

Synthesis of 1-(Phenylsulfanyl/Phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-diones

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ABSTRACT: A convenient method is devised to synthesize 1-(phenylsulfanyl/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione analogs in high yield for the first time by condensation of 2-bromo-*N*-(9,10-dioxo-dihydro-anthracen-1-yl)-acetamide with benzenethiol/phenol using potassium carbonate. © 2008 Wiley Periodicals, Inc. *Heteroatom Chem* 19:221–227, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20399

INTRODUCTION

Respiratory syncytial virus (RSV) infections occur all over the world, and each year RSV infections cause more than 125,000 hospitalizations and about 2500 deaths. RSV infects nearly all children by age 2 years, and it causes considerable illness and death in certain high-risk pediatric populations. Historically, treatment for RSV has been symptomatic, and developing a safe and effective vaccine has been a challenge. Therefore, research efforts have turned to passive immunization as the best option to control RSV infections. Benzanthrone analogs [1–3] in (shown in Fig. 1) **1** and **2** have been reported to have variable antiviral activity against RSV, with EC₅₀ values ranging from 0.03 to 57 µg/mL in vitro

F-inhibition assays [4]. Also, multidrug resistance to antitumor agents, which are structurally dissimilar and having different intracellular targets, is the major problem in cancer therapy. The multidrug resistance phenomenon is associated with the presence of membrane proteins, which belong to the ATP-binding cassette family transporters that are responsible for the active drug efflux leading to the decreased intracellular accumulation [4]. The prolonged clinical use of chemotherapeutic agents often causes the appearance of multidrug resistance toward numerous antitumor compounds [6]. This effect currently constitutes one of the major problems in clinical chemotherapy and has not yet been successfully solved. Many efforts have been directed toward the search for new benzanthrone analogs, anthracenedione derivatives with increased effectiveness against multidrug resistance tumor cell lines. The majority of DNA-intercalating anticancer drugs possess linear or angular polycyclic chromophores. An increasing number of examples of “fused” tetracyclic systems have been reported, including the azonafides **3** [7,8], imidazoacridones **4** [9–11], pyrimido[5,6,1-*de*]acridines **5** [12], benzo[*e*]pyrimidines **6,7** [13,14], and 3(*H*)-naphtho[1,2,3-*de*]quinoline-2,7-dione **1,2** [15]. Although the presence of a fused heterocyclic ring is essential to overcome the multidrug resistance, appropriate substituents were necessary to achieve the optimal results. In the present context, because of the industrial production of synthetic dyes that may contain nitrogen analogs of polycyclic aromatic hydrocarbons, benzo[*de*]anthracen-7-one [16]

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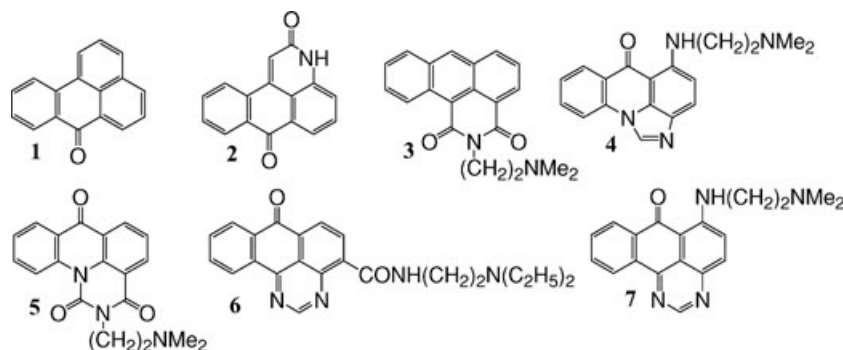


FIGURE 1 Examples of fused tetracyclic systems.

(benzanthrone) derivatives are interesting compounds owing to their excellent color characteristics and high photostability [17]. They have been widely used as dyes for polymers [18], textiles [19], daylight fluorescent pigments [20], and laser dyes [21].

The main aim of the search for new structures within the mentioned groups is not only to develop novel synthetic compounds with antiviral and antitumor activities but also to overcome the major undesirable properties of related anthracene antibiotics, their cytotoxicity (peroxidating activity), and the ability to induce resistance. Although the rationale for the design of nonperoxidating compounds has been recently proposed, the clear concepts for the development of agents active on resistant tumor cells are still lacking. The synthesis of novel structural types of benzanthrone, anthracenedione, acridine, and their analogs could be a way to find the desired leads.

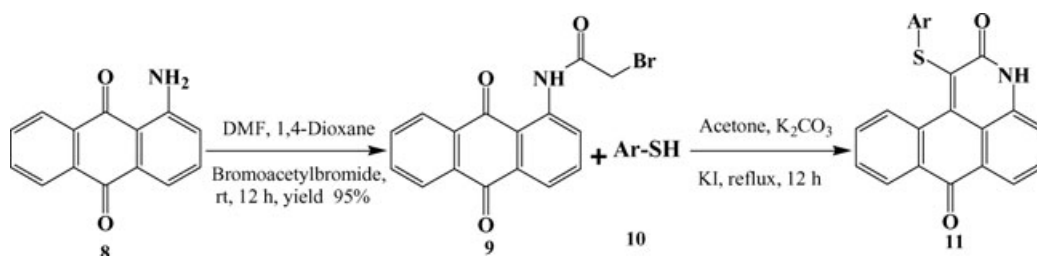
RESULTS AND DISCUSSION

Although many methods for the synthesis of benzanthrone have already been published, no one has used the strategy adopted in this work. Our strategy has the following advantages: (i) It is easier to introduce the substituent at the first position of the benzanthrone ring. (ii) The reactivity of the β -carbon

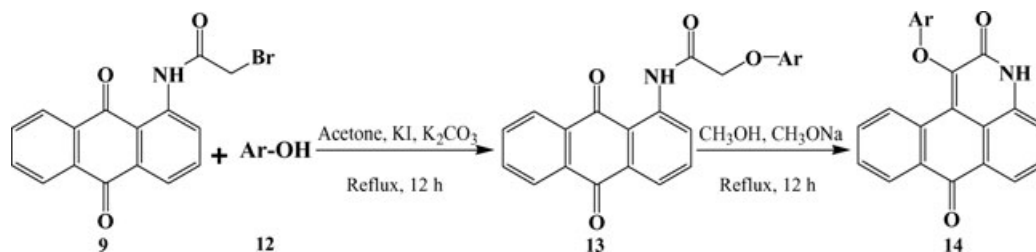
in **9** and the carbonyl carbon in **13** allows the regiospecific introduction of a wide range of phenols and benzenethiols, bearing both electron donor and electron-withdrawing substituents.

In this paper, we describe the synthesis of 1-(phenylsulfanyl/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione derivatives, which are modified with an additional quinolinone ring incorporated into the chromophore. A series of compounds bearing [(substituted phenylsulfanyl/phenoxy)] side chain at position 1 to the chromophore moiety have been obtained. These derivatives are structurally related to the antitumor agent benzanthrone and mitoxantrone. The presence of phenylsulfanyl/phenoxy side chain could modify the physicochemical properties and solubility of the above-mentioned derivatives and enhance their cytotoxic activity. Therefore, 1-(phenylsulfanyl/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione analogs have been synthesized.

In this section, for the first time we report the synthesis of 1-(phenylsulfanyl/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione from easily accessible 2-aminoanthraquinone. As a result of our studies, we found a heterocyclization method to synthesize a series of 1-(phenylsulfanyl/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione using mild basic conditions. The synthetic pathways leading



SCHEME 1



SCHEME 2

to 1-(phenylsulfanyl/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione derivatives are shown in Schemes 1 and 2. The formation of the compounds (Table 1, entries **11a–i**) can be rationalized in terms of the reaction of 2-aminoanthraquinone in *N,N*-dimethylformamide and 1,4-dioxane in the ratio of 1:1 with bromoacetyl bromide that afford (2-bromo-*N*-(9,10-dioxo-dihydro-anthracen-1-yl)acetamide. This intermediate compound was further treated with various benzenethiols and substituted phenols in the presence of anhydrous potassium carbonate in acetone to give 1-(phenylsulfanyl)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione. Whereas, phenols formed *N*-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-2-phenoxy acetamides when further treated with sodium methoxide in methanol and furnished the desired product 1-phenoxy-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione (Table 2). It is noteworthy that when benzenethiols were allowed to react with 2-bromo-*N*-(9,10-dioxo-dihydro-anthracen-1-yl)acetamide, the expected *N*-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-2-phenylthio acetamides were not isolated, instead the reaction proceeded on to the next step and directly yielded cyclized products 1-(phenylsulfanyl)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione. This can be rationalized because the sulfur atom renders the hydrogen atom of the adjacent group highly acidic, and a carbanion is formed readily in the presence of potassium carbonate, thus facilitating the quinolinone ring formation.

CONCLUSION

In conclusion, we have developed a convenient procedure to obtain new heteropolycycles as 1-(phenylthio/phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione, derived from 2-aminoanthraquinone, thiophenols, and phenols involving the isolation of *N*-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-2-phenoxy acetamide intermediates. We hope that the new benzanthrones described here will contribute to a combinatorial library of benzanthone derivatives, and also aim to determine a more potent drug and its action pathway as a respiratory syncytial virus and antitumor agent. The evaluation of biological activity is being investigated and is to be unraveled.

EXPERIMENTAL

Unless otherwise indicated, all the common reagents and solvents were used as obtained from commercial suppliers without further purification. The melting points were determined on a Mel-Temp 3.0 melting point apparatus and uncorrected. ¹H NMR spectra were determined on a Varian 300 MHz spectrometer, and the chemical shifts are reported in parts per million (δ , ppm). Tetramethylsilane is used as an internal standard. Elemental analyses were carried out by Atlantic Microlab, GA.

TABLE 1 Synthetic Data of 1-(Phenylsulfanyl)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione (**11a–i**)

Entry	Amide (9) Ar	Product (11)	Time (h)	Melting Point ($^{\circ}$ C)	Yield (%) ^a
1	C ₆ H ₅	11a	12	223–225	95
2	2-Cl-C ₆ H ₄	11b	12	315–317	88
3	4-Cl-C ₆ H ₄	11c	10	297–299	90
3	2-F-C ₆ H ₄	11d	11	201–203	87
4	3-F-C ₆ H ₄	11e	12	185–187	89
5	4-F-C ₆ H ₄	11f	10	158–160	90
6	3-CH ₃ O-C ₆ H ₄	11g	11	261–263	92
7	4-CH ₃ O-C ₆ H ₄	11h	11	286–288	94
8	4-CF ₃ -C ₆ H ₄	11i	12	301–303	88

^aIsolated yields.

TABLE 2 Synthetic Data of 1-(Phenoxy)-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione (**14a–i**)

Entry	Amide (13) Ar	Product (14)	Time (h)	Melting Point (°C)	Yield (%) ^a
1	C ₆ H ₅	14a	12	196–198	92
2	4-CH ₃ CO-C ₆ H ₄	14d	10	217–219	96
3	4-Br-C ₆ H ₄	14b	11	230–232	90
4	4-O ₂ N-C ₆ H ₄	14c	11	239–241	85
5	3-Cl-4-CH ₃ -C ₆ H ₃	14e	12	243–245	90
6	2,4,6-(Br) ₃ -C ₆ H ₂	14g	11	257–259	89
7	2,4,6-(Cl) ₃ -C ₆ H ₂	14f	10	266–268	91
8	3,5-(CF ₃) ₂ -C ₆ H ₃	14h	12	183–185	88
9	2,3,4,5,6-F ₅ C ₆	14i	12	167–169	90

^aIsolated yields.

General Procedure

Synthesis of 2-Bromo-*N*-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)acetamide (9). To a solution of 2-aminoanthraquinone (15 g, 67.19 mmol) in a round-bottom flask, dimethyl formamide (35 mL) and 1,4-dioxane (35 mL) were added, which was cooled to 0°C. Then, bromoacetyl bromide (6.44 mL, 73.90 mmol) was slowly added, so that temperature did not rise to 1°C. At the end of the addition, the temperature was maintained at 0°C for further 15 min, and then the mixture was stirred for overnight at room temperature. The contents of the flask were poured into water (400 mL), and the resulting precipitate was filtered, washed with water (3 × 100 mL), dried. Then orange-colored solid was obtained.

Yield, 95.13%; mp 188–190°C; ¹H NMR (300 MHz, CDCl₃), δ (ppm): 13.10 (s, 1H), 9.10 (d, 1H, *J* = 7.5 Hz), 8.40–8.20 (m, 2H), 8.14 (d, 1H, *J* = 7.5 Hz), 7.85–7.75 (m, 3H), 4.30 (s, 2H).

Synthesis of 1-Phenylsulfanyl-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione (11a). To a solution of 2-bromo-*N*-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-acetamide (547 mg, 1.59 mmol) and benzenethiol (175 mg, 1.59 mmol) in acetone (10 mL), K₂CO₃ (439 mg, 3.18 mmol) and KI (26.3 mg, 0.159 mmol) were added. Then, the reaction mixture was refluxed for 12 h. There after, the reaction mixture was cooled to room temperature and acetone was removed on rotary vapor. The brown color precipitate was diluted with water (15 mL) and neutralized with 10% aqueous hydrochloric acid (10 mL). The brown-colored solid was separated through filtration, washed with water (2 × 20 mL), and dried.

¹H NMR (300 MHz, DMSO-*d*₆), δ (ppm): 12.80 (s, NH), 8.20 (d, 2H, *J* = 6.6 Hz), 8.10 (d, 2H, *J* = 6.0 Hz), 7.76–7.94 (m, 3H), 7.50 (t, 1H, *J* = 8.1 Hz), 7.36 (d, 2H, *J* = 7.2 Hz), 7.15 (d, 2H, *J* = 6.9 Hz). ¹³C NMR (300 MHz, DMSO-*d*₆), δ (ppm): 178.90, 163.84, 148.82,

143.88, 135.94, 135.59, 132.13, 132.36, 131.21, 130.82, 129.80, 129.69, 129.53, 129.43, 128.29, 128.28, 127.62, 124.60, 124.01, 123.17, 121.52, 115.40. Anal. Calcd for C₂₂H₁₃NO₂S: C, 74.35; H, 3.69; N, 3.94. Found: C, 74.21; H, 3.57; N, 3.85.

Synthesis of *N*-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-phenoxy-acetamide (13a). To a solution of 2-bromo-*N*-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-acetamide (547 mg, 1.59 mmol) and phenol (150 mg, 1.59 mmol) in acetone (10 mL), K₂CO₃ (439 mg, 3.18 mmol) and KI (26.3 mg, 0.159 mmol) were added. Then, the reaction mixture was refluxed for 12 h. After that the reaction mixture was cooled to room temperature, and acetone was removed on rotary vapor. It was diluted with water (15 mL) and neutralized with 10% aqueous hydrochloric acid (10 mL). The resulting solid was separated through filtration, washed with water (2 × 20 mL), and dried. Then, orange-colored solid was obtained.

Yield, 90%; mp 187–189°C; ¹H NMR (300 MHz, CD₃OD), δ (ppm) 13.04 (s, NH), 9.10 (d, 1H, *J* = 7.5 Hz), 8.20–8.40 (m, 3H), 8.10 (d, 1H, *J* = 7.6 Hz), 7.70–7.90 (m, 4H), 7.60 (d, 1H, *J* = 7.5 Hz), 7.40 (t, 1H, *J* = 7.6 Hz), 7.00 (d, 1H, *J* = 7.5 Hz), 4.30 (s, 2H).

Synthesis of 1-Phenoxy-3*H*-naphtho[1,2,3-*de*]quinoline-2,7-dione (14a). A mixture of anhydrous methanol (3 mL) and sodium metal (13 gm, 0.54 mmol) was stirred at 0°C, and the solution of *N*-(9,10-dihydro-anthracen-1-yl)-2-phenoxy-acetamide (100 mg, 0.27 mmol) in methanol (2 mL) was added to the mixture dropwise at the same temperature (0°C). Stirring was continued for another 10 min at room temperature, and then the reaction mixture was refluxed for 12 h. The reaction mixture was cooled to room temperature and poured into ice cold water (15 mL), and it was neutralized with 10% aqueous hydrochloric acid (10 mL). The

orange-colored solid was filtered, washed with water (2×20 mL), and dried.

^1H NMR (300 MHz, CD_3OD), δ (ppm): 12.60 (s, NH, 1H), 8.20 (d, 2H, $J = 6.8$ Hz), 8.10 (d, 2H, $J = 6.4$ Hz), 7.80–8.00 (m, 3H), 7.50 (t, 1H, $J = 7.9$ Hz), 7.40 (d, 2H, $J = 7.5$ Hz), 7.20 (d, 2H, $J = 7.2$ Hz). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 158.05, 155.53, 154.42, 152.76, 136.08, 134.54, 133.13, 132.59, 130.43, 129.08, 129.06, 128.94, 127.83, 125.23, 122.45, 121.67, 120.80, 116.01, 115.98, 113.01, 103.01. Anal. Calcd for $\text{C}_{22}\text{H}_{13}\text{NO}_3$: C, 77.87; H, 3.86; N, 4.13. Found: C, 77.72; H, 3.75; N, 4.02.

1-(2-Chloro-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11b). ^1H NMR (300 MHz, $\text{DMSO}-d_6$), δ (ppm): 12.50 (s, NH), 8.66 (d, 1H, $J = 8.1$ Hz), 8.18 (d, 1H, $J = 7.2$ Hz), 8.02 (d, 1H, $J = 7.2$ Hz), 7.98 (t, 1H, $J = 7.5$ Hz), 7.58–7.70 (m, 3H), 7.40 (d, 1H, $J = 8.1$ Hz), 7.00–7.16 (m, 3H). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 163.84, 143.88, 148.82, 135.65, 135.36, 134.97, 133.25, 132.36, 132.13, 131.21, 130.82, 130.58, 129.00, 128.29, 127.62, 127.41, 124.63, 124.60, 123.17, 121.52, 115.17. Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{ClNO}_2\text{S}$: C, 67.78; H, 3.10; N, 3.59. Found: C, 67.66; H, 3.53; N, 3.41.

1-(4-Chloro-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11c). ^1H NMR (300 MHz, $\text{DMSO}-d_6$), δ (ppm): 12.40 (s, NH), 8.60 (d, 1H, $J = 7.5$ Hz), 8.12 (d, 1H, $J = 9.0$ Hz), 7.98 (d, 1H, $J = 7.2$ Hz), 7.70 (t, 1H, $J = 7.5$ Hz), 7.50–7.66 (m, 3H), 7.10 (d, 2H, $J = 9.0$ Hz), 6.68 (d, 2H, $J = 8.7$ Hz). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 163.84, 148.82, 143.88, 135.65, 135.63, 135.59, 135.57, 132.91, 132.36, 132.13, 131.21, 130.82, 128.50, 128.46, 128.29, 127.62, 124.60, 124.01, 123.52, 121.17, 115.40. Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{ClNO}_2\text{S}$: C, 67.78; H, 3.10; N, 3.59. Found: C, 67.63; H, 3.55; N, 3.47.

1-(2-Fluoro-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11d). ^1H NMR (300 MHz, $\text{DMSO}-d_6$), δ (ppm): 12.40 (s, NH), 8.70 (d, 1H, $J = 7.5$ Hz), 8.20 (d, 1H, $J = 7.2$ Hz), 8.00 (d, 1H, $J = 7.5$ Hz), 7.80 (t, 1H, $J = 7.5$ Hz), 7.60–7.75 (m, 3H), 7.10–7.20 (m, 2H), 7.00 (d, 1H, $J = 8.0$ Hz), 6.80–6.90 (m, 1H). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 167.57, 163.84, 148.88, 143.82, 138.72, 134.60, 132.36, 132.24, 132.13, 131.21, 130.82, 128.29, 127.62, 125.87, 124.60, 123.17, 122.96, 121.52, 118.18, 115.52, 114.42. Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{FNO}_2\text{S}$: C, 70.76; H, 3.24; N, 3.75. Found: C, 70.63; H, 3.17; N, 3.69.

1-(3-Fluoro-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11e). ^1H NMR (300 MHz, $\text{DMSO}-d_6$), δ (ppm): 12.40 (s, 1H, NH), 8.70 (d, 1H, $J = 7.5$ Hz), 8.18–8.24 (dd, 2H, $J = 1.8, 9.0$ Hz), 8.0 (d, 1H, $J = 7.2$ Hz), 7.74–7.80 (t, 1H, $J = 7.5$ Hz), 7.60–7.70 (m, 2H), 7.10–7.20 (m, 2H), 7.04–7.08 (d, 1H, $J = 8.1$ Hz), 6.88–6.96 (m, 1H). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 163.84, 161.55, 148.82, 143.88, 138.01, 135.59, 132.36, 132.13, 131.21, 130.82, 129.21, 128.82, 128.29, 127.62, 124.60, 124.01, 123.17, 122.87, 121.52, 116.33, 115.40. Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{FNO}_2\text{S}$: C, 70.76; H, 3.24; N, 3.75. Found: C, 70.67; H, 3.15; N, 3.66.

1-(4-Fluoro-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11f). ^1H NMR (300 MHz, $\text{DMSO}-d_6$), δ (ppm): 12.40 (s, 1H, NH), 8.60 (d, 1H, $J = 7.5$ Hz), 8.18 (dd, 1H, $J = 2.1, 9.3$ Hz), 8.00 (dd, 1H, $J = 1.5, 7.2$ Hz), 7.70–7.80 (t, 1H, $J = 7.8$ Hz), 7.56–7.68 (m, 3H), 7.20–7.30 (m, 2H), 6.90–7.00 (t, 2H, $J = 9.0$ Hz). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 164.05, 163.84, 148.82, 143.88, 138.78, 138.72, 135.59, 132.30, 132.13, 131.21, 130.82, 128.29, 127.85, 127.62, 124.60, 124.01, 123.17, 121.52, 115.71, 115.69, 115.40. Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{FNO}_2\text{S}$: C, 70.76; H, 3.24; N, 3.75. Found: C, 70.64; H, 3.19; N, 3.63.

1-(3-Methoxy-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11g). ^1H NMR (300 MHz, CD_3OD), δ (ppm): 12.40 (s, 1H, NH), 8.60 (d, 1H, $J = 7.7$ Hz), 8.12 (d, 1H, $J = 7.5$ Hz), 8.00 (d, 1H, $J = 7.2$ Hz), 7.70 (t, 1H, $J = 7.5$ Hz), 7.64–7.50 (m, 3H), 7.24 (t, 1H, $J = 7.8$ Hz), 6.67–6.80 (m, 2H), 6.60 (d, 1H, $J = 7.5$ Hz), 3.80 (s, 3H). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 163.84, 159.44, 148.82, 143.88, 135.59, 135.49, 132.36, 132.13, 131.21, 130.82, 129.44, 128.42, 128.29, 127.62, 124.60, 124.01, 123.17, 121.52, 118.42, 115.40, 114.42, 55.09. Anal. Calcd for $\text{C}_{23}\text{H}_{15}\text{NO}_3\text{S}$: C, 71.67; H, 3.92; N, 3.63. Found: C, 71.55; H, 3.81; N, 3.54.

1-(4-Methoxy-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11h). ^1H NMR (300 MHz, CD_3OD), δ (ppm): 12.40 (s, 1H, NH), 8.60 (d, 1H, $J = 7.7$ Hz), 8.12 (d, 1H, $J = 7.5$ Hz), 7.98 (d, 1H, $J = 7.2$ Hz), 7.70 (t, 1H, $J = 7.5$ Hz), 7.64–7.50 (m, 3H), 7.20 (d, 2H, $J = 9.0$ Hz), 6.68 (d, 2H, $J = 8.7$ Hz), 3.60 (s, 3H). ^{13}C NMR (300 MHz, $\text{DMSO}-d_6$): 178.90, 163.84, 161.84, 148.88, 143.82, 138.92, 138.90, 135.59, 132.36, 132.13, 130.82, 131.21, 128.29, 127.62, 126.16, 124.60, 124.01, 123.17, 121.52, 115.40, 114.92, 114.90, 55.26. Anal. Calcd for $\text{C}_{23}\text{H}_{15}\text{NO}_3\text{S}$: C, 71.67; H, 3.92; N, 3.63. Found: C, 71.59; H, 3.85; N, 3.50.

1-(4-Trifluoromethyl-phenylsulfanyl)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (11i). $^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$): δ (ppm): 12.50 (s, 1H, NH), 8.74 (d, 1H, $J = 7.2$ Hz), 8.22 (d, 1H, $J = 6.9$ Hz), 8.04 (d, 1H, $J = 7.5$ Hz), 7.78 (t, 1H, $J = 7.5$ Hz), 7.72–7.62 (m, 3H), 7.50 (d, 2H, $J = 8.4$ Hz), 7.42 (d, 2H, $J = 8.1$ Hz). $^{13}\text{C NMR}$ (300 MHz, $\text{DMSO-}d_6$): 178.90, 163.84, 148.82, 143.88, 139.98, 137.07, 137.05, 135.59, 132.36, 132.13, 131.58, 131.21, 130.82, 128.29, 127.62, 124.60, 124.43, 124.41, 124.14, 124.01, 123.17, 121.52, 115.40. Anal. Calcd for $\text{C}_{23}\text{H}_{12}\text{F}_3\text{NO}_2\text{S}$: C, 65.24; H, 2.86; N, 3.31. Found: C, 65.17; H, 2.74; N, 3.19.

N-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-(4-acetyl-phenoxy)-acetamide (13b). Yield, 92%; mp 201–203°C; $^1\text{H NMR}$ (300 MHz, CDCl_3), δ (ppm): 12.60 (s, NH), 9.20 (d, 1H, $J = 7.5$ Hz), 8.20–8.30 (m, 2H), 8.10 (d, 1H, $J = 7.6$ Hz), 7.70–7.90 (m, 3H), 7.60 (d, 1H, $J = 8.9$ Hz), 7.40 (t, 1H, $J = 7.8$ Hz), 7.00 (d, 2H, $J = 8.7$ Hz), 4.30 (s, 2H), 1.40 (s, 3H).

N-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-(4-bromo-phenoxy)-acetamide (13c). Yield, 92%; mp 205–207°C; $^1\text{H NMR}$ (300 MHz, CDCl_3), δ (ppm): 13.30 (s, 1H, NH), 9.20 (d, 1H, $J = 7.5$ Hz), 8.40–8.22 (m, 2H), 8.10 (d, 1H, $J = 7.5$ Hz), 7.85–7.75 (m, 3H), 7.50 (d, 2H, $J = 9.0$ Hz), 7.06 (d, 2H, $J = 8.7$ Hz), 4.62 (s, 2H).

N-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-(4-nitro-phenoxy)-acetamide (13d). Yield, 86%; mp 175–177°C; $^1\text{H NMR}$ (300 MHz, CD_3OD), δ (ppm): 12.90 (s, 1H, NH), 9.40 (d, 1H, $J = 7.5$ Hz), 8.60–8.40 (m, 2H), 8.30 (d, 1H, $J = 7.5$ Hz), 8.05–7.90 (m, 3H), 7.80 (d, 2H, $J = 8.8$ Hz), 7.20 (d, 2H, $J = 8.70$ Hz), 4.30 (s, 2H).

2-(3-Chloro-4-methyl-phenoxy)-N-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-acetamide (13e). Yield, 90%; mp 210–211°C; $^1\text{H NMR}$ (300 MHz, CDCl_3), δ (ppm): 13.20 (s, 1H, NH), 9.20 (d, 1H, $J = 7.5$ Hz), 8.40–8.20 (m, 2H), 8.10 (d, 1H, $J = 7.5$ Hz), 7.84–7.72 (m, 3H), 7.34 (d, 1H, $J = 7.2$ Hz), 7.10 (d, 1H, $J = 1.8$ Hz), 6.85 (s, 1H, NH), 4.70 (s, 2H), 2.40 (s, 3H).

N-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-(2,4,6-tribromo-phenoxy)-acetamide (13f). Yield, 83%; mp 231–233°C; $^1\text{H NMR}$ (300 MHz, CDCl_3), δ (ppm): 13.20 (s, 1H, NH), 9.10 (d, 1H, $J = 7.5$ Hz), 8.20–8.10 (m, 2H), 8.00 (d, 1H, $J = 7.5$ Hz), 7.80–7.60 (m, 3H), 7.28 (s, 1H), 7.14 (s, 1H), 4.60 (s, 2H).

N-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-(2,4,6-trichloro-phenoxy)-acetamide (13g). Yield, 85%; mp 205–207°C; $^1\text{H NMR}$ (300 MHz, CDCl_3), δ (ppm): 13.10 (s, 1H, NH), 9.10 (d, 1H, $J = 7.5$ Hz), 8.10–8.20 (m, 2H), 8.00 (d, 1H, $J = 7.7$ Hz), 7.60–7.80 (m, 3H), 7.30 (s, 1H), 7.10 (s, 1H), 4.60 (s, 2H).

2-(3,5-Bis-trifluorosulfanyl-phenoxy)-N-(9,10-dioxo-9,10-dihydro-anthracen-1-yl)-acetamide (13h). $^1\text{H NMR}$ (300 MHz, CDCl_3), δ (ppm): 13.50 (s, 1H, NH), 8.56 (d, 1H, $J = 9.0$ Hz), 8.34 (d, 1H, $J = 6.0$ Hz), 8.24 (d, 1H, $J = 7.6$ Hz), 8.14 (d, 1H, $J = 7.5$ Hz), 7.94 (t, 1H, $J = 7.5$ Hz), 7.80 (t, 1H, $J = 7.5$ Hz), 7.66 (s, 2H), 7.55 (t, 1H, $J = 6.0$ Hz), 7.30 (s, 1H), 4.45 (s, 2H).

N-(9,10-Dioxo-9,10-dihydro-anthracen-1-yl)-2-pentafluorophenyloxy-acetamide (13i). Yield, 92%; mp 224–225°C; $^1\text{H NMR}$ (300 MHz, $\text{DMSO-}d_6$), δ (ppm): 12.60 (s, 1H, NH), 9.00 (dd, 1H, $J = 1.2, 9.6$ Hz), 8.18–8.22 (m, 1H), 8.12–8.16 (m, 1H), 7.88–7.98 (m, 4H), 4.60 (s, 2H).

1-(4-Acetylphenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14b). $^1\text{HNMR}$: (300 MHz, CDCl_3), δ (ppm): 8.20 (t, 3H, $J = 7.8$ Hz), 7.60 (m, 4H), 7.50 (t, 2H, $J = 7.5$ Hz), 7.00 (d, 2H, $J = 9.0$ Hz), 6.80 (s, NH), 1.20 (s, 3H). $^{13}\text{C NMR}$ (300 MHz, $\text{DMSO-}d_6$): 197.80, 178.90, 157.95, 155.53, 154.42, 152.76, 136.08, 135.46, 134.54, 133.13, 132.59, 130.43, 129.73, 129.71, 128.94, 127.83, 125.23, 122.45, 120.80, 114.91, 114.89, 113.01, 103.01, 26.31. Anal. Calcd for $\text{C}_{24}\text{H}_{15}\text{NO}_4$: C, 75.58; H, 3.96; N, 3.67. Found: C, 75.47; H, 3.85; N, 3.58.

1-(4-Bromophenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14c). $^1\text{HNMR}$ (300 MHz, CDCl_3), δ (ppm): 8.20 (t, 3H, $J = 7.8$ Hz), 7.80 (m, 3H), 7.60 (d, 1H, $J = 8.8$ Hz), 7.50 (t, 2H, $J = 7.5$ Hz), 7.00 (d, 2H, $J = 9.0$ Hz), 6.80 (s, NH). $^{13}\text{C NMR}$ (300 MHz, $\text{DMSO-}d_6$): 178.90, 155.53, 155.26, 154.42, 152.76, 136.08, 134.54, 133.13, 132.59, 132.15, 132.13, 130.43, 128.94, 127.83, 125.23, 122.45, 121.20, 121.19, 120.80, 114.56, 113.01, 103.01. Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{BrNO}_3$: C, 63.18; H, 2.89; N, 3.35. Found: C, 63.07; H, 2.77; N, 3.28.

1-(4-Nitrophenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14d). $^1\text{HNMR}$ (300 MHz, CDCl_3), δ (ppm): 8.20 (t, 3H, $J = 7.8$ Hz), 7.80 (m, 3H), 7.60 (d, 1H, $J = 9.0$ Hz), 7.50 (t, 2H, $J = 7.5$ Hz), 7.00 (d, 2H, $J = 9.0$ Hz), 6.80 (s, NH). $^{13}\text{C NMR}$ (300 MHz, $\text{DMSO-}d_6$): 178.90, 160.03, 155.53, 154.42, 152.76, 146.17, 136.08, 134.54, 133.13, 132.59, 130.43, 128.94, 127.83, 126.68, 126.64, 125.23, 122.45,

120.80, 120.38, 120.36, 113.01, 103.01. Anal. Calcd for C₂₂H₁₂N₂O₅: C, 68.75; H, 3.15; N, 7.29. Found: C, 68.67; H, 3.01; N, 7.18.

1-(3-Chloro-4-methyl-phenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14e). ¹HNMR (300 MHz, CDCl₃), δ (ppm): 8.20 (t, 3H, *J* = 7.8 Hz), 7.80 (m, 3H), 7.60 (d, 1H, *J* = 9.0 Hz), 7.40 (t, 1H, *J* = 7.5 Hz), 6.80 (s, 1H, NH), 2.35 (s, 3H). ¹³C NMR (300 MHz, DMSO-*d*₆): 178.90, 158.00, 155.53, 154.76, 152.42, 136.08, 134.54, 133.13, 132.87, 132.59, 132.54, 130.43, 130.19, 128.94, 127.83, 125.23, 122.45, 120.80, 116.72, 113.63, 113.01, 103.01, 19.90. Anal. Calcd for C₂₃H₁₄ClNO₃: C, 71.23; H, 3.64; N, 3.61. Found: C, 69.93; H, 3.37; N, 3.28.

1-(2,4,6-Tribromophenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14f). ¹HNMR (CDCl₃), δ (ppm): 8.20 (t, 2H, *J* = 7.8 Hz), 7.60 (m, 3H), 7.50 (t, 2H, *J* = 7.5 Hz), 7.00 (d, 2H, *J* = 9.0 Hz), 6.80 (s, NH). ¹³C NMR (300 MHz, DMSO-*d*₆): 178.90, 154.70, 154.42, 153.75, 152.76, 136.08, 134.56, 133.85, 133.83, 133.13, 132.59, 130.43, 128.94, 127.83, 125.23, 122.45, 120.80, 119.60, 116.22, 116.20, 113.04, 103.01. Anal. Calcd for C₂₂H₁₀Br₃NO₃: C, 45.87; H, 1.75; N, 2.43. Found: C, 45.76; H, 1.67; N, 2.33.

1-(2,4,6-Trichlorophenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14g). ¹HNMR (300 MHz, CDCl₃), δ (ppm): 8.20 (t, 3H, *J* = 7.8 Hz), 7.60 (m, 4H), 7.50 (t, 2H, *J* = 7.5 Hz), 7.00 (d, 2H, *J* = 9.0 Hz), 6.80 (s, NH). ¹³C NMR (300 MHz, DMSO-*d*₆): 178.90, 156.76, 154.42, 152.76, 144.86, 136.08, 134.08, 133.13, 132.59, 131.08, 130.43, 129.77, 129.75, 128.94, 127.89, 127.87, 127.83, 125.32, 122.45, 120.80, 112.56, 103.01. Anal. Calcd for C₂₂H₁₀Cl₃NO₃: C, 59.69; H, 2.28; N, 3.16. Found: C, 59.58; H, 2.19; N, 3.07.

1-(3,5-Bis(trifluoromethylthio)phenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14h). ¹HNMR (300 MHz, CDCl₃), δ (ppm): 8.20 (t, 2H, *J* = 7.8 Hz), 7.60 (m, 4H), 7.50 (t, 2H, *J* = 7.5 Hz), 7.00 (d, 2H, *J* = 9.0 Hz), 6.80 (s, NH). ¹³C NMR (300 MHz, DMSO-*d*₆): 178.90, 169.19, 155.53, 154.42, 152.76, 136.08, 134.54, 134.24, 134.22, 133.12, 131.49, 131.47, 132.59, 130.43, 128.94, 127.83, 127.32, 125.23, 122.45, 120.80, 114.41, 114.39, 113.01, 103.01. Anal. Calcd for C₂₄H₁₁F₆NO₃S₂: C, 53.43; H, 2.06; N, 2.60. Found: C, 53.36; H, 1.95; N, 2.55.

1-(Perfluorophenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (14i). ¹HNMR (CDCl₃), δ (ppm): 8.20 (t, 1H, *J* = 7.8 Hz), 7.60 (m, 4H), 7.50 (t, 2H, *J* = 7.5 Hz), 7.00 (d, 2H, *J* = 9.0 Hz), 6.80 (s, NH). ¹³C NMR (300 MHz, DMSO-*d*₆): 178.90, 154.42, 152.76, 143.87, 143.30, 143.28, 137.66, 136.08, 135.65, 133.13, 132.59, 132.57, 131.29, 131.27, 130.43, 128.94, 127.83, 125.23, 122.45, 120.80, 111.05, 103.01. Anal. Calcd for C₂₂H₈F₅NO₃: C, 61.55; H, 1.88; N, 3.26. Found: C, 61.47; H, 1.74; N, 3.55.

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