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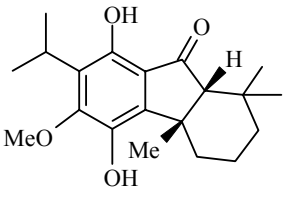
DIELS-ALDER REACTION WITH CYCLIC SULFONES. 9.* SYNTHESIS OF 10-OXO-1H-TETRAHYDROFLUORENO[2,1-*b*]THIOPHENE DIOXIDES*[2]

E. E. Shults[1], G. N. Andreev[2], M. M. Shakirov[1], I. Yu. Bagryanskaya[1], and G. A. Tolstikov[1]

The treatment of 5-aryl-4',6'-dioxo-2,3,3a,4,5,6-hexahydrospiro-[benzothiophene-4,5'-1,3-dioxane] 1,1-dioxides with boron trifluoride etherate in dichloroethane leads to the formation of products of intramolecular acylation, namely, the corresponding 10-oxo-1H-5,5a,10a,10b-tetrahydrofluoreno-[2,1-b]thiophene dioxides. In all cases, 5-aryl-4-carboxyhexahydrobenzo[b]thiophene 1,1-dioxides were also isolated. The product ratio depends on the structure of the aromatic substituent at C(5) of the spiro- adducts. The structure of 4-carboxy-5-(2-methoxyphenyl)-7-methyl -2,3,3a,4,5,6-hexahydro-benzo[b]thiophene 1,1-dioxide was confirmed by X-ray diffraction structural analysis.

Keywords: benzo[*b*]thiophene dioxides, fluoreno[2,1-*b*]thiophene dioxides, intramolecular Friedel-Crafts acylation, Diels-Alder reaction.

Plant-derived tricyclic diterpenoids, containing the unusual 4a-methyltetrahydrofluorene or hexahydrofluorene unit [taiwaniaquinol B (**1**), taiwaniaquinol D (**2**), and standishinal (**3**)], are rare plant metabolites. These compounds characteristically display inhibitory activity relative to aromatases [2, 3] and, thus, these metabolites and their analogs hold interest as leader compounds for the development of new antitumor agents [2-5]. Schemes have been proposed for the synthesis of taiwaniaquinoids [6-9].



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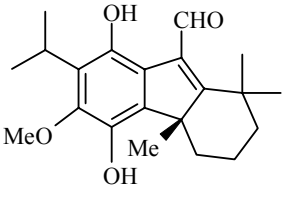

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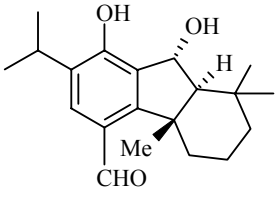

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* For Communication 9 see [1].

*[2] Dedicated to Academician of the Russian Academy of Sciences B. A. Trofimov on his 70th jubilee.

[1]N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk 630090, Russia; e-mail: schultz@nioch.nsc.ru. [2]M. K. Ammosov Yakutsk State University, Yakutsk 677000, Russia; e-mail: chemvoodoo@mail.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1503-1512, October, 2008. Original article submitted June 11, 2008, submitted after revision July 14, 2008.

In the present work, we describe an approach to the synthesis of sulfur analogs of these compounds, namely, 10-oxo-1H-5,5a,10a,10b-tetrahydrofluoreno[2,1-*b*]thiophene dioxides **4a-d** from the corresponding 5-aryl-4',6'-dioxo-2,3,3a,4,5,6-hexahydrospiro-[benzothiophene-4,5'-1,3-dioxane] 1,1-dioxides **5a-d** [10]. We established that brief heating of a solution of spiro-compound **5a-d** in dichloroethane or dioxane in the presence of boron trifluoride etherate leads to products of intramolecular acylation **4a-d** in 12-82% yield. In addition, the corresponding 5-aryl-4-carboxy-7-methyl-2,3,3a,4,5,6-hexahydrobenzo[*b*]thiophene 1,1-dioxides **6a-d** were also isolated in 8-55% yield (Table 1).

The data in Table 1 show that the composition of the reaction products depends on the substituent at C(5) of the spiro-adducts. The greatest yield of 10-oxotetrahydrofluoreno[2,1-*b*]thiophene dioxides **4** is found using spiro-adducts containing a 3-methoxy or 3-hydroxy group in the aromatic substituent. The presence of a methoxy group at C(2) or C(4) in the aromatic substituent leads to a reduced yield of the product of intramolecular acylation and increase in the yield of 5-aryl-4-carboxy-7-methylhexahydrobenzo[*b*]thiophene dioxides **6**. These findings are in accord with the results of the acylation of benzyl derivatives of Meldrum's acid, catalyzed by triflates [11], and 5-alkylidene derivatives of Meldrum's acid in the presence of boron trifluoride etherate [12]. Variation of the reaction conditions such as the solvent, reaction temperature, and amount of $BF_3 \cdot Et_2O$ has only a slight effect on the product composition. Some increase in the yield of 10-oxotetrahydrofluoreno[2,1-*b*]thiophene dioxide **4c** is observed following the gradual addition of Lewis acid (Table 1, example 6).

Tetrahydrofluoreno[2,1-*b*] **4b** may also be obtained without isolation of the spiro-adduct by treatment of the reaction mixture obtained in the cycloaddition of 5-isopropenyl-2,3-dihydrothiophene 1,1-dioxide (**7**) to 5-(2,3-dimethoxybenzylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**8b**) with boron trifluoride etherate (Table 1). 4-Carboxy -5-(2-methoxyphenyl) -7-methylhexahydrobenzo[*b*]thiophene 1,1-dioxide **6a** was isolated as the major product upon analogous treatment of the reaction product obtained in the Diels-Alder reaction of diene **7** with 5-(2-methoxybenzylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (**8a**).

TABLE 1. Conditions and Yields of the Acylation of 5-Arylhexahydro-spiro-(benzothiophenedioxido-1,3-dioxane-4,6-diones)

Example	Starting compounds	Reaction conditions	Reaction product	Yield, %
1	**5a**	0.10 mmol $BF_3 \cdot Et_2O$, $(CH_2Cl)_2$, 80°C, 30 min	**4a** **6a**	12 55
2	**5b**	0.10 mmol $BF_3 \cdot Et_2O$, $(CH_2Cl)_2$, 80°C, 30 min	**4b** **6b**	82 8
3	**5c**	0.10 mmol $BF_3 \cdot Et_2O$, $(CH_2Cl)_2$, 80°C, 30 min	**4c** **6c**	52 22
4	**5c**	0.20 mmol $BF_3 \cdot Et_2O$, $(CH_2Cl)_2$, 80°C, 20 min	**4c** **6c**	32 12
5	**5c**	0.15 mmol $BF_3 \cdot Et_2O$, dioxane, 80°C, 30 min	**4c** **6c**	50 20
6	**5c**	0.05 mol $BF_3 \cdot Et_2O$, (CH_2Cl_2), 60°C, 30 min, then an additional 0.05 mol %, 80°C, 20 min	**4c** **6c**	58 20
7	**5d**	0.10 mol $BF_3 \cdot Et_2O$, $(CH_2Cl)_2$, 80°C, 30 min	**4d** **6d**	18 52
8	**7** + **8a**	Heating a solution of **7** and **8a** (2.25 mmol each) in dioxane at reflux, 25 h, then treatment with 0.23 mmol $BF_3 \cdot Et_2O$, 100°C, 30 min	**4a** **6a**	8 51
9	**7** + **8b**	Heating a solution of **7** and **8b** (2.25 mmol each) in dioxane, 25 h, then treatment as in example 8	**4b** **6b**	58 5

All the compounds were isolated by column chromatography and subsequent crystallization. Products **4a-d** and **6a-d** were obtained as chromatographically pure compounds, whose structure was established unequivocally using the spectral and elemental analysis data.

The IR spectra of the derivatives of oxotetrahydrofluorenothiophene dioxides and hexahydro-benzothiophene dioxides have sulfone stretching bands at ν 1100-1120 and 1295-1330 cm^{-1}. The IR spectra of fluorenones **4a-d** characteristically display stretching bands of the conjugated carbonyl group at ν 1676-1684 cm^{-1}, while benzo-thiophene dioxides **6a-d** characteristically display stretching bands of the carboxylic groups at ν 1710-1720 and 3420-3430 cm^{-1}. The ^{1}H NMR spectra of 10-oxotetrahydro-fluoreno[2,1-*b*]thiophene dioxides 4**a-d** have characteristics, which permit us to identify these products as the (5a*S*,10a*S*,10b*R*)-stereoisomers. Analysis of the vicinal coupling constants for H-5a and H-10a indicates their *cis* arrangement (J = 5.0-6.3 Hz). The *trans* arrangement of H-10a and H-10b was shown using the axial-axial coupling constant between these protons (J = 10.6-11.2 Hz). The mutual orientation of H-5, H-10a, and H-10b in **4a-d** was confirmed by the NOE data for **4c**: H-10b has a NOE effect on the upfield H-5 proton, while H-10a has a cross peak with the downfield H-5 proton. A significant increase in the difference between the chemical shifts of H-5 protons and an unusually upfield shift for one of these protons, for example, δ 1.92 and 2.98 ppm for **4c**, are characteristic for the ^{1}H NMR spectra of fused fluorenones **4a-d**. The peak for H-10a in the spectra of 10-oxo-1H-tetrahydro-fluoreno[2,1-*b*]thiophene dioxides **4a-d** is shifted considerably downfield relative to H-4 in benzothiophene dioxides **6a-d**, which is attributed to the effect of the carbonyl substituent in the α-position of the cyclic system in **4a-d**. The *trans* arrangement of H-3a and H-4 in the substituted hexahydro-benzo[*b*]thiophene dioxides follows from the axial-axial coupling constant between these protons (J = 11.2-11.6 Hz).

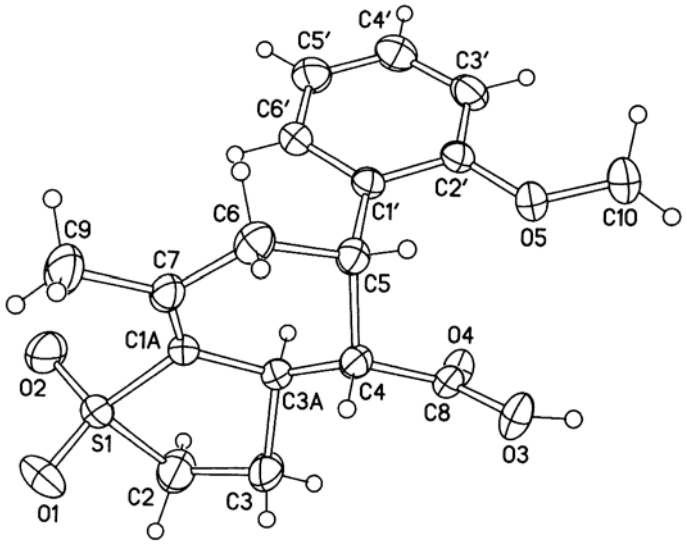
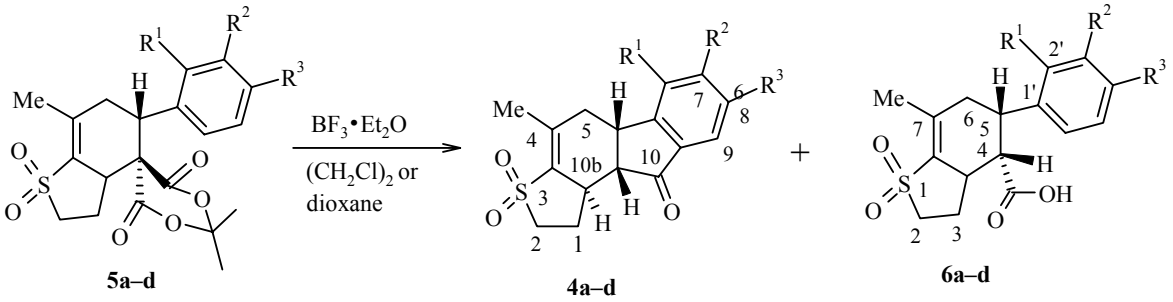


Fig. 1. Three-dimensional structure of **6a** from X-ray diffraction structural analysis.

The structure of 4-carboxy-5-(2-methoxyphenyl)-7-methyl-2,3,3a,4,5,6-hexahydrobenzo[*b*]thiophene 1,1-dioxide **6a** was confirmed by X-ray diffraction structural analysis (Fig. 1). The analysis of the structure and conformation of the rings as well as the intermolecular interactions was carried out using the PLATON program [13]. The bond lengths in this molecule are close to mean values [14] and coincide within ±3σ with the values for 4-carbamoyl-4-carboxy-7-methyl-2,3,3a,4,5,6-hexahydrobenzo[*b*]thiophene dioxide [10] and (+)-3-benzyl-oxy-5(4H)oxo-2,3,3a,7a-tetrahydrobenzo[*b*]thiophene dioxide [15] described in our previous work. The five-membered ring has envelope conformation with extrusion of C(3) by 0.623(5) Å from the plane of the

Scheme 1



5a–d **4a–d** **6a–d**

4–6 a R^1 = OMe, R^2 = R^3 = H, **b** R^1 = R^2 = OMe, R^3 = H, **c** R^1 = H, R^2 = OH, R^3 = OMe, **d** R^1 = R^2 = R^3 = OMe

other four atoms (with mean-square deviation of 0.026 Å). The cyclohexene fragment has slightly deformed *half-chair* conformation: C(4) extrudes from the plane, in which the other five atoms are located by 0.701(3) Å (the mean-square deviation of C(5), C(6), C(7), C(1A), and C(3A) from the plane is 0.049 Å). The carboxylic group is twisted toward the abovementioned plane at an angle of 56.1(2)°, while the phenyl ring is twisted toward this plane at an angle of 87.77(7)°.

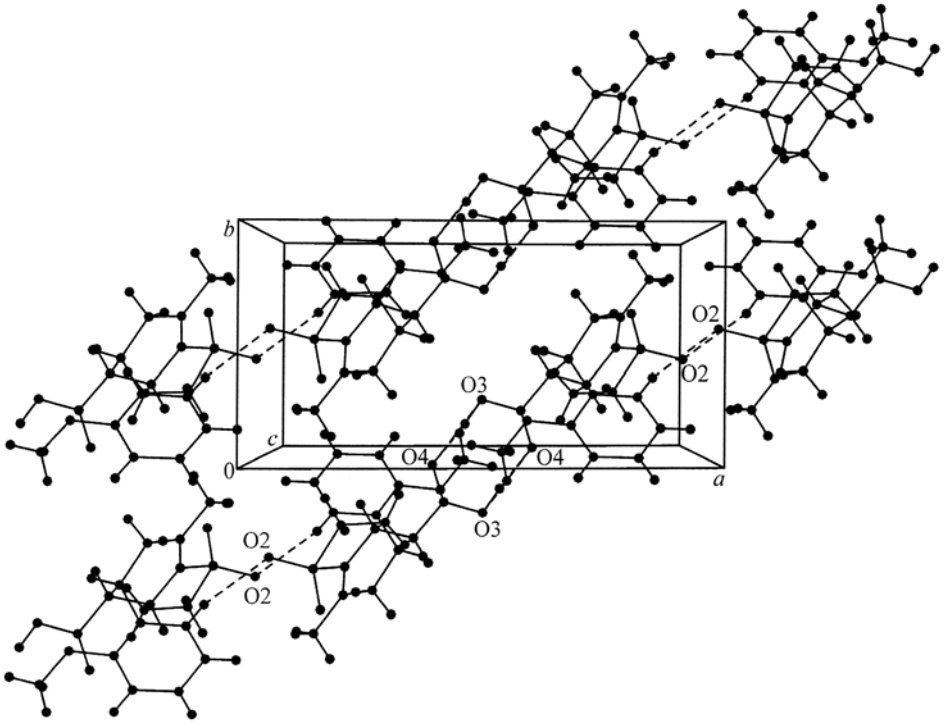
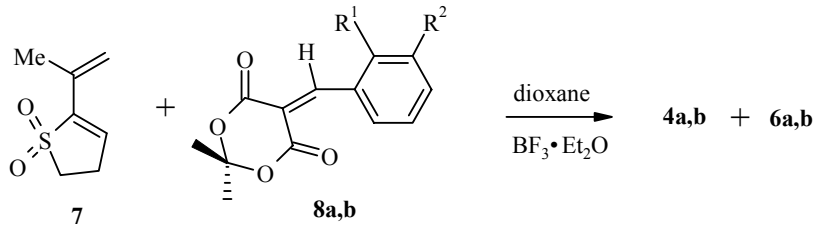


Fig. 2. Molecular packing in the crystal of **6a** along the *c*-axis.

The molecules of **6a** in the crystal forms dimers due to hydrogen bonding (C=O···H–O [16]) typical for structures with a carboxylic group (O(3)H(1)···O(4): O(3)-H(1), 0.94(3) Å; H(1)···O(4), 1.67(3) Å; O(3)···O(4), 2.612(2) Å, angle 177(3)°). The dimers, in turn, are linked in infinite chains to form a one-dimensional supramolecular pattern in the crystal by means of a weaker C–H···O hydrogen bond (C(6')–H(6'A)···O(2): C(6')–H(6'A), 0.93 Å; H(6'A)···O(2), 2.56 Å; C(6')···O(2), 3.272(3) Å, angle 134°) (Fig. 2).



8 a R^1 = OMe, R^2 = H, **b** R^1 = R^2 = OMe

Thus, a one-step method is proposed for the synthesis of pharmacologically attractive 4-methyl-10H-oxo-5,5a,10a,10b-tetrahydro-1H-fluoreno[2,1-*b*]thiophene dioxides from β-aryl-substituted spiro-fused derivatives of Meldrum's acid. The yield of the intramolecular acylation product was found to depend on the substituents in the aromatic fragment.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra of solutions of the compounds were obtained on Bruker AV-300 (300 and 75 MHz), AM-400 (400 and 101 MHz), and Bruker DRX-500 spectrometers (500 and 126 MHz). The signals were assigned in the NMR spectra using various types of proton-proton and carbon-proton shift correlation spectroscopy (COSY, COLOC) as well as Overhauser effect ^{1}H NMR 2D-spectroscopy NOESY for **4a-d**. A high-resolution Finnigan MAT-8200 mass spectrometer with 70 eV ionizing radiation was used to determine the molecular masses and elemental composition. The injector temperature was 270-300°C. The IR spectra were taken on a VECTOR-22 spectrometer for KBr pellets. The UV spectra were taken on an HP 8453 UV-vis spectrometer for solutions in ethanol (c 10^{-4} mol/liter). The X-ray diffraction structural analysis measurements for compound **6a** were taken on a Bruker P4 diffractometer with MoKα radiation, graphite monochromator, and 2θ/θ-scanning in the range $2\theta \leq 52°$.

The reaction course and purity of the products obtained were monitored by thin-layer chromatography on Silufol UV-254 plates with development in an iodine chamber. The products were separated by column chromatography on silica gel using chloroform–ethanol as the eluent.

The syntheses and characteristics of 5-aryl-4',6'-dioxo-2,3,3a,4,5,6-hexahydrospiro-[benzothiophene-4,5'-1,3-dioxane] 1,1-dioxides **5a-d** and 5-arylidene-2,2-dimethyl-1,3-dioxane-1,3-diones **8a,b** were described in our previous work [10]. A sample of 5-isopropenyl-2,3-dihydrothiophene 1,1-dioxide (**7**) was obtained according to Argyle et al. [17]. The sample of $BF_3 \cdot Et_2O$ used was freshly distilled over calcium hydride.

(5a*S*,10a*S*,10b*R*)-6-Methoxy-4-methyl-10-oxo-5,5a,10a,10b-tetrahydro-1H-fluoreno[2,1-*b*]thiophene dioxide (4a) and (3a*R*,4*S*,5*S*)-4-carboxy-5-(2-methoxyphenyl)-7-methyl-2,3,3a,4,5,6-hexahydrobenzo-[*b*]thiophene 1,1-dioxide (6a). A. A solution of boron trifluoride etherate (0.13 ml, 0.1 mmol) in dichloroethane (2 ml) was added with stirring in an argon stream to a solution of spiro-adduct **5a** (0.42 g, 1 mmol) in dichloroethane (5 ml). The solution was heated at 80°C for 30 min and left overnight. The reaction mixture was diluted by adding 20 ml methylene chloride, washed with saturated aqueous NaCl, dried over $MgSO_4$, and evaporated. The residue was subjected to chromatography on silica gel to give consecutively 0.19 g (55%) compound **6a** and 0.039 g (12%) compound **4a**.

B. A solution of diene **7** (0.36 g, 2.25 mmol) and 5-(2-methoxybenzylidene)-2,2-dimethyl-1,3-dioxane-dione (**8a**) (0.59 g, 2.25 mmol) in dioxane (10 ml) was heated at reflux for 25 h with monitoring by thin-layer chromatography until compound **8a** had disappeared. After cooling in an argon stream, a solution of 0.028 ml $BF_3 \cdot Et_2O$ in 2 ml dioxane was added. The solution was heated at 100°C over 30 min and then cooled. Methylene chloride (20 ml) was added. The solution was washed with saturated aqueous NaCl,

dried over $MgSO_4$, and evaporated. The residue was subjected to chromatography on silica gel to give consecutively 0.38 g (51%) compound **6a** and 0.056 g (8%) compound **4a**.

Dioxide 4a, mp 131-134°C (ether). IR spectrum, cm^{-1}: 732, 798, 834, 918, 1011, 1089, 1120, 1295, 1324, 1506, 1597, 1694. ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.79 (1H, ddd, *J* = 15.0, *J* = 11.1, *J* = 1.2, H-5); 2.33 (1H, m, H-1); 2.30 (3H, d, *J* = 2.2, CH_3); 2.68 (1H, m, H-10b); 2.81 (1H, dd, *J* = 10.6, *J* = 6.3, H-10a); 2.82-3.09 (3H, m, H-1, H-2, H-5); 3.24 (1H, m, H-2); 3.62 (1H, ddd, *J* = 11.1, *J* = 7.0, *J* = 6.3, H-5a); 3.78 (3H, s, OCH_3); 7.09 (1H, d, *J* = 7.7, H-7); 7.27 (1H, d, *J* = 7.7, H-9). 7.45 (1H, t, *J* = 7.7, H-8). ^{13}C NMR spectrum, δ, ppm: 18.83 (q, CH_3); 26.68 (t, C-1); 36.02 (t, C-5); 36.86 (d, C-10b); 37.76 (d, C-5a); 51.52 (t, C-2); 53.45 (d, C-10a); 55.12 (q, OCH_3 at C-6); 117.22 (d, C-7); 120.31 (d, C-9); 126.42 (d, C-8); 135.61 (s, C-3a); 137.81 (s, C-9a); 139.32 (s, C-5b); 143.12 (s, C-4); 156.12 (s, C-6); 204.48 (s, C-10). Found, %: C 64.32; H 5.3; S 10.36. $C_{17}H_{18}O_4S$. Calculated, %: C 64.13; H 5.70; S 10.07.

Dioxide 6a, mp 238-241°C (ethyl acetate). IR spectrum, cm^{-1}: 728, 760, 961, 1027, 1089, 1120, 1296, 1334, 1586, 1602, 1615, 1712, 3420. UV spectrum, λ_{max}, nm (log ε): 204 (3.72), 275 (2.49), 282 (2.46). ^1H NMR spectrum (400 MHz, CD_3OD), δ, ppm (*J*, Hz): 1.67 (1H, m, H-3); 2.21 (3H, d, *J* = 2.4, CH_3); 2.36 (1H, m, H-3); 2.44 (1H, dd, *J* = 19.4, *J* = 2.4, H-6); 2.56 (1H, dd, *J* = 11.0, *J* = 3.7, H-4); 2.67 (1H, m, H-3a); 2.86 (1H, ddd, *J* = 19.4, *J* = 7.0, *J* = 4.6, H-6); 2.96 (1H, m, H-2); 3.17 (1H, m, H-2); 3.75 (3H, s, OCH_3); 4.14 (1H, dd, *J* = 7.0, *J* = 3.7, H-5); 6.84 (1H, dd, *J* = 8.3, *J* = 1.2, H-3'); 6.87 (1H, t, *J* = 7.6, H-5'); 6.96 (1H, dd, *J* = 7.6, *J* = 1.8, H-6'); 7.21 (1H, dt, *J* = 8.3, *J* = 1.8, H-4'). ^{13}C NMR spectrum, δ, ppm: 18.43 (q, CH_3); 25.94 (t, C-3); 33.38 (d, C-5); 35.69 (d, C-3a); 39.75 (t, C-6); 50.01 (d, C-4); 51.50 (t, C-2); 55.01 (q, OCH_3); 110.64 (d, C-3'); 121.09 (d, C-5'); 127.98 (d, C-6'); 128.90 (d, C-4'); 129.56 (s, C-1'); 135.45 (s, C-7a); 142.73 (s, C-7); 157.86 (s, C-2'); 174.87 (s, CO_2H). Mass spectrum, *m/z* (I_{rel}, %): 336 $[M]^+$ (16), 304 (41), 290 (100), 275 (36), 260 (20), 226 (19), 211 (21), 197 (27), 183 (53), 121 (28), 108 (77), 94 (32), 77 (55). Found: *m/z* 336.10554 $[M]^+$. $C_{17}H_{20}O_5S$. Calculated: M 336.10314.

(5a*S*,10a*S*,10b*R*)-6,7-Dimethoxy-4-methyl-10-oxo-5,5a,10a,10b-tetrahydro-1H-fluoreno[2,1-*b*]thiophene dioxide (4b) and (3a*R*,4*S*,5*S*)-4-carboxy-5-(2,3-dimethoxyphenyl)-7-methyl-2,3,3a,4,5,6-hexahydrobenzo[*b*]thiophene 1,1-dioxide (6b) were obtained by analogy to the procedures for **4a** and **6a** using method A (adduct **5b**) or method B (reaction of diene **7** (0.32 g) and 4-arylidene-2,2-dimethyl-1,3-dioxanedione **8b** (0.63 g) in dioxane (10 ml)). The yields are given in Table 1.

Dioxide 4b, mp 198-200°C (ethyl acetate). IR spectrum, cm^{-1}: 733, 777, 834, 868, 1010, 1080, 1100, 1133, 1284, 1322, 1498, 1596, 1678. UV spectrum, λ_{max}, nm (log ε): 207 (3.76), 285 (3.41). ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.87 (1H, ddd, *J* = 14.8, *J* = 11.4, *J* = 1.2, H-5); 2.38 (1H, m, H-1); 2.31 (3H, d, *J* = 2.2, CH_3); 2.64 (1H, m, H-10b); 2.81 (1H, dd, *J* = 11.0, *J* = 6.2, H-10a); 2.86-3.06 (3H, m, H-1, H-2, H-5); 3.22 (1H, m, H-2); 3.60 (1H, ddd, *J* = 11.4, *J* = 7.0, *J* = 6.2, H-5a); 3.96 (3H, s, OCH_3); 4.03 (3H, s, OCH_3); 7.04 (1H, d, *J* = 8.2, H-8); 7.56 (1H, d, *J* = 8.2, H-9). ^{13}C NMR spectrum, δ, ppm: 18.90 (q, CH_3); 27.11 (t, C-1); 36.62 (t, C-5); 36.73 (d, C-10b); 37.54 (d, C-5a); 51.46 (t, C-2); 53.52 (d, C-10a); 56.20 (q, OCH_3 at C-7); 60.60 (q, OCH_3 at C-6); 113.32 (d, C-8); 120.63 (d, C-9); 129.78 (C-9a); 135.09 (s, C-3a); 143.38 (s, C-4); 145.12 (s, C-5); 148.66 (s, C-6); 158.39 (s, C-7); 204.25 (s, C-10). Mass spectrum, *m/z* (I_{rel}, %): 348 $[M]^+$ (37), 320 (1), 269 (11), 255 (11), 241 (12), 225 (13), 190 (19), 167 (31), 138 (18), 91 (54), 43 (100). Found: *m/z* 348.10416 $[M]^+$. $C_{18}H_{20}O_5S$. Calculated: M 348.10314.

Dioxide 6b, mp 243-245°C (ethyl acetate). IR spectrum, cm^{-1}: 730, 752, 870, 985, 1049, 1092, 1108, 1128, 1291, 1586, 1600, 1626, 1710, 1726, 3195, 3430. UV spectrum, λ_{max}, nm (log ε): 204 (3.82), 280 (2.57). ^1H NMR spectrum (500 MHz, CD_3OD), δ, ppm (*J*, Hz): 1.57 (1H, m, H-3); 2.19 (3H, d, *J* = 2.4, CH_3); 2.38-2.42 (2H, m, H-3, H-6); 2.56 (1H, dd, *J* = 11.2, *J* = 4.0, H-4); 2.67 (1H, m, H-3a); 2.86 (1H, ddd, *J* = 19.2, *J* = 7.2, *J* = 4.6, H-6); 2.98 (1H, m, H-2); 3.20 (1H, m, H-2); 3.79 (3H, s, OCH_3); 3.86 (3H, s, OCH_3); 4.08 (1H, dd, *J* = 7.2, *J* = 4.0, H-5); 6.64 (1H, dd, *J* = 8.0, *J* = 1.8, H-4'); 6.88 (1H, dd, *J* = 8.0, *J* = 1.8, H-6'); 6.98 (1H, t, *J* = 8.0, H-5'). ^{13}C NMR spectrum, δ, ppm: 17.66 (q, CH_3); 24.34 (t, C-3); 32.62 (d, C-5); 34.91 (d, C-3a); 39.26 (t, C-6); 49.81 (d, C-4); 50.38 (t, C-2); 54.91 (q, OCH_3 at C-3'); 59.87 (q, OCH_3 at C-2'); 111.52 (d, C-4'); 119.23(d, C-6');

123.37 (d, C-5'); 133.87 (s, C-1'); 134.86 (s, C-7a); 140.98 (s, C-7); 146.72 (s, C-2'); 152.16 (s, C-3'); 174.65 (s, CO_2H). Mass spectrum, *m/z* (I_{rel}, %): 366 $[M]^+$ (55), 334 (30), 305 (45), 256 (21), 241 (20), 227 (21), 176 (25), 164 (81), 151 (22), 138 (100), 124 (30), 115 (24), 77 (54). Found: *m/z* 366.11420 $[M]^+$. $C_{18}H_{22}O_6S$. Calculated: M 366.11370.

(5a*S*,10a*S*,10b*R*)-7-Hydroxy-8-methoxy-4-methyl-10-oxo-5,5a,10a,10b-tetrahydro-1H-fluoreno-[2,1-*b*]thiophene dioxide (4c) and (3a*R*,4*S*,5*S*)-4-carboxy-5-(3-hydroxy-4-methoxyphenyl)-7-methyl-2,3,3a,4,5,6-hexahydrobenzo[*b*]thiophene 1,1-dioxide (6c). A. A solution of boron trifluoride etherate (0.026 ml, 0.2 mmol) in dichloroethane (2 ml) was added with stirring in an argon stream to a solution of spiro-adduct **5c** (0.44 g, 1 mmol) in dichloroethane (5 ml). The solution was heated at 80°C for 20 min. The reaction mixture was diluted by adding 20 ml methylene chloride, washed with saturated aqueous NaCl, dried over $MgSO_4$, and evaporated. The residue was subjected to chromatography on silica gel to give consecutively 0.042 g (12%) compound **6c** and 0.11 g (32%) compound **4c**.

Spiro-adduct **5c** (0.44 g, 1 mmol) was treated with boron trifluoride etherate (0.07 ml) in dichloroethane (5 ml). The mixture was heated for 30 min at 60°C and then the same amount of reagent was again added at 60°C to give compound **4c** in 58% yield and compound **6c** in 20% yield.

C. Heating adduct **5c** (0.65 g, 1.5 mmol) with $BF_3 \cdot Et_2O$ (0.03 ml) in dioxane (8 ml) for 30 min at 80°C gave 0.11 g (20%) compound **6c** and 0.26 g (50%) compound **4c**.

Dioxide 4c, mp 228-230°C (ethyl acetate). IR spectrum, cm^{-1}: 725, 773, 832, 857, 875, 1010, 1026, 1051, 1098, 1121, 1288, 1320, 1343, 1499, 1583, 1612, 1676, 3377. ^1H NMR spectrum (500 MHz, CD_3OD), δ, ppm (*J*, Hz): 1.92 (1H, ddd, *J* = 14.9, *J* = 11.1, *J* = 1.4, H-5); 2.26 (1H, m, H-1); 2.30 (3H, d, *J* = 2.2, CH_3); 2.67 (1H, m, H-10b); 2.75 (1H, dd, *J* = 10.2, *J* = 5.4, H-10a); 2.88 (1H, m, H-1); 2.98 (1H, m, H-5); 3.22 (1H, m, H-2); 3.32 (1H, m, H-2); 3.50 (1H, ddd, *J* = 11.1, *J* = 7.5, *J* = 5.4, H-5a); 3.95 (3H, s, OCH_3); 7.04 (1H, s, H-6); 7.22 (1H, s, H-9). ^{13}C NMR spectrum, δ, ppm: 18.96 (q, CH_3); 27.95 (t, C-1); 38.71 (t, C-5); 39.09 (d, C-10b); 39.48 (d, C-5a); 52.49 (t, C-2); 54.74 (d, C-10a); 56.71 (q, OCH_3 at C-8); 105.68 (d, C-6); 112.09 (d, C-9); 128.71 (s, C-9a); 136.67 (s, C-3a); 144.62 (s, C-4); 150.27 (s, C-5b); 154.31 (s, C-8); 156.16 (s, C-7); 206.33 (s, C-10). Mass spectrum, *m/z* (I_{rel}, %): 334 $[M]^+$ (8), 320 (7), 270 (7), 177 (18), 161 (13), 108 (37), 93 (100), 91 (23), 77 (35), 44 (39), 28 (50). Found: *m/z* 334.08490 $[M]^+$. $C_{17}H_{18}O_5S$. Calculated: M 334.08411.

Dioxide 6c, mp 265-268°C (ethyl acetate). IR spectrum, cm^{-1}: 730, 755, 872, 985, 1019, 1068, 1096, 1112, 1130, 1295, 1318, 1589, 1600, 1625, 1642, 1715, 3176, 3377, 3420. ^1H NMR spectrum (500 MHz, CD_3OD), δ, ppm (*J*, Hz): 1.62 (1H, m, H-3); 2.21 (3H, d, *J* = 2.5, CH_3); 2.36-2.42 (2H, m, H-3, H-6); 2.60 (1H, dd, *J* = 11.6, *J* = 4.2, H-4); 2.70 (1H, m, H-3a); 2.82 (1H, ddd, *J* = 19.0, *J* = 7.5, *J* = 4.8, H-6); 2.92 (1H, m, H-2); 3.25 (1H, m, H-2); 3.92 (3H, s, OCH_3); 4.12 (1H, dd, *J* = 7.5, *J* = 4.2, H-5); 6.87 (1H, d, *J* = 8.4, H-5'); 7.06 (1H, d, *J* = 1.5, H-2'); 7.12 (1H, dd, *J* = 8.4, *J* = 1.5, H-6'). ^{13}C NMR spectrum, δ, ppm: 17.68 (q, CH_3); 24.87 (t, C-3); 33.12 (d, C-5); 34.98 (d, C-3a); 39.61 (t, C-6); 50.09 (d, C-4); 51.18 (t, C-2); 55.16 (q, OCH_3 at C-4'); 111.93 (d, C-5'); 116.38 (d, C-2'); 122.86 (d, C-6'); 132.25 (s, C-1'); 134.86 (s, C-7a); 140.98 (s, C-7); 147.08 (s, C-3'); 149.01 (s, C-4'); 174.65 (s, CO_2H). Found, %: C 58.02; H 5.78; S 9.61. $C_{17}H_{20}O_6S$. Calculated, %: C 57.94; H 5.72; S 9.10.

(5a*S*,10a*S*,10bR)-6,7,8-Trimethoxy-4-methyl-10-oxo-5a,10a,10b-tetrahydro-1H-fluoreno[2,1-*b*]thiophene 1,1-dioxide (4d) and (3a*R*,4*S*,5*S*)-4-carboxy-7-methyl-5-(2,3,4-trimethoxyphenyl)-2,3,3a,4,5,6-hexahydrobenzo[*b*]thiophene 1,1-dioxide (6d) were obtained analogously using method A. The products yields are given in Table 1.

Dioxide 4d, mp 206-209°C (ethyl acetate). IR spectrum, cm^{-1}: 735, 778, 830, 870, 1010, 1026, 1067, 1096, 1130, 1292, 1333, 1500, 1600, 1620, 1715. ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.87 (1H, ddd, *J* = 14.7, *J* = 11.2, *J* = 1.6, H-5); 2.18 (1H, m, H-1); 2.31 (3H, d, *J* = 2.2, CH_3); 2.60 (1H, m, H-10b); 2.80 (1H, dd, *J* = 10.2, *J* = 5.0, H-10a); 2.82-3.08 (3H, m, H-1, H-2, H-5); 3.20 (1H, m, H-2); 3.68 (1H, ddd, *J* = 11.4, *J* = 7.0, *J* = 5.0, H-5a); 3.77 (3H, s, OCH_3); 3.85 (3H, s, OCH_3); 3.93 (3H, s, OCH_3); 6.41 (1H, s, H-9). ^{13}C NMR spectrum, δ, ppm: 18.32 (q, CH_3); 28.15 (t, C-1); 32.84 (t, C-5); 33.79 (d, C-10b); 34.57 (d, C-5a);

50.77 (t, C-2); 53.42 (d, C-10a); 55.81 (q, OCH_3 at C-8); 60.79 (q, OCH_3 at C-6); 60.94 (q, OCH_3 at C-7); 103.40 (d, C-9); 123.12 (s, C-5b); 132.01 (s, C-9a); 134.90 (s, C-3a); 141.94 (s, C-4); 150.80 (s, C-7); 151.37 (s, C-8); 152.88 (s, C-6); 204.86 (s, C-10). Found, %: C 60.08; H 5.48; S 8.10. $C_{19}H_{22}O_6S$. Calculated, %: C 60.30; H 5.86; S 8.47.

Dioxide 6d, mp 272-274°C (ethyl acetate). IR spectrum, cm^{-1}: 699, 720, 749, 779, 873, 927, 1022, 1066, 1096, 1128, 1289, 1300, 1495, 1601, 1703, 1734, 3208, 3443. ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.63 (1H, m, H-3); 2.21 (3H, d, *J* = 2.1, CH_3); 2.32-2.40 (2H, m, H-3, H-6); 2.53 (1H, dd, *J* = 11.2, *J* = 4.2, H-4); 2.67 (1H, m, H-3a); 2.86 (1H, ddd, *J* = 19.0, *J* = 7.2, *J* = 3.8, H-6); 2.92 (1H, m, H-2); 3.20 (1H, m, H-2); 3.77 (3H, s, OCH_3); 3.79 (3H, s, OCH_3); 3.85 (3H, s, OCH_3); 3.95 (1H, dd, *J* = 7.2, *J* = 4.2, H-5); 6.60 (1H, d, *J* = 8.0, H-5'); 6.68 (1H, d, *J* = 8.0, H-6'). ^{13}C NMR spectrum, δ, ppm: 18.13 (q, CH_3); 24.98 (t, C-3); 33.18 (d, C-5); 34.37 (d, C-3a); 39.33 (t, C-6); 49.17 (d, C-4); 50.64 (t, C-2); 55.67 (q, OCH_3 at C-4'); 60.29 (q, OCH_3 at C-2'); 60.34 (q, OCH_3 at C-3'); 106.99 (d, C-5'); 121.72 (d, C-6'); 125.50 (s, C-1'); 134.58 (s, C-7a); 141.33 (s, C-7 and C-3'); 151.48 (s, C-4'); 152.85 (s, C-2'); 177.43 (s, CO_2H). Found, %: C 52.71; H 6.38; S 8.22. $C_{19}H_{24}O_7S$. Calculated, %: C 57.56; H 6.10; S 8.09.

X-ray diffraction structural analysis of compound 6a. A 0.50×0.46×0.12-mm crystal of compound **6a** was grown from ethyl acetate. The unit cell parameters of the monoclinic crystal are as follows: *a* = 13.954(1), *b* = 7.0022(8), *c* = 17.688(2) Å, β = 94.241(8)°, *V* = 1723.5(3)$Å^3$, space group $P2_1/n$, *Z* = 4, $C_{17}H_{20}O_5S$, d_{calc} = 1.296 g/cm^3, μ = 0.209 mm^{-1}. The intensities of 3391 independent reflections were measured. An absorption correction was introduced using the Psi curve method (transmission 0.84-0.94). The structure was solved by the direct method using the SHELX-97 program [18]. The structural parameters were refined by the method of least squares in the full-matrix anisotropic approximation (isotropic for the hydrogen atom in the OH group) using the SHELX-97 program [18]. The parameters of the other hydrogen atoms were calculated in each refinement using the coordinates of the corresponding carbon atoms (horse rider model). The final structure refinement was carried out over all F_2 to give wR_2 = 0.1313, *S* = 1.02; 212 parameters were refined (*R* = 0.0463 for 2670 $F > 4\sigma$).

The structure **6a** was registered with the Cambridge Center for Crystallographic Data (deposit No. CCDC690623). The X-ray diffraction structural analysis data are available at http://www.ccdc.cam.ac.uk/data_request/cif deposit.

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