Efficient Synthesis of Dihydrofurans with Sulfide Groups by Ceric(IV) Ammonium Nitrate-Mediated Oxidative Cycloaddition of 1,3-Dicarbonyl Compounds to Vinyl Sulfides. Application to the Synthesis of Benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione and First Total Synthesis of Millettocalyxins C and Pongamol Methyl Ether

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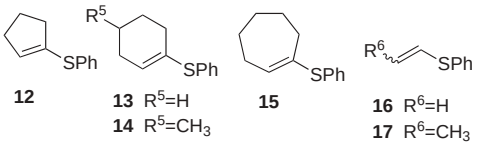
Received 2 April 2003; revised 30 May 2003

Abstract: Ceric(IV) ammonium nitrate-mediated oxidative cycloaddition of 1,3-dicarbonyls to vinyl sulfides afforded substituted dihydrofurans with sulfide groups in moderate yields. This new synthetic method has been applied to the synthesis of benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione and furanoflavone natural products such as millettocalyxins C and pongol methyl ether.

Key words: furans, natural products, cycloadditions, oxidations, millettocalyxins C, pongol methyl ether

Oxidative cycloaddition reactions mediated by metal salts (Mn^{III}, Ce^{IV}, Co^{II}, and V^{V}) have received considerable attention in organic synthesis for the construction of carbon–carbon bonds.[1] Among these, manganese(III) acetate and ceric(IV) ammonium nitrate (CAN) have been used most efficiently. CAN-mediated oxidative cycloaddition of 1,3-dicarbonyl compounds to alkenes,[2] vinyl acetates,[3] enol silyl ethers,[4] and enol ethers[5] has been studied extensively. We have reported on the CAN-mediated oxidative cycloaddition of 1,3-dicarbonyl compounds with conjugated compounds.[6] While continuing our work based on the CAN-mediated oxidative cycloaddition, we have expanded this work to the synthesis of dihydrofurans with sulfide groups.[7] In order to examine the breadth and generality of the reactions described in our preliminary results,[7] we have reviewed additional reactions of a number of 1,3-dicarbonyl compounds and vinyl sulfides. Here, we report the efficient synthesis of a variety of substituted dihydrofurans and its application to the biologically interesting benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione and furanoflavone natural products such as millettocalyxins C and pongol methyl ether.

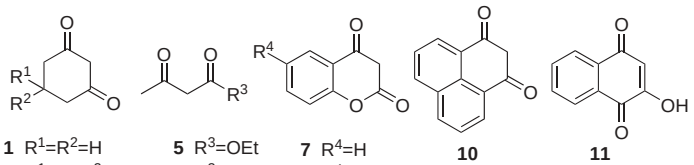
The 1,3-dicarbonyl compounds used in this study included the commercially available cyclohexane-1,3-diones **1**–**4**, ethyl acetoacetate (**5**), 2,4-pentanedione (**6**), 4-hydroxycoumarins **7**–**9**, 3-hydroxy-1*H*-phenalen-1-one (**10**), and 2-hydroxy-1,4-naphthoquinone (**11**) (Figure 1). The vinyl sulfides **12**–**15** used to react with the dicarbonyl compounds were readily prepared with a known procedure (Figure 2).[8]



12 **13** R^5=H **14** R^5=CH_3 **15** **16** R^6=H **17** R^6=CH_3

Figure 2

Reaction of 1,3-dicarbonyl compound **1** with vinyl sulfide **13** was first examined utilizing the two oxidizing agents $Mn(OAc)_3{\cdot}2\ H_2O$ and $Ce(NH_4)_2(NO_3)_6$. Both manganese(III) acetate dihydrate (80 °C, 7 h) in HOAc and ceric(IV) ammonium nitrate (0 °C, 6 h) in acetonitrile provided the dihydrofuran **18** in 65 and 79% yields, respectively (Table 1). However, we found that ceric(IV) ammonium nitrate was a much superior reagent for this cycloaddition than manganese(III) acetate dihydrate, with the advantage of more mild reaction conditions and a higher yield. The formation of **18** was confirmed by the



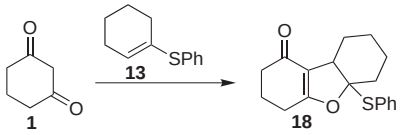
1 R^1=R^2=H **2** R^1=H, R^2=CH_3 **3** R^1=H, R^2=Ph **4** R^1=R^2=CH_3 **5** R^3=OEt **6** R^3=CH_3 **7** R^4=H **8** R^4=Cl **9** R^4=CH_3 **10** **11**

Figure 1

Synthesis 2003, No. 13, Print: 18 09 2003. Web: 19 08 2003.
Art Id.1437-210X,E;2003,0,13,1977,1988,ftx,en;F03003SS.pdf.
DOI: 10.1055/s-2003-41023

observation of a carbonyl peak of the enone at 1638 cm^{-1} in the IR spectrum, and the expected chemical shifts associated with the methine proton of the dihydrofuran ring at δ = 3.16. In order to find the optimized reaction conditions, we surveyed several solvents in the presence of $Ce(NH_4)_2(NO_3)_6$. The best yield was obtained in THF (86%). Other solvents included methanol (27%) and benzene (12%). Our finding was very surprising in comparison with the reported result that CAN(IV)-mediated oxidative reactions have usually been used in polar solvents such as acetonitrile and methanol.[1–5]

Table 1 Effect of Oxidants and Solvents in the Reaction of **1** and **13**



Oxidant	Solvent	Temperature (°C)	Time (h)	Yield (%)
$Mn(OAc)_3 \cdot 2\ H_2O$	HOAc	80	7	65
$Ce(NH_4)_2(NO_3)_6$	MeCN	0	6	79
$Ce(NH_4)_2(NO_3)_6$	THF	r.t.	6	86
$Ce(NH_4)_2(NO_3)_6$	MeOH	r.t	18	27
$Ce(NH_4)_2(NO_3)_6$	benzene	r.t	24	12

In order to extend the utility of these oxidative cycloadditions, additional reactions of 1,3-dicarbonyl compounds with other sulfides were next investigated. In the treatment of **1** and **4** with vinyl sulfide **12** in the presence of 2.2 equiv of CAN(IV) at room temperature for 6 hours in THF, cycloadducts **19** and **20** were obtained in 79% and 84% yields, respectively (entries 1, 2, Table 1). With the acyclic 1,3-dicarbonyl compound, the cycloaddition reaction was successful. When ethyl acetoacetate (**5**) was treated with vinyl sulfide **12** in THF, dihydrofuran **21** was obtained with 40% yield (entry 3). Vinyl sulfide **14,** with a larger ring system, gave cycloadducts **23**–**26** in 49–87% yields (entries 5–8). The stereochemistry of **19**–**26** is assigned as *cis* by spectral analysis and by analogy with earlier reported data.[9] The reaction was also successful with the acyclic vinyl sulfides **16** and **17**. Treatment of **1** with vinyl sulfide **16** in THF gave cycloadduct **27** with 74% yield (entry 9). With vinyl sulfide **17** with a 3:2 ratio of stereoisomers, there is a moderate solvent dependence in yield and stereoselectivity. In acetonitrile the reaction afforded cycloadduct **28** in 64% yield with a 32:68 mixture of the *cis*- and *trans*-isomers (entry 10), whereas in THF the reaction gave **28** with a higher yield (71%) and a lower stereoseletivity toward the *trans*-isomer (entry 11). The stereochemical assignment of the *cis*- and *trans*-isomers was defined by the observation of the coupling constants between vicinal protons (J_{cis} = 8.8 Hz, J_{trans} = 5.3 Hz) of the dihydrofuran ring. The results are summarized in Table 2.

In order to synthesize biologically interesting dihydrofurocoumarin derivatives, reaction of 4-hydroxycoumarins **7**–**9** with vinyl sulfides was next examined. Treatment of **7** with vinyl sulfide **12** in the presence of 2.2 equivalents of CAN(IV) in THF gave dihydrofurocoumarins **29** (42%), without any formation of possible regioisomers (entry 1, Table 3). Compound **29** has been clearly shown to be angular by spectral analysis and by comparison with reported data in the literature.[10,11] With other vinyl sulfides **13** and **15**, the expected dihydrofurocoumarins **30**–**32** were also obtained in 40–72% yields, respectively (entries 2–4). Similarly, reaction of **7** and **9** with acyclic vinyl sulfide **16** afforded cycloadducts **33** and **34** in 46% and 60% yields, respectively (entries 5, 6). The results are summarized in Table 3. These reactions provide a rapid route to the preparation of dihydrofurocoumarin derivatives which are known to have a number of biological activities such as anticoagulant, insecticidal, anthelminthic, hypnotic, and antifungal.[12]

Next, reaction of 3-hydroxy-1*H*-phenalen-1-one (**10**) with vinyl sulfides was investigated. Treatment of **10** with vinyl sulfide **12** gave dihydrofurophenalenone **35** with a yield of 87% (entry 1, Table 4). Similarly, reaction with sulfides **13** and **15** afforded dihydrofurophenalenone derivatives **36** and **37** in 77 and 74% yields, respectively (entries 2, 3). Reaction with vinyl sulfide **17** afforded cycloadduct **39** (92%) with a 34:66 mixture of *cis*- and *trans*-isomers (entry 5). This reaction also affords the *trans*-compound as the major product, despite the fact that the *cis*-vinyl sulfide was the major reagent. The results are summarized in Table 4. Importantly, these reactions provide a rapid route for the synthesis of biologically interesting dihydrofurophenalenone derivatives which are reported to have various biological activities such as antibiotics, antimicrobial, antifungal, and phytoalexin.[13]

Finally, the reaction of 2-hydroxy-1,4-naphthoquinone (**11**) with vinyl sulfides was investigated. Treatment of **11** with vinyl sulfide **12** resulted in dihydrofuronaphthoquinone **40** (30%) and **41** (19%) as a mixture of linear and angular regioisomers (entry 1, Table 5). The products were easily purified by column chromatography and the structures of the two isomers were determined by their spectroscopic data, and by comparison with data that had been reported in the literature.[14] The clear assignments came from the IR carbonyl absorptions at 1690 and 1647 cm^{-1} for the two carbonyls in **40** and at 1701and 1653 cm^{-1} in **41**. Similarly, with other sulfides **13**–**16**, cycloadducts **42**–**47** were obtained as a mixture of regioisomers (entries 2–4). However, reaction with vinyl sulfide **16** at room temperature in THF afforded solely dihydrofuronaphthoquinone **48** in 53% yield, without formation of the other possible regioisomer (entry 5). The results are summarized in Table 5. These reactions also provided a rapid entry to the synthesis of biologically active dihydrofuronaphthoquinone derivatives.[15]

As an application of this methodology, the synthesized adducts can be elaborated toward other biologically and

Table 2 Reaction of Cyclic and Acyclic 1,3-Dicarbonyl Compounds **1**–**6** with Vinyl Sulfides

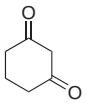
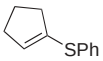
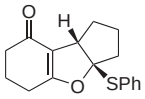
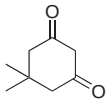
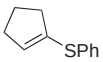
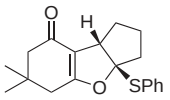
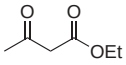
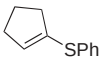
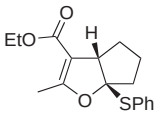
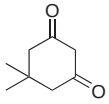
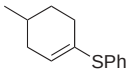
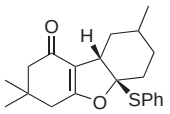
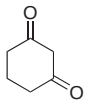
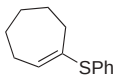
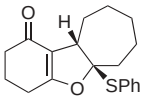
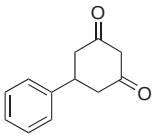
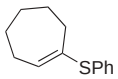
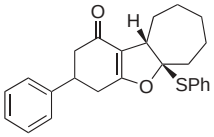
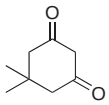
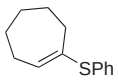
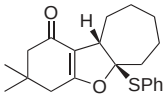
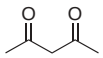
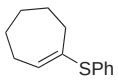
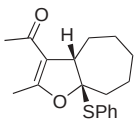
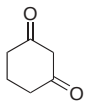
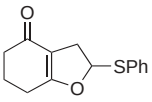
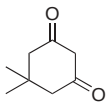
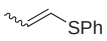
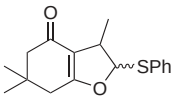
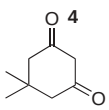
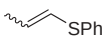
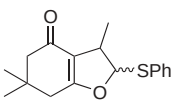
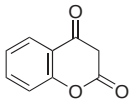
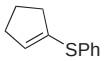
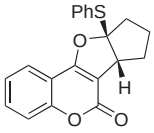
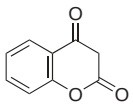
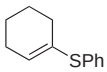
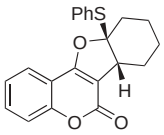
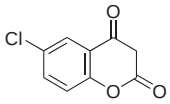
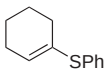
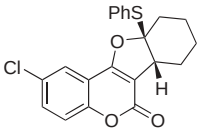
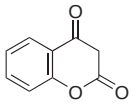
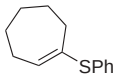
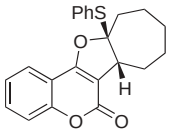
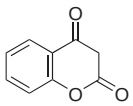
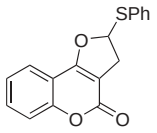
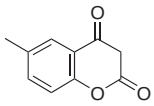
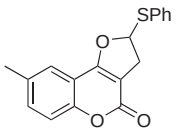
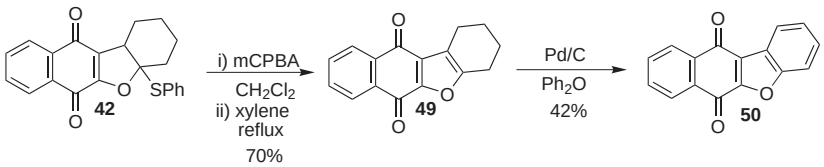
Entry	1,3-Dicarbonyl compound	Vinyl sulfide	Solvent	Product	Yield (%)
1	 **1**	 **12**	THF	 **19**	79
2	 **4**	 **12**	THF	 **20**	84
3	 **5**	 **12**	THF	 **21**	40
4	 **4**	 **14**	THF	 **22**	71
5	 **1**	 **15**	THF	 **23**	81
6	 **3**	 **15**	THF	 **24**	87
7	 **4**	 **15**	THF	 **25**	85
8	 **6**	 **15**	THF	 **26**	49
9	 **1**	 **16**	THF	 **27**	74
10	 **4**	 **17** (*cis–trans*, 60:40)	MeCN	 **28** (*cis*:*trans* = 32:68)	64
11	 **2**	 **17** (*cis–trans*, 60:40)	THF	 **28** (*cis*:*trans* = 46:54)	71

Table 3 Reaction of 4-Hydroxycoumarins **7**–**9** with Vinyl Sulfides

Entry	4-Hydroxycoumarin	Vinyl sulfide	solvent	Product	Yield (%)
1	 **7**	 **12**	THF	 **29**	42
2	 **7**	 **13**	THF	 **30**	40
3	 **8**	 **13**	THF	 **31**	41
4	 **7**	 **15**	THF	 **32**	72
5	 **7**	 **16**	THF	 **33**	46
6	 **9**	 **16**	THF	 **34**	60

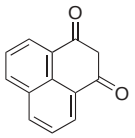
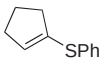
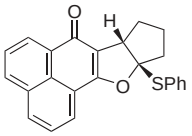
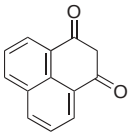
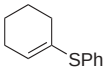
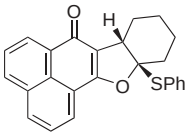
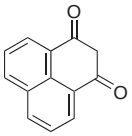
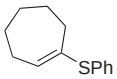
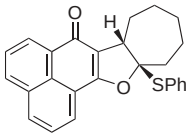
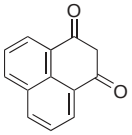
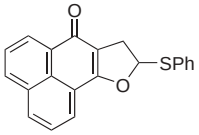
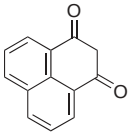
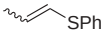
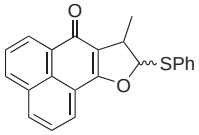
pharmacologically interesting compounds. For example, dihydrofuran **42** can be readily converted to benzofuronaphthoquinone derivative **50** which has been reported to have significant biological activities such as antipruritic, antitumor, topo II-mediate DNA cleavage.[16] Although several synthetic methods for the preparation of benzofuronaphthoquinone derivatives have been reported, their synthetic exploitation has been limited due to many reaction steps, low yield, and the difficulty in availability of the required starting materials.[17] Reaction of **42** with MCPBA in CH_2Cl_2 at room temperature for 24 hours afforded the corresponding sulfoxide, which upon refluxing for 5 hours in xylene gave furan **49** in 70% yield (Scheme 1). When **49** was treated with Pd/C at reflux for 5 hours in phenyl ether, benzofuronaphthofurandione **50** was produced in 42% yield. The structural assignment of **50** was easily made with the new aromatic peaks in the ^{1}H NMR spectrum.

As another application, a synthetic route to furanoflavone natural products starting from the obtained dihydrofuran was next investigated (Scheme 2). Furanoflavones are an abundant subclass of the flavonoid and are widely distributed in nature.[18] Members of the furanoflavones have been associated with a wide variety of biological activities such as insecticide, pesticidal, anticancer and antiulcer,[19] and are used in traditional medicines for the treatment of



Scheme 1

Table 4 Reaction of 3-Hydroxy-1*H*-phenalen-1-one (**10**) with Vinyl Sulfides

Entry	3-Hydroxy-1*H*-phenalen-1-one	Vinyl sulfide	Solvent	Product	Yield (%)
1	 **10**	 **12**	THF	 **35**	87
2	 **10**	 **13**	THF	 **36**	77
3	 **10**	 **15**	THF	 **37**	74
4	 **10**	 **16**	THF	 **38**	62
5	 **10**	 **17** (*cis–trans*, 60:40)	THF	 **39** (*cis–trans*, 34:66)	92

tumours, piles, skin diseases, wounds, ulcers, etc.[20] Very recently, new furanoflavones, millettocalyxins C **55** and pongol methyl ether **56**, were isolated from the stem bark of *Millettia erythrocalyx*.[21] Currently, the bark of this plant has been used by the local people in Thailand for treating stomach pain. However, the total synthesis of millettocalyxins C **55** and pongol methyl ether **56** has not been reported.

The conversion of dihydrofuran **27** to both of these natural products **55** and **56** was begun by *syn*-elimination with MCPBA to give compound **51** (70%). Transformation of **51** into the sodium enolate with an excess of NaH in the presence of a catalytic amount of KH was followed by treatment with dimethyl carbonate to form **52** in 90% yield. The DDQ-mediated oxidation of **52** in refluxing dioxane gives the compound **53** (85%), which was treated with the dimsyl anion in benzene to form the β-keto sulfoxide **54** (83%).[22] The β-keto sulfoxide **54** is easily converted by treatment with 2,5-dimethoxybenzaldehyde and 3-methoxybenzaldehyde in the presence of piperidine, first at 40 °C and then at 110 °C, to the corresponding furanoflavones **55** and **56** in 78% and 88% yield, respectively. The spectroscopic properties of our synthetic materials agreed well with those reported in the literature.[21]

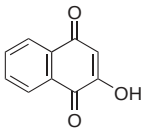
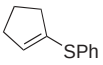
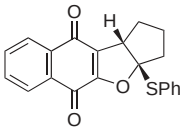
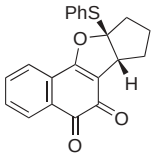
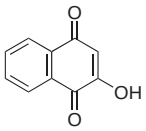
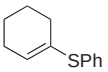
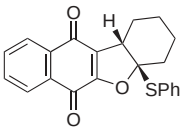
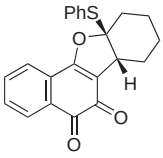
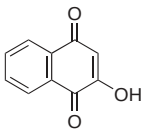
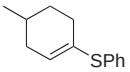
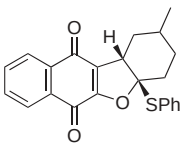
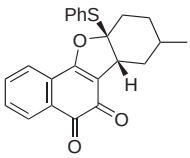
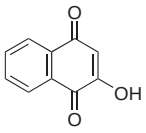
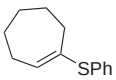
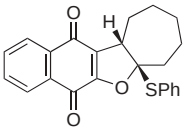
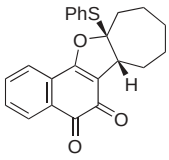
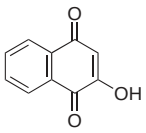
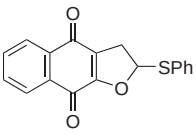
In conclusion, CAN-mediated oxidative cycloaddition of 1,3-dicarbonyls to vinyl sulfides is described. This method provides a simple and efficient synthesis of substituted dihydrofurans. As an application of this methodology, the synthesis of benzofuronaphthoquinone and the natural furanoflavones is carried out starting from obtained dihydrofurans.

All experiments were carried out under a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Mps were determined with microcover glasses on a Fisher–Johns apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Model ARX (300 MHz) spectrometer. ^{13}C NMR spectra were recorded on a Bruker Model ARX (75 MHz) spectrometer in $CDCl_3$ using δ = 77.0 as the solvent chemical shift. IR spectra were recorded on a JASCO FTIR 5300 spectrophotometer. Mass and high resolution mass spectra were obtained with a JEOL JMS-700 spectrometer at the Korea Basic Science Institute (Daegu). Elementary analyses were performed by the Korea Basic Science Institute (Daegu).

Dihydrofurans; General Procedure

To a solution of 1,3-dicarbonyl compound (1.0 mmol) and vinyl sulfide (2.0 mmol) in MeCN (20 mL) or THF (20 mmol) was added CAN (1.206 g, 2.2 mmol) and $NaHCO_3$ (420 mg, 5.0 mmol) at 0 °C

Table 5 Reaction of 2-Hydroxy-1,4-naphthoquinone (**11**) with Vinyl Sulfides

Entry	2-Hydroxy-1,4-naphthoquinone	Vinyl sulfide	Solvent	Product	Yield (%)
1	 **11**	 **12**	THF	 **40**	40	 **41**	19
2	 **11**	 **13**	THF	 **42**	45	 **43**	23
3	 **11**	 **14**	THF	 **44**	43	 **45**	19
4	 **11**	 **15**	THF	 **46**	44	 **47**	23
5	 **11**	 **16**	THF	 **48**	53		

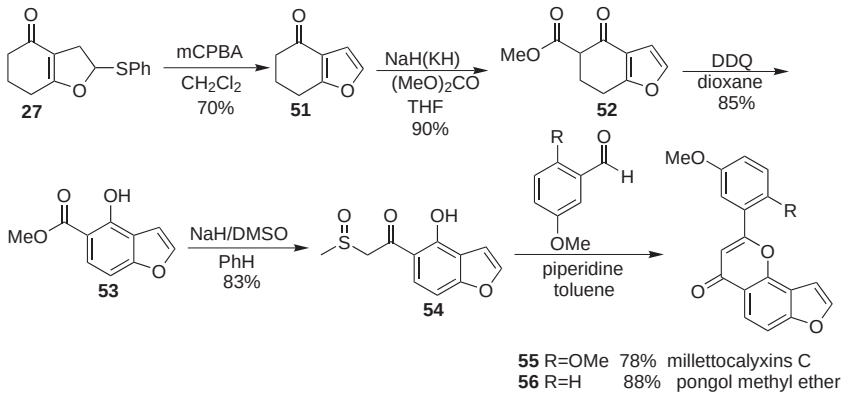
or r.t. The reaction mixture was stirred for 6 h at 0 °C in MeCN or for 6 h at r.t. in THF. The mixture was diluted with H_2O and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure to give the residue. The residue was purified by flash column chromatography on silica gel to give product.

5a-Phenylsulfanyl-3,4,5a,6,7,8,9,9a-octahydro-2*H*-dibenzofuran-1-one (18)

Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with vinyl sulfide **13** (381 mg, 2 mmol) in THF (20 mL) afforded **18**.

Yield: 258 mg (86%); solid; mp 96–97 °C.

IR (KBr): 3057, 2946, 2866, 1638, 1474, 1454, 1439, 1399, 1248, 1181, 1136, 1061, 999 cm^{-1}.



Scheme 2

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.53 (2 H, m), 7.37–7.29 (3 H, m), 3.16 (1 H, dd, *J* = 6.7, 5.9 Hz), 2.41–2.37 (2 H, m), 2.27–2.18 (2 H, m), 1.98–1.89 (4 H, m), 1.60–1.41 (6 H).

HRMS: *m*/*z* calcd for $C_{18}H_{20}O_2S$ (M^+): 300.1185; found: 300.1184.

8a-Phenylsulfanyl-1,2,3,3a,5,6,7,8a-octahydro-8-oxacyclopenta[*a*]inden-4-one (19)

Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with vinyl sulfide **12** (353 mg, 2 mmol) in THF (20 mL) afforded **19**.

Yield: 226 mg (79%); solid; mp 42–43 °C.

IR (KBr): 3057, 2946, 2868, 1638, 1476, 1439, 1399, 1364, 1258, 1213, 1181, 1138, 1055, 1003, 909 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.56 (2 H, m), 7.35–7.26 (3 H, m), 3.52 (1 H, d, *J* = 9.1 Hz), 2.41–1.48 (m, 12 H).

HRMS: *m*/*z* calcd for $C_{17}H_{18}O_2S$ (M^+): 286.1028; found: 286.1025.

6,6-Dimethyl-8a-phenylsulfanyl-1,2,3,3a,5,6,7,8a-octahydro-8-oxacyclopenta[*a*]inden-4-one (20)

Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**4**) (140 mg, 1 mmol) with vinyl sulfide **12** (353 mg, 2 mmol) in THF (20 mL) afforded **20**.

Yield: 264 mg (84%); solid; mp 73–74 °C.

IR (KBr): 3059, 2959, 2870, 1640, 1472, 1400, 1350, 1302, 1250, 1208, 1163, 1142, 1034, 912 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.56 (2 H, m), 7.36–7.22 (3 H, m), 3.56 (1 H, d, *J* = 8.3 Hz), 2.27–1.91 (6 H, m), 1.82–1.75 (2 H, m), 1.60–1.45 (2 H, m), 1.02 (3 H, s), 0.85 (3 H, s).

HRMS: *m*/*z* calcd for $C_{19}H_{22}O_2S$ (M^+): 314.1341; found: 314.1337.

2-Methyl-6a-phenylsulfanyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*b*]furan-3-carboxylic Acid Ethyl Ester (21)

Reaction of ethyl acetoactate (**5**) (130 mg, 1 mmol) with vinyl sulfide **12** (353 mg, 2 mmol) in THF (20 mL) afforded **21** (122 mg, 40%).

Liquid.

IR (neat): 2961, 1699, 1649, 1476, 1441, 1379, 1277, 1246, 1208, 1130, 1071, 1022, 972, 912, 846, 802 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.54 (2 H, m), 7.31–7.24 (3 H, m), 4.16–4.04 (2 H, m), 3.47 (1 H, d, *J* = 8.0 Hz), 2.09 (s, 3 H), 2.00–1.90 (2 H, m), 1.76–1.65 (2 H, m), 1.61–1.47 (2 H, m), 1.20 (3 H, t, *J* = 7.1 Hz).

HRMS: *m*/*z* calcd for $C_{17}H_{20}O_3S$ (M^+): 304.1134; found: 314.1136.

3,3,8-Trimethyl-5a-phenylsulfanyl-3,4,5a,6,7,8,9,9a-octahydro-2*H*-dibenzofuran-1-one (22)

Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**4**) (140 mg, 1 mmol) with vinyl sulfide **14** (409 mg, 2 mmol) in THF (20 mL) afforded **22** as an inseparable diastereommer.

Yield: 243mg (71%).

IR (KBr): 3050, 2957, 1634, 1456, 1437, 1399, 1343, 1263, 1233, 1198, 1167, 1134, 1042, 984, 957, 870, 843 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.50 (2 H, m), 7.37–7.27 (3 H, m), 3.24 (0.6 H, br d, *J* = 3.0 Hz) and 3.06 (0.4 H, dd, *J* = 5.9, 5.8 Hz), 2.31–2.23 (2 H, m), 2.18–2.15 (2 H, m), 2.10–2.01 (2 H, m), 1.00–1.91 (1 H, m), 1.86–1.82 (1 H, m), 1.69–1.46 (1 H, m), 1.41–1.34 (1 H, m), 1.15–1.10 (1 H, m), 1.07 and 1.05 (3 H, s), 1.04 and 1.01 (3 H, s), 0.89 (1.8 H, d, *J* = 6.6 Hz) and 0.87 (1.2 H, d, *J* = 7.1 Hz).

HRMS: *m*/*z* calcd for $C_{21}H_{26}O_2S$ (M^+): 342.1655; found: 342.1652.

9a-Phenylsulfanyl-1,2,3,4b,5,6,7,8,9a-decahydro-10-oxabenzo-[*a*]azulen-4-one (23)

Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in THF (20 mL) afforded **23** (255 mg, 81%).

Solid; mp 80–81 °C.

IR (KBr): 3057, 2930, 2853, 1642, 1453, 1439, 1397, 1362, 1277, 1256, 1225, 1179, 1136, 1063, 995, 984 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.51 (2 H, m), 7.42–7.29 (3 H, m), 3.21 (1 H, d, *J* = 9.2 Hz), 2.43–2.38 (2 H, m), 2.32–2.16 (2 H, m), 2.04–1.89 (4 H, m), 1.76–1.35 (8 H, m).

MS (EI): *m*/*z* = 204 (M^+ – PhSH) (100), 189 (30), 176 (63), 175 (46), 148 (43), 125 (20), 105 (17), 91 (20), 77 (14), 55 (18).

HRMS: *m*/*z* calcd for $C_{13}H_{16}O_2$ (M^+ – PhSH): 204.1150; found: 204.1152.

Anal. Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05; S, 10.20. Found: C, 72.35; H, 6. 98; S, 10.42.

2-Phenyl-9a-phenylsulfanyl-1,2,3,4b,5,6,7,8,9,9a-decahydro-10-oxabenzo[*a*]azulen-4-one (24)

Reaction of 5-phenyl-1,3-cyclohexanedione (**3**) (188 mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in THF (20 mL) afforded **24** as an inseparable diastereomer.

Yield: 349 mg (87%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.46 (2 H, m), 7.37, 7.40–7.32 (5 H, m), 7.29–7.20 (3 H, m), 3.42–3.28 (1 H, m), 3.23 (1 H, d, *J* = 9.3 Hz), 2.75–2.62 (2 H, m), 2.59–2.40 (2 H, m), 2.06–1.96 (3 H, m), 1.75–1.58 (5 H, m), 1.50–1.40 (2 H, m).

IR (KBr): 3057, 3029, 2922, 2855, 1640, 1195, 1476, 1454, 1439, 1418, 1397, 1323, 1211, 1179, 1134, 1051, 1009, 983, 966, 906, 891, 860 cm^{-1}.

MS (EI): *m*/*z* = 280 (M^+ – PhSH) (85), 256 (13), 176 (100), 148 (45), 129 (66), 110 (30), 91 (23), 71 (30), 57 (44).

HRMS: *m*/*z* calcd for $C_{19}H_{20}O_2$ (M^+ – PhSH): 280.1463; found: 280.1461.

2,2-Dimethyl-9a-phenylsulfanyl-1,2,3,4b,5,6,7,8,9a-decahydro-10-oxabenzo[*a*]azulen-4-one (25)

Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**4**) (140 mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in MeCN (20 mL) afforded **25**.

Yield: 291 mg (85%); solid; mp 102–103 °C.

IR (KBr): 2943, 1640, 1481, 1440, 1394, 1222, 1178, 1058, 1021, 900, 870, 839 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.50 (2 H, m), 7.37–7.21 (3 H, m), 3.21 (1 H, d, *J* = 9.2 Hz), 2.29 (2 H, m), 2.16 (2 H, m), 1.98–1.90 (4 H, m), 1.66–1.38 (6 H, m), 1.10 (3 H, s), 1.08 (3 H, s).

MS: *m*/*z* = 232 (M^+ – PhSH) (81), 204 (10), 176 (33), 167 (5), 153 (24), 148 (15), 110 (27), 97 (23), 81 (20), 58 (33).

HRMS: *m*/*z* calcd for $C_{15}H_{20}O_2$ (M^+ – PhSH): 232.1463; found: 232.1466.

1-(2-Methyl-8a-phenylsulfanyl-4,5,6,7,8,8a-hexahydro-3aH-cyclohepta[*b*]furan-3-yl)ethanone (26)

Reaction of 2,4-pentanedione (**6**) (100 mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in THF (20 mL) afforded **26**.

Yield: 148 mg (49%); liquid.

IR (neat): 3059, 2928, 2855, 1672, 1628, 1439, 1385, 1281, 1260, 1215, 1067, 1024, 983, 947, 924 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.48 (2 H, m), 7.35–7.27 (3 H, m), 3.13 (1 H, d, *J* = 9.5 Hz), 2.21 (3 H, s), 2.18 (3 H, s), 1.96–1.20 (10 H, m).

HRMS: *m*/*z* calcd for $C_{12}H_{16}O_2$ (M^+ – PhSH): 192.1150; found: 192.1150.

2-Phenylsulfanyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (27)
Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with phenyl vinyl sulfide (**16**) (272 mg, 2 mmol) in THF (20 mL) afforded **27**.

Yield: 182 mg (74%); liquid.

IR (neat): 2943, 1640, 1481, 1440, 1394, 1222, 1178, 1058, 1021, 900, 870, 839 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.33 (5 H, m), 6.09 (1 H, dd, *J* = 9.9, 5.9 Hz), 3.25 (1 H, dd, *J* = 15.5, 9.9 Hz), 2.83 (1 H, dd, *J* = 15.5, 5.9 Hz), 2.45 (2 H, m), 2.32 (2 H, m), 2.02 (2 H, m).

HRMS: *m*/*z* calcd for $C_{14}H_{14}O_2S$ (M^+): 246.0715; found: 246.0716.

3,6,6-Trimethyl-2-phenylsulfanyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (28)[23]
Method A
Reaction of 5-methyl-1,3-cyclohexanedione (**2**) (126 mg, 1 mmol) with phenyl 1-propenyl sulfide (**17**) (308 mg, 2 mmol) in MeCN (20 mL) afforded **28** as a 32:68 mixture of *cis*- and *trans*-isomers.

Yield: 185 mg (64%).

***cis*-Isomer**
IR (neat): 3059, 2962, 2872, 1642, 1583, 1470, 1440, 1397, 1213, 1168, 1126, 1030, 914, 864 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.53 (2 H, m), 7.34–7.28 (3 H, m), 6.07 (1 H, d, *J* = 8.8 Hz), 3.61–3.51 (1 H, m), 2.31 (2 H, q), 2.21 (2 H, s), 1.34 (3 H, d, *J* = 7.0 Hz), 1.09 (3 H, s), 1.07 (3 H, s).

***trans*-Isomer**
IR (neat): 3059, 2959, 2872, 1644, 1584, 1470, 1441, 1399, 1277, 1215, 1167, 1109, 1030, 914, 880 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.47 (2 H, m), 7.33–7.28 (3 H, m), 5.53 (1 H, d, *J* = 5.3 Hz), 3.21–3.17 (1 H, m), 2.28 (2 H, s), 2.17 (2 H,s), 1.29 (3 H, d, *J* = 6.8 Hz), 1.06 (3 H, s), 1.05 (3 H, s).

Method B
Reaction of 5-methyl-1,3-cyclohexanedione (**2**) (126 mg, 1 mmol) with vinyl sulfide **17** (308 mg, 2 mmol) in THF (20 mL) afforded **28** as a 46:54 mixture of *cis*- and *trans*-isomers.

Yield: 205 mg (71%).

9a-Phenylsulfanyl-7,8,9,9a-tetrahydro-6b*H*-5,10-dioxapentaleno[2,1-*a*]naphthalen-6-one (29)
Reaction of 4-hydroxycoumarin (**7**) (162mg, 1 mmol) with vinyl sulfide **12** (353 mg, 2 mmol) in THF (20 mL) afforded **29**.

Yield: 141 mg (42%); solid; mp 64–66 °C.

IR (KBr): 3075, 2957, 2934, 2868, 1726, 1649, 1607, 1570, 1499, 1406, 1348, 1323, 1227, 1202, 1182, 1091, 1051, 1030, 1001, 945, 906 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69–7.67 (1 H, m), 7.59–7.53 (3 H, m), 7.31–7.20 (5 H, m), 3.79 (1 H, dd, *J* = 8.2, 2.6 Hz), 2.43–2.40 (1 H, m), 2.17–2.02 (3 H, m), 1.85–1.80 (1 H, m), 1.70–1.58 (1 H, m).

HRMS: *m*/*z* calcd for $C_{20}H_{16}O_3S$ (M^+): 336.0821; found: 336.0824.

10a-Phenylsulfanyl-6b,7,8,9,10,10a-hexahydrobenzo[4,5]furo[3,2-*c*]chromen-6-one (30)
Reaction of 4-hydroxycoumarin (**7**) (162mg, 1 mmol) with vinyl sulfide **13** (381 mg, 2 mmol) in THF (20 mL) afforded **30**.

Yield: 140 mg (40%); solid; mp 125–126 °C.

IR (KBr) 3061, 2942, 2865, 1725, 1647, 1609, 1566, 1499, 1456, 1406, 1306, 1161, 1028, 943, 883, 845 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.67 (1 H, m), 7.58–7.53 (3 H, m), 7.36–7.26 (5 H, m), 3.40 (1 H, t, *J* = 6.1 Hz), 2.07–1.96 (3 H, m), 1.90–1.82 (1 H, m), 1.65–1.46 (4 H, m).

HRMS: *m*/*z* calcd for $C_{21}H_{18}O_3S$ (M^+): 350.0977; found: 350.0975.

2-Chloro-10a-phenylsulfanyl-6b,7,8,9,10,10a-hexahydrobenzo[4,5]furo[3,2-*c*]chromen-6-one (31)
Reaction of 6-chloro-4-hydroxycoumarin (**8**) (197mg, 1 mmol) with vinyl sulfide **13** (381 mg, 2 mmol) in THF (20 mL) afforded **31**.

Yield: 158 mg (41%); solid; mp 126–128 °C.

IR (KBr) 3069, 2961, 2940, 2870. 1726, 1651, 1564, 1493, 1431, 1391, 1265, 1123, 1065, 1011, 966, 939, 827 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (1 H, d, *J* = 2.5 Hz), 7.59–7.53 (2 H, m), 7.49 (1 H, dd, *J* = 8.9, 2,5 Hz), 7.37–7.26 (4 H, m), 3.41 (1 H, t, *J* = 6.1 Hz), 2.10–1.95 (3 H, m), 1.91–1.802 (1 H, m), 1.66–1.46 (4 H, m).

HRMS: *m*/*z* calcd for $C_{21}H_{17}ClO_3S$ (M^+): 384.0588; found: 384.0589.

11a-Phenylsulfanyl-7,8,9,10,11,11a-hexahydro-6b*H*-5,12-dioxanaphtho[2,1-*a*]azulen-6-one (32)
Reaction of 4-hydroxycoumarin (**7**) (162mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in THF (20 mL) afforded **32**.

Yield: 262 mg (72%); solid; mp 116–118 °C.

IR (KBr): 3057, 2932, 2855, 1707, 1645, 1607, 1570, 1499, 1474, 1439, 1404, 1327, 1275, 1235, 1196, 1165, 1094, 1028, 963, 895 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67–7.62 (1 H, m), 7.59–7.51 (3 H, m), 7.39–7.27 (5 H, m), 3.40 (1 H, dd, *J* = 9.6, 2.8 Hz), 2.19–2.06 (3 H, m), 2.03–1.60 (6 H, m), 1.48–1.38 (1 H, m).

HRMS: *m*/*z* calcd for $C_{16}H_{14}O_3$ (M^+ – PhSH): 254.0943; found: 254.0948.

Anal. Calcd for $C_{22}H_{20}O_3S$: C, 72.50; H, 5.53; S, 8.80. Found: C, 72.21; H, 5.42; S, 8.75.

2-Phenylsulfanyl-2,3-dihydrofuro[3,2-*c*]chromen-4-one (33)
Reaction of 4-hydroxycoumarin (**7**) (162mg, 1 mmol) with phenyl vinyl sulfide (**16**) (272 mg, 2 mmol) in THF (20 mL) afforded **33**.

Yield: 136 mg (46%); solid; mp 125–126 °C.

IR (KBr): 3061, 2926, 1724, 1649, 1608, 1570, 1498, 1440, 1410, 1344, 1325, 1269, 1207, 1157, 1091, 1028, 941, 895, 860 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68 (1 H, d, *J* = 7.8 Hz), 7.60–7.52 (3 H, m), 7.39–7.28 (5 H, m), 6.39 (1 H, dd, *J* = 9.8, 6.1 Hz), 3.64 (1 H, dd, *J* = 16.4, 9.8 Hz), 3.16 (1 H, dd, *J* = 16.4, 6.1 Hz).

HRMS: *m*/*z* calcd for $C_{17}H_{12}O_3S$ (M^+): 296.0508; found: 296.0505.

8-Methyl-2-phenylsulfanyl-2,3-dihydrofuro[3,2-*c*]chromen-4-one (34)
Reaction of 4-hydroxyl-6-methylcoumarin (**7**) (176mg, 1 mmol) with phenyl vinyl sulfide (**16**) (272 mg, 2 mmol) in THF (20 mL) afforded **34**.

Yield: 186 mg (60%); solid; mp 109–110 °C.

IR (KBr): 3076, 2982, 1714, 1649, 1610, 1577, 1494, 1439, 1394, 1271, 1203, 1095, 1035, 1006, 914, 858, 829. 798 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.54 (2 H, m), 7.44 (1 H, s), 7.37–7.26 (5 H, m), 6.37 (1 H, dd, *J* = 9.8, 6.3 Hz), 3.61 (1 H, d, *J* = 16.4, 9.8 Hz), 3.13 (1 H, dd, *J* = 16.4, 6.3 Hz), 2.41 (3 H, s).

HRMS: *m*/*z* calcd for $C_{18}H_{14}O_3S$ (M^+): 310.0663; found: 310.0661.

Dihydrofurophenalenone 35
Reaction of 3-hydroxy-1*H*-phenalen-1-one (**10**) (196 mg, 1 mmol) with vinyl sulfide **12** (353 mg, 2 mmol) in THF (20 mL) afforded **35**.

Yield: 322 mg (87%); solid; mp 157–159 °C.

IR (KBr): 3063, 2957, 2936, 1630, 1591, 1508, 1472, 1431, 1418, 1381, 1327, 1308, 1206, 1069, 1020, 926, 882, 833 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.52 (1 H, d, *J* = 7.3 Hz), 8.10–8.03 (3 H, m), 7.71–7.59 (4 H, m), 7.21–7.14 (3 H, m), 3.90 (1 H, dd, *J* = 8.5, 2.5 Hz), 2.41–2,36 (1 H, m), 2.22–2.02 (3 H, m), 1.81–1.79 (1 H, m), 1.67–1.56 (1 H, m).

HRMS: *m*/*z* (M^+) calcd for $C_{24}H_{18}O_2S$: 370.1028; found: 370.1027.

11a-Phenylsulfanyl-7b,8,9,10,11,11a-hexahydro-12-oxa-indeno[2,1-*a*]phenalen-7-one (36)
Reaction of 3-hydroxy-1*H*-phenalen-1-one (**10**) (196 mg, 1 mmol) with vinyl sulfide **13** (381 mg, 2 mmol) in THF (20 mL) afforded **36**.

Yield: 296 mg (77%); solid; mp 154–156 °C.

IR (KBr): 3063, 2946, 2864, 1628, 1589, 1508, 1468, 1433, 1418, 1383, 1318, 1292, 1225, 1194, 1150, 1101, 1020, 937, 887, 860, 839 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.57 (1 H, dd, *J* = 7.4, 1.1 Hz), 8.11 (1 H, dd, *J* = 7.8, 1.1 Hz), 8.06 (2 H, d, *J* = 7.8 Hz), 7.72 (1 H, dd, *J* = 7.8, 7.4 Hz), 7.63 (1 H, dd, *J* = 7.8, 7.4 Hz), 7.60–7.56 (2 H, m), 7.39–7.30 (3 H, m), 3.50 (1 H, dd, *J* = 6.7, 6.0 Hz), 2.18–2.08 (3 H, m), 1.91–1.79 (1 H, m), 1.72–1.60 (1 H, m), 1.53–1.47 (3 H, m).

HRMS: *m*/*z* calcd for $C_{25}H_{20}O_2S$ (M^+): 384.1184. found: 384.1187.

Dihydrofurophenalenone 37
Reaction of 3-hydroxy-1*H*-phenalen-1-one (**10**) (196 mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in THF (20 mL) afforded **37**.

Yield: 295 mg (74%); solid; mp 150–151 °C.

IR (KBr): 3059, 2928, 2853, 1628, 1589, 1508, 1464, 1418m 1379, 1314, 1213, 1165, 1019, 960, 931, 895, 864, 845 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.59 (1 H, d, *J* = 7.6 Hz), 8.11 (1 H, d, *J* = 7.8 Hz), 8.07 (1 H, d, *J* = 7.8 Hz), 8.02 (1 H, d, *J* = 7.4 Hz), 7.72 (1 H, dd, *J* = 7.8, 7.4 Hz), 7.63 (1 H, dd, *J* = 7.8, 7.6 Hz), 7,58–7.53 (2 H, m), 7.39–7.26 (3 H, m), 3.57 (1 H, dd, *J* = 9.4, 2.9 Hz), 2.67–2.19 (1 H, m), 2.14–2.11 (2 H, m), 1.86–1.69 (5 H, m), 1.56–1.41 (2 H, m).

HRMS: *m*/*z* calcd for $C_{20}H_{16}O_2$ (M^+ – PhSH): 288.1150; found: 288.1147.

9-Phenylsulfanyl-8,9-dihydrophenaleno[1,2-*b*]furan-7-one (38)
Reaction of 3-hydroxy-1*H*-phenalen-1-one (**10**) (196 mg, 1 mmol) with vinyl sulfide **16** (272 mg, 2 mmol) in THF (20 mL) afforded **38**.

Yield: 205 mg (62%); solid; mp 113–115 °C.

IR (KBr): 3057, 2928, 1628, 1585, 1568, 1433, 1420, 1379, 1217, 1144, 1098, 1017, 926, 876, 851 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.59 (1 H, dd, *J* = 7.3, 1.2 Hz), 8.13–8.04 (3 H, m), 7.72 (1 H, dd, *J* = 7.5, 7.4 Hz), 7.63–7.58 (3 H, m), 7.37–7.30 (3 H, m), 6.38 (1 H, dd, *J* = 9.7, 6.0 Hz), 3.67 (1 H, dd, *J* = 16.6, 9.7 Hz), 3.23 (1 H, dd, *J* = 16.6, 6.0 Hz).

HRMS: *m*/*z* calcd for $C_{21}H_{14}O_2S$ (M^+): 330.0715; found: 330.0714.

8-Methyl-9-phenylsulfanyl-8,9-dihydrophenaleno[1,2-*b*]furan-7-one (39)
Reaction of 3-hydroxy-1*H*-phenalen-1-one (**10**) (196 mg, 1 mmol) with vinyl sulfide **17** (308 mg, 2 mmol) in THF (20 mL) afforded **39** as a 34:66 mixture of *cis*- and *trans*-isomers.

Yield: 317 mg (92%).

^1H NMR (300 MHz, $CDCl_3$): δ = 8.63–8.58 (1 H, m), 8.13–8.05 (3 H, m), 7.75–7.67 (1 H, m), 7.64–7.59 (3 H, m), 7.42–7.28 (3 H, m), 6.37 (0.34 H, d, *J* = 8.7 Hz, *cis*) and 5.85 (0.66 H, d, *J* = 5.2 Hz, *trans*), 4.06–3.96 (0.34 H, *cis*) and 3.66–3.58 (0.66 H, *trans*), 1.58 (0.34 H, d, *J* = 7.0 Hz, *cis*) and 1.52 (0.66 H, d, *J* = 6.9 Hz).

IR (KBr): 3059, 2968, 2930, 2870, 1630, 1588, 1435, 1418, 1379, 1281, 1211, 1192, 1150, 1090, 1022, 966, 910, 870, 845 cm^{-1}.

HRMS: *m*/*z* calcd for $C_{22}H_{16}O_2S$ (M^+): 344.0871; found: 344.0870.

10a-Phenylsulfanyl-2,3,3a,10a-tetrahydro-1*H*-10-oxapentaleno[1,2-*b*]naphthalene-4,9-dione (40) and 9a-Phenylsulfanyl-7,8,9,9a-tetrahydro-6b*H*-10-oxapentaleno[2,1-*a*]naphthalene-5,6-dione (41)
Reaction of 2-hydroxy-1,4-naphthoquinone (**11**) (174 mg, 1 mmol) with vinyl sulfide **12** (353 mg, 2 mmol) in THF (20 mL) afforded **40** (139 mg, 40%) and **41** (66 mg, 19%) as a mixture.

Compound 40
Mp 93–94 °C.

IR (KBr): 3054, 2957, 2866, 1690, 1647, 1628, 1595, 1572, 1391, 1364, 1252, 1204, 1071, 966, 936 880 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.03–8.01 (1 H, m), 7.99–7.94 (1 H, m), 7.69–7.59 (4 H, m), 7.26–7.22 (3 H, m), 3.82 (1 H, d, *J* = 9.0, 2.6 Hz), 2.44–2.35 (1 H, m), 2.21–2.02 (2 H, m), 2.01–1.80 (2 H, m), 1.74–1.59 (1 H, m).

HRMS: *m*/*z* calcd for $C_{21}H_{16}O_3S$ (M^+): 348.0820; found: 348.0818.

Compound 41
Mp 108–110 °C.

IR (KBr): 3057, 2963, 1701, 1653, 1620, 1574, 1439, 1402, 1346, 1221, 1082, 912, 885 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (1 H, d, *J* = 7.9 Hz), 7.68–7.65 (2 H, m), 7.59–7.54 (3 H, m), 7.28–7.17 (3 H, m), 3.77 (1 H, dd, *J* = 8.4, 1.8 Hz), 2.15–2.05 (2 H, m), 1.94–1.80 (2 H, m), 1.70–1.55 (2 H, m).

HRMS: *m*/*z* calcd for $C_{21}H_{16}O_3S$ (M^+): 348.0820; found: 348.0821.

4a-Phenylsulfanyl-1,2,3,4,4a,11b-hexahydrobenzo[*b*]naphtho[2,3-*d*]furan-6,11-dione (42) and 10a-Phenylsulfanyl-6b,7,8,9,10,10a-hexahydrobenzo[*b*]naphtho[2,1-*d*]furan-5,6-dione (43)
Reaction of 2-hydroxy-1,4-naphthoquinone (**11**) (174 mg, 1 mmol) with vinyl sulfide **13** (381 mg, 2 mmol) in THF (20 mL) afforded **42** (163 mg, 45%) and **43** (83 mg, 23%) as a mixture.

Compound 42
Mp 94–95 °C.

IR (KBr): 3063, 2944, 2865, 1680, 1651, 1624, 1595, 1476, 1439, 1387, 1360, 1248, 1202, 1161, 951, 901, 849 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07–7.97 (2 H, m), 7.72–7.62 (2 H, m), 7.60–7.54 (2 H, m), 7.30–7.27 (3 H, m), 3.42 (1 H, dd, *J* = 6.4, 6.3 Hz), 2.18–1.97 (2 H, m), 1.69–1.47 (6 H, m).

HRMS: *m*/*z* calcd for $C_{22}H_{18}O_3S$ (M^+): 362.0977; found: 362.0979.

Compound 43
Mp 118–120 °C.

IR (KBr): 3071, 2942, 1698, 1653, 1620, 1572, 1400, 1350, 1254, 1215, 1163, 1055, 1022, 986, 862 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (1 H, d, *J* = 8.2 Hz), 7.68–7.66 (2 H, m), 7.57–7.52 (3 H, m), 7.35–7.15 (3 H, m), 3.41 (1 H, dd, *J* = 6.1, 6.0 Hz), 2.09–1.96 (2 H, m), 1.82–1.44 (6 H, m).

HRMS: *m*/*z* calcd for $C_{22}H_{18}O_3S$ (M^+): 362.0977; found: 362.0980.

2-Methyl-4a-phenylsulfanyl-1,2,3,4,4a,11b-hexahydrobenzo[*b*]naphtho[2,3-*d*]furan-6,11-dione(44) and 8-Methyl-10a-phenylsulfanyl-6b,7,8,9,10,10a-hexahydrobenzo[*b*]naphtho[2,1-*d*]furan-5,6-dione (45)
Reaction of 2-hydroxy-1,4-naphthoquinone (**11**) (174 mg, 1 mmol) with vinyl sulfide **14** (409 mg, 2 mmol) in THF (20 mL) afforded **44** (162mg, 43%) and **45** (72 mg, 19%) as a mixture.

Compound 44
Mp 91–93 °C.

IR (KBr): 3065, 2951, 1682, 1651, 1624, 1595, 1574, 1541, 1385, 1358, 1267, 1204, 1005, 945, 839 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07–7.98 (2 H, m), 7.71–7.64 (2 H, m), 7.60–7.54 (2 H, m), 7.32–7.26 (3 H, m), 3.54 (1 H, dd, *J* = 6.0, 3.0 Hz), 2.21–2.02 (2 H, m), 1.68–1.53 (3 H, m), 1.26–1.16 (2 H, m), 0.94 (3 H, d, *J* = 6.0 Hz).

HRMS: *m*/*z* calcd for $C_{23}H_{20}O_3S$ (M^+): 376.1133; found: 376.1132.

Compound 45
Mp 151–153 °C.

IR (KBr): 2926, 1701, 1651, 1620, 1589, 1572, 1454, 1399, 1221, 1163, 1067, 841 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8. 04 (1 H, d, *J* = 7.6 Hz), 7.67–7.64 (2 H, m), 7.59–7.50 (3 H, m), 7.35–7.26 (3 H, m), 3.49 (1 H, dd, *J* = 6.0, 3.0 Hz), 2.30–2.21 (1 H, m), 2.15–2.07 (1 H, m), 2.03–1.90 (1 H, m), 1.74–1.60 (2 H, m), 1.27–1.86 (2 H, m), 0.93 (3 H, d, *J* = 6.0 Hz).

HRMS: *m*/*z* calcd for $C_{23}H_{20}O_3S$ (M^+): 376.1133; found: 376.1135.

10a-Phenylsulfanyl-6,7,8,9,10,10a-hexahydro-5b*H*-11-oxanaphtho[2,3-*a*]azulene-5,12-dione (46) and 11a-Phenylsulfanyl-7,8,9,10,11,11a-hexahydro-6b*H*-12-oxanaphtho[2,1-*a*]azulene-5,6-dione (47)
Reaction of 2-hydroxy-1,4-naphthoquinone (**11**) (174 mg, 1 mmol) with vinyl sulfide **15** (409 mg, 2 mmol) in THF (20 mL) afforded **46** (166 mg, 44%) and **47** (87 mg, 23%) as a mixture.

Compound 46
Mp 135–137 °C.

IR (KBr): 2932, 1682, 1647, 1624, 1593, 1389, 1366, 1273, 1221, 1206, 1169, 970, 951, 804 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09–8.02 (2 H, m), 7.73–7.63 (2 H, m), 7.58–7.54 (2 H, m), 7.32–7.28 (3 H, m), 3.50 (1 H, dd, *J* = 9.5, 2.9 Hz), 2.15–2.03 (3 H, m), 1.79–1.40 (7 H, m).

HRMS: *m*/*z* calcd for $C_{17}H_{14}O_3$ (M^+ – PhSH): 266.0943; found: 266.0945.

Anal. Calcd for $C_{23}H_{20}O_3S$: C, 73.38; H, 5.35; S, 8.52. Found: C, 73.11; H, 5.30; S, 8.48.

Compound 47
Mp 143–145 °C.

IR (KBr): 3067, 2938, 2855, 1698, 1651, 1620, 1589, 1574, 1474, 1443, 1399, 1319, 1223, 1084, 960, 876 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (1 H, d, *J* = 7.5 Hz), 7.70–7.50 (5 H, m), 7.39–7.26 (3 H, m), 3.48 (1 H, dd, *J* = 9.5, 2.9 Hz), 2.13–2.07 (3 H, m), 1.88–1.59 (7 H, m).

HRMS: *m*/*z* calcd for $C_{17}H_{14}O_3$ (M^+ – PhSH): 266.0943; found: 266.0938.

Anal. Calcd for $C_{23}H_{20}O_3S$: C, 73.38; H, 5.35; S, 8.52. Found: C, 73.14; H, 5.26; S, 8.56.

2-Phenylsulfanyl-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (48)
Reaction of 2-hydroxy-1,4-naphthoquinone (**11**) (174 mg, 1 mmol) with vinyl sulfide **16** (272 mg, 2 mmol) in THF (20 mL) afforded **48**.

Yield: 163 mg (53%); mp 151–152 °C.

IR (KBr): 3059, 2955, 1678, 1645, 1593, 1485, 1391, 1289, 1173, 1092, 999, 897, 789 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15–8.02 (2 H, m), 7.73–7.64 (2 H, m), 7.59–7.57 (2 H, m), 7.34–7.31 (3 H, m), 6.26 (1 H, dd, *J* = 10.0, 6.1 Hz), 3.63 (1 H, dd, *J* = 18.2, 10.0 Hz), 3.18 (1 H, dd, *J* = 18.2, 6.1 Hz).

HRMS: *m*/*z* calcd for $C_{18}H_{12}O_3S$ (M^+): 308.0508; found: 308.0508.

1,2,3,4-Tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan-6,11-dione (49)
To a solution of **42** (181 mg, 0.5 mmol) in CH_2Cl_2 (10 mL) was added MCPBA (247 mg, 70%, 1.0 mmol) at r.t. and the reaction mixture was stirred under nitrogen for 24 h. Sat. aq $NaHCO_3$ was added, and the aq layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure to give the residue. The residue was refluxed for 5 h in xylene (10 mL) and then cooled to r.t. Evaporation of solvent and purification by flash column chromatography (sillica gel) gave **49**.

Yield: 88 mg (70%); solid; mp 162–164 °C.

IR (KBr): 3067, 2940, 2865, 1667, 1593, 1537, 1468, 1429, 1379, 1329, 1279, 1236, 1208, 1148, 990, 953, 930. 823 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19–8.10 (2 H, m), 7.73–7.67 (2 H, m), 2.82–2.73 (4 H, m), 1.95–1.55 (4 H, m).

HRMS: *m*/*z* calcd for $C_{16}H_{12}O_3$ (M^+): 252.0787; found: 252.0785.

Benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione (50)
To a stirred solution of **49** (100 mg, 0.4 mmol) in diphenyl ether (5 mL) was added Pd/C (100 mg, 10 wt.%). The mixture was refluxed for 5 h and cooled to r.t. The suspension was filtered off and the inorganic material was washed with EtOAc (3 × 25 mL). The solvent was evaporated under reduced pressure to give the residue. The residue was purified by flash column chromatography (silica gel) to give **50**.

Yield: 41 mg (42%); mp 247 °C.

IR (KBr): 3079, 2963, 1667, 1593, 1578, 1566, 1487, 1445, 1372, 1325, 1182, 1040, 1011, 990, 914, 874, 802 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (1 H, d, *J* = 7.2 Hz), 8.27–8.20 (2 H, m), 7.82–7.76 (2 H, m), 7.70 (1 H, d, *J* = 8.3 Hz), 7.58 (1 H, dd, *J* = 8.3, 7.2 Hz), 7.49 (1 H, dd, *J* = 8.2, 7.9 Hz).

HRMS: *m*/*z* calcd for $C_{16}H_8O_3$ (M^+): 248.0474; found: 248.0476.

6,7-Dihydro-5*H*-benzofuran-4-one (51)[24]

To a solution of **27** (2.10 g, 8.52 mmol) in CH_2Cl_2 (50 mL) was added MCPBA (1.54 g, 70%, 10.4 mmol) at 0 °C. The reaction mixture was stirred for 24 h at r.t., and then poured into sat. aq Na_2CO_3. The mixture was extracted with CH_2Cl_2 (3 × 50 mL), washed with brine, and dried ($MgSO_4$). Evapotation of solvent gave an oil which was purified by chromatography (silica gel) to give the **51**.

Yield: 812 mg (70%); liquid.

IR (neat): 3131, 2948, 1677, 1595, 1516, 1447, 1414, 1294, 1242, 1184, 1119, 1026 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32 (1 H, d, *J* = 2.0 Hz), 6.67 (1 H, d, *J* = 2.0 Hz), 2.89 (2 H, m), 2.50 (2 H, m), 2.18 (2 H, m).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.9, 166.7, 142.2, 120.6, 105.9, 37.2, 22.8, 22.2.

MS (EI) 136 (M^+), 121, 108, 94, 80, 77, 63, 55, 52.

4-Oxo-4,5,6,7-tetrahydrobenzofuran-5-carboxylic Acid Methyl Ester (52)

To a stirred suspension of NaH (1.175 g, 29.4 mmol, 60%) and KH (50 mg, 35 wt% dispersion in oil) in anhyd THF (50 mL) under N_2 was added **52** (800 mg, 5.9 mmol) in anhyd THF (3 mL) at 0 °C. The mixture was stirred for 30 min and dimethyl carbonate (1.593 g, 17.7 mmol) in THF (2 mL) was added slowly over 10 min. The ice bath was removed and the reaction mixture was heated at reflux for 2 h. After cooling to r.t., H_2O (10 mL) and sat. aq NH_4Cl solution (40 mL) were added carefully dropwise and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel; hexane–EtOAc, 3:1) to give **52**.

Yield: 1.027 g (90%).

IR (neat): 3144, 3113, 2955, 1733, 1675, 1582, 1454, 1433, 1276, 1208, 1164, 1122, 1025, 983, 903, 861 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.34 (1 H, d, *J* = 2.0 Hz), 6.69 (1 H, d, *J* = 2.0 Hz), 3.76 (3 H, s), 3.52 (1 H, t, *J* = 4.8 Hz), 3.05–2.91 (2 H, m), 2.56–2.38 (2 H, m).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.5, 170.1, 166.5, 140.0, 120.2, 106.6, 53.0, 52.3, 25.6, 21.7.

HRMS: *m*/*z* calcd for $C_{10}H_{10}O_4$ (M^+): 194.0579. Found: 194.0575.

4-Hydroxybenzofuran-5-carboxylic Acid Methyl Ester (53)

A mixture of **52** (0.90 g, 4.63 mmol) and DDQ (1.261 g, 5.56 mmol) in dioxane (30 mL) was heated under reflux for 3 h. The resulting mixture was cooled in an ice bath and solids were removed by filtration through Celite. The filtrate was evaporated under reduced pressure and purified by flash column chromatography (silica gel; hexane–EtOAc, 5:1) to give **53**.

Yield: 0.756 g (85%); solid; mp 105 °C.

IR (KBr): 3500, 3071, 2950, 1677, 1629, 1471, 1446, 1358, 1288, 1234, 1195, 1169, 1134, 1052 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.78 (1 H, d, *J* = 8.9 Hz), 7.57 (1 H, d, *J* = 2.1 Hz), 7.03 (1 H, d, *J* = 8.9 Hz), 6.98 (1 H, d, *J* = 2.1 Hz), 3.97 (3 H, s).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.2, 159.5, 157.4, 144.3, 125.9, 117.1, 104.9, 104.7, 103.8, 52.2.

HRMS: *m*/*z* calcd for $C_{10}H_8O_4$ (M^+): 192.0422; found: 192.0426.

1-(4-Hydroxybenzofuran-5-yl)-2-methanesulfinylethanone (54)

A mixture of anhyd DMSO (2.0 mL) and NaH (0.76 g, 19 mmol, 60%) in anhyd benzene (30 mL) was heated at reflux for 2 h under N_2. The mixture was cooled to 35 °C and treated dropwise with **53** (0.73 g, 3.80 mmol) in anhyd benzene (4 mL). The reaction mixture was then stirred for 1 h and then quenched with a sat. aq NH_4Cl solution (30 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel; EtOAc) to give **54**.

Yield: 0.751 g (83%); solid; mp 113 °C.

IR (KBr): 3435, 3115, 2993, 2905, 1632, 1614, 1474, 1435, 1335, 1298, 1214, 1135, 1092, 1045, 1027 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.65 (1 H, d, *J* = 9.0 Hz), 7.60 (1 H, d, *J* = 2.2 Hz), 7.12 (1 H, d, *J* = 9.0 Hz), 7.00 (1 H, d, *J* = 2.2 Hz), 4.40 (2 H, q), 2.79 (3 H, s).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.2, 160.5, 159.7, 145.0, 127.3, 117.7, 114.2, 105.1, 104.9, 62.0, 39.5.

HRMS: *m*/*z* calcd for $C_{11}H_{10}O_4S$ (M^+): 238.0301; found: 238.0305.

Millettocalyxins C (55)[21]

2,5-Dimethoxybenzaldehyde (0.157 g, 0.94 mmol) in anhyd toluene (3 mL) was slowly added to a warm solution (40 °C) of **54** (0.150 g, 0.63 mmol) in anhyd toluene (20 mL) containing a catalytic amount of piperidine (4 drops) and the resulting mixture was allowed to reflux for 3 h. After distillation of the solvent, the residue was purified by flash column chromatogaraphy (silica gel; hexane–EtOAc, 6:1) to give **55**.

Yield: 0.158 g (78%); solid; mp 167–168 °C.

IR (KBr): 3102, 2998, 2938, 2836, 1628, 1589, 1574, 1505, 1466, 1410, 1362, 1263, 1238, 1186, 1146, 1074, 1053, 852, 839, 814 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.15 (1 H, d, *J* = 8.8 Hz), 7.73 (1 H, d, *J* = 2.1 Hz), 7.54 (1 H, d, *J* = 8.8 Hz), 7.50 (1 H, d, *J* = 2.9 Hz), 7.21 (1 H, s), 7.15 (1 H, d, J = 2.1 Hz), 7.02 (1 H, dd, *J* = 8.8, 2.9 Hz), 6.99 (1 H, d, *J* = 8.8 Hz), 3.90 (3 H, s), 3.84 (3 H, s).

Pongol Methyl Ether (56)[21]

3-Methoxybenzaldehyde (0.129 g, 0.94 mmol) in anhyd toluene (3 mL) was slowly added to a warm solution (40 °C) of **54** (0.150 g, 0.63 mmol) in anhyd toluene (20 mL) containing a catalytic amount of piperidine (4 drops) and the resulting mixture was allowed to reflux for 3 h. After distillation of the solvent, the residue was purified by flash column chromatogaraphy (silica gel; hexane–EtOAc, 6:1) to give **56**.

Yield: 0.162 g (88%); solid; mp 156–157 °C.

IR (KBr): 3055, 2988, 2949, 2843, 1651, 1607, 1491, 1451, 1433, 1402, 1358, 1296, 1273, 1254, 1215, 1165, 1140, 1067, 1043, 1030 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.16 (1 H, d, *J* = 8.8 Hz), 7.76 (1 H, d, *J* = 2.2 Hz), 7.57 (1 H, d, *J* = 8.8 Hz), 7.54 (1 H, d, *J* = 7.8 Hz), 7.48 (1 H, d, *J* = 3.0 Hz), 7.46 (1 H, dd, *J* = 7.8, 7.8 Hz), 7.20 (1 H, d, *J* = 2.2 Hz), 7.11 (1 H, dd, *J* = 7.8, 3.0 Hz), 6.86 (1 H, s), 3.90 (3 H, s).

Acknowledgment

This work was supported by the Korea Research Foundation Grant (KRF-99-042-F00167). Dr. Ronald Tepper's help with this work is greatly appreciated.

References

(1) (a) Melikyan, G. G. *Synthesis* **1993**, 833. (b) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.
(2) Nair, V.; Mathew, J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 187.

(3) (a) Baciocchi, E.; Ruzziconi, R. *Synth. Commun.* **1988**, *18*, 1841. (b) Baciocchi, E.; Civatarese, G.; Ruzziconi, R. *Tetrahedron Lett.* **1987**, *28*, 5357.
(4) Baciocchi, E.; Casu, A.; Ruzziconi, R. *Tetrahedron Lett.* **1989**, *30*, 3707.
(5) Roy, S. C.; Mandel, P. K. *Tetrahedron* **1996**, *52*, 12495.
(6) Lee, Y. R.; Kim, B. S.; Kim, D. H. *Tetrahedron* **2000**, *56*, 8845.
(7) Lee, Y. R.; Lee, G. J.; Kang, K. Y. *Bull. Korean Chem. Soc.* **2002**, *23*, 1477.
(8) Labiad, B.; Villemin, D. *Synthesis* **1989**, 143.
(9) Roy, S. C.; Mandal, P. K. *Tetrahedron* **1996**, *52*, 2193.
(10) (a) Darbarwar, M.; Sundaramurthy, V. *Synthesis* **1982**, 337. (b) Steinmeyer, A.; Bohlmann, F. *Tetrahedron Lett.* **1986**, *27*, 5359. (c) Chenevert, R.; Page, J.; Voyer, N. *Synth. Commun.* **1984**, *14*, 737. (d) Bohlmann, F.; Wolfrum, C. *Liebigs Ann. Chem.* **1989**, 295. (e) Majumdar, K. C.; Choudhury, P. K.; Nethaji, M. *Tetrahedron Lett.* **1994**, *35*, 5927.
(11) (a) Pirrung, M. C.; Blume, F. *J. Org. Chem.* **1999**, *64*, 3642. (b) Senboku, H.; Takashima, M.; Suzuki, M.; Kobayashi, K.; Suginome, H. *Tetrahedron* **1996**, *52*, 6126. (c) Suginome, H.; Kobayashi, K.; Itoh, M.; Seko, S. *J. Org. Chem.* **1990**, *55*, 4933.
(12) (a) Feuer, G. In *Progress in Medicinal Chemistry*; Ellis, G. P.; West, G. B., Eds.; North-Holland Publishing: New York, **1974**. (b) Deana, A. A. *J. Med. Chem.* **1983**, *26*, 580. (c) Wenkert, E.; Buckwalter, B. L. *J. Am. Chem. Soc.* **1972**, *94*, 4367. (d) Miski, M.; Jakupovic, J. *Phytochemistry* **1990**, *29*, 1995. (e) Schuster, N.; Christiansen, C.; Jakupovic, J.; Mungai, M. *Phytochemistry* **1993**, *34*, 1179. (f) Bittner, M.; Jakupovic, J.; Grenz, M.; Silva, M. *Phytochemistry* **1988**, *27*, 3263. (g) Rustalyan, A.; Nazarians, L.; Bohlmann, F. *Phytochemistry* **1980**, *19*, 1254. (h) Zdero, C.; Bohlmann, F.; King, R. M.; Robinson, H. *Phytochemistry* **1986**, *25*, 509.
(13) (a) Narasimhachari, N.; Gopalkrishnam, K. S.; Haskins, R. H.; Vining, L. C. *Can. J. Microbiol.* **1963**, *9*, 134. (b) Luis, J. G.; Esheverri, F.; Quiñones, W.; Brito, I.; Lópes, M.; Torres, F.; Cardona, G.; Aguiar, Z.; Pelaez, C.; Rojas, M. *J. Org. Chem.* **1993**, *58*, 4306. (c) Luis, J. G.; Lahlou, E. I. H.; Andres, L. S.; Echeverri, F.; Fletcher, W. Q. *Tetrahedron* **1997**, *53*, 8249.
(14) Kobayashi, K.; Uneda, T.; Tanaka, K.; Mori, M.; Tanaka, H.; Morikawa, O.; Konishi, H. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1691.
(15) (a) Wagner, H.; Kreher, B.; Lotter, H. *Helv. Chim. Acta* **1989**, *72*, 659. (b) Abbott, B. J.; Hartwell, J. L.; Leiter, J.; Perdue, R. E.; Schepartz, S. A. *Cancer Res. (Suppl.)* **1967**, *27*, 190.
(16) (a) Cheng, C. C. *Structural Aspects of Antineoplastic Agents - A New Approach* In *Progress of Medicinal Chemistry*, Vol. 25; Ellis, G. P.; West, G. B., Eds.; Elsevier Science Publishers, B. V. (Biomedical Division): Amsterdam, **1988**, 35–83. (b) Cheng, C. C.; Dong, Q.; Liu, D.-F.; Luo, Y.-I.; Liu, L. F.; Chen, A. Y.; Yu, C.; Savaraj, N.; Chou, T.-C. *J. Med. Chem.* **1993**, *36*, 4108.
(17) (a) Martínez, E.; Estévez, J. C.; Estévez, R. J.; Castedo, L. *Tetrahedron Lett.* **2000**, *41*, 2365. (b) Martínez, E.; Martínez, L.; Mónica, T.; Estévez, J. C.; Estévez, R. J.; Castedo, L. *Tetrahedron* **2000**, *56*, 6023. (c) Martínez, E.; Martínez, L.; Estévez, J. C.; Estévez, R. J.; Castedo, L. *Tetrahedron Lett.* **1998**, *39*, 2175. (d) Yoshida, K.; Adachi, T.; Oga, N.; Kubo, Y. *Chem. Lett.* **1990**, 2049. (e) Yoshida, K.; Yamanaka, Y.; Ueno, Y. *Chem. Lett.* **1994**, 2051.
(18) (a) Harborne, J. B.; Baxter, H. In *The Handbook of Natural Flavonoids*, Vols. 1and 2; Wiley: Chichester, **1999**. (b) Wagner, H.; Farkas, L. In *The Flavonoids*; Harborne, J. B.; Mabry, T. J.; Mabry, H., Eds.; Academic Press: New York, **1975**, 127. (c) Gripenberg, J. In *The Chemistry of Flavonoids Compounds*; Geissman, T. A., Ed.; MacMillan: New York, **1962**, 409.
(19) (a) Welton, A. F.; Tobias, L. D.; Fiedler-Nagy, C.; Anderson, W.; Hope, W.; Meyers, K.; Coffey, J. W. In *Plant Flavnoids in Biology and Medicine*; Cody, V.; Middleton, E. Jr.; Harborne, J. B.; Alan, R., Eds.; Liss Inc.: New York, **1986**, 231. (b) Hagiwara, M.; Inoue, S.; Tanaka, T.; Nunoki, K.; Ito, M.; Hidaka, H. *Biochem. Pharmacol.* **1988**, *37*, 2987. (c) Chopra, R. N.; Nayyer, S. L.; Chopra, I. C. In *Glossary of Indian Medicinal Plants*; C. S. I. R.: New Delhi, **1956**, 241. (d) Saxena, B. N.; Dubey, D. N.; Nair, A. L. *Def. Sci. J.* **1974**, *24*, 43.
(20) Parmar, B. S.; Sahrawat, K. K.; Mukerjee, S. K. *J. Sci. India Res.* **1976**, *35*, 608.
(21) Sritularak, B.; Likhitwitayawuid, K.; Conrad, J.; Vogler, B.; Reeb, S.; Klaiber, I.; Kraus, W. *J. Nat. Prod.* **2002**, *65*, 589.
(22) von Strandtmann, M.; Klutchko, S.; Cohen, M. P.; Shavel, J. *J. Heterocycl. Chem.* **1972**, *9*, 171.
(23) Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *J. Chem. Soc., Chem. Commun.* **1978**, 362.
(24) Lee, Y. R.; Kim, N. S.; Kim, B. S. *Tetrahedron Lett.* **1997**, *38*, 5671.