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

Jagan Reddy Etukala[1] and J. S. Yadav[2]

[1]*College of Pharmacy and Pharmaceutical Sciences, Florida A&M University, Tallahassee, FL 32307*

[2]*Indian Institute of Chemical Technology, Organic Chemistry Division-I, Hyderabad 500 007, India*

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ABSTRACT: *A convenient method is devised to synthesize 1-(phenylsulfanyl/phenoxy)-3H-naptho[1,2,3-de]quinoline-2,7-dione analogs in high yield for the first time by condensation of 2-bromo-N-(9,10-dixo-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 EC_{50} values ranging from 00.03 to 57 μg/mL in 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 benzanthone 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*)-naptho[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]

Correspondence to: Jagan Reddy Etukala; e-mail: jaganreddy.etukala@famu.edu.

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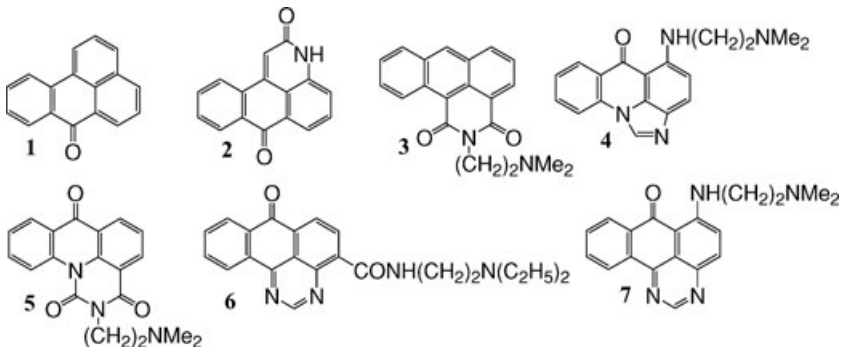


FIGURE 1 Examples of fused tetracyclic systems.

(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].

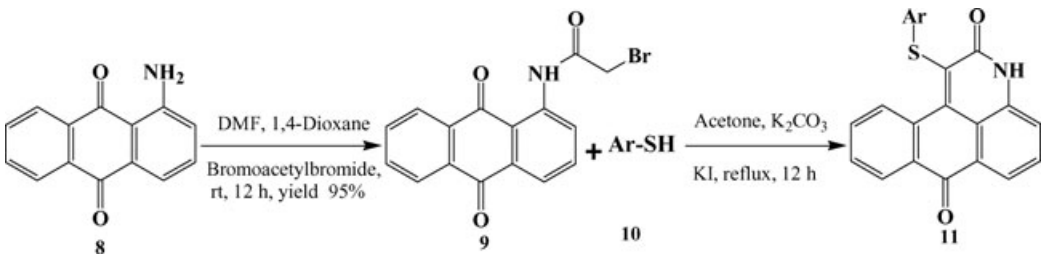
The main aim of the search for new structures within the mentioned groups is not only to develop novel synthetic compounds with antiviral and antitumor activities but also to overcome the major undesirable properties of related anthracycline antibiotics, their cytotoxicity (peroxidating activity), and 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 benzanthrones, anthracenedione, acridine, and their analogs could be a way to find the desired leads.

RESULTS AND DISCUSSION

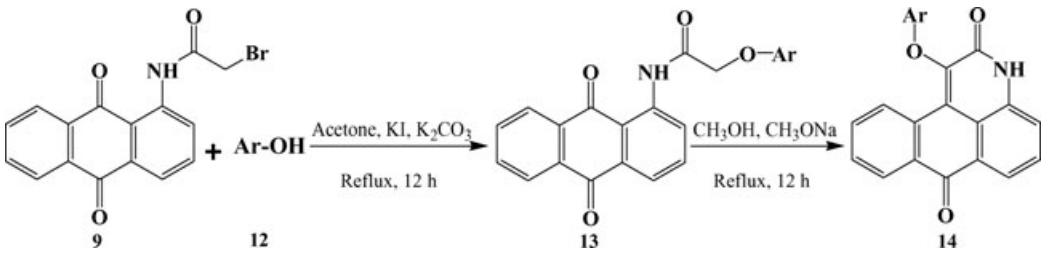
Although many methods for the synthesis of benzanthrones have already been published, no one has used the strategy adopted in this work. Our strategy has the following advantages: (i) It is easier to introduce the substituent at the first position of the benzanthrone ring. (ii) The reactivity of the 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*-naptho[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 physiochemical properties and solubility of the abovementioned derivatives and enhance their cytotoxic activity. Therefore, 1-(phenylsulfanyl/phenoxy)-3*H*-naptho[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*-naptho[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*-naptho[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*-naptho[1,2,3-*de*]-quninoline-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*-dimethylformaide and 1,4-dixane in the ratio of 1:1 with bromoacetyl bromide that afford (2-bromo-*N*-(9,10-dixo-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*-naptho[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-phenoxyl-3*H*-naptho[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*-naptho[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*-naptho[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. ^{1}H 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*-naptho[1,2,3-*de*]quinoline-2,7-dione (**11a–i**)

Entry	*Amide* (**9**) *Ar*	*Product* (**11**)	*Time (h)*	*Melting Point (°C)*	*Yield (%)*[a]
1	C_6H_5	**11a**	12	223–225	95
2	2-Cl-C_6H_4	**11b**	12	315–317	88
3	4-Cl-C_6H_4	**11c**	10	297–299	90
3	2-F-C_6H_4	**11d**	11	201–203	87
4	3-F-C_6H_4	**11e**	12	185–187	89
5	4-F-C_6H_4	**11f**	10	158–160	90
6	3-CH_3O-C_6H_4	**11g**	11	261–263	92
7	4-CH_3O-C_6H_4	**11h**	11	286–288	94
8	4-CF_3-C_6H_4	**11i**	12	301–303	88

[a]Isolated yields.

TABLE 2 Synthetic Data of 1-(Phenoxy)-3*H*-naptho[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_6H_5	**14a**	12	196–198	92
2	4-CH_3CO-C_6H_4	**14d**	10	217–219	96
3	4-Br-C_6H_4	**14b**	11	230–232	90
4	4-O_2N-C_6H_4	**14c**	11	239–241	85
5	3-Cl-4-CH_3-C_6H_3	**14e**	12	243–245	90
6	2,4,6-$(Br)_3$-C_6H_2	**14g**	11	257–259	89
7	2,4,6-$(Cl)_3$-C_6H_2	**14f**	10	266–268	91
8	3,5-$(CF_3S)_2$-C_6H_3	**14h**	12	183–185	88
9	2,3,4,5,6-F_5C_6	**14i**	12	167–169	90

[a]Isolated 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, bromoacetylbromide (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; ^{1}H NMR (300 MHz, $CDCl_3$), 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-3H-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), K_2CO_3 (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.

^{1}H 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). ^{13}C NMR (300 MHz, DMSO-d_6),: 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 $C_{22}H_{13}NO_2S$: 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), K_2CO_3 (439 gm, 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; ^{1}H NMR (300 MHz, CD_3OD), 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-3H-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.

^{1}H 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, 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 $C_{22}H_{13}NO_3$: 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**). ^{1}H NMR (300 MHz, 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, 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 $C_{22}H_{12}ClNO_2S$: 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**). ^{1}H NMR (300 MHz, 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, 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 $C_{22}H_{12}ClNO_2S$: 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**). ^{1}H NMR (300 MHz, DMSO-d_6), δ 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, 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 $C_{22}H_{12}FNO_2S$: 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**). ^{1}H NMR (300 MHz, 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, 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 $C_{22}H_{12}FNO_2S$: 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**). ^{1}H NMR (300 MHz, 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, 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 $C_{22}H_{12}FNO_2S$: 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**). ^{1}H 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, 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 $C_{23}H_{15}NO_3S$: 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**). ^{1}H 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, 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 $C_{23}H_{15}NO_3S$: C, 71.67; H, 3.92; N, 3.63. Found: C, 71.59; H, 3.85; N, 3.50.

*1-(4-Trifluoromethyl-phenylsulfanyl)-3H-naphthao-[1,2,3-de]quinoline-2,7-dione (**11i**).* ^{1}H-NMR (300 MHz, 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}C NMR (300 MHz, 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 $C_{23}H_{12}F_3NO_2S$: 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}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}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}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}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}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}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}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}H NMR (300 MHz, 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-Acetylhenoxy)-3H-naphtho[1,2,3-de]quinoline-2,7-dione (**14b**).* ^{1}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}C NMR (300 MHz, 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 $C_{24}H_{15}NO_4$: 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}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}C NMR (300 MHz, 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 $C_{22}H_{12}BrNO_3$: 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}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}C NMR (300 MHz, 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 $C_{22}H_{12}N_2O_5$: 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***).* ^{1}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), 7.40 (t, 1H, $J = 7.5$ Hz), 6.80 (s, 1H, NH), 2.35 (s, 3H). ^{13}C 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 $C_{23}H_{14}ClNO_3$: 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***).* ^{1}HNMR ($CDCl_3$), 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). ^{13}C 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 $C_{22}H_{10}Br_3NO_3$: 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***).* ^{1}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). ^{13}C 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 $C_{22}H_{10}Cl_3NO_3$: 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***).* ^{1}HNMR (300 MHz, $CDCl_3$), 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). ^{13}C 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 $C_{24}H_{11}F_6NO_3S_2$: 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***).* ^{1}HNMR ($CDCl_3$), 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). ^{13}C 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 $C_{22}H_8F_5NO_3$: C, 61.55; H, 1.88; N, 3.26. Found: C, 61.47; H, 1.74; N, 3.55.

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