.65; N, 7.25. ^{1}H NMR, δ: 4.47 (d, 2 H, NCH_2Ph, J = 5.5 Hz); 7.24—7.41 (m, 5 H, NCH_2Ph); 7.92—8.01 (m, 2 H, H-6, H-7); 8.11—8.26 (m, 2 H, H-5, H-8); 8.21 (d, 1 H, H-4, J = 8.4 Hz); 8.46 (d, 1 H, H-3); 9.58 (t, 1 H, $NHCH_2Ph$).

***N*-Methoxycarbonylmethyl-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (8e).** Methyl glycinate hydrochloride (0.14 g, 1.14 mmol) and NaOAc (0.093 g, 1.14 mmol) were added with stirring to a solution of acid chloride **7** (0.30 g, 0.95 mmol) in anhydrous benzene (15 mL). The reaction mixture was stirred at 15 °C for 2.5 h and worked up conventionally to give compound **8e**, yield 51%, m.p. 212—215 °C (THF—ethanol, 2 : 1). Found (%): C, 58.77; H, 3.15; N, 7.50 $C_{18}H_{12}N_2O_7$. Calculated (%): C, 58.70; H, 3.28; N, 7.61. ^{1}H NMR, δ: 3.69 (s, 3 H, $NHCH_2COOMe$); 4.05 (d, 2 H, $NHCH_2COOMe$); 7.93—8.01 (m, 2 H, H-6, H-7); 8.11—8.24 (m, 3 H, H-5, H-8, H-4); 8.49 (d, 1 H, H-3, J = 8.7 Hz); 9.54 (t, 1 H, $NHCH_2COOMe$, J = 5.9 Hz).

The reaction of *N*-benzyl-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (8d) with α-toluenethiol. α-Toluenethiol (0.3 mL, 2.4 mmol) was added to a solution of amide **8b** (0.25 g, 0.9 mmol) in anhydrous DMF (3.5 mL). Finely ground K_2CO_3 (0.1 g, 0.95 mmol) was then added with vigorous stirring. The reaction mixture was stirred in an atmosphere of argon at 50 °C for 5 h and poured into 5% HCl (15 mL). The precipitate that formed was filtered off, washed with water (3×10 mL), and chromatographed on silica gel L (40/100) in toluene and then in toluene—ethyl acetate (2 : 1) to give a complex mixture of products (0.11 g) containing ***N*-methyl-6-oxo-1-phenyl-6*H*-anthra[1,9-*bc*]thiophene-3-carboxamide (9)** (^{1}H NMR data). ^{1}H NMR (**9**), δ: 2.91 (d, 3H, NHMe, J = 5.5 Hz); 7.50—7.71 (m, 7 H, Ph, H-8, H-9); 8.29—8.36 (m, 2 H, H-7, H-10); 8.31 (d, 1 H, H-5, J = 7.8 Hz); 8.40 (d, 1 H, H-4); 9.10 (br.s, 1H, NHMe).

1-Methylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10a). A mixture of amide **8a** (0.20 g, 0.68 mmol), DMF (4 mL), and MeSNa (0.06 g, 0.87 mmol) was stirred at 15 °C for 12 h, poured into water (20 mL), and acidified with HCl to acid reaction. The precipitate that formed was filtered off, washed with water (3×10 mL), and recrystallized from THF—ethanol (2 : 1) to give amide **10a**, yield 0.16 g (82%), m.p. 256—260 °C. Found (%): C, 64.85; H, 3.51; N, 4.94, S, 10.52 $C_{16}H_{11}NO_3S$. Calculated (%): C, 64.63; H, 3.73; N, 4.71, S, 10.78. ^{1}H NMR, δ: 2.44 (s, 3 H, SMe); 7.75 (d, 1 H, H-4, J = 7.9 Hz); 7.78 (s, 1 H, NH_2); 7.84—7.99 (m, 2 H, H-6, H-7); 8.11 (d, 1 H, H-3); 8.13—8.22 (m, 3 H, H-5, H-8, NH_2).

Amides **10b—d** were prepared analogously.

***N*-Methyl-1-methylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10b).** Yield 87%, m.p. 227—230 °C. Found (%): C, 65.61; H, 4.32; N, 4.32, S, 10.21 $C_{17}H_{13}NO_3S$. Calculated (%): C, 65.58; H, 4.21; N, 4.50, S, 10.30. ^{1}H NMR, δ: 2.39 (s, 3 H, SMe); 2.82 (d, 3 H, NHMe), 7.75 (d, 1 H, H-4, J = 7.93 Hz); 7.89—8.01 (m, 2 H, H-6, H-7); 8.09—8.22 (m, 3 H, H-5, H-8, H-3); 8.62 (q, 1 H, NHMe, J = 4.0 Hz).

1-Methylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxanilide (10c). Yield 75%, m.p. 225—227 °C. Found (%): C, 70.54; H, 4.34; N, 3.63, S, 8.62 $C_{22}H_{15}NO_3S$. Calculated (%): C, 70.76; H, 4.05; N, 3.75, S, 8.59. ^{1}H NMR, δ: 2.42 (s, 3 H, SMe); 7.12 (t, 1 H, (NHPh) H-*p*); 7.38 (dd, 2 H, (NHPh) H_m, $J_{m,p}$ = 6.9 Hz, $J_{m,o}$ = 8.2 Hz); 7.74 (d, 2 H, (NHPh) H_o); 7.92 (d, 1 H, H-4, J = 7.8 Hz); 7.88—8.01 (m, 2 H, H-6, H-7); 8.20 (d, 1 H, H-3); 8.15—8.23 (m, 2 H, H-5, H-8); 10.74 (s, 1 H, NHPh).

***N*-Benzyl-1-methylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10d).** Yield 71%, m.p. 198—200 °C. Found (%): C, 71.65; H, 4.83; N, 3.21, S, 7.85 $C_{24}H_{19}NO_3S$. Calculated (%): C, 71.80; H, 4.77; N, 3.49, S, 7.99. ^{1}H NMR, δ: 2.49 (s, 3 H, SMe); 4.49 (d, 2 H, $NHCH_2Ph$, J = 5.2 Hz); 7.22—7.47 (m, 5 H, $NHCH_2Ph$), 7.78 (d, 1 H, H-4, J = 7.2 Hz); 7.86—8.01 (m, 2 H, H-6, H-7); 8.08—8.25 (m, 3 H, H-3, H-5, H-8); 9.22 (t, 1 H, $NHCH_2Ph$, J = 4.6 Hz).

1-Ethylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10e). A mixture of amide **8a** (0.20 g, 0.68 mmol), DMF (4 mL), and EtSNa (0.07 g, 0.83 mmol) was stirred at 15 °C for 12 h, poured into water (20 mL), and acidified with HCl to acid reaction. The precipitate that formed was filtered off, washed with water (3×10 mL), and recrystallized from THF—ethanol (2 : 1) to give amide **10e**, yield 0.17 g (81%), m.p. 224—226 °C. Found (%): C, 65.67; H, 4.34; N, 4.37, S, 10.21 $C_{17}H_{13}NO_3S$. Calculated (%): C, 65.58; H, 4.21; N, 4.50, S, 10.30. ^{1}H NMR, δ: 1.12 (t, 3 H, SCH_2CH_3, J = 7.2 Hz); 2.94 (q, 2 H, SCH_2CH_3); 7.70—7.82 (m, 2 H, H-4, NH); 7.99—7.84 (m, 2 H, H-6, H-7); 8.05—8.23 (m, 4 H, H-5, H-8, H-3, NH).

Amides **10f—h** were prepared analogously.

1-Ethylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxanilide (10f). Yield 86%, m.p. 194—196 °C. Found (%): C, 71.42; H, 4.35; N, 3.51, S, 8.44 $C_{23}H_{17}NO_3S$. Calculated (%): C, 71.30; H, 4.42; N, 3.62, S, 8.28. ^{1}H NMR, δ: 1.08 (t, 3 H, SCH_2CH_3, J = 7.2 Hz); 2.91 (q, 2 H, SCH_2CH_3); 7.13 (t, 1 H, (NHPh) H_p, $J_{m,p}$ = 7.2 Hz); 7.37 (dd, 2 H, (NHPh) H_m, $J_{m,o}$ = 7.7 Hz); 7.73 (d, 2 H, (NHPh) H_o); 7.92 (d, 1 H, H-4, J = 8.2 Hz); 7.89—8.01 (m, 2 H, H-6, H-7); 8.23 (d, 1 H, H-3); 8.15—8.27 (m, 2 H, H-5, H-8); 10.67 (s, 1 H, NHPh).

***N*-Benzyl-1-ethylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10g).** Yield 72%, m.p. 205—206 °C. Found (%): C, 71.80; H, 4.77; N, 3.49, S, 7.99 $C_{24}H_{19}NO_3S$. Calculated (%): C, 71.80; H, 4.77; N, 3.49, S, 7.99. ^{1}H NMR, δ: 1.03 (t, 3 H, S CH_2CH_3, J = 7.2 Hz); 2.78 (q, 2 H, SCH_2CH_3); 4.50 (d, 2 H, $NHCH_2Ph$, J = 5.5 Hz); 7.26—7.46 (m, 5 H, $NHCH_2Ph$); 7.79 (d, 1 H, H-4, J = 8.2 Hz); 7.89—8.00 (m, 2 H, H-6, H-7); 8.14—8.24 (m, 3 H, H-5, H-8, H-3); 9.19 (t, 1 H, $NHCH_2Ph$).

***N*-Methoxycarbonylmethyl-1-ethylthio-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10h).** Yield 89%, m.p. 165—175 °C. Found (%): C, 62.76; H, 4.22; N, 3.75, S, 8.12 $C_{20}H_{17}NO_5S$. Calculated (%): C, 62.65; H, 4.47; N, 3.65, S, 8.36. ^{1}H NMR, δ: 1.09 (t, 3 H, $SCH_2C\underline{H}_3$, J = 7.7 Hz); 2.89 (q, 2 H, $SC\underline{H}_2CH_3$); 3.69 (s, 3 H, COOMe); 4.06 (d, 2 H, $NHC\underline{H}_2$, J = 5.5 Hz); 7.76 (d, 1 H, H-4, J = 7.7 Hz); 7.83—8.03 (m, 2 H, H-6, H-7); 8.17 (d, 1 H, H-3); 8.13—8.20 (m, 2 H, H-5, H-8); 9.13 (t, 1 H, $N\underline{H}CH_2$).

2,3,6,11-Tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione (11a). Sulfuryl chloride (0.1 mL, 1.24 mmol) was added with vigorous stirring to a suspension of amide **10a** (0.30 g, 1.01 mmol) in anhydrous CH_2Cl_2 (5 mL). The precipitate dissolved almost immediately to give a red solution, from which the reaction product started to precipitate after 5 to 8 s. The reaction mixture was stirred at 15 °C for 1.5 h. The solvent was removed *in vacuo*, and the precipitate was recrystallized from THF to give trione **11a**, yield 0.20 g (72%), m.p. 328—333 °C.

Isothiazolone **11a** was also obtained by treating **10e** with sulfuryl chloride (yield 82%). Found (%): C, 64.27; H, 2.43; N, 5.02, S, 11.67 $C_{15}H_7NO_3S$. Calculated (%): C, 64.05; H, 2.51; N, 4.98, S, 11.40. ^{1}H NMR, δ: 7.94—8.03 (m, 2 H, H-8, H-9); 8.20—8.30 (m, 3 H, H-7, H-10, H-5); 8.38 (d, 1 H, H-4, J = 7.7 Hz).

Compounds **11b—e** were obtained analogously.

2-Methyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione (11b). Yield 67%, m.p. 272—276 °C. Found (%): C, 65.25; H, 2.96; N, 4.52, S, 10.98 $C_{16}H_9NO_3S$. Calculated (%): C, 65.07; H, 3.07; N, 4.74, S, 10.86. ^{1}H NMR, δ: 3.42 (s, 3 H, NMe); 7.94—8.02 (m, 2 H, H-8, H-9); 8.20 (d, 1 H, H-5, J = 7.2 Hz); 8.16—8.28 (m, 2 H, H-7, H-10); 8.34 (d, 1 H, H-4).

2-Phenyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione (11c). Yield 63% (from amide **10c**), m.p. 262—268 °C. Isothiazolone **11c** was also obtained from amide **10f** (yield 72%). Found (%): C, 70.66; H, 3.04; N, 4.04, S, 8.84 $C_{21}H_{11}NO_3S$. Calculated (%): C, 70.58; H, 3.10; N, 3.92, S, 8.97. ^{1}H NMR, δ: 7.42 (t, 1 H, (NPh) H_p); 7.57 (dd, 2 H, (NPh) H_m, $J_{m,p}$ = 7.2 Hz, $J_{m,o}$ = 7 Hz); 7.77 (d, 2 H, (NPh) H_o); 7.91—8.06 (m, 2 H, H-8, H-9); 8.16—8.33 (m, 3 H, H-7, H-10, H-5); 8.42 (d, 1 H, H-4, J = 7.2 Hz).

2-Benzyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione (11d). Yield 71%, m.p. 214—217 °C. Isothiazolone **11d** was also obtained from amide **10d** (yield 75%). Found (%): C, 71.36; H, 3.21; N, 3.92, S, 8.38 $C_{22}H_{13}NO_3S$. Calculated (%): C, 71.14; H, 3.53; N, 3.77, S, 8.63. ^{1}H NMR, δ: 5.09 (s, 2 H, $C\underline{H}_2Ph$); 7.28—7.46 (m, 5 H, $CH_2\underline{Ph}$); 7.91—8.02 (m, 2 H, H-8, H-9); 8.19—8.25 (m, 3 H, H-7, H-10, H-5); 8.48 (d, 1 H, H-4, J = 7.2 Hz).

2-Methoxycarbonylmethyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione (11e). Yield 64%, m.p. 225—230 °C. Found (%): C, 61.35; H, 3.25; N, 3.72, S, 9.11 $C_{18}H_{11}NO_5S$. Calculated (%): C, 61.18; H, 3.14; N, 3.96, S, 9.07. ^{1}H NMR, δ: 3.72 (s, 3 H, COOMe); 4.77 (s, 2 H, $NC\underline{H}_2COOMe$); 7.89—8.05 (m, 2 H, H-8, H-9); 8.11—8.28 (m, 3 H, H-7, H-10, H-5); 8.34 (d, 1 H, H-4, J = 7.4 Hz).

2-Methyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione 1,1-dioxide (12) was obtained in 36% yield from isothiazolone **11b** (0.30 g, 1.01 mmol) and 50% H_2O_2 (0.9 mL) as it was described for *S*-monoxide **13a**, m.p. 320—325 °C. Found (%): C, 58.94; H, 2.53; N, 4.36, S, 9.71 $C_{16}H_9NO_5S$. Calculated (%): C, 58.71; H, 2.77; N, 4.28, S, 9.80. ^{1}H NMR, δ: 3.25 (s, 3 H, NMe); 7.98—8.05 (m, 2 H, H-8, H-9); 8.23—8.34 (m, 2 H, H-7, H-10); 8.52 (d, 1 H, H-5, J = 8.7 Hz); 8.70 (d, 1 H, H-4).

2-Phenyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione 1-oxide (13a). A mixture of isothiazolone **11c** (0.20 g, 0.56 mmol), AcOH (5 mL), and 50% H_2O_2 (0.50 mL) was stirred at 50 °C for 48 h, cooled, and poured into water (20 mL). The precipitate that formed was filtered off, washed with water (3×10 mL), and recrystallized from THF to give *S*-monoxide **13a**, yield 0.09 g (42%), m.p. 265—270 °C. Found (%): C, 67.77; H, 2.72; N, 3.63, S, 8.72 $C_{21}H_{11}NO_4S$. Calculated (%): C, 67.55; H, 2.97; N, 3.75, S, 8.59. ^{1}H NMR, δ: 7.49—7.72 (m, 5 H, NPh); 7.97—8.11 (m, 2 H, H-8, H-9); 8.25—8.36 (m, 2 H, H-7, H-10); 8.48 (d, 1 H, H-4, J = 8.1 Hz); 8.67 (d, 1 H, H-5).

S-Oxides **13b,c** were obtained analogously.

2-Benzyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione 1-oxide (13b). Yield 56% (from isothiazolone **11d**), m.p. 262—265 °C. Found (%): C, 68.53; H, 3.24; N, 3.51, S, 8.31 $C_{22}H_{13}NO_4S$. Calculated (%): C, 68.21; H, 3.38; N, 3.62, S, 8.28. ^{1}H NMR, δ: 4.84 (d, 1 H, $NC\underline{H}_2Ph$, J = 15.4 Hz); 5.24 (d, 1 H, $NC\underline{H}_2Ph$); 7.26—7.54 (m, 5 H, $NCH_2\underline{Ph}$); 7.93—8.09 (m, 2 H, H-8, H-9); 8.18—8.33 (m, 2 H, H-7, H-10); 8.41 (d, 1 H, H-5, J = 7.2 Hz); 8.61 (d, 1 H, H-4).

2-Methoxycarbonylmethyl-2,3,6,11-tetrahydroanthra[2,1-*d*]isothiazole-3,6,11-trione 1-oxide (13e). Yield 46% (from isothiazolone **11e**), m.p. 255—260 °C. Found (%): C, 68.53; H, 3.24; N, 3.51, S, 8.31 $C_{18}H_{11}NO_6S$. Calculated (%): C, 58.53; H, 3.00; N, 3.79, S, 8.68. ^{1}H NMR, δ: 3.73 (s, 3 H, COOMe); 4.73 (d, 1 H, $NC\underline{H}_2COOMe$, J = 18.1 Hz); 4.82 (d, 1 H, $NC\underline{H}_2COOMe$); 7.97—8.04 (m, 2 H, H-8, H-9); 8.22—8.28 (m, 2 H, H-7, H-10); 8.41 (d, 1 H, H-5, J = 7.3 Hz); 8.61 (d, 1 H, H-4).

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Received January 15, 2001;
in revised form May 23, 2001