Preparations of Anthraquinone and Naphthoquinone Derivatives and Their Cytotoxic Effects

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Chrysophanol and 1,8-di-*O*-hexylchrysophanol derivatives having nucleic acid bases at position 5 were synthesized. Furthermore, derivatives of menadione substituted at position 11 (type A naphthoquinone derivatives) or methylmenadione substituted at position 7 (type B naphthoquinone derivatives) modified with nucleic acid bases, amines and thiocyano, selenocyano or thioacetyl groups were synthesized. The cytotoxic effects of these derivatives on HCT 116 cells, which poorly express P-glycoprotein (P-gp), and Hep G2 cells, which stably express P-gp, were evaluated by performing 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Results were compared with those obtained using 5-fluorouracil (5-FU), which has been used clinically. Several of these derivatives exhibited markedly higher potent cytotoxic effects not only on HCT cancer cells but also Hep G2 cancer cells as compared with 5-FU.

Key words anthraquinone derivative; naphthoquinone derivative; cytotoxic effect; HCT 116 cell; Hep G2 cell

Previously, we reported[1] a comparison of the cytotoxic effects of naturally occurring hydroxyanthraquinone derivatives, isolated from the root of Rhubarb (*Rheum palmatum* (Polygonaceae)) and hydroxynaphthoquinone derivatives, isolated from the roots of *Lithosperumum erythrorhizon* Sieb. *et* Zucc. and *Macrotomia euchroma* (Royle) Pauls. (Boraginaceae), using human colorectal (HCT 116)[2] and human hepatoma (Hep G2)[3] cell lines. In addition, we prepared 1,8-di-*O*-alkylaloe-emodins and 15-amino-, 15-thiocyano- and 15-selenochrysophanol derivatives from aloe-emodin, which is one of hydroxyanthraquinone compounds isolated from the root of Rhubarb. A comparison of cytotoxic acivities of the derivatives using the same cancer cell lines were also reported.[4]

The present study deals with preparations of chrysophanol and 18-di-*O*-hexylchrysophanol derivatives having various nucleic acid bases at position of 15 from aloe-emodin and 18-di-*O*-hexylaloe-emodin, respectively. We also synthesize napthoquinone derivatives having various nucleic acid bases, amines, and thiocyanato (-SCN), selenocyanato (-SeCN) and thioacetyl (-SAc) groups on the side chains of the naphthoquinone skeletons derived from menadione (Vitamin K_3, 2-methylnaphthoquinone). Furthermore, we evaluate the cytotoxic effects of the synthetic derivatives using HCT 116 and Hep G2 cancer cell lines, and compare the effects with those of 5-fluorouracil (5-FU).

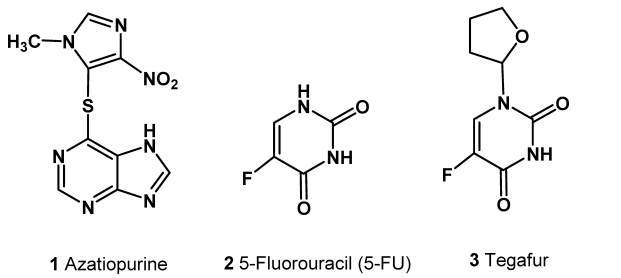

Fig. 1. Purine and Pyrymidine Base Derivatives Used in Clinical Chemotherapy

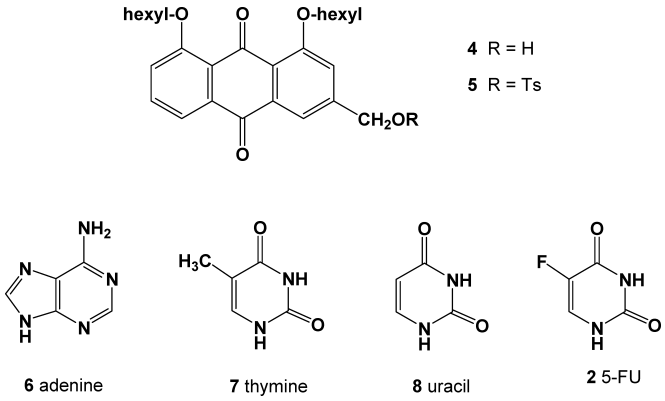

Fig. 2. Structures of Compounds **4** and **5** and Nucleic Acid Bases **6**, **7**, **8** and **2** Used in This Study

Chemical Results and Dicscussion

Several cytotoxic compounds having purine or pyrimidine bases in the molecule, such as azathiopurine **1**,[5,6] 5-fluorouracil **2** (5-FU)[7—10] and tegafur **3**,[11,12] have been synthesized and used in clinical chemotherapy. In this study, syntheses of anthraquinone derivatives having nucleic acid bases (adenine, thymine, uracil or 5-FU) on the side chain of the anthraquinone skeleton were performed (Fig. 1).

Firstly, anthraquinone derivatives having the nucleic acid bases at position 15 were synthesized. 1,8-Di-*O*-hexylaloe-emodin **4**, which displayed the highest cytotoxic activity of the synthesized 1,8-*O*-alkylaloe-emodins,[4] was selected as the starting material. The synthesis of tosylate **5** from **4** was previously reported.[13] Compound **5** was reacted with adenine **6**, thymine **7**, uracil **8** or 5-FU **2** in the presence of NaH in *N*,*N*-dimethylformamide (DMF) to give **9**, **10**, **11** and **12** in 19.5%, 27.9%, 39.7% and 55.9% yield, respectively (Fig. 2). The substituted positions of the nucleic acid bases of compounds **9**—**12** were confirmed from the heteronuclear multiple bond connectivity (HMBC) spectra shown in Fig. 3. In the spectrum of compound **9**, correlations between the proton signals due to the methylene group (CH_2) on the anthraquinone residue at δ 5.43 and the carbon signal at δ 117.2 due to C-4 on the quinone residue and those at δ 153.4 and 140.2

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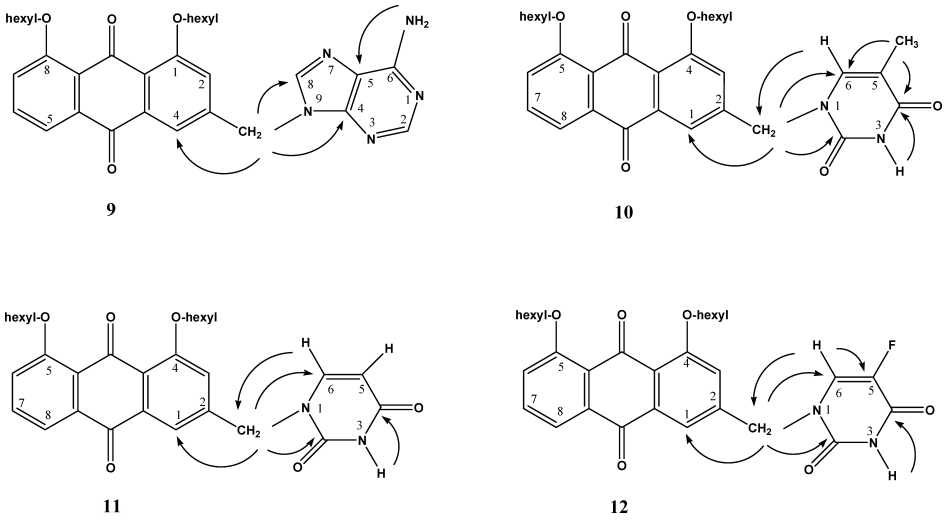


Fig. 3. Structures of Compounds **9**—**12** and ^{1}H–^{13}C Long-Range Correlations Observed for Compounds **9**—**12**

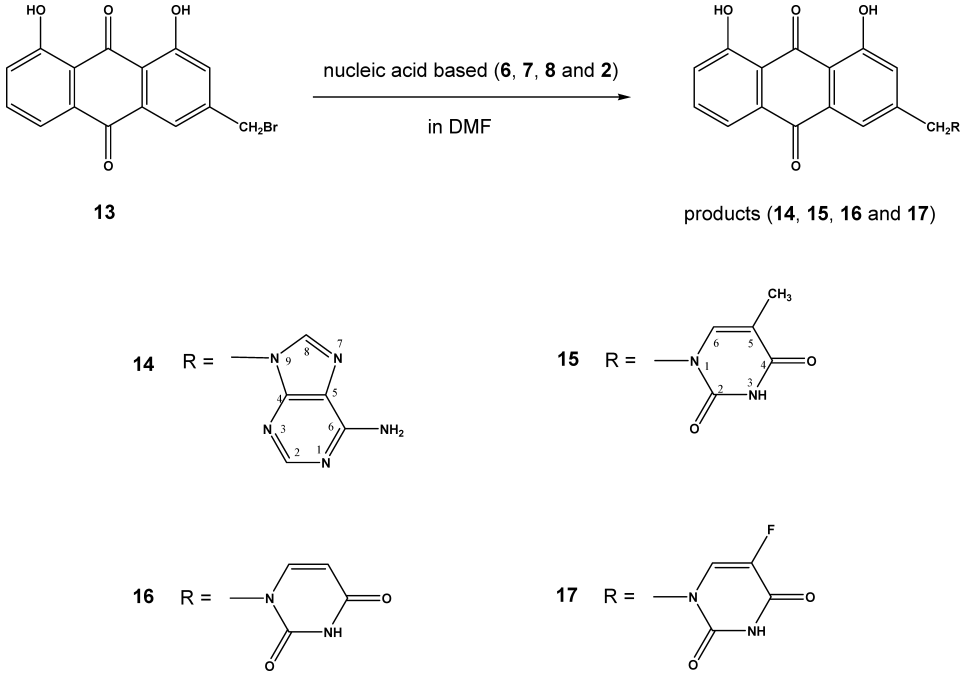


Fig. 4. Structures of Compounds **14**—**17** Obtained by the Reactions of **13** with **6**, **7**, **8** and **2**, Respectively

due to C-4 and C-8 on the adenine residue, respectively, were observed. Thus, compound **9** was confirmed as 3-[(6-amino-9*H*-purin-9-yl)-methyl]-1,8-bis(hexyloxy)anthracene-9,10-dione. Correlations between proton signals at δ 4.94, 4.98 and 4.93 due to the methylene groups on the anthraquinone residues of **10**, **11** and **12**, respectively, and carbon signals due to C-2 and C-6 at δ 150.9 and 136.4, δ 150.7 and 143.6, and δ 149.3 and 127.9 on the thymine, uracil and 5-fluorouracil residues, respectively, were observed. As a result, compounds **10**, **11** and **12** are confirmed as 1-([4,5-bis (hexyloxy)-9,10-dinoe-9,10-dihydroanthracene-2yl]methyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione, 1-([4,5-bis(hexyloxy)-9,10-dinoe-9,10-dihydroanthracene-2yl]methyl)pyrimidine-2,4(1*H*,3*H*)-dione and, 1-([4,5-bis(hexyloxy)-9,10-dinoe-9, 10-dihydroanthracene-2yl]methyl)-5-fluoropyrimidine-2, 4(1*H*,3*H*)-dione, respectively.

1,8-Dihydroxyl anthraquinone derivatives having nucleic acid bases were synthesized as follows. 15-Bromochrysophanol **13**[4] was reacted with adenine **6**, thymine **7**, uracil **8** or 5-FU **2** in the presence of NaH in DMF to give compounds **14**, **15**, **16** and **17** in 18.1%, 57.0%, 68.2% and 45.9% yield, respectively (Fig. 4).

Next, naphthoquinone derivatives having various nucleic acid bases or amines, and thiocyanato (-SCN), selenocyanato (-SeCN) and thioacetyl (-SAc) groups on the side chains of the naphthoquinone skeletons were synthesized. In this study, we aimed to obtain two types of naphthoquinone derivatives (type A and B shown in Fig. 5) from menadione **18** (Vitamin K_3, an easily obtainable compound from commercial suppliers) in order to investigate the structure–cytotoxic activity relationships of the products.

A key 2-bromomethoxy-1,4-dimethoxynaphthalene **19** for

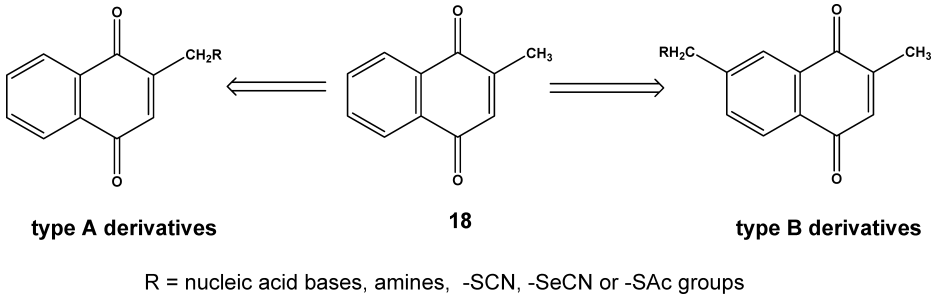


Fig. 5. Structures of Compound **18** and Type A and B Derivatives

the preparation of type A (Fig. 5) derivatives was synthesized as follows. Compound **18** was reacted with $SnCl_2$ in acidic MeOH, followed by treatment with dimethyl-sulfate and K_2CO_3 in acetone[14] to give **20** in 71.5% yield. Compound **20** was oxidized with $KMnO_4$ in aqueous pyridine to give compound **21** in 32.3% yield, and then reduced with $LiAlH_4$ to obtain alcohol **22** (57.1% yield). The alcohol was then reacted with CBr_4 and PPh_3 in ether to give compound **19** (50.3% yield) (Fig. 6).

A key 7-bromomethoxy-1,4-dimethoxynaphthalene **23** for the preparation of type B derivatives (Fig. 5) was synthesized as follows. Friedel–Crafts reaction[15] of compound **20** with CH_3COCl gave **24** in 65.2% yield. The position of the substituted acetyl group ($COCH_3$) of **24** was confirmed from the HMBC spectrum (Fig. 7). Correlation between proton signals at δ 8.06 and 8.83 due to H-6 and H-8, respectively, and carbon signal at δ 198.1, due to the newly introduced acetyl group, and that between the methyl proton signal at δ 2.73 of the acetyl group and carbon signals at 133.2 and 124.5 due to C-7 and C-8, respectively, were observed. The NMR data shows compound **24** is 7-acetyl-1,4-dimethoxy-2-methylnaphthalene.

Compound **24** was successively treated with KOH,[16] reduced with $LiAlH_4$ and brominated with CBr_4 and PPh_3 to give **25**, **26** and **23**, in 43.5%, 64.7% and 65.8% yield, respectively. Bromide **19** was reacted with adenine, thymine, uracil and 5-fluorouracil in the presence of NaH in DMF to give compounds **27**, **28**, **29** and **30** in 28.3%, 53.7%, 41.9% and 54.7% yield, respectively (Fig. 8). The same reactions with bromide **23** afforded compounds **31**, **32**, **33** and **34** in 57.0, 54.7, 56.6 and 47.8% yield, respectively. Cleavage of the protecting group of **27** was carried out by three different methods; i) hydrolysis with HNO_3 in AcOH, ii) treatment with $(NH_4)_2Ce(NO_3)_6$ (CAN) in aqueous CH_3CN[14] and iii) treatment with *N*-bromosuccinimide (NBS) in acidified aqueous tetrahydrofuran (THF).[17] Most of the procedures gave mixtures, although treatment of compounds **28**—**34** by the method i) afforded the desired products **35**, **36**, **37**, **38**, **39**, **40** and **41** in 53.2%, 47.8%, 51.7%, 21.9%, 64.1%, 63.5% and 56.1% yield, respectively.

Naphthoquinone derivatives having various amines at the side chain in the molecules were synthesized next (Fig. 9). Bromide **19** was reacted with pyrrolidine, 1-methylpiperazine, morpholine, imidazole, theophylline and theobromine in THF to give compounds **42**, **43**, **44**, **45**, **46** and **47** in 64.2, 51.4, 62.6, 46.7, 32.6 and 55.5% yield, respectively. Bromide **23** was reacted with morpholine in THF to give compound **48** in 49.8% yield. Bromide **23** was reacted with theophylline

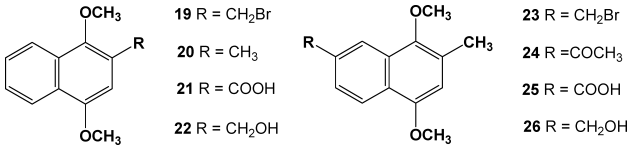


Fig. 6. Structures of Compounds **19**—**26**

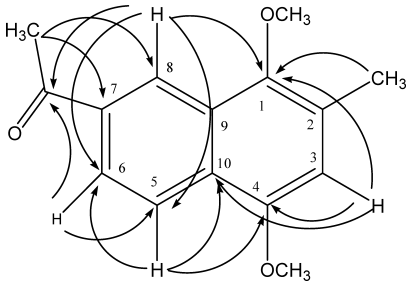


Fig. 7. ^1H–^{13}C Long-Range Correlations Observed for Compound **24**

and theobromine in the presence of NaH in DMF to afford compounds **49** and **50** in 38.4% and 69.8% yield, respectively. Cleavage of the protecting group of **42** and **43** by the method iii) (described earlier) gave compounds **51** and **52** in 59.0% and 54.8% yield, respectively. Compounds **44** and **46** were deprotected by the method ii) to afford compounds **53** and **54** in 63.5% and 53.7% yield, respectively. The protecting group of **47** was cleaved by the method i) to give compound **55** in 58.6% yield. Unfortunately, cleavage of the protecting group of **45** gave a mixture of products using each of the three methods. The cleavages of the protecting group of compounds **48**—**50** by the method iii) gave compounds **56**—**58** in 49.5%, 41.2% and 38.5% yield, respectively.

Finally, type A and B naphthoqinone derivatives (Fig. 5) having thiocyanato (-SCN), selenocyanato (-SeCN) and thioacetyl (-SAc) groups at the side chains of the molecules were prepared. In these preparations, bromide **19** and bromide **23** were also utilized as starting materials. Bromide **19** was reacted with KSCN, KSeCN and KOAc to give naphthalene derivatives **59**—**61** in 73.6%, 76.4% and 55.3% yield, respectively. Reactions of bromide **23** with KSCN, KSeCN and KOAc gave naphthalene derivatives **62**—**64** in the yields of 65.3%, 52.2% and 48.3% yield, respectively. Cleavage of the protecting groups of compounds **59**—**64** was carried out by the three methods described earlier. Method i) was used to obtain compounds **65**—**70** in 46.6%, 38.9%, 45.3%, 42.3%, 41.8% and 71.5% yield, respectively.

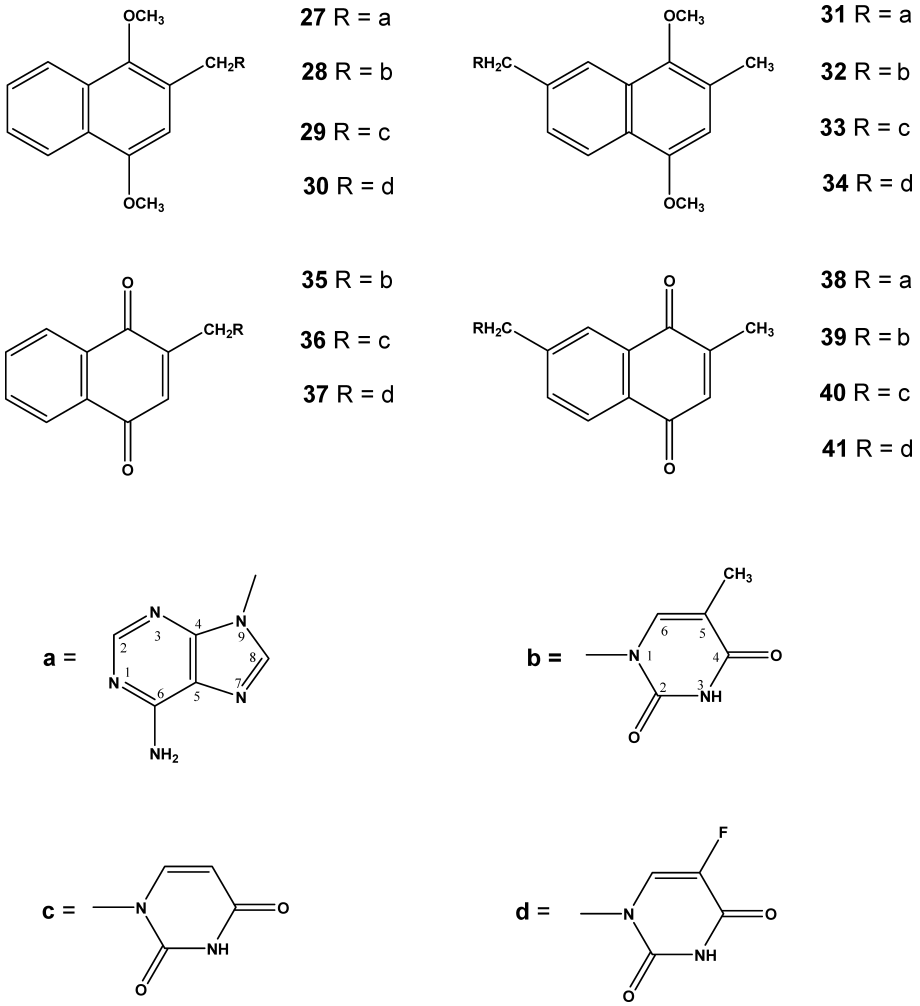


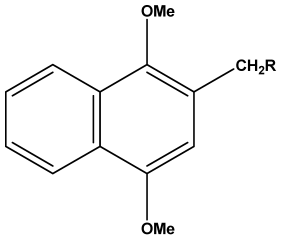
Fig. 8. Structures of Compounds **27**—**41**

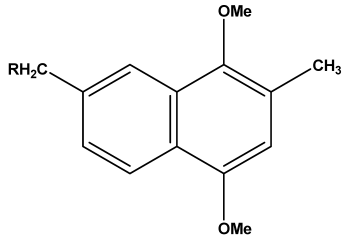
Pharmacological Results and Discussion

Cytotoxic effects of all anthraquinone and naphthoquinone derivatives prepared in this study were tested against HCT 116 and Hep G2 cancer cell lines using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay[18] and compared with those of 5-FU, which has been used clinically. In this study, the effects are represented by IC_{50} values *i.e.*, concentration of compound required to give 50% inhibition of cell growth. Although multidrug resistance 1 (MDR 1) (P-glycoprotein; P-gp)[2] is overexpressed in Hep G2 cells, it is barely expressed in HCT 116 cells.[3] P-gp acts as an efflux pump to remove several antitumor agents such as Ca^{2+} antagonists, cyclosporine and digoxin from cells.[19]

Table 1 shows the comparison of cytotoxic effects of 1,8-di-*O*-hexylchrysophanol derivatives **9**—**12** and chrysophanol derivatives **14**—**17** having nucleic acid bases at position 15 with those of clinically used 5-fluorouracil (5-FU) **2** against HCT 116 and Hep G2 cancer cells. In the case of compounds **9**—**12**, **9** and **10** substituted with adenine and thymine, respectively, showed more potent effects on the both cell lines (IC_{50}: 8.1±1.1 and 3.8±0.11 μM, respectively, on HCT 116 cells, and 10.4±3.6 and 4.2±0.4 μM, respectively, on Hep G2 cells) than those of **2** (IC_{50}: 45.0±6.8 and 50.8±3.7 μM on HCT 116 and Hep G2 cells, respectively). Compounds **11** and **12** substituted with uracil and 5-fluorouracil, respectively, have, however, slightly greater effects (IC_{50}: 29.3±6.9 and 39.6±4.4 μM, respectively) on HCT 116 cells than that of **2**. Using Hep G2 cells, compound **12** displayed only a marginally greater effect (IC_{50}: 45.3±10.5 μM) than that of **2**, while the effect of compound **11** (IC_{50}: more than 100 μM) was weaker than that of **2** on the same cells. We also tested the biological effect of chrysophanol derivatives **14**—**17** substituted with adenine, thymine, uracil or 5-fluorouracil, respectively. All these derivatives showed greater effects than those of **2** both on TCT 116 cells and Hep G2 cells. Among these compounds, **14**, **16** and **17** had potent effects both on HCT 116 cells (IC_{50}: 2.8±0.4—7.8±0.4 μM) and Hep G2 cells (IC_{50}: 3.1±0.4—9.8±0.6 μM), although the exact IC_{50} values for **15** were not obtained because of problems with turbidity.

Next, cytotoxic effects of type A and B naphthoquinone derivatives having nucleic acid bases (Fig. 8) were evaluated and compared with those of **2** (5-FU). Table 2 shows the cytotoxic effects of compounds **35**—**37** (type A) and compounds **38**—**41** (type B). Both types of compounds had potent effects on HCT 116 cells (IC_{50}: 1.8±0.1—3.0±0.1 μM for **35**—**37** and 1.8±0.1—8.6±0.6 μM for **38**—**41**) and Hep G2 cells (IC_{50}: 2.3±0.1—4.1±0.2 μM for **35**—**37** and 2.5±0.2—7.8±0.3 μM for **38**—**41**). The effects of type A and type B derivatives against HCT 116 and Hep G2 cells





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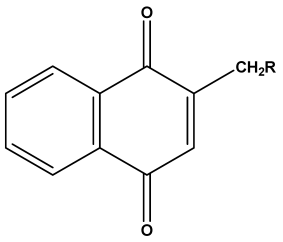
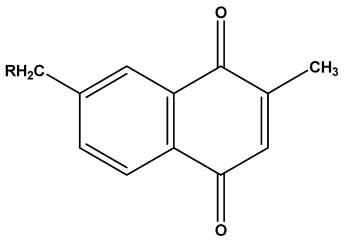
44 R = g **45** R = h

46 R = i **47** R = j

48 R = g **49** R = i

50 R = j





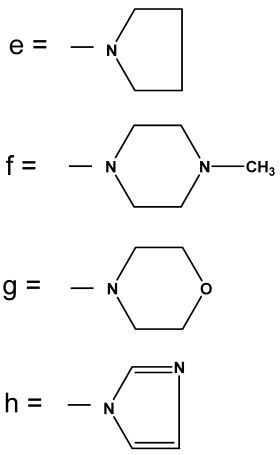
51 R = e **52** R = f

53 R = g **54** R = i

55 R = j

56 R = g **57** R = i

58 R = j



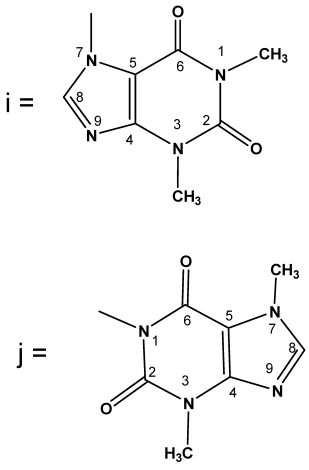


Fig. 9. Structures of Compounds **42**—**58**

were 5.2—25.0 and 6.5—22.1 times higher than those of **2** (IC_{50}: 45.0±6.8 and 50.8±3.7 μM, respectively). However, there was no significant difference between the effects of type A derivatives and those of type B derivatives.

Amino derivatives **51**—**54** (type A) and **56**—**58** (type B) also showed more potent effects on HCT 116 cells (IC_{50}: 1.6±0.1—6.7±0.1 μM) and Hep G2 cells (IC_{50}: 2.1±0.3—8.5±0.4 μM) (Table 3) than the corresponding effect of compound **2**. In this case, no significant difference between type A and type B amines was also observed.

Finally, cytotoxic effects of type A and B naphthoquinone derivatives **65**—**67** and **68**—**70**, respectively, having -SCN, -SeCN and -SAc groups (Fig. 10) were evaluated and compared with those of **2** (5-FU) (Table 4). All these type A and B compounds displayed a greater biological effects (IC_{50}: 2.7±0.1—16.0±0.5 μM on HCT 116 cells, 4.4±0.1—20.9±1.4 μM on Hep G2 cells) than compound **2** using both cell lines. A comparison of the effects shown in Table 4 between type A and type B compounds illustrates that there is no difference in the structure–activity relationships. Interes-

Table 1. Comparison of the Cytotoxic Effects of Anthraquinone Derivatives **9**—**12** and **14**—**17** with Those of 5-FU (**2**)[a]

Compound	IC_{50}±S.D. (μM)[b]	
	HCT 116 cells	Hep G2 cells
2 (5-FU)	45.0±6.8	50.8±3.7
9	8.1±1.1	10.4±3.6
10	3.8±0.1	4.2±0.4
11	29.3±6.9	>100[c]
12	39.6±4.4	45.3±10.5
14	7.8±0.4	3.1±0.4
15	29.4±1.9[d]	21.5±0.6[d]
16	5.1±0.2	3.9±0.5
17	2.8±0.4	9.8±0.6

a) Each experiment was performed in duplicate wells, and drug treatments were performed separately three times. *b*) IC_{50} values (mean±S.D.) are the concentrations at which 50% of the cells are inhibited from growing. *c*) IC_{50} values more than 100 μM are indicated as >100. *d*) Precise values for compound **15** were not obtained because the turbidity of the solution was too great at the concentrations of compound giving 50% growth inhibition.

Table 2. Comparison of the Cytotoxic Effects of Compounds **35**—**41** with Those of 5-FU (**2**)[a]

Compound	IC_{50}±S.D. (μM)[b]	
	HCT 116 cells	Hep G2 cells
2 (5-FU)	45.0±6.8	50.8±3.7
35	1.8±0.1	2.8±0.1
36	3.0±0.1	3.5±0.1
37	2.5±0.2	4.1±0.2
38	1.8±0.1	2.5±0.2
39	2.7±0.1	2.3±0.1
40	5.8±0.3	7.8±0.3
41	8.6±0.6	6.4±0.1

a) Each experiment was carried out in duplicate wells, and drug treatments were performed separately three times. *b*) IC_{50} values (mean±S.D.) are the concentrations at which 50% of the cells are inhibited from growing.

Table 3. Comparison of the Cytotoxic Effects of Compounds **51**—**58** with Those of 5-FU (**2**)[a]

Compound	IC_{50}±S.D. (μM)[b]	
	HCT 116 cells	Hep G2 cells
2 (5-FU)	45.0±6.8	50.8±3.7
51	5.3±0.1	4.1±0.1
52	1.6±0.1	4.5±0.2
53	5.4±0.2	4.7±0.3
54	1.9±0.1	2.1±0.3
55	2.9±0.1	3.8±0.1
56	6.7±0.1	8.5±0.4
57	4.2±0.1	6.8±0.1
58	3.1±0.1	3.8±0.1

a) Each experiment was carried out in duplicate wells, and drug treatments were performed separately three times. *b*) IC_{50} values (mean±S.D.) are the concentrations at which 50% of the cells are inhibited from growing.

tigly, the effect of compounds **65** and **67**—**70** on HCT 116 cells was greater than the corresponding effect on Hep G2 cells. However, in the case of compound **66**, both cell lines were affected to a similar extent. Among these compounds **65**—**70**, compound **68** (type B derivative having -SCN group) in particular displayed a remarkably potent effects against both the HCT 116 cells (IC_{50}: 2.7±0.1 μM) and Hep G2 cells (IC_{50}: 4.4±0.1 μM) lines.

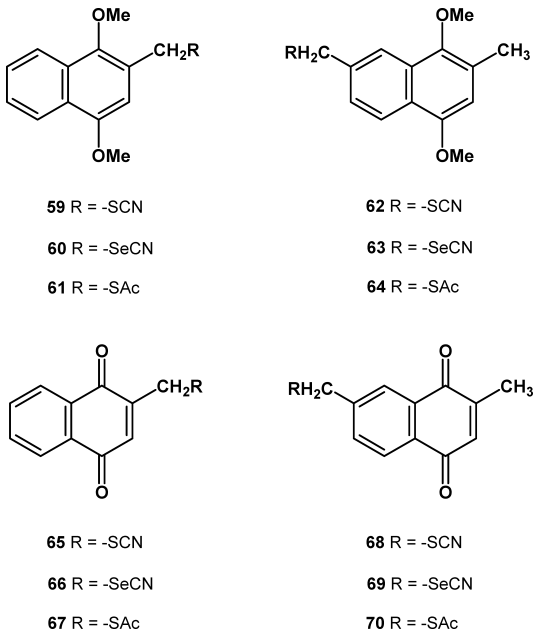


Fig. 10. Structures of Compounds **59**—**70**

Table 4. Comparison of the Cytotoxic Effects of Compounds **65**—**70** with Those of 5-FU (**2**)[a]

Compound	IC_{50}±S.D. (μM)[b]	
	HCT 116 cells	Hep G2 cells
2 (5-FU)	45.0±6.8	50.8±3.7
65	16.0±0.5	20.9±1.4
66	8.5±0.2	7.9±0.8
67	3.8±0.6	6.6±0.2
68	2.7±0.1	4.4±0.1
69	4.1±0.1	10.1±0.1
70	6.5±0.1	13.4±0.3

a) Each experiment was carried out in duplicate wells, and drug treatments were performed separately three times. *b*) IC_{50} values (mean±S.D.) are the concentrations at which 50% of the cells are inhibited from growing.

Conclusion

In this study, anthraquinone and naphthoquinone derivatized with various nucleic acid bases, amines and thiocyanato, selenocyanato or thioacetyl groups were synthesized. From 1,8-di-*O*-hexyl-15-*O*-tosylchrysophanol **5**, 1,8-di-*O*-hexylchrysophanol derivatives **9**—**12** substituted with adenine, thymine, uracil and 5-fluorouracil, respectively, were prepared. Starting from 15-bromochrysophanol **13**, chrysophanol derivatives **14**—**17** substituted with adenine, thymine, uracil and 5-fluorouracil, respectively, were prepared. For the preparations of naphthoquinone derivatives, 1,4-dimethoxynaphthalene **20** derived from menadione **18** (Vitamin K_3) was used as a key intermediate. From compound **20**, both type A and type B bromides (11-bromo-1,4-dimethoxynaphthalene **19** and 7-bromomethyl-1,4-dimethoxynaphthalene **23**, respectively) were obtained. Substitutions of **19** with nucleic acid bases, amines and potassium salts (KSCN, KSeCN and KSAc), followed by cleavage of the protecting groups, gave **35**, **36** and **37** as type A derivatives bearing thymine, uracil and 5-fluolouracil moieties, respec-

tively. Compounds **51**—**55** represent the same type of derivatives having amines (pyrrolidine, 1-methylpiperazine, morpholine, imidazole, theophylline or theobromine, respectively). Likewise compounds **65**—**67** are corresponding derivatives having -SCN, -SeCN and -SAc groups, respectively. Similarly, from bromide **23**, the type B naphthoquinone derivatives **38**—**41** having adenine, thymine, uracil and 5-fluorouracil, respectively, were synthesized. The same type derivatives **56**—**58** having morpholine, theophylline and theobromine, respectively, and the same type derivatives **68**—**70** having -SCN, -SeCN and -SAc, respectively, were also obtained.

The cytotoxic effects of each synthetic derivative was evaluated using the HCT 116 cell and Hep G2 cancer cell lines. These cell lines were chosen because MDR 1 (P-glycoprotein, P-gp)[2] is known to be overexpressed in the Hep G2 cell lines but barely expressed in the HCT 116 cell lines.[3] The cytotoxic activity of each compound was then compared to that of 5-fluorouracil (5-FU). Among anthraquinones **9**—**17**, 1,8-di-*O*-hexylchrysophanols **9** and **10** and chrysophanols **14**, **16** and **17** showed potent effects both on HCT 116 and Hep G2 cells (Table 1). Interestingly, compounds **14** and **16** displayed enhanced activity using both Hep G2 cells and HCT 116 cells. Indeed, of all the anthraquinones, **14** and **16** seemed to be the strongest inhibitors of the efflux function of P-gp. Moreover, all the naphthoquinone derivatives synthesized in this study also displayed potent effects both on HCT 116 and Hep G2 cell lines (see Tables 2—4). We analized the structure–activity relationships between type A and B derivatives and the various substituents. However, no firm conclusions could be made from this analysis. Interestingly, however, many of the compounds had potent effects against Hep G2 cells, which overexpress P-gp. We anticipate these derivatives may help to overcome the problem of drug excretion from cancer cells stably expressing P-gp. Indeed, excretion of anticancer agents is a major cause of multidrug resistance. Further work is required to establish the precise structure–activity relationship for the various derivatives in terms of their affinity for the target proteins and the corresponding intracellular accumulation.

Experimental

General Methods Reagent-grade chemicals and solvents were obtained from commercial suppliers. The melting points (mp) were determined using a Yanagimoto micromelting point apparatus and were uncorrected. Kieselgel 60 F_{254} (E. Merck, Germany) was used in thin-layer chromatography (TLC). Spots were detected by spraying plates with 1 : 9 $Ce(SO_4)_2$–10% H_2SO_4 reagent, followed by heating the plates at 200 °C for 4—5 min. Column chromatography was carried out using Kieselgel 60 (E. Merck), then the eluates were monitored by TLC. ^{1}H- and ^{13}C-NMR spectroscopy investigations were carried out at 500 and 125 MHz, respectively, and ^{1}H–^{1}H and ^{1}H–^{13}C correlation spectroscopy (COSY) and HMBC spectra were obtained using a JEOL JNM-A500 FT-NMR spectrometer. Tetramethylsilane was used as an internal standard. The chemical shifts are given in ppm. The multiplicities of the ^{1}H-NMR signals are indicated as s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet) and m (multiplet). Electron impact mass spectra (EI-MS) were recorded using a JEOL JMS-DX 300 mass spectrometer. First-atom-bombardment mass spectra (FAB-MS) and high resolution mass (HR-MS) spectra were recorded using a JEOL JMS-700 mass spectrometer.

3-[(6-Amino-9*H*-purin-9-yl)methyl]-1,8-bis(hexyloxy)anthracene-9,10-dione (9) A solution of **5** (110 mg, 0.19 mmol), NaH (42.5 mg, 1.8 mmol) and **6** (118.5 mg, 0.88 mmol) in DMF (5 ml) was stirred at 85 °C for 35 h. The reaction mixture was poured into ice-water (20 ml) and extracted with $CHCl_3$ (30 ml×2). The organic extracts were successively washed with brine and water, dried over absolute $MgSO_4$, and then filtered. The filtrate was evaporated to give a residue, which was subjected to silica gel column chromatography (a gradient of 0—10% MeOH in $CHCl_3$) to afford compound **9** (20.1 mg, 19.5% yield) as yellowish needles (mp 194—196 °C). FAB-MS: *m/z* 556 $[M+H]^+$. HR-MS: *m/z* Calcd for $C_{32}H_{38}N_5O_4$ $[M+H]^+$; 556.2925, Found; 556.2923. ^{1}H-NMR ($CDCl_3$) δ: 8.40 (1H, s, 8′-H), 7.85 (1H, s, 2′-H), 7.77 (1H, dd, *J*=7.7, 0.9 Hz, H-5), 7.70 (1H, d, *J*=1.5 Hz, H-4), 7.58 (1H, dd, *J*=8.2, 7.7 Hz, H-6), 7.28 (1H, dd, *J*=8.2, 0.9 Hz, H-7), 7.23 (1H, d, *J*=1.5 Hz, H-2), 5.73 (2H, br s, 6′-NH_2), 5.43 (2H, s, 15-CH_2), 4.11 and 4.03 (each 2H, t, *J*=6.6 Hz, 1- or 8-OCH_2), 1.88 (4H, m, CH_2×2), 1.54 (4H, m, CH_2×2), 1.34 (8H, m, CH_2×4), 0.91 (6H, m, CH_3×2). ^{13}C-NMR ($CDCl_3$): δ 183.9 (C-10), 181.4 (C-9), 159.7 (C-8), 159.0 (C-1), 155.6 (C-6′), 153.4 (C-4′), 150.2 (C-2′), 141.3 (C-3), 140.2 (C-8′), 135.4 (C-14), 134.7 (C-11), 133.6 (C-6), 124.5 (C-12), 124.4 (C-13), 119.8 (C-7), 119.6 (C-5′), 118.9 (C-5), 118.4 (C-2), 117.2 (C-4), 69.9 and 70.0 (each OCH_2), 47.1 (C-15), 22.6—31.6 (CH_2×8), 14.0 (CH_3×2).

1-([4,5-Bis(hexyloxy)-9,10-dioxo-9,10-dihydroanthracen-2-yl]methyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (10) The same reaction and procedure using **5** (52.4 mg, 0.09 mmol), **7** (53.9 mg, 0.43 mmol) and NaH (21.9 mg, 0.91 mmol) as described for **9** gave compound **10** (13.5 mg, 27.9% yield) as yellowish needles (mp 194—196 °C). FAB-MS: *m/z* 547 $[M+H]^+$. HR-MS: *m/z* Calcd for $C_{32}H_{39}N_2O_6$ $[M+H]^+$; 547.2809, Found; 547.2808. ^{1}H-NMR ($CDCl_3$) δ: 8.64 (1H, br s, 3′-H), 7.79 (1H, dd, *J*=7.6, 0.9 Hz, H-5), 7.67 (1H, d, *J*=1.5 Hz, H-4), 7.62 (1H, dd, *J*=8.2, 7.6 Hz, H-6), 7.29 (1H, dd, *J*=8.2, 0.9 Hz, H-7), 7.23 (1H, d, *J*=1.5 Hz, H-2), 7.03 (1H, s, 6′-H), 4.94 (2H, s, 15-CH_2), 4.12 and 4.10 (each 2H, t, *J*=6.4 Hz, 1- or 8-OCH_2), 1.92 (3H, m, 5′-CH_3), 1.92 (4H, m, CH_2×2), 1.56 (4H, m, CH_2×2), 1.37 (8H, m, CH_2×4), 0.92 (6H, m, CH_3×2); ^{13}C-NMR ($CDCl_3$): δ 184.0 (C-10), 181.4 (C-9), 159.7 (C-8), 159.0 (C-1), 163.6 (C-4′), 150.9 (C-2′), 141.3 (C-3), 136.6 (C-11), 136.4 (C-6′), 135.5 (C-14), 133.7 (C-16), 124.6 (C-12), 124.5 (C-13), 119.8 (C-7), 118.9 (C-5), 118.6 (C-2), 117.4 (C-4), 111.9 (C-5′), 69.9 and 70.0 (each OCH_2), 51.0 (C-15), 22.6—31.6 (CH_2×8), 14.0 (CH_3×2), 12.4 (5′-CH_3).

1-([4,5-Bis(hexyloxy)-9,10-dioxo-9,10-dihydroanthracen-2-yl]-methyl)pyrimidine-2,4(1*H*,3*H*)-dione (11) The same reaction and procedure using **5** (64.4 mg, 0.11 mmol), **8** (16.7 mg, 0.12 mmol) and NaH (5.5 mg, 0.23 mmol) as described for **9** gave compound **11** (23.0 mg, 39.7% yield) as yellowish needles (mp 196—198 °C). FAB-MS: *m/z* 533 $[M+H]^+$. HR-MS: *m/z* Calcd for $C_{31}H_{37}N_2O_6$ $[M+H]^+$; 533.2630, Found; 533.2652. ^{1}H-NMR ($CDCl_3$) δ: 8.50 (1H, br s, 3′-H), 7.81 (1H, dd, *J*=7.7, 0.9 Hz, H-5), 7.69 (1H, d, *J*=1.6 Hz, H-4), 7.62 (1H, dd, *J*=8.3, 7.7 Hz, H-6), 7.31 (1H, dd, *J*=8.3, 0.9 Hz, H-7), 7.25 (1H, d, *J*=8.0 Hz, H-6′), 7.25 (1H, s, H-2), 5.77 (1H, d, *J*=8.0 Hz, H-5′), 4.98 (2H, s, 15-CH_2), 4.14 and 4.12 (each 2H, t, *J*=6.4 Hz, 1- or 8-OCH_2), 1.92 (4H, m, CH_2×2), 1.58 (4H, m, CH_2×2), 1.39 (8H, m, CH_2×4), 0.94 (6H, m, CH_3×2). ^{13}C-NMR ($CDCl_3$) δ: 183.9 (C-10), 181.4 (C-9), 162.8 (C-4′), 159.7 (C-8), 159.0 (C-1), 150.7 (C-2′), 143.6 (C-6′), 140.8 (C-3), 135.3 (C-14), 134.5 (C-11), 133.7 (C-6), 124.6 (C-12), 124.3 (C-13), 119.7 (C-7), 118.8 (C-5), 118.4 (C-2), 117.3 (C-4), 103.2 (C-5′), 69.8 and 70.0 (each OCH_2), 51.2 (C-15), 22.6—31.5 (CH_2×8), 14.0 (CH_3×2).

1-([4,5-Bis(hexyloxy)-9,10-dioxo-9,10-dihydroanthracen-2-yl]methyl)-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (12) The same reaction and procedure using **5** (41.4 mg, 0.07 mmol), **2** (16.7 mg, 0.12 mmol) and NaH (5.5 mg, 0.23 mmol) as described for **9** gave compound **12** (21.5 mg, 55.9% yield) as yellowish needles (mp 210—212 °C). FAB-MS: *m/z* 551 $[M+H]^+$. HR-MS: *m/z* Calcd for $C_{31}H_{36}O_6N_2F$ $[M+H]^+$; 551.2564, Found; 551.2552. ^{1}H-NMR ($CDCl_3$) δ: 8.66 (1H, br s, 3′-H), 7.80 (1H, dd, *J*=7.9, 0.9 Hz, H-5), 7.69 (1H, d, *J*=1.5 Hz, H-4), 7.62 (1H, dd, *J*=8.2, 7.9 Hz, H-6), 7.31 (1H, m, H-6′), 7.31 (1H, dd, *J*=8.2, 0.9 Hz, H-7), 7.21 (1H, d, *J*=1.5 Hz, H-2), 4.93 (2H, s, 15-CH_2), 4.12 and 4.10 (each 2H, t, *J*=6.4 Hz, 1- or 8-OCH_2), 1.91 (4H, m, CH_2×2), 1.56 (4H, m, CH_2×2), 1.37 (8H, m, CH_2×4), 0.92 (6H, m, CH_3×2). ^{13}C-NMR ($CDCl_3$) δ: 183.8 (C-10), 181.3 (C-9), 159.8 (C-8), 159.1 (C-4′), 159.0 (C-1), 149.3 (C-2′), 140.2 (C-3), 140.2 (C-5′), 135.5 (C-14), 134.6 (C-11), 133.8 (C-6), 127.9 (C-6′), 124.9 (C-12), 124.4 (C-13), 119.9 (C-7), 118.9 (C-5), 118.6 (C-2), 117.5 (C-4), 69.8 and 70.1 (each OCH_2), 51.5 (C-15), 22.6 – 31.6 (CH_2×8), 14.0 (CH_3×2).

3-[(6-Amino-9*H*-purin-9-yl)methyl]-1,8-dihydroxyanthracene-9,10-dione (14) A solution of **13** (96 mg, 0.29 mmol), NaH (22.0 mg, 0.9 mmol) and **6** (77.4 mg, 0.57 mmol) in DMF (15 ml) was stirred at room temperature for 3 h. The reaction mixture was poured into ice-water (30 ml) and extracted with AcOEt (100 ml×3). The organic extracts were successively washed with brine and water, dried over absolute $MgSO_4$, and then filtered. The filtrate was evaporated to give a residue, which was subjected to silica gel column chromatography (a gradient of 0—10% MeOH in $CHCl_3$) to afford compound **14** (20.2 mg, 18.1% yield) as yellowish needles (mp more than

300 °C). FAB-MS: *m/z* 387 $[M+H]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{12}O_6N_2$ $[M+H]^+$; 387.0968, Found; 387.1002. ^{1}H-NMR (DMSO-d_6) δ: 11.97 (2H, br s, 1- and 8-OH), 8.34 (1H, s, H-8′), 8.15 (1H, s, H-2′), 7.78 (1H, t, J=8.1 Hz, H-6), 7.67 (1H, dd, J=8.1, 1.0 Hz, H-7), 7.56 (1H, d, J=1.2 Hz, H-2), 7.37 (1H, dd, J=8.1, 1.0 Hz, H-5), 7.32 (2H, br s, 6′-NH_2), 7.22 (1H, d, J=1.2 Hz, H-4), 5.52 (2H, s, H-15). ^{13}C-NMR (DMSO-d_6) δ: 183.9 (C-10), 181.2 (C-9), 161.6 (C-1), 161.4 (C-8), 156.0 (C-6′), 152.7 (C-2′), 149.4 (C-4′), 146.8 (C-8′), 140.8 (C-3), 137.2 (C-6), 133.7 (C-14), 133.2 (C-11), 124.4 (C-5), 122.5 (C-4), 119.2 (C-7), 118.6 (C′-6), 117.6 (C-2), 115.9 (C-12), 115.4 (C-13), 45.7 (C-15).

1-[(4,5-Dihydroxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)methyl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (15) The same reaction and procedure using **13** (41.0 mg, 0.12 mmol), **7** (32.0 mg, 0.25 mmol) and NaH (14.0 mg, 0.58 mmol) as described for the preparation of **14** gave compound **15** (26.6 mg, 57.0% yield) as yellowish needles (mp more than 300 °C). EI-MS: *m/z* 378 $[M]^+$. HR-MS: *m/z* Calcd for $C_{20}H_{14}N_2O_6$ $[M]^+$; 378.0852, Found; 378.0857. ^{1}H-NMR (pyridine-d_5) δ: 13.52 (1H, br s, H-3′), 12.12 (2H, br s, 1- and 8-OH), 8.06 (1H, d, J=1.8 Hz, H-2), 7.89 (1H, dd, J=8.2, 0.9 Hz, H-7), 7.64 (1H, t, J=8.2 Hz, H-6), 7.56 (1H, q, J=1.2 Hz, H-6′), 7.54 (1H, d, J=1.8 Hz, H-4), 7.37 (1H, dd, J=8.2, 0.92 Hz, H-5), 5.19 (2H, s, H-15), 1.96 (3H, d, J=1.2 Hz, 5′-CH_3).

1-[(4,5-Dihydroxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)-methyl]pyrimidine-2,4(1*H*,3*H*)-dione (16) The same reaction and procedure using **13** (41.0 mg, 0.12 mmol), **8** (39.1 mg, 0.35 mmol) and NaH (15.1 mg, 0.63 mmol) as described for the preparation of **14** gave compound **16** (30.6 mg, 68.2% yield) as yellowish needles (mp 282—283 °C). EI-MS: *m/z* 364 $[M]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{12}N_2O_6$ $[M]^+$; 364.0695, Found; 364.0715. ^{1}H-NMR (pyridine-d_5) δ: 13.58 (1H, br s, H-3′), 12.08 (2H, br s, 1- and 8-OH), 8.01 (1H, d, J=1.5 Hz, H-2), 7.86 (1H, dd, J=8.2, 0.9 Hz, H-7), 7.79 (1H, d, J=7.9 Hz, H-6′), 7.61 (1H, t, J=8.2 Hz, H-6), 7.50 (1H, d, J=1.5 Hz, H-4), 7.35 (1H, dd, J=8.2, 0.9 Hz, H-5), 5.91 (1H, d, J=7.9 Hz, H-5′), 5.19 (2H, s, H-15). ^{13}C-NMR (pyridine-d_5) δ: 192.6 (C-10), 181.5 (C-9), 164.7 (C-4′), 163.0 (C-1), 162.9 (C-8), 152.3 (C-2′), 147.6 (C-3), 144.9 (C-6′), 137.6 (C-6), 134.5 (C-11), 134.0 (C-14), 124.8 (C-5), 123.0 (C-4), 120.0 (C-7), 118.9 (C-2), 116.3 (C-12), 115.8 (C-13), 103.0 (C-5′), 51.2 (C-15).

1-[(4,5-Dihydroxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)methyl]-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (17) The same reaction and procedure using **13** (42.0 mg, 0.13 mmol), **2** (34.5 mg, 0.27 mmol) and NaH (20.4 mg, 0.85 mmol) as described for the preparation of **14** gave compound **17** (22.1 mg, 45.9% yield) as yellowish needles (mp 290—293 °C). EI-MS: *m/z* 382 $[M]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{11}FN_2O_6$ $[M]^+$; 383.0601, Found; 382.0587. ^{1}H-NMR (pyridine-d_5) δ: 13.69 (3H, m, 1- and 8-OH and H-3′), 8.27 (1H, d, J=6.1 Hz, H-6′), 8.07 (1H, d, J=1.8 Hz, H-2), 7.88 (2H, dd, J=8.2, 0.9 Hz, H-7), 7.63 (1H, t, J=8.2 Hz, H-6), 7.58 (1H, d, J=1.8 Hz, H-4), 7.36 (1H, dd, J=8.2, 0.9 Hz, H-5), 5.22 (2H, s, H-15). ^{13}C-NMR (pyridine-d_5) δ: 192.6 (C-10), 181.5 (C-9), 163.1 (C-8), 162.7 (C-1), 158.5 (C′-4), 151.1 (C′-2), 147.2 (C-3), 140.6 (C′-5), 137.6 (C-6), 134.6 (C-11), 134.0 (C-14), 129.5 (C′-6), 124.9 (C-5), 123.1 (C-4), 120.0 (C-7), 119.0 (C-2), 116.4 (C-12), 116.0 (C-13), 51.4 (C-15).

1,4-Dimethoxy-2-methylnaphthalene (20) A solution of tin(II)chloride (60.0 g, 0.32 mmol) in 12 M HCl (60.0 ml, 0.72 mmol) was added dropwise over a period of 30 min to a solution of **18** (15.0 g, 87.1 mmol) in MeOH (250 ml). The mixture was stirred for 30 min, then MeOH was evaporated *in vacuo* and the residue was poured into water (100 ml). The resulting precipitate was collected by filtration and dissolved in acetone (200 ml). The solution was dried over $MgSO_4$ and then filtered. To the acetone filtrate, K_2CO_3 (90.0 g, 0.65 mol) and dimethyl sulfate (59.9 g, 0.48 mol) were added, then refluxed for 4 h before being filtered. The filtrate was evaporated *in vacuo* and the residue was dissolved in ether (200 ml) and aqueous 20% KOH (200 ml). After the mixture was stirred vigorously for 1 h, the organic layer was separated and dried over $MgSO_4$. The solvent was evaporated to give a residue, which was subjected to column chromatography (toluene) to obtain compound **20** (12.6 g, 71.5% yield). EI-MS: *m/z* 202 $[M]^+$. HR-MS: *m/z* Calcd for $C_{13}H_{14}O_2$ $[M]^+$; 202.0994, Found; 202.1005. ^{1}H-NMR ($CDCl_3$) δ: 8.19 and 8.02 (each 1H, m, H-5 or 8), 7.50 and 7.42 (each 1H, m, H-6 or 7), 6.60 (1H, s, H-3), 3.96 and 3.86 (each 3H, s, 1- or 4-OCH_3), 2.44 (3H, s, 2-CH_3). ^{13}C-NMR ($CDCl_3$) δ: 151.5 (C-4), 147.0 (C-1), 128.6 (C-9), 126.5 (C-10), 125.6 (C-7), 125.2 (C-6), 124.6 (C-5), 122.2 (C-8), 121.5 (C-2), 106.8 (C-3), 61.2 (OCH_3), 55.6 (OCH_3), 16.3 (C-11).

1,4-Dimethoxynaphthalene-2-carboxylic Acid (21) $KMnO_4$ (63.4 g, 0.4 mol) was added to a solution of compound **20** (16.2 g, 80.1 mmol) in pyridine (250 ml) and water (250 ml) before stirring the mixture at 100 °C for 24 h. The reaction mixture was filtered and half the filtrate was removed by distillation at reduced pressure. Water (250 ml) was then added to the mixture before extracting with Et_2O (100 ml×3). The organic extracts were successively washed with brine and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—50% MeOH in $CHCl_3$) to obtain compound **21** (6.0 g, 32.3% yield) as colorless needles (mp 160—162 °C). EI-MS: *m/z* 232 $[M]^+$. HR-MS: *m/z* Calcd for $C_{13}H_{12}O_4$ $[M]^+$; 232.0736, Found; 232.0734. ^{1}H-NMR ($CDCl_3$) δ: 11.05 (1H, br s, OH), 8.31 and 8.11 (each 1H, m, H-5 or 8), 7.65 (2H, m, H-6 and 7), 7.37 (1H, s, H-3), 4.12 and 4.05 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR ($CDCl_3$) δ: 166.2 (COOH), 152.6 (C-1), 151.1 (C-4), 129.6 (C-10), 128.4 (C-6), 127.7 (C-9), 127.3 (C-7), 123.0 (C-8), 122.7 (C-5), 117.4 (C-3), 103.2 (C-2), 64.3 (OCH_3), 56.0 (OCH_3).

(1,4-Dimethoxynaphthlen-2-yl)methanol (22) $LiAlH_4$ (3.8 g, 100 mmol) was added to a solution of **21** (5.8 g, 25.0 mmol) in THF (150 ml) and the mixture was stirred at room temperature for 12 h. The reaction mixture was neutralized by dropwise addition of 10% aqueous H_2SO_4. After pouring into water (100 ml) the mixture was extracted with Et_2O (50 ml×3). The organic extracts were washed with water and dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—5% acetone in toluene) to obtain compound **22** (3.1 g, 57.1% yield) as colorless needles (mp 59—65 °C). EI-MS: *m/z* 218 $[M]^+$. HR-MS: *m/z* Calcd for $C_{13}H_{14}O_3$ $[M]^+$; 218.0943, Found; 218.0919. ^{1}H-NMR ($CDCl_3$) δ: 8.23 and 8.03 (each 1H, m, H-5 or 8), 7.54 and 7.48 (each 1H, m, H-6 or 7), 6.81 (1H, s, H-3), 4.88 (2H, s, H-11), 3.98 and 3.91 (each 3H, s, 1- or 4-OCH_3), 2.03 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) δ: 145.0 (C-4), 139.8 (C-1), 121.4 (C-2), 121.3 (C-9), 119.6 (C-10), 119.1 (C-7), 118.4 (C-6), 115.3 (C-5), 114.6 (C-8), 96.6 (C-3), 55.5 (C-11), 53.9 (OCH_3), 48.5 (OCH_3).

2-(Bromomethyl)-1,4-dimethoxynaphthalene (19) CBr_4 (13.2 g, 39.9 mmol) and PPh_3 (10.5 g, 39.9 mmol) were added to a solution of **22** (2.9 g, 13.3 mmol) in Et_2O (100 ml). The reaction mixture was stirred at room temperature for 4 h, then filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography ($CHCl_3$) to obtain compound **19** (1.88 g, 50.3% yield) as colorless needles (mp 89—91 °C). EI-MS: *m/z* 280 $[M]^+$ and 282 $[M+2]^+$. HR-MS: *m/z* Calcd for $C_{13}H_{13}BrO_2$ $[M]^+$; 280.0099, Found; 280.0081. ^{1}H-NMR ($CDCl_3$) δ: 8.22 and 8.05 (each 1H, m, H-5 or 8), 7.55 and 7.50 (each 1H, m, H-6 or 7), 6.72 (1H, s, H-3), 4.77 (2H, s, H-11), 4.01 and 4.00 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR ($CDCl_3$) δ: 152.2 (C-4), 147.9 (C-1), 128.4 (C-9), 127.01 (C-10), 126.98 (C-7), 126.2 (C-6), 125.7 (C-5), 122.5 (C-8), 122.3 (C-2), 104.7 (C-3), 62.4 (OCH_3), 55.7 (OCH_3), 29.1 (C-11).

1-(5,8-Dimethoxy-7-methylnaphthalen-2-yl)ethanone (24) To a solution of compound **20** (100 mg, 0.49 mmol) in CH_2Cl_2 (15 ml), CH_3COCl (0.17 ml, 1.69 mmol) and $AlCl_3$ (220 mg, 1.69 mmol) were added. The mixture was stirred at room temperature for 40 min, then poured into ice-water (50 ml), neutralized with $NaHCO_3$ and extracted with $CHCl_3$ (30 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (a gradient of 0—5% acetone in toluene) to obtain compound **24** (78.8 mg, 65.2% yield) as colorless solid (mp 115—116 °C). EI-MS: *m/z* 244 $[M]^+$. HR-MS: *m/z* Calcd for $C_{15}H_{16}O_3$ $[M]^+$; 244.1099, Found; 244.1089. ^{1}H-NMR ($CDCl_3$) δ: 8.83 (1H, H-8*), 8.06 (2H, H-5* and 6*) (peaks with an asterisk show virtual coupling),[20] 6.66 (1H, s, H-3), 4.01 (3H, s, 4-OCH_3), 3.86 (3H, s, 1-OCH_3), 2.73 (3H, s, $COCH_3$), 2.47 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 198.1 ($COCH_3$), 152.5 (C-4), 147.0 (C-1), 133.2 (C-7), 130.7 (C-10), 129.5 (C-9), 124.9 (C-5), 124.5 (C-8), 124.2 (C-2), 122.0 (C-6), 107.7 (C-3), 61.3 (OCH_3), 55.6 (OCH_3), 26.6 ($CO\underline{C}H_3$), 16.3 (C-11).

5,8-Dimethoxy-7-methylnaphthalene-2-carboxylic Acid (25) Finely powdered KOH (130 mg, 2.3 mmol) was added to a solution of **24** (100 mg, 0.41 mmol) in DMF (10 ml) and the mixture was then stirred at 68 °C for 3 h. After a second addition of finely powderd KOH (130 mg, 2.3 mmol) the mixture was stirred at the same temperature for a further 12 h. The reaction mixture was then poured into ice-water (100 ml) and extracted with $CHCl_3$ (50 ml×3). The chloroform extracts were acidified by addition of 5% aqueous HCl and extracted with $CHCl_3$ (50 ml×3). The extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—3% MeOH in $CHCl_3$) to obtain compound **25** (43.5 mg, 43.2% yield) as needles (mp 197—199 °C). EI-MS: *m/z* 246 $[M]^+$. HR-MS: *m/z* Calcd for $C_{14}H_{14}O_4$ $[M]^+$; 246.0892, Found; 246.0879. ^{1}H-NMR ($CDCl_3$) δ: 13.01 (1H, br s, COOH), 8.77 (1H, H-8*), 8.02 (2H, H-5* and 6*) (peaks with an asterisk show virtual coupling),[20] 6.95 (1H, s, H-3), 4.04 (3H, s, 4-OCH_3),

3.84 (3H, s, 1-OCH_3), 2.47 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 167.4 (COOH), 151.6 (C-4), 146.3 (C-1), 129.9 (C-10), 129.1 (C-6), 126.7 (C-9), 125.9 (C-7), 124.6 (C-8), 123.5 (C-2), 121.8 (C-5), 108.2 (C-3), 61.0 (OCH_3), 55.8 (OCH_3), 16.2 (C-11).

(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methanol (26) $LiAlH_4$ (62.3 mg, 1.64 mmol) was added to a solution of **25** (100 mg, 0.41 mmol) in THF (10 ml) and the mixture was then stirred at room temperature for 12 h. The reaction mixture was neutralized by addition of 10% aqueous H_2SO_4, poured into ice-water (100 ml) and extracted with $CHCl_3$ (50 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—5% acetone in toluene) to obtain compound **26** (61.2 mg, 64.7% yield) as colorless needles (mp 99—100 °C). EI-MS: *m/z* 232 $[M]^+$. HR-MS: *m/z* Calcd for $C_{14}H_{16}O_3$ $[M]^+$; 232.1099, Found; 232.1091. ^{1}H-NMR ($CDCl_3$) δ: 8.15 (1H, d, *J*=1.8 Hz, H-8), 8.00 (1H, d, *J*=8.6 Hz, H-5), 7.52 (1H, dd, *J*=8.6, 1.8 Hz, H-6), 6.60 (1H, s, H-3), 4.83 (2H, s, H-12), 3.96 (3H, s, 4-OCH_3), 3.85 (3H, s, 1-OCH_3), 2.44 (3H, s, H-11), 1.76 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) δ: 151.5 (C-4), 147.0 (C-1), 137.1 (C-7), 128.1 (C-10), 125.9 (C-5), 125.7 (C-9), 125.0 (C-2), 122.1 (C-8), 120.1 (C-6), 107.2 (C-3), 65.7 (7-$\underline{C}H_2OH$), 61.2 (OCH_3), 55.6 (OCH_3), 16.3 (C-11).

7-(Bromomethyl)-1,4-dimethoxy-2-methylnaphthalene (23) CBr_4 (554 mg, 1.67 mmol) and PPh_3 (438 mg, 1.67 mmol) were added to a solution of **26** (100 mg, 0.43 mmol) in Et_2O (100 ml) and the mixture was stirred at room temperature for 4 h. The reaction mixture was filtered and the filtrate was evaporated to give a residue, which was subjected to column chromatography ($CHCl_3$) to obtain compound **23** (83.3 mg, 65.8% yield). EI-MS: *m/z* 294 $[M]^+$ and 296 $[M+2]^+$. HR-MS: *m/z* Calcd for $C_{14}H_{15}BrO_2$ $[M]^+$; 294.0255, Found; 294.0247. ^{1}H-NMR ($CDCl_3$) δ: 8.19 (1H, d, *J*=1.8 Hz, H-8), 8.00 (1H, d, *J*=8.6 Hz, H-5), 7.54 (1H, dd, *J*=8.6, 1.8 Hz, H-6), 6.61 (2H, s, CH_2Br), 3.96 (3H, s, 4-OCH_3), 3.84 (3H, s, 1-OCH_3), 2.44 (3H, s, 11-CH_3). ^{13}C-NMR ($CDCl_3$) δ: 151.5 (C-4), 147.0 (C-1), 133.8 (C-7), 128.3 (C-10), 127.3 (C-6), 126.7 (C-9), 124.9 (C-2), 122.6 (C-8), 122.5 (C-5), 107.5 (C-3), 61.3 (OCH_3), 55.6 (OCH_3), 34.5 (7-CH_2Br), 16.3 (C-11).

9-[(1,4-Dimethoxynaphthalen-2-yl)methyl]-9*H*-purin-6-amine (27) Compound **6** (220 mg, 1.62 mmol) and NaH (12.8 mg, 0.53 mmol) were added to a solution of **19** (150 mg, 0.53 mmol) in DMF (20 ml) and the mixture was then stirred at 80 °C for 5 h. The reaction mixture was poured into ice-water (100 ml), neutralized with 5% aqueous $NaHCO_3$, and extracted with $CHCl_3$ (50 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—10% MeOH in $CHCl_3$) to obtain compound **27** (50.6 mg, 28.3% yield) as a solid (mp 233—236 °C). EI-MS: *m/z* 335 $[M]^+$. HR-MS: *m/z* Calcd for $C_{18}H_{17}N_5O_2$ $[M]^+$; 335.1382, Found; 335.1372. ^{1}H-NMR (DMSO-d_6) δ: 8.45 (1H, s, H-8′), 8.12 and 8.02 (each 1H, m, H-5 or 8), 7.91 (2H, br s, 6′-NH_2), 7.77 (1H, s, H-2′), 7.61 and 7.54 (each 1H, m, H-6 or 7), 6.94 (1H, s, H-3), 5.69 (2H, s, H-11), 3.94 and 3.84 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR (DMSO-d_6) δ: 154.8 (C′-6), 152.4 (C-2′), 151.1 (C-4′), 149.9 (C-4), 147.4 (C-1), 143.6 (C-8′), 127.7 (C-9), 127.0 (C-10), 126.1 (C-7), 125.8 (C-6), 123.7 (C-5′), 121.9 (C-5), 121.9 (C-8), 120.3 (C-2), 105.0 (C-3), 62.3 (OCH_3), 55.6 (OCH_3), 47.9 (C-11).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (28) The same reaction and procedure using **19** (80.0 mg, 0.29 mmol), **7** (72.0 mg, 0.57 mmol) and NaH (6.9 mg, 0.29 mmol) as for the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—20% acetone in toluene) to afford compound **28** (49.9 mg, 53.7% yield) as a solid (mp 208—210 °C). EI-MS: *m/z* 326 $[M]^+$. HR-MS: *m/z* Calcd for $C_{18}H_{18}N_2O_4$ $[M]^+$; 326.1267, Found; 326.1275. ^{1}H-NMR (pyridine-d_5) δ: 13.35 (1H, br s, H-3′), 8.39 and 8.18 (each 1H, m, H-5 or 8), 7.60 and 7.55 (each 1H, m, H-6 or 7), 7.44 (1H, q, *J*=0.9 Hz, H-6′), 7.05 (1H, s, H-3), 5.29 (2H, s, H-11), 3.94 and 3.78 (each 3H, s, 1- or 4-OCH_3), 1.91 (3H, d, *J*=0.9 Hz, 5′-CH_3). ^{13}C-NMR (pyridine-d_5) δ: 165.3 (C-4′), 152.7 (C-2′), 152.6 (C-4), 148.3 (C-1), 140.8 (C-6′), 128.9 (C-9), 127.4 (C-10), 127.0 (C-7), 126.3 (C-6), 125.4 (C-5), 123.0 (C-8), 122.5 (C-2), 110.6 (C-5′), 104.9 (C-3), 62.6 (OCH_3), 55.6 (OCH_3), 46.0 (C-11), 12.5 (5′-CH_3).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl]pyrimidine-2,4(1*H*,3*H*)-dione (29) The same reaction and procedure using **19** (150 mg, 0.53 mmol), **8** (178 mg, 1.60 mmol) and NaH (12.8 mg, 0.54 mmol) as the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—15% acetone in toluene) to afford compound **29** (69.8 mg, 41.9% yield) as a solid (mp 224—227 °C). EI-MS: *m/z* 312 $[M]^+$. HR-MS: *m/z* Calcd for $C_{17}H_{16}N_2O_4$ $[M]^+$; 312.1110, Found; 312.1127. ^{1}H-NMR (pyridine-d_5) δ: 13.43 (1H, br s, H-3′), 8.40 and 8.18 (each 1H, m, H-5 or 8), 7.65 (1H, d, *J*=7.9 Hz, H-6′), 7.61 and 7.56 (each 1H, m, H-6 or 7), 7.01 (1H, s, H-3), 5.86 (1H, d, *J*=7.9 Hz, H-5′), 5.26 (2H, s, H-11), 3.92 and 3.78 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR (pyridine-d_5) δ: 164.8 (C-4′), 152.63 (C-2′), 152.60 (C-4), 148.5 (C-1), 145.1 (C-6′), 128.9 (C-9), 127.4 (C-10), 127.1 (C-7), 126.3 (C-6), 125.0 (C-5), 123.0 (C-8), 122.6 (C-2), 105.0 (C-3), 102.4 (C-5′), 62.6 (OCH_3), 55.6 (OCH_3), 46.5 (C-11).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl]-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (30) The same reaction and procedure using **19** (150 mg, 0.53 mmol), **2** (277 mg, 2.13 mmol) and NaH (18.8 mg, 0.78 mmol) as the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—10% MeOH in $CHCl_3$) to afford compound **30** (95.0 mg, 54.7% yield) as a solid (mp 191—193 °C). EI-MS: *m/z* 330 $[M]^+$. HR-MS: *m/z* Calcd for $C_{17}H_{15}FN_2O_4$ $[M]^+$; 330.1016, Found; 3301.005. ^{1}H-NMR (pyridine-d_5) δ: 14.12 (1H, br s, H-3′), 8.41 and 8.19 (each 1H, m, H-5 or 8), 8.00 (1H, d, *J*=6.4 Hz, H-6′), 7.62 and 7.57 (each 1H, m, H-6 or 7), 7.06 (1H, s, H-3), 5.28 (2H, s,H-11), 3.94 and 3.80 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR (pyridine-d_5) δ: 158.5 (C-4′), 152.7 (C-2′), 151.2 (C-4), 148.6 (C-1), 142.1 (C-5′), 129.5 (C-6′), 129.2 (C-9), 127.5 (C-10), 127.2 (C-7), 126.4 (C-6), 124.6 (C-5), 123.0 (C-8), 122.6 (C-2), 105.1 (C-3), 62.7 (OCH_3), 55.7 (OCH_3), 46.7 (C-11).

9-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]-9*H*-purin-6-amine (31) The same reaction and procedure using **23** (200 mg, 0.68 mmol), **6** (276 mg, 2.13 mmol) and NaH (54.6 mg, 1.36 mmol) as the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—7% MeOH in $CHCl_3$) to give compound **31** (135.1 mg, 57.0% yield) as a solid (mp 134—136 °C). EI-MS: *m/z* 349 $[M]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{19}N_5O_2$ $[M]^+$; 349.1539, Found; 349.1541. ^{1}H-NMR (DMSO-d_6) δ: 8.31 (1H, s, H-8′), 8.17 (1H, s, H-2′), 8.01 (1H, d, *J*=1.8 Hz, H-8), 7.91 (1H, d, *J*=8.9 Hz, H-5), 7.51 (1H, dd, *J*=8.9, 1.8 Hz, H-6), 7.22 (2H, br s, 6′-NH_2), 6.80 (1H, s, H-3), 5.53 (2H, s, 7-CH_2-), 4.01 (3H, s, 4-OCH_3), 3.91 (3H, s, 1-OCH_3), 2.37 (3H, s, H-11). ^{13}C-NMR (DMSO-d_6) δ: 156.0 (C-6′), 152.6 (C-2′), 150.6 (C-4), 149.5 (C-4′), 146.4 (C-1), 140.8 (C-8′), 133.4 (C-7), 127.4 (C-9), 126.1 (C-6), 125.9 (C-2), 124.1 (C-10), 122.0 (C-5), 120.5 (C-8), 118.7 (C-5′), 107.8 (C-3), 60.8 (OCH_3), 55.5 (OCH_3), 46.4 (7-CH_2-), 15.9 (C-11).

1-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (32) The same reaction and procedure using **23** (100 mg, 0.34 mmol), **7** (130 mg, 1.0 mmol) and NaH (13.6 mg, 0.34 mmol) as described for the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—5% MeOH in $CHCl_3$) to afford compound **32** (63.1 mg, 54.7% yield) as a solid (mp 234—237 °C). EI-MS: *m/z* 340 $[M]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{20}N_2O_4$ $[M]^+$; 340.1423, Found; 340.1415. ^{1}H-NMR (DMSO-d_6) δ: 11.36 (1H, br s, H-3′), 8.01 (1H, d, *J*=1.8 Hz, H-8), 7.94 (1H, d, *J*=8.9 Hz, H-5), 7.69 (1H, s, H-6′), 7.50 (1H, dd, *J*=8.9, 1.8 Hz, H-6), 6.82 (1H, s, H-3), 4.99 (2H, s, 7-CH_2-), 3.93 (3H, s, 4-OCH_3), 3.75 (3H, s, 1-OCH_3), 2.38 (3H, s, H-11), 1.75 (3H, s, 5′-CH_3). ^{13}C-NMR (DMSO-d_6) δ: 164.2 (C-4′), 151.1 (C-2′), 150.7 (C-4), 146.4 (C-1), 141.3 (C-6′), 133.3 (C-7), 127.4 (C-10), 126.2 (C-5), 125.9 (C-9), 124.2 (C-2), 122.1 (C-6), 120.7 (C-8), 109.1 (C-5′), 107.8 (C-3), 60.9 (OCH_3), 55.6 (OCH_3), 50.3 (7-CH_2-), 16.0 (C-11), 11.9 (5′-CH_3).

1-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]pyrimidine-2,4(1*H*,3*H*)-dione (33) The same reaction and procedure using **23** (300 mg, 1.01 mmol), **8** (330 mg, 3.00 mmol) and NaH (120 mg, 3.00 mmol) as the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—15% MeOH in toluene) to afford compound **33** (187.7 mg, 56.6% yield) as a solid (mp more than 300 °C). EI-MS: *m/z* 326 $[M]^+$. HR-MS: *m/z* Calcd for $C_{18}H_{18}N_2O_4$ $[M]^+$; 326.1267, Found; 326.1260. ^{1}H-NMR (DMSO-d_6) δ: 11.36 (1H, br s, H-3′), 7.99 (1H, d, *J*=1.8 Hz, H-8), 7.92 (1H, d, *J*=8.9 Hz, H-5), 7.82 (1H, d, *J*=7.9 Hz, H-6′), 7.48 (1H, dd, *J*=8.9, 1.8 Hz, H-6), 6.81 (1H, s, H-3), 5.61 (1H, d, *J*=7.9 Hz, H-5′), 5.01 (2H, s, 7-CH_2-), 3.91 (3H, s, 4-OCH_3), 3.74 (3H, s, 1-OCH_3), 2.36 (3H, s, H-11). ^{13}C-NMR (DMSO-d_6) δ: 163.7 (C-4′), 151.1 (C-2′), 152.6 (C-4), 146.4 (C-1), 145.7 (C-6′), 133.2 (C-7), 127.4 (C-10), 126.3 (C-5), 126.0 (C-9), 124.2 (C-2), 122.1 (C-8), 120.6 (C-6), 107.8 (C-3), 101.4 (C-5′), 60.9 (OCH_3), 55.6 (OCH_3), 50.5 (7-CH_2), 16.0 (C-11).

1-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (34) The same reaction and procedure using **23** (170 mg, 0.58 mmol), **2** (222 mg, 1.73 mmol) and NaH (46.2 mg, 1.15 mmol) as the preparation of **27** gave a residue, which was subjected to column chromatography (a gradient of 0—10% MeOH in toluene) to afford compound **34** (94.0 mg, 47.8% yield) as a solid (mp 257—260 °C). EI-MS: *m/z* 344 $[M]^+$. HR-MS: *m/z* Calcd for $C_{18}H_{17}FN_2O_4$ $[M]^+$; 344.1172, Found; 344.1158. ^{1}H-NMR (DMSO-d_6) δ: 12.81 (1H, br s, H-3′), 8.31 (1H, d,

J=6.7 Hz, H-6′), 8.04 (1H, d, J=1.8 Hz, H-8), 7.95 (1H, d, J=8.9 Hz, H-5), 7.60 (1H, dd, J=8.9, 1.8 Hz, H-6), 6.83 (1H, s, H-3), 4.98 (2H, s, 7-CH_2-), 3.94 (3H, s, 4-OCH_3), 3.76 (3H, s, 1-OCH_3), 2.37 (3H, s, H-11). ^{13}C-NMR (DMSO-d_6) δ: 157.5 (C-4′), 157.3 (C-2′), 150.7 (C-4), 149.7 (C-1), 146.4 (C-5′), 132.8 (C′-6), 130.2 (C-7), 127.5 (C-9), 126.3 (C-6), 126.0 (C-2), 124.2 (C-10), 121.6 (C-5), 120.8 (C-8), 107.5 (C-3), 60.7 (OCH_3), 55.6 (OCH_3), 50.9 (7-CH_2), 16.0 (C-11).

1-[(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (35) To a solution of **28** (45.0 mg, 0.14 mmol) in AcOH (5 ml), HNO_3 (0.28 g, 2.90 mmol) was added, and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured into ice-water (50 ml) and extracted with $CHCl_3$ (50 ml×3). The organic extracts were neutralized with 5% aqueous $NaHCO_3$, washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give compound **35** (21.7 mg, 53.2% yield) as a solid (mp 206—207 °C). EI-MS: m/z 296 $[M]^+$. HR-MS: m/z Calcd for $C_{16}H_{12}N_2O_4$ $[M]^+$; 296.0797, Found; 296.0792. ^{1}H-NMR ($CDCl_3$) δ: 9.05 (1H, br s, H-3′), 8.09 (2H, m, H-5 and 8), 7.78 (2H, m, H-6 and 7), 7.24 (1H, q, J=1.2 Hz, H-6′), 6.94 (1H, t, J=1.2 Hz, H-3), 4.80 (2H, d, J=1.2 Hz, H-11), 1.95 (3H, d, J=1.2 Hz, 5′-CH_3). ^{13}C-NMR ($CDCl_3$) δ: 184.8 (C-1), 184.4 (C-4), 163.9 (C-4′), 150.7 (C-2′), 143.1 (C-2), 140.5 (C-6′), 136.8 (C-3), 134.4 (C-7), 134.1 (C-6), 132.0 (C-9), 131.7 (C-10), 126.6 (C-8), 126.5 (C-5), 111.5 (C-5′), 46.7 (C-11), 12.4 (5′-CH_3).

1-[(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl]pyrimidine-2,4(1*H*,3*H*)-dione (36) The same reaction and preparation using **29** (700 mg, 0.22 mmol) as described for the preparation of **35** gave compound **36** (302.4 mg, 47.8%yield) as solid (mp 236—237 °C). EI-MS: m/z 282 $[M]^+$. HR-MS: m/z Calcd for $C_{15}H_{10}N_2O_4$ $[M]^+$; 282.0641, Found; 282.0643. ^{1}H-NMR (DMSO-d_6) δ: 11.37 (1H, br s, H-3′), 8.04 and 7.99 (each 1H, m, H-5 or 8), 7.90 (2H, m, H-6 and 7), 7.67 (1H, d, J=7.9 Hz, H-6′), 6.70 (1H, t, J=1.5 Hz, H-3), 5.65 (1H, d, J=7.9 Hz, H-5′), 4.81 (2H, d, J=1.5 Hz, H-11). ^{13}C-NMR (DMSO-d_6) δ: 184.3 (C-1), 184.0 (C-4), 163.7 (C-4′), 150.9 (C-2′), 145.6 (C-2), 145.0 (C-6′), 134.4 (C-7), 134.3 (C-6), 134.0 (C-3), 131.6 (C-9), 131.5 (C-10), 126.1 (C-8), 125.8 (C-5), 101.6 (C-5′), 46.0 (C-11).

1-[(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl]-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (37) The same reaction and procedure using **30** (80.0 mg, 0.24 mmol) as described for the preparation of **35** gave compound **37** (37.6 mg, 51.7% yield) as solid (mp 90—92 °C). EI-MS: m/z 300 $[M]^+$. HR-MS: m/z Calcd for $C_{15}H_9FN_2O_4$ $[M]^+$; 300.0546, Found; 300.0543. ^{1}H-NMR (DMSO-d_6) δ: 11.87 (1H, br s, H-3′), 8.05 and 8.00 (each 1H, m, H-5 or 8), 8.04 (1H, d, J=6.7 Hz, H-6′), 7.90 (2H, m, H-6 and 7), 6.89 (1H, t, J=1.5 Hz, H-3), 4.77 (2H, d, J=1.5 Hz, H-11). ^{13}C-NMR (DMSO-d_6) δ: 184.4 (C-1), 184.1 (C-4), 157.7 (C-4′), 1489.7 (C-2′), 144.6 (C-2), 139.1 (C-5′), 134.4 (C-3), 134.3 (C-7), 134.2 (C-6), 131.6 (C-6′), 130.0 (C-10), 129.8 (C-9), 126.1 (C-8), 125.8 (C-5), 46.3 (C-11).

7-[(6-Amino-9*H*-purin-9-yl)methyl]-2-methylnaphthalene-1,4-dione (38) The same reaction and procedure using **31** (100 mg, 0.29 mmol) as described for the preparation of **35** gave a residue, which was subjected to column chromatography (a gradient of 0—5% MeOH in toluene) to afford compound **38** (20.0 mg, 21.9% yield) as a pale yellowish solid (mp 134—135 °C). EI-MS: m/z 319 $[M]^+$. HR-MS: m/z Calcd for $C_{17}H_{13}N_5O_2$ $[M]^+$; 319.1069, Found; 319.1064. ^{1}H-NMR (DMSO-d_6) δ: 8.33 (1H, s, H-8′), 8.14 (1H, s, H-2′), 7.98 (1H, d, J=8.2 Hz, H-5), 7.83 (1H, d, J=1.8 Hz, H-8), 7.74 (1H, dd, J=8.2, 1.8 Hz, H-6), 7.30 (2H, br s, 6′-NH_2), 6.95 (1H, q, J=1.2 Hz, H-3), 5.53 (2H, s, H-12), 2.09 (3H, d, J=1.2 Hz, H-11). ^{13}C-NMR (DMSO-d_6) δ: 184.5 (C-1) , 184.2 (C-4), 156.0 (C-6′), 152.7 (C-2′), 149.4 (C-4′), 148.0 (C-8′), 143.2 (C-7), 135.1 (C-9), 133.2 (C-3), 132.6 (C-6), 131.9 (C-10), 131.0 (C-2), 126.6 (C-5), 124.2 (C-8), 118.6 (C-5′), 45.7 (C-12), 15.8 (C-11).

5-Methyl-1-[(7-methyl-5,8-dioxo-5,8-dihydronaphthalen-2-yl)methyl]pyrimidine-2,4(1*H*,3*H*)-dione (39) The same reaction and procedure using **32** (65.0 mg, 0.19 mmol) as described for the preparation of **35** gave a residue, which was subjected to column chromatography (a gradient of 0—3% MeOH in $CHCl_3$) to give compound **39** (38.0 mg, 64.1% yield) as a solid (mp 267 —269 °C). EI-MS: m/z 310 $[M]^+$. HR-MS: m/z Calcd for $C_{17}H_{14}N_2O_4$ $[M]^+$; 310.0954, Found; 310.0953. ^{1}H-NMR (DMSO-d_6) δ: 11.41 (1H, br s, H-3′), 8.00 (1H, d, J=8.2 Hz, H-5), 7.85 (1H, d, J=1.8 Hz, H-8), 7.73 (1H, dd, J=8.2, 1.8 Hz, H-6), 7.71 (1H, q, J=1.2 Hz, H-6′), 6.97 (1H, q, J=1.53 Hz, H-3), 5.00 (2H, s, H-12), 2.11 (3H, d, J=1.5 Hz, H-11), 1.73 (3H, d, J=1.2 Hz, 5′-CH_3). ^{13}C-NMR (DMSO-d_6) δ: 184.6 (C-1), 184.3 (C-4), 164.1 (C-4′), 150.9 (C-2′), 148.0 (C-2), 143.2 (C-7), 141.2 (C-6′), 135.1 (C-3), 132.6 (C-6), 131.9 (C-9), 130.1 (C-10), 126.6 (C-5), 124.2 (C-8), 109.2 (C-5′), 49.9 (C-12), 15.8 (C-11), 11.9 (5′-CH_3).

1-[(7-Methyl-5,8-dioxo-5,8-dihydronaphthalen-2-yl)methyl]pyrimidine-2,4(1*H*,3*H*)-dione (40) The same reaction and procedure using **33** (70.0 mg, 0.21 mmol) as described for the preparation of **35** gave a residue, which was subjected to column chromatography (a gradient of 0—5% MeOH in $CHCl_3$) to afford compound **40** (40.4 mg, 63.5% yield) as a solid (mp more than 300 °C). EI-MS: m/z 296 $[M]^+$. HR-MS: m/z Calcd for $C_{16}H_{12}N_2O_4$ $[M]^+$; 296.0797, Found; 296.0790. ^{1}H-NMR (DMSO-d_6) δ: 11.41 (1H, br s, H-3′), 8.01 (1H, d, J=7.9 Hz, H-5), 7.86 (1H, d, J=7.6 Hz, H-6′), 7.84 (1H, d, J=1.8 Hz, H-8), 7.76 (1H, dd, J=7.9, 1.8 Hz, H-6), 6.98 (1H, q, J=1.5 Hz, H-3), 5.66 (1H, d, J=7.6 Hz, H-5′), 5.04 (2H, s, H-12), 2.11 (3H, d, J=1.5 Hz, H-11). ^{13}C-NMR (DMSO-d_6) δ: 184.7 (C-1), 184.4 (C-4), 163.7 (C-4′), 151.0 (C-2′), 148.1 (C-2), 145.6 (C-7), 143.2 (C-6′), 135.2 (C-3), 132.7 (C-6), 131.9 (C-9), 131.1 (C-10), 126.7 (C-5), 124.2 (C-8), 101.6 (C-5′), 50.2 (C-12), 15.9 (C-11).

5-Fluoro-1-[(7-methyl-5,8-dioxo-5,8-dihydronapphthalen-2-yl)-methyl]pyrimidine-2,4(1*H*,3*H*)-dione (41) The same reaction and procedure using **34** (80.0 mg, 0.23 mmol) as described for the preparation of **35** gave a residue, which was subjected to column chromatography (a gradient of 0—5% MeOH in $CHCl_3$) to afford compound **41** (41.0 mg, 56.1% yield) as a solid (mp 155—157 °C). EI-MS: m/z 314 $[M]^+$. HR-MS: m/z Calcd for $C_{16}H_{11}FN_2O_4$ $[M]^+$; 314.0703, Found; 314.0703. ^{1}H-NMR (DMSO-d_6) δ: 11.92 (1H, br s, H-3′), 8.30 (1H, d, J=6.7 Hz, H-6′), 8.00 (1H, d, J=7.9 Hz, H-5), 7.89 (1H, d, J=1.8 Hz, H-8), 7.79 (1H, dd, J=7.9, 1.8 Hz, H-6), 6.98 (1H, q, J=1.5 Hz, H-3), 4.98 (2H, s, H-12), 2.11 (3H, d, J=1.5 Hz, H-11). ^{13}C-NMR (DMSO-d_6) δ: 184.6 (C-1), 184.4 (C-4), 157.5 (C-4′), 149.7 (C-2′), 148.1 (C-2), 142.7 (C-7), 135.2 (C-5′), 132.8 (C-3), 132.7 (C-6), 131.9 (C-6), 131.1 (C-5), 130.1 (C-9), 129.9 (C-10), 126.6 (C-8), 124.4 (C-6′), 50.5 (C-12), 15.9 (C-11).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl]pyrrolidine (42) Pyrrolidine (91 μl, 1.1 mmol) was added to a solution of **19** (50 mg, 0.18 mmol) in DMF (10 ml) and the mixture was then stirred at room temperature for 30 min. The reaction mixture was poured into ice-water (100 ml), neutralized with 5% aqueous $NaHCO_3$, and extracted with Et_2O (50 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—5% MeOH in toluene) to obtain compound **42** (31.2 mg, 64.7% yield). EI-MS: m/z 271 $[M]^+$. HR-MS: m/z Calcd for $C_{17}H_{21}NO_2$ $[M]^+$; 271.1572, Found; 271.1571. ^{1}H-NMR ($CDCl_3$) δ: 8.20 (1H, d, J=8.2 Hz, H-5) 8.00 (1H, d, J=8.2 Hz, H-8), 7.52 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-6) or 7.46 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-7), 6.98 (1H, s, H-3), 4.00 and 3.89 (each 3H, s, 1- or 4-OCH_3), 3.88 (2H, s, H-11), 2.64 (4H, s, –NCH_2– ×2) and 4.12 (4H, s, –NCH_2– ×2); ^{13}C-NMR ($CDCl_3$) δ: 151.8 (C-4), 147.2 (C-1), 128.5 (C-9), 126.4 (C-10), 125.9 (C-7), 125.1 (C-6), 122.3 (C-5), 121.9 (C-8), 105.4 (C-2), 96.1 (C-3), 62.2 (1-OCH_3), 55.8 (4-OCH_3), 54.3 (–N<u>C</u>$H_2$$CH_2$– ×2), 54.1 (C-11), 23.6 (–NCH_2<u>C</u>H_2– ×2).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl]-4-methylpiperazine (43) The same reaction and preparation using **19** (100.0 mg, 0.36 mmol) and 1-methylpiperazine (280 μl, 2.3 mmol) as described for the preparation of **42** gave compound **43** (57.0 mg, 51.4% yield). EI-MS: m/z 300 $[M]^+$. HR-MS: m/z Calcd for $C_{18}H_{24}N_2O_2$ $[M]^+$; 300.1838, Found; 300.1829. ^{1}H-NMR ($CDCl_3$) δ: 8.21 (1H, d, J=8.2 Hz, H-5) 8.03 (1H, d, J=8.2 Hz, H-8), 7.50 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-6) or 7.43 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-7), 6.90 (1H, s, H-3), 3.97 and 3.86 (each 3H, s, 1- or 4-OCH_3), 3.34 (2H, s, H-11), 2.50 (8H, m, N<u>C</u>H_2×4) and 2.27 (3H, s, N–<u>C</u>H_3). ^{13}C-NMR ($CDCl_3$) δ: 151.8 (C-4), 148.0 (C-1), 128.4 (C-9), 126.5 (C-10), 126.0 (C-7), 125.7 (C-6), 125.3 (C-5), 122.2 (C-8), 121.8 (C-2), 105.2 (C-3), 56.4 (1-OCH_3), 55.7 (4-OCH_3), 55.3 (–N<u>C</u>H_2<u>C</u>H_2×2), 53.2 (C-11), 46.1 (–NCH_3).

4-[(1,4-Dimethoxynaphthalen-2-yl)methyl]morpholine (44) The same reaction and procedure fusing **19** (100.0 mg, 0.36 mmol) and 1-methylpiperazine (217 μl, 2.5 mmol) as described for the preparation of **42** gave compound **44** (64.0 mg, 62.6% yield) as a solid (mp 56—58 °C). EI-MS: m/z 287 $[M]^+$. HR-MS: m/z Calcd for $C_{18}H_{24}N_2O_2$ $[M]^+$; 287.1521, Found; 287.1526. ^{1}H-NMR ($CDCl_3$) δ: 8.22 (1H, d, J=8.2 Hz, H-5) 8.04 (1H, d, J=8.2 Hz, H-8), 7.52 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-6) or 7.46 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-7), 6.91 (1H, s, H-3) 3.99 and 3.89 (each 3H, s, 1- or 4-OCH_3), 3.71 (2H, s, H-11), 3.72 (4H, s, –N<u>C</u>H_2×2) and 2.53 (4H, m, –<u>C</u>H_2O<u>C</u>H_2–). ^{13}C-NMR ($CDCl_3$) δ: 151.8 (C-4), 148.0 (C-1), 128.4 (C-9), 126.5 (C-10), 126.0 (C-7), 125.7 (C-6), 125.3 (C-5), 122.2 (C-8), 121.8 (C-2), 105.2 (C-3), 67.1 (–<u>C</u>H_2O<u>C</u>H_2–), 62.4 (1-OCH_3), 56.8 (4-OCH_3), 55.7 (–NCH_2×2), 53.7 (C-11).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl]-1*H*-imidazole (45) The same reaction and procedure using **19** (100.0 mg, 0.36 mmol) and imidazol (120 mg, 1.78 mmol) as described for the preparation of **42** gave compound **45** (44.6 mg, 46.7% yield) as a solid (mp 88—90 °C). EI-MS: m/z 268 $[M]^+$. HR-MS: m/z Calcd for $C_{16}H_{16}N_2O_2$ $[M]^+$; 268.1212, Found; 268.1220. ^{1}H-

NMR ($CDCl_3$) δ: 8.23 (1H, d, J=8.2 Hz, H-5) 8.05 (1H, d, J=8.2 Hz, H-8), 7.58 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-6) and 7.52 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-7), 7.63, 7.08 and 6.96 (each 1H, proton on the imidazol group), 6.39 (1H, s, H-3), 3.71 (2H, s, H-11), 3.89 and 3.86 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR ($CDCl_3$) δ: 152.5 (C-4), 147.5 (C-1), 137.5 (–N<u>C</u>=N–), 129.7 (–NC=<u>C</u>–), 128.3 (C-9), 127.1 (C-10), 126.7 (C-7), 126.1 (C-6), 123.5 (C-5), 122.6 (C-8), 122.0 (–N<u>C</u>=C–), 119.3 (C-2), 103.4 (C-3), 62.6 (C-11), 55.7 (1-OCH_3), 45.8 (4-O<u>C</u>H_3).

7-[(1,4-Dimethoxynaphthalen-2-yl)methyl]1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (46) K_2CO_3 (50 mg, 0.36 mmol) was added to a solution of **19** (50.0 mg, 0.18 mmol) and theophylline (64.0 mg, 0.36 mmol) in DMF (10 ml) and the mixture was then stirred at room temperature for 12 h. The mixture was poured into ice-water and neutralized with 5% $NaHCO_3$ and extracted with Et_2O (50 ml×3). The organic extracts was washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (a gradient of 0—10% acetone in toluene) to obtain compound **46** (22.1 mg, 32.6% yield) as a solid (mp 170—172 °C). EI-MS: m/z 380 $[M]^+$. HR-MS: m/z Calcd for $C_{20}H_{20}N_4O_4$ $[M]^+$; 380.1485, Found; 380.1471. ^{1}H-NMR ($CDCl_3$) δ: 8.23 (1H, dd, J=8.2, 1.2 Hz, H-5) or 8.05 (1H, dd, J=8.2, 1.2 Hz, H-8), 7.64 (1H, s, H-8′), 7.58 (1H, ddd, J=8.24, 7.0, 1.2 Hz, H-6) or 7.52 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-7), 6.83 (1H, s, H-3) 5.68 (2H, s, H-11), 3.98 and 3.93 (each 3H, s, 1- or 4-OCH_3), 3.59 and 3.44 (each 3H, s, 1′- or 3′-NCH_3). ^{13}C-NMR ($CDCl_3$) δ: 155.5 (C′-6), 152.5 (C-2′), 151.7 (C-4′), 148.7 (C-4), 148.1 (C-8′), 141.7 (C-1), 128.2 (C-9), 127.1 (C-10), 126.9 (C-7), 126.2 (C-6), 123.1 (C-5), 122.6 (C-8), 122.1 (C-2), 107.0 (C-5′) 104.2 (C-3), 62.8 (1-OCH_3), 55.8 (4-OCH_3), 45.3 (C-11), 29.8 (7-N′CH_3), 28.0 (3-N′CH_3).

1-[(1,4-Dimethoxynaphthalen-2-yl)methyl-3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (47) The same reaction and procedure using **9** (50 mg, 0.18 mmol), theobromine (250 mg, 1.42 mmol) and K_2CO_3 (50 mg, 0.36 mmol) as described for the preparation of **46** gave compound **47** (36.4 mg, 55.5% yield) as a solid (mp 159—161 °C). EI-MS: m/z 380 $[M]^+$. HR-MS: m/z Calcd for $C_{20}H_{20}N_4O_4$ $[M]^+$; 380.1485, Found; 380.1475. ^{1}H-NMR ($CDCl_3$) δ: 8.17 (1H, dd, J=8.2, 1.2 Hz, H-5) or 8.04 (1H, dd, J=8.2, 1.2 Hz, H-8), 7.52 (1H, s, H-8′), 7.51 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-6) or 7.44 (1H, ddd, J=8.2, 7.0, 1.2 Hz, H-7), 6.63 (1H, s, H-3) 5.45 (2H, s, H-11), 4.03 and 3.99 (each 3H, s, 1- or 4-OCH_3), 3.89 and 3.60 (each 3H, s, 3′- or 7′-NCH_3). ^{13}C-NMR ($CDCl_3$) δ: 155.4 (C-6′), 152.0 (C-2′), 151.9 (C-4′), 149.0 (C-4), 146.98 (C-8′), 141.6 (C-1), 128.5 (C-9), 126.7 (C-10), 126.5 (C-7), 125.3 (C-6), 122.3 (C-5), 122.1 (C-8), 107.7 (C-2), 103.8 (C-3), 103.4 (C-5′), 62.3 (1-OCH_3), 55.7 (4-OCH_3), 40.0 (C-11), 30.7 (7′-NCH_3), 30.0 (3′-NCH_3).

4-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]morpholine (48) The same reaction and procedure using **23** (330.0 mg, 1.12 mmol) and morpholine (1.59 mg, 18.3 mmol) as described for the preparation of **42** gave compound **48** (167.8 mg, 49.8% yield) as a solid (mp 91—93 °C). EI-MS: m/z 301 $[M]^+$. HR-MS: m/z Calcd for $C_{18}H_{23}NO_3$ $[M]^+$; 301.1678, Found; 301.1671. ^{1}H-NMR ($CDCl_3$) δ: 8.05 (1H, s, H-8), 7.98 (1H, d, J=8.9 Hz, H-5), 7.52 (1H, d, J=8.9 Hz, H-6), 6.59 (1H, s, H-3), 3.96 and 3.85 (each 3H, s, 1- or 4-OCH_3), 3.72 (4H, m, –CH_2OCH_2–) and 3.65 (2H, s, 7-CH_2–), 2.48 (4H,m, –CH_2NCH_2–) 2.43 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 151.3 (C-4), 147.0 (C-1), 134.0 (C-7), 128.0 (C-9), 125.4 (C-6), 124.9 (C-10), 122.3 (C-2), 121.7 (C-8), 107.0 (C-5), 96.1 (C-3), 67.2 (–CH_2OCH_2–), 66.4 (C-12), 63.8 (OCH_3), 61.2 (OCH_3), 55.5 (–CH_2NCH_2–), 16.2 (C-11).

7-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]-1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (49) To a solution of **23** (330.0 mg, 1.12 mmol) in DMF (20 ml), theophylline (540 mg, 3.36 mmol) and NaH (135 mg, 3.36 mmol) was added. The mixture was stirred at 80 °C for 2 h. The reaction mixture was poured into ice-water (100 ml), neutralized with 5% aqueous $NaHCO_3$ and extracted with $CHCl_3$ (50 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and then filtered. The filtrate was subjected to column chromatography (a gradient of 0—3% MeOH in toluene) to obtain compound **49** (169.3 mg, 38.4% yield) as a solid (mp 182—184 °C). EI-MS: m/z 394 $[M]^+$. HR-MS: m/z Calcd for $C_{21}H_{22}N_4O_4$ $[M]^+$; 394.1641, Found; 394.1639. ^{1}H-NMR ($CDCl_3$) δ: 8.13 (1H, d, J=1.8 Hz, H-8), 8.02 (1H, d, J=8.9 Hz, H-5), 7.56 (1H, s, H-8′), 7.46 (1H, dd, J=8.9, 1.8 Hz, H-6), 6.62 (1H, s, H-3), 5.65 (2H, s, 7-CH_2–), 3.95 and 3.82 (each 3H, s, 1- or 4-OCH_3), 3.82 and 3.59 (each 3H, s, 3′-CH_3 or 7′-CH_3), 2.43 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 155.3 (C-6′), 151.7 (C-2′), 151.4 (C-4′), 148.8 (C-4), 147.0 (C-1), 141.0 (C-8′), 132.2 (C-7), 128.5 (C-9), 126.7 (C-6), 126.1 (C-5), 125.0 (C-10), 122.9 (C-8), 122.0 (C-2), 107.6 (C-5′), 96.1 (C-3), 61.2 (OCH_3), 55.6 (OCH_3), 50.6 (7′-CH_2-), 29.8 and 28.0 (1′- and 3′-CH_3), 16.3 (C-11).

1-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl]-1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (50) The same reaction and procedure uisng **23** (250 mg, 0.85 mmol), theobromine (460 mg, 2.56 mmol) and NaH (102 mg, 2.56 mmol) as described for the preparation of **49** gave compound **50** (232.7 mg, 69.8% yield) as a solid (mp 155—156 °C). EI-MS: m/z 394 $[M]^+$. HR-MS: m/z Calcd for $C_{21}H_{22}N_4O_4$ $[M]^+$; 394.1641, Found; 394.1646. ^{1}H-NMR ($CDCl_3$) δ: 8.27 (1H, s, H-8′), 7.95 (1H, d, J=8.6 Hz, H-5), 7.63 (1H, dd, J=8.6, 1.8 Hz, H-6), 7.48 (1H, d, J=1.8 Hz, H-8), 6.55 (1H, s, H-3), 5.35 (2H, s, –CH_2–), 3.98 and 3.85 (each 3H, s, 1- or 4-OCH_3), 3.80 and 3.57 (each 3H, s, 1′- or 3′-CH_3), 2.38 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 157.9 (C-6′), 155.3 (C-2′), 151.4 (C-4′), 148.9 (C-4), 146.1 (C-1), 141.5 (C-8′), 133.5 (C-7), 128.0 (C-9), 127.2 (C-5), 125.1 (C-6), 125.1 (C-10), 122.2 (C-8), 121.9 (C-2), 107.7 (C-5′), 107.0 (C-3), 61.2 (OCH_3), 55.5 (OCH_3), 44.8 (7′-CH_2–), 33.6 and 29.8 (3′- and 7′-CH_3), 16.2 (C-11).

2-[(Pyrrolidin-1-yl)methyl]naphthalene-1,4-dione (51) To a solution of **42** (100 mg, 0.37 mmol) in THF (25 ml) and H_2O (5 ml), NBS (72.2 mg, 0.41 mmol) and 0.1 M aqueous H_2SO_4 (0.05 ml) were added, and the mixture was then stirred at room temperature for 5 min. The reaction mixture was poured into ice-water (100 ml), neutralized with 5% aqueous $NaHCO_3$, and extracted with Et_2O (50 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—3% MeOH in $CHCl_3$) to obtain compound **51** (52.9 mg, 59.0% yield). EI-MS: m/z 241 $[M]^+$. HR-MS: m/z Calcd for $C_{15}H_{15}NO_2$ $[M]^+$; 270.1103, Found; 270.1099. ^{1}H-NMR ($CDCl_3$) δ: 8.09 (each 1H, m, H-5 or 8), 7.73 (each 1H, m, H-6 or 7), 7.05 (1H, t, J=1.8 Hz, H-3), 3.65 (2H, d, J=1.8 Hz, H-11), 2.63 (4H, m, –CH_2NCH_2–) and 2.52 (4H, m, –CH_2CH_2–). ^{13}C-NMR ($CDCl_3$) δ: 185.3 (C-1), 185.3 (C-4), 148.5 (C-2), 135.3 (C-3), 133.7 (C-7), 133.6 (C-6), 132.4 (C-9), 132.1 (C-10), 126.4 (C-8), 126.1 (C-5), 53.4 (C-11), 54.5 and 23.7 (signals on the pyrrolidinyl group).

2-[(4-Methylpyrerazin-1-yl)methyl]naphthalene-1,4-dione (52) The same reaction and procedure using **43** (62 mg, 0.21 mmol) and NBS (120 mg, 0.62 mmol) as described for the preparation of **51** gave compound **52** (30.6mg, 54.8% yield). EI-MS: m/z 270 $[M]^+$. HR-MS: m/z Calcd for $C_{16}H_{18}N_2O_2$ $[M]^+$; 270.1368, Found; 270.1364. ^{1}H-NMR ($CDCl_3$) δ: 8.08 (each 1H, m, H-5 or 8), 7.74 (each 1H, m, H-6 or 7), 7.06 (1H, t, J=1.8 Hz, H-3) 3.45 (2H, d, J=1.8 Hz, H-11), 2.61 and 2.52 (8H, m, –NCH_2CH_2– ×2) and 2.27 (3H, s, –NCH_3). ^{13}C-NMR ($CDCl_3$) δ: 185.4 (C-1), 185.3 (C-4), 147.4 (C-2), 135.3 (C-3), 133.8 (C-7), 133.7 (C-6), 132.3 (C-9), 132.1 (C-10), 126.4 (C-8), 126.1 (C-5), 55.7 (C-11), 55.1 (–N<u>C</u>H_2CH_2– ×2), 53.3 (–NCH_2<u>C</u>H_2– ×2), 45.9 (–NCH_3).

2-[(Morpholin-4-yl)methyl]naphthalene-1,4-dione (53) A solution of **44** (70 mg, 0.34 mmol) and CAN (400 mg, 0.73 mmol) in acetonitrile (25 ml) and H_2O (25 ml) was stirred at room temperature for 1 h. The reaction mixture was poured into ice-water (100 ml), and extracted with Et_2O (50 ml×3). The organic extracts were washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—3% MeOH in $CHCl_3$) to obtain compound **53** (39.8 mg, 63.5% yield). EI-MS: m/z 257 $[M]^+$. HR-MS:m/z Calcd for $C_{16}H_{18}N_2O_2$ $[M]^+$; 257.1052, Found; 270.1042. ^{1}H-NMR ($CDCl_3$) δ: 8.04 (each 1H, m, H-5 or 8), 7.70 (each 1H, m, H-6 or 7), 7.04 (1H, s, H-3), 3.47 (2H, s, H-11), 3.72 (4H, t, J=4.6 Hz, –CH_2OCH_2–), 2.52 (4H, t, J=4.6 Hz, –NCH_2×2). ^{13}C-NMR ($CDCl_3$) δ: 185.2 (C-1), 185.2 (C-4), 147.0 (C-2), 135.3 (C-3), 133.8 (C-7), 133.7 (C-6), 132.3 (C-9), 132.0 (C-10), 126.4 (C-8), 126.1 (C-5), 66.9 (–<u>C</u>H_2O<u>C</u>H_2–), 55.7 (C-11), 29.9 and 28.0 (–<u>C</u>H_2N<u>C</u>H_2–).

7-[(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl]-1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (54) The same reaction and procedure using **46** (60 mg, 0.16 mmol) and CAN (400 mg, 0.73 mmol) as described for the preparation of **53** gave compound **54** (29.6 mg, 53.7% yield) as a solid (mp 183—185 °C). EI-MS: m/z 350 $[M]^+$. HR-MS: m/z Calcd for $C_{18}H_{14}N_4O_4$ $[M]^+$; 350.1015, Found; 350.1016. ^{1}H-NMR ($CDCl_3$) δ: 8.11 and 8.07 (each 1H, m, H-5 or 8), 7.80 (1H, s, H-8′), 7.77 (2H, m, H-6 and 7), 6.84 (1H, s, H-3), 5.46 (2H, s, H-11), 3.60 and 3.38 (each 3H, s, 1′- or 3′-NCH_3). ^{13}C-NMR ($CDCl_3$) δ: 184.4 (C-1), 184.1 (C-4), 155.01 (C-6′), 151.6 (C-2′), 148.9 (C-2), 144.0 (C-4′), 142.2 (C-8′), 136.1 (C-3), 134.4 (C-7), 134.1 (C-6), 132.0 (C-9), 131.6 (C-10), 126.7 (C-8), 126.5 (C-5), 106.7 (C-5′), 44.5 (C-11), 29.9 and 28.0 (1′- and 3′-NCH_3).

7-[(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl]-3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (55) A solution of **47** (100 mg, 0.26 mmol) and HNO_3 (0.28 g, 2.9 mmol) in AcOH (10 ml) was stirred at room temperature for 1 h. The reaction mixture was poured into ice-water (50 ml), and the mixture was neutralized with 5% aqueous $NaHCO_3$, and extracted with $CHCl_3$ (50 ml×3). The extracts were evaporated to give a residue which was subjected to column chromatography (a gradient of 0—3% MeOH in

$CHCl_3$) to obtain compound **55** (44.8 mg, 58.6% yield) as a solid (mp 168—170 °C). EI-MS: *m/z* 350 $[M]^+$. HR-MS: *m/z* Calcd for $C_{18}H_{14}N_4O_4$ $[M]^+$; 350.1015, Found; 350.1034. ^{1}H-NMR ($CDCl_3$) δ: 8.14 and 8.04 (each 1H, m, H-5 or 8), 7.77 (2H, m, H-6 and 7), 7.59 (1H, s, H-8′), 6.44 (1H, s, H-3), 5.20 (2H, s, H-11), 4.00 and 3.61 (each 3H, s, 1′- or 3′-NCH_3). ^{13}C-NMR ($CDCl_3$) δ: 184.7 (C-1), 184.3 (C-4), 154.6 (C-6′), 151.1 (C-2), 149.3 (C-2′), 145.9 (C-4′), 142.1 (C-8′), 135.2 (C-3), 134.0 (C-7), 133.9 (C-6), 132.2 (C-9), 132.1 (C-10), 126.6 (C-8), 126.3 (C-5), 107.5 (C-5′), 39.5 (C-11), 33.7 and 30.0 (3′- and 7′-NCH_3).

2-Methyl-7-[(morpholin-4-yl)methyl]naphthalene-1,4-dione (56) A solution of **48** (80 mg, 0.27 mmol) and HNO_3 (0.28 g, 2.9 mmol) in AcOH (50 ml) was stirred at room temperature for 1 h. The reaction mixture was poured into ice-water (50 ml), and extracted with $CHCl_3$ (50 ml×3). The organic extracts were washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (toluene) to obtain compound **56** (57.3 mg, 49.5% yield) as a solid (mp 115—117 °C). EI-MS: *m/z* 271 $[M]^+$. HR-MS: *m/z* Calcd for $C_{16}H_{17}NO_3$ $[M]^+$; 271.1208, Found; 271.1209. ^{1}H-NMR ($CDCl_3$) δ: 8.01 (1H, d, *J*=7.9 Hz, H-5), 8.00 (1H, d, *J*=1.8 Hz, H-8), 7.74 (1H, dd, *J*=7.9, 1.8 Hz, H-6), 6.83 (1H, d, *J*=1.5 Hz, H-3), 3.73 (4H, m, –CH_2OCH_2–), 3.61 (2H, s, 7′-CH_2–), 3.47 (4H, m, –CH_2NCH_2–), 2.20 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 185.3 (C-1), 185.1 (C-4), 148.2 (C-2), 144.7 (C-7), 135.6 (C-3), 134.0 (C-6), 132.2 (C-9), 131.3 (C-10), 126.8 (C-5), 126.4 (C-8), 66.9 (–$\underline{C}H_2O\underline{C}H_2$–), 62.8 (7′-$CH_2$–), 53.6 (–$\underline{C}H_2N\underline{C}H_2$–), 16.4 (C-11).

1,3-Dimethyl-7-[(7-methyl-5,8-dioxo-5,8-dihydronaphthalen-2-yl)methyl]-3,7-dihydro-1*H*-purine-2,6-dione (57) The same reaction and procedure using **49** (80 mg, 0.20 mmol) as described for the preparation of **56** gave compound **57** (28.8 mg, 41.2% yield) as a solid (mp 238—240 °C). EI-MS: *m/z* 364 $[M]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{16}N_4O_4$ $[M]^+$; 364.1172, Found; 364.1185. ^{1}H-NMR ($CDCl_3$) δ: 8.35 (1H, d, *J*=1.8 Hz, H-8), 7.97 (1H, d, *J*=7.9 Hz, H-5), 7.87 (1H, s, H-6′), 7.74 (1H, dd, *J*=7.9, 1.8 Hz, H-6), 6.96 (1H, q, *J*=1.5 Hz, H-3), 5.64 (2H, s, 7-CH_2–), 3.43 and 3.17 (each 3H, s, 1′- or 3′-CH_3), 2.10 (3H, d, *J*=1.5 Hz, H-11). ^{13}C-NMR ($CDCl_3$) δ: 184.5 (C-1), 184.2 (C-4), 154.2 (C-6′), 150.9 (C-2′), 148.5 (C-4′), 148.0 (C-2), 142.9 (C-7), 142.7 (C-8′), 135.1 (C-3), 132.6 (C-9), 131.9 (C-6), 131.2 (C-5), 126.6 (C-8), 124.3 (C-10), 105.7 (C-5′), 48.6 (7-CH_2–), 29.4 and 27.4 (1′- and 3′-CH_3), 15.8 (C-11).

3,7-Dimethyl-1-[(7-methyl-5,8-dioxo-5,8-dihydronaphthalen-2-yl)methyl]-3,7-dihydro-1*H*-purine-2,6-dione (58) The same reaction and procedure using **50** (100 mg, 0.25 mmol) as described for the preparation of **57** gave compound **58** (84.0 mg, 92.0% yield) as a solid (mp 224—225 °C). EI-MS: *m/z* 364 $[M]^+$. HR-MS: *m/z* Calcd for $C_{19}H_{16}N_4O_4$ $[M]^+$; 364.1172, Found; 364.1189. ^{1}H-NMR ($CDCl_3$) δ: 8.05 (1H, d, *J*=7.9 Hz, H-5), 8.02 (1H, s, H-8′), 7.76 (1H, dd, *J*=7.9, 1.8 Hz, H-6), 7.55 (1H, d, *J*=1.8 Hz, H-8), 6.80 (1H, q, *J*=1.5 Hz, H-3), 5.30 (2H, s, 7-CH_2–), 4.00 (3H, s, 7′-CH_3), 3.61 (3H, s, 3′-CH_3), 2.17 (3H, d, *J*=1.5 Hz, H-11). ^{13}C-NMR ($CDCl_3$) δ: 185.3 (C-1), 184.9 (C-4), 167.8 (C-6′), 155.0 (C-2′), 151.4 (C-4′), 143.7 (C-7), 141.9 (C-8′), 135.1 (C-3), 133.3 (C-6), 132.4 (C-2), 131.3 (C-10), 130.9 (C-9), 127.0 (C-5), 125.5 (C-8), 107.6 (C-5′), 44.2 (7′-CH_2–), 33.7 and 29.7 (3′- and 7′-CH_3), 16.4 (C-11).

1,4-Dimethoxynaphthalen-2-yl)methyl Thiocyanate (59) KSCN (430 mg, 4.28 mmol) was added to a solution of **19** (300 mg, 1.07 mmol) in DMF (50 ml) and the mixture was then stirred at 60 °C for 2 h. The reaction mixture was poured into ice-water (100 ml) and extracted with $CHCl_3$ (50 ml×3). The organic extracts were washed successively with brine and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (a gradient of 0—5% acetone in toluene) to obtain compound **59** (203.7 mg, 73.6% yield) as a solid (mp 94—97 °C). EI-MS: *m/z* 259 $[M]^+$. HR-MS: *m/z* Calcd for $C_{14}H_{13}NO_2S$ $[M]^+$; 259.0667, Found; 259.0658. ^{1}H-NMR ($CDCl_3$) δ: 8.25 and 8.03 (each 1H, m, H-5 or 8), 7.58 and 7.52 (each 1H, m, H-6 or 7), 6.72 (1H, s, H-3), 4.43 (2H, s, H-11), 4.01 and 3.97 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR ($CDCl_3$) δ: 152.4 (C-4), 148.2 (C-1), 128.2 (C-9), 127.2 (C-10), 127.1 (C-7), 126.3 (C-6), 122.7 (C-5), 122.3 (C-8), 122.2 (C-2), 112.5 (SCN), 104.0 (C-3), 63.1 (OCH_3), 55.8 (OCH_3), 33.7 (C-11).

(1,4-Dimethoxynaphthalen-2-yl)methyl Selenocyanate (60) The same reaction and preparation using **19** (286 mg, 0.95 mmol) and KSeCN (548 mg, 3.81 mmol) as described for the preparation of **59** gave compound **60** (238.0 mg, 76.4% yield) as a solid (mp 95—96 °C). EI-MS: *m/z* 307 $[M]^+$. HR-MS: *m/z* Calcd for $C_{14}H_{13}NO_2Se$ $[M]^+$; 307.0112, Found; 307.0120. ^{1}H-NMR ($CDCl_3$) δ: 8.24 and 8.02 (each 1H, m, H-5 or 8), 7.55 and 7.51 (each 1H, m, H-6 or 7), 6.71 (1H, s, H-3), 4.55 (2H, s, H-11), 4.01 and 3.97 (each 3H, s, 1- or 4-OCH_3). ^{13}C-NMR ($CDCl_3$) δ: 152.3 (C-4), 148.0 (C-1), 128.3 (C-9), 127.2 (C-10), 127.0 (C-7), 126.2 (C-6), 123.4 (C-5), 122.7 (C-8), 122.0 (C-2), 104.2 (C-3), 102.5 (SeCN), 62.7 (OCH_3), 55.8 (OCH_3), 28.3 (C-11).

***S*-[(1,4-Dimethoxynaphthalin-2-yl)methyl] Ethanethionate (61)** The same reaction and procedure using **19** (300 mg, 1.07 mmol) and KSeAc (430 mg, 3.78 mmol) as described for the preparation of **59** gave compound **61** (163.1mg, 55.3% yield). EI-MS: *m/z* 276 $[M]^+$. HR-MS: *m/z* Calcd for $C_{15}H_{16}O_3S$ $[M]^+$; 276.0820, Found; 276.0828. ^{1}H-NMR ($CDCl_3$) δ: 8.20 and 8.01 (each 1H, m, H-5 or 8), 7.53 and 7.46 (each 1H, m, H-6 or 7), 6.70 (1H, s, H-3), 4.35 (2H, s, H-11), 3.96 and 3.92 (each 3H, s, 1- or 4-OCH_3), 2.38 (3H, s, $COCH_3$). ^{13}C-NMR ($CDCl_3$) δ: 195.7 (11-S$\underline{C}OCH_3$), 152.1 (C-4), 147.6 (C-1), 128.4 (C-9), 126.8 (C-10), 126.3 (C-7), 125.5 (C-6), 125.2 (C-5), 122.4 (C-8), 121.9 (C-2), 105.1 (C-3), 62.5 (OCH_3), 55.7 (OCH_3), 30.4 (C-11), 28.4 (11-SCO$\underline{C}H_3$).

(5,8-Dimethoxynaphthalen-2-yl)methyl Thiocyanate (62) The same reaction and procedure using **23** (300 mg, 1.02 mmol) and KSCN (430 mg, 4.28 mmol) as described for the preparation of **59** gave compound **62** (181.4 mg, 65.3% yield) as a solid (mp 58—60 °C). EI-MS: *m/z* 273 $[M]^+$. HR-MS: *m/z* Calcd for $C_{15}H_{15}NO_2S$ $[M]^+$; 273.0824, Found; 273.0825. ^{1}H-NMR ($CDCl_3$) δ: 8.16 (1H, d, *J*=1.8 Hz, H-8), 8.04 (1H, d, *J*=8.6 Hz, H-5), 7.48 (1H, dd, *J*=8.6, 1.8 Hz, H-6), 6.63 (1H, s, H-3), 4.34 (2H, s, 7-CH_2–), 3.98 (3H, s, 4-OCH_3), 3.85 (3H, s, 1-OCH_3), 2.44 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 151.4 (C-4), 147.0 (C-1), 130.2 (C-7), 128.5 (C-9), 127.0 (C-10), 126.7 (C-6), 125.0 (C-2), 123.1 (C-5), 122.9 (C-8), 112.0 (SCN), 107.7 (C-3), 61.3 (OCH_3), 55.6 (OCH_3), 39.1 (7-$\underline{C}H_2$–), 16.8 (C-11).

(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl Selenocyanate (63) The same reaction and procedure using **23** (260 mg, 0.89 mmol) and KSeCN (548 mg, 3.81 mmol) as described for the preparation of **62** gave compound **63** (147.2 mg, 52.2% yield) as a solid (mp 105—108 °C). EI-MS: *m/z* 321 $[M]^+$. HR-MS: *m/z* Calcd for $C_{15}H_{15}NO_2Se$ $[M]^+$; 321.0268, Found; 321.0264. ^{1}H-NMR ($CDCl_3$) δ: 8.16 (1H, d, *J*=1.8 Hz, H-8), 8.03 (1H, d, *J*=8.6 Hz, H-5), 7.48 (1H, dd, *J*=8.6, 1.8 Hz, H-6), 6.62 (1H, s, H-3), 4.51 (2H, s, 7-CH_2–), 3.96 (3H, s, 4-OCH_3), 3.85 (3H, s, 1-OCH_3), 2.44 (3H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 151.4 (C-4), 147.0 (C-1), 131.1 (C-7), 128.4 (C-9), 127.0 (C-10), 126.9 (C-6), 125.0 (C-2), 123.0 (C-5), 107.7 (C-8), 102.0 (C-3), 96.1 (SeCN), 61.3 (OCH_3), 55.7 (OCH_3), 33.7 (7-$\underline{C}H_2$–), 16.4 (C-11).

***S*-[(5,8-Dimethoxy-7-methylnaphthalen-2-yl)methyl Ethanethioate (64)** The same reaction and procedure using **23** (300 mg, 1.02 mmol) and KSAc (468 mg, 4.06 mmol) as described for the preparation of **59** gave compound **64** (142.5 mg, 48.3% yield). EI-MS: *m/z* 290 $[M]^+$. HR-MS: *m/z* Calcd for $C_{16}H_{18}O_3S$ $[M]^+$; 290.0977, Found; 290.0980. ^{1}H-NMR ($CDCl_3$) δ: 8.09 (1H, d, *J*=1.8 Hz, H-8), 7.96 (1H, d, *J*=8.5 Hz, H-5), 7.42 (1H, dd, *J*=8.5, 1.8 Hz, H-6), 6.59 (1H, s, H-3), 4.23 (2H, s, 7-CH_2–), 3.95 (3H, s, 4-OCH_3), 3.83 (3H, s, 1-OCH_3), 2.42 (3H, s, H-11) 2.36 (3H, s, $SCOCH_3$). ^{13}C-NMR ($CDCl_3$) δ: 151.7 (C-4), 146.9 (C-1), 131.1 (C-7), 128.6 (C-9), 127.4 (C-6), 125.8 (C-10), 125.1 (C-2), 122.3 (C-8), 122.0 (C-5), 107.3 (C-3), 102.0 (SeCN), 61.2 (OCH_3), 55.6 (OCH_3), 33.9 (7-CH_2–), 30.3 (7-SCO$\underline{C}H_3$), 16.3 (C-11).

(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl Thiocyanate (65) A solution of compound **59** (50 mg, 0.19 mmol) and HNO_3 (0.28 g, 2.90 mmol) in AcOH (10 ml) was stirred at room temperature for 1 h. The mixture was poured into ice-water (50 ml) and extracted with Et_2O (50 ml×3). The organic extracts were washed successively with 5% aqueous $NaHCO_3$ and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (a gradient of 0—10% acetone in toluene) to obtain compound **65** (20.6 mg, 46.6% yield) as a solid (mp 79—81 °C). EI-MS: 229 $[M]^+$. HR-MS: *m/z* Calcd for $C_{12}H_7NO_2S$ $[M]^+$; 229.0197, Found; 229.0201. ^{1}H-NMR ($CDCl_3$) δ: 8.13 (2H, m, H-5 and 8), 7.80 (2H, m, H-6 and 7), 7.07 (1H, s, H-3), 3.99 (2H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 183.9 (C-4), 183.2 (C-1), 143.3 (C-2), 136.7 (C-3), 134.5 (C-7), 134.2 (C-6), 132.2 (C-9), 131.6 (C-10), 126.9 (C-5), 126.6 (C-8), 111.3 (11-SCN), 31.9 (C-11).

(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl Selenocyanate (66) The same reaction and procedure using **60** (50.0 mg, 0.16 mmol) as described for the preparation of **65** gave compound **66** (17.5 mg, 38.9% yield) as a solid (mp 121—123 °C). EI-MS: *m/z* 276 $[M]^+$. HR-MS: *m/z* Calcd for $C_{12}H_7O_2NSe$ $[M]^+$; 276.9642, Found; 276.9662. ^{1}H-NMR ($CDCl_3$) δ: 8.12 (2H, m, H-5 and 8), 7.80 (2H, m, H-6 and 7), 7.03 (1H, s, H-3), 4.03 (2H, s, H-11). ^{13}C-NMR ($CDCl_3$) δ: 183.9 (C-1), 183.8 (C-4), 145.0 (C-2), 135.6 (C-3), 134.6 (C-7), 134.1 (C-6), 132.3 (C-9), 131.6 (C-10), 126.9 (C-8), 126.7 (C-5), 101.7 (11-SeCN), 25.7 (C-11).

***S*-[(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)methyl] Ethanethioate (67)** The same reaction and procedure using **61** (80 mg, 0.29 mmol) as described

for the preparation of **66** gave compound **67** (32.3 mg, 45.3% yield) as a solid (mp 75—78 °C). EI-MS: *m/z* 246 $[M]^+$. HR-MS: *m/z* Calcd for $C_{13}H_{10}O_3S$ $[M]^+$; 246.0351, Found; 246.0353. ^{1}H-NMR ($CDCl_3$) δ: 8.11 and 8.07 (each 1H, m, H-5 or 8), 7.75 (2H, m, H-6 and 7), 7.05 (1H, t, J=0.9 Hz, H-3), 4.00 (2H, d, J=0.9 Hz, H-11), 2.36 (3H, s, $SCOCH_3$). ^{13}C-NMR ($CDCl_3$) δ: 194.3 (11-S<u>C</u>OCH_3), 184.9 (C-1), 184.3 (C-4), 146.4 (C-2), 135.9 (C-3), 134.0 (C-7), 133.8 (C-6), 132.1 (C-9), 131.9 (C-10), 126.7 (C-8), 126.3 (C-5), 30.3 (C-11), 27.3 (11-SCO<u>C</u>H_3).

(7-Methyl-5,8-dioxo-5,8-dihydronaphthalen-2-yl)methyl Thiocyanate (68) The same reaction and procedure fusing **62** (70.0 mg, 0.26 mmol) as described for the preparation of **59** gave compound **68** (26.4 mg, 42.3% yield) as a solid (mp 135—136 °C). EI-MS: *m/z* 243 $[M]^+$. HR-MS: *m/z* Calcd for $C_{13}H_9NO_2S$ $[M]^+$; 243.0354, Found; 243.0330. ^{1}H-NMR ($CDCl_3$) δ: 8.15 (1H, d, J=7.9 Hz, H-5), 8.06 (1H, d, J=1.8 Hz, H-8), 7.75 (1H, dd, J=7.9, 1.8 Hz, H-6), 6.88 (1H, q, J=1.5 Hz, H-3), 4.23 (2H, s, 7-CH_2–), 2.22 (3H, d, J=1.5 Hz, H-11). ^{13}C-NMR ($CDCl_3$) δ: 184.8 (C-1), 184.2 (C-4), 148.5 (C-2), 140.5 (C-7), 135.7 (C-3), 133.8 (C-6), 132.8 (C-9), 132.2 (C-10), 127.7 (C-5), 126.6 (C-8), 111.8 (7-CH_2S<u>C</u>N), 37.4 (7-<u>C</u>H_2–), 16.5 (C-11).

7-(Methyl-5,8-dioxo-5,8-dihydronaphthalen-2-yl)methyl Selenocyanate (69) The same reaction and procedure for **63** (70.0 mg, 0.22 mmol) as described for the preparation of **59** gave compound **69** (26.5 mg, 41.8% yield) as a solid (mp 147—148 °C). EI-MS: *m/z* 290 $[M]^+$. HR-MS: *m/z* Calcd for $C_{13}H_9O_2NSe$ $[M]^+$; 290.9798, Found; 290.9810. ^{1}H-NMR ($CDCl_3$) δ: 8.13 (1H, d, J=7.9 Hz, H-5), 8.05 (1H, d, J=1.5 Hz, H-8), 7.74 (1H, dd, J=7.9, 1.5 Hz, H-5), 6.83 (1H, q, J=1.2 Hz, H-3), 4.36 (2H, s, 7-CH_2–), 2.21 (3H, d, J=1.2 Hz, H-11). ^{13}C-NMR ($CDCl_3$) δ: 184.8 (C-1), 184.3 (C-4), 148.6 (C-2), 141.9 (C-7), 141.9 (C-3), 135.6 (C-6), 133.8 (C-9), 132.8 (C-10), 127.6 (C-5), 126.5 (C-8), 100.6 (7-CH_2Se<u>C</u>N), 31.4 (7-<u>C</u>H_2–), 16.5 (C-11).

***S*-[(7-Methyl-5,8-dioxo-5,8-dihydromaphthalen-2-yl)methyl] Ethanethionate (70)** The same reaction and procedure using **63** (70.0 mg, 0.24 mmol) as described for the preparation of **59** gave compound **70** (32.3 mg, 51.5% yield) as a solid (mp 122—124 °C). EI-MS: *m/z* 260 $[M]^+$. HR-MS: *m/z* Calcd for $C_{14}H_{12}O_3S$ $[M]^+$; 260.0507, Found; 260.0497. ^{1}H-NMR ($CDCl_3$) δ: 8.03 (1H, d, J=7.9 Hz, H-5), 7.96 (1H, d, J=1.8 Hz, H-8), 7.66 (1H, dd, J=7.9, 1.8 Hz, H-5), 6.83 (1H, q, J=1.5 Hz, H-3), 4.20 (2H, s, 7-CH_2–), 2.37 (3H, s, $SCOCH_3$), 2.19 (3H, d, J=1.5 Hz, H-11). ^{13}C-NMR ($CDCl_3$) δ: 194.2 (S<u>C</u>OCH_3), 185.6 (C-1), 184.7 (C-4), 148.2 (C-2), 144.3 (C-7), 135.6 (C-3), 133.9 (C-6), 132.4 (C-9), 131.1 (C-10), 127.1 (C-5), 126.3 (C-8), 33.0 (7-<u>C</u>H_2–), 30.3 (SCO<u>C</u>H_3), 16.5 (C-11).

Cytotoxic Effects. Cell Lines and Culture The human colorectal carcinoma cell line (HCT 116, ATCC No. CCL-247) and human hepatoma cell line (Hep G2 No. RCB0459) were purchased from Dainippon Pharmaceutical Co., Ltd. (Osaka, Japan) and RIKEN Cell Bank (Tsukuba, Japan), respectively. Dulbecco's modified Eagle's medium (DMEM), McCoy's 5A medium, fetal bovine serum (FBS) and penicillin–streptomycin mixture (100 U/ml penicillin and 100 μg/ml streptomycin) were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan), Sigma-Aldrich (St. Louis, MO, U.S.A.), BioSource International (Camarillo, CA, U.S.A.) and Bio Whittaker (Walkersville, MD, U.S.A.), respectively. The HCT 116 cells were maintained in McCoy's 5A medium and Hep G2 cells were cultured in DMEM. Each medium was supplemented with 10% FBS and a penicillin–streptomycin mixture. Cell cultures performed at 37 °C in a humidified atmosphere containing 5% CO_2 in air.

Assay Procedure Aliquots (200 μl) of 5×10^3 cells per ml of HCT 116 and Hep G2 cells were seeded in 96 well flat-bottomed plates (Microtest™ Tissue Culture Plate, 96 Well, Flat Bottom with Low Evaporation Ltd., Falcon, NJ, U.S.A.). Cell cultures were incubated in a medium containing 10% FBS and a penicillin–streptomycin mixture at 37 °C in a humidified atmosphere of 5% CO_2 for 24 h. The test drugs were dissolved in dimethyl sulfoxide (DMSO). The incubation medium was replaced with each test medium giving a final concentration of 0.1—500 μmol/l of test compounds and no drug in 2 μl DMSO over 2 d. The ability of the drug to inhibit cellular growth was determined by performing the MTT assay.[18] The cytotoxic effects of the test drugs were determined as previously described.[21] Each experiment was performed in duplicate wells, and all the experiments involving a control (DMSO only) and the drug treatments were performed separately three to five times. The data represent mean±S.D. values.

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