The Synthesis of Substituted [1]Benzothieno[2,3-*c*]quinolines and their *N*-methyl Quaternary Salts

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Four substituted [1]benzothieno[2,3-*c*]quinolines **14a-14d** were prepared by photocyclization of the appropriate carboxamides **8a-8d** to the corresponding [1]benzothieno[2,3-*c*]quinolin-6(5*H*)-ones **12a-12d** followed by chlorination to 6-chloro[1]benzothieno[2,3-*c*]quinolines **13a-13d** and dechlorination resulting in the title compounds. Treatment of **14a-14d** with iodomethane furnished the corresponding *N*-methyl quaternary salts **5a-5d**.

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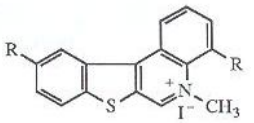
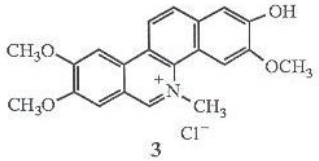
We have been interested in the synthesis of substituted [1]benzothieno[2,3-*c*]quinolines *via* photocyclization of the appropriate anilides [2-6]. This led us to the discovery of antileukemic activity against L-1210 of 5-methyl[1]benzothieno[2,3-*c*]quinolinium iodide **1** [4,7] and its 4,10-dimethoxy-substituted derivative **2** [2,7] as sulfur-containing analogs of the naturally occurring antileukemic alkaloids fagaronine (**3**) [8] and nitidine (**4**) [9]. A recent report [10] revealed that fagaronine chloride (**3**) and nitidine chloride (**4**) exhibit potent activity against HIV-1 reverse transcriptase. These findings prompted us to report the synthesis of 2,3,9,10-tetramethoxy-5-methyl[1]benzothieno[2,3-*c*]quinolinium iodide (**5a**), 4-fluoro-9,10-dimethoxy-5-methyl[1]-



1 R = H
2 R = OCH_3



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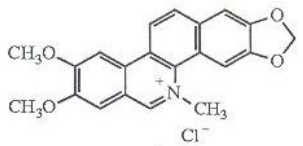

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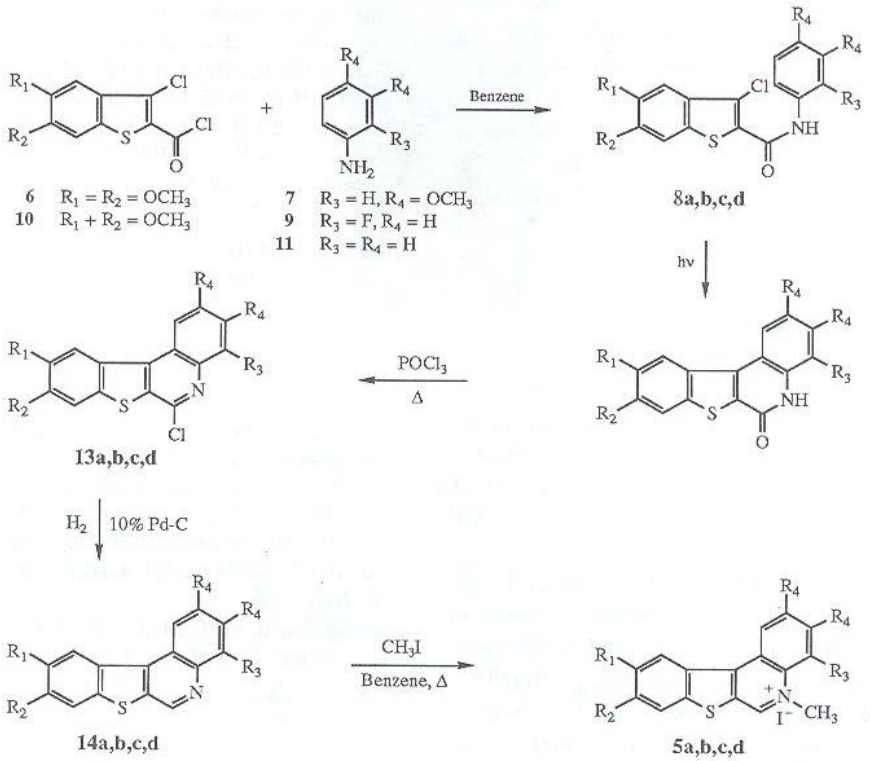
Scheme I



6 $R_1 = R_2 = OCH_3$
10 $R_1 + R_2 = OCH_3$
7 $R_3 = H, R_4 = OCH_3$
9 $R_3 = F, R_4 = H$
11 $R_3 = R_4 = H$

8a,b,c,d
13a,b,c,d
14a,b,c,d
5a,b,c,d

a, $R_1 = R_2 = R_4 = OCH_3, R_3 = H$
b, $R_1 = R_2 = OCH_3, R_3 = F, R_4 = H$
c, $R_1 + R_2 = OCH_2O, R_3 = R_4 = H$
d, $R_1 + R_2 = OCH_2O, R_3 = F, R_4 = H$

benzothieno[2,3-*c*]quinolinium iodide (**5b**), 5-methyl-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinolinium iodide (**5c**) and 4-fluoro-5-methyl-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinolinium iodide (**5d**) for biological evaluation.

Thus when 3-chloro-5,6-dimethoxybenzo[*b*]thiophene-2-carbonyl chloride (**6**), prepared by the reaction of 3-(3,4-dimethoxyphenyl)propenoic acid [11] with the thionyl chloride in the presence of pyridine [12,13] was allowed to react with 3,4-dimethoxyaniline (**7**) a 62% yield of 3-chloro-5,6-dimethoxy-*N*-(3,4-dimethoxyphenyl)benzo[*b*]thiophene-2-carboxamide (**8a**) resulted as shown in Scheme I. The reaction of 2-fluoroaniline (**9**) with **6** afforded 3-chloro-*N*-(2-fluorophenyl)-5,6-dimethoxybenzo[*b*]thiophene-2-carboxamide (**8b**) in 87% yield. Likewise, 3-chloro-5,6-methylenedioxybenzo[*b*]thiophene-2-carbonyl chloride (**10**) [12,13], obtained from 3-(3,4-methylenedioxyphenyl)-propenoic acid [14], was treated with aniline (**11**) and 2-fluoroaniline (**9**) to yield 3-chloro-5,6-methylenedioxy-*N*-phenylbenzo[*b*]thiophene-2-carboxamide (**8c**) (75%) and 3-chloro-*N*-(2-fluorophenyl)-5,6-methylenedioxybenzo[*b*]thiophene-2-carboxamide (**8d**) (90%), respectively.

Photoinduced cyclization of the carboxamides **8a**, **8b**, **8c** and **8d** was carried out by irradiating a mixture of equimolar amounts of the carboxamide and triethylamine with a 450 watt Hanovia medium pressure mercury vapor lamp using the appropriate solvent to yield the corresponding [1]benzothieno[2,3-*c*]quinolin-6(5*H*)-ones **12a** (58%), **12b** (86%), **12c** (59%) and **12d** (98%), respectively. The higher yields of **12b** and **12d** compared with **12a** and **12c** are in line with those previously reported for the *m*-methoxy compounds [2]. It should be noted that the isomeric product of **12a** was not isolated in the photocyclization of **8a**. Verification of the structure of **12a** was demonstrated by its ^{1}H nmr spectrum which exhibits eight singlets as expected.

The lactams **12a-12d** were chlorinated by refluxing phosphorus oxychloride to yield 6-chloro-2,3,9,10-tetramethoxy[1]benzothieno[2,3-*c*]quinoline (**13a**) (79%), 6-chloro-4-fluoro-9,10-dimethoxy[1]benzothieno[2,3-*c*]quinoline (**13b**) (89%), 6-chloro-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinoline (**13c**) (39%) and 6-chloro-4-fluoro-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinoline (**13d**) (67%), respectively.

Catalytic reduction of **13a-13d** with hydrogen and 10% Pd-C as the catalyst in 1:1 benzene-methanol solution in the presence of potassium hydroxide resulted in the corresponding dechlorinated quinolines **14a** (69%), **14b** (73%), **14c** (72%) and **14d** (77%), respectively. By treatment of **14a-14d** with iodomethane in benzene in a sealed tube at 100-110°, the corresponding [1]benzothieno[2,3-*c*]quinolinium iodides **5a** (65%), **5b** (94%), **5c** (61%) and **5d** (35%) were obtained. It is of interest to note that the quaternary salts **5b** and **5d** exhibited a doublet resonating a δ 4.77 with J = 9.2 Hz, 9.5 Hz, respectively, for the *N*-methyl group in their ^{1}H nmr spectra. This observation was consistent with our previous report [6] and can be attributed to the through-space spin-spin splitting involving the protons of the methyl group and the proximate fluorine atom [15].

These quaternary salts will be submitted for biological screening and these data will be reported elsewhere.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Beckman FT 1100 spectrometer as potassium bromide pellets and frequencies are expressed in cm^{-1}. Routine ^{1}H nmr spectra were obtained on a JEOL FX90Q spectrometer in the solvent indicated with TMS as the internal standard and chemical shifts reported in ppm (δ) and J values in Hz. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona.

3-Chloro-5,6-dimethoxy-*N*-(3,4-dimethoxyphenyl)benzo[*b*]thiophene-2-carboxamide (**8a**).

A mixture of 8.0 g (27.5 mmoles) of 3-chloro-5,6-dimethoxybenzo[*b*]thiophene-2-carbonyl chloride (**6**) [12,13], 4.21 g (27.5 mmoles) of 3,4-dimethoxyaniline (**7**), and 3.9 ml of triethylamine in 800 ml of benzene was heated under reflux for 4 hours. After cooling, the solid was collected by filtration and recrystallized from benzene to give 7.0 g (17.2 mmoles, 62%) of **8a** as fine white clusters, mp 204-206°; ir (potassium bromide): 3399 (NH stretching), 1635 (C=O stretching); ^{1}H nmr (deuteriochloroform): 500 MHz, δ 3.87 (s, 3H, CH_3), 3.92 (s, 3H, CH_3), 3.96 (s, 3H, CH_3), 3.99 (s, 3H, CH_3), 6.84 (d, $J_{5',6'}$ = 8.6 Hz, 1H, H5'), 6.99 (dd, $J_{5',6'}$ = 8.6 Hz, $J_{2',6'}$ = 2.4 Hz, 1H, H6'), 7.16 (s, 1H, H7), 7.19 (s, 1H, H4), 7.54 (d, $J_{2',6'}$ = 2.4 Hz, 1H, H2'), 8.76 (br s, 1H, NH).

Anal. Calcd. for $C_{19}H_{18}ClNO_5S$: C, 55.94; H, 4.45; N, 3.43. Found: C, 55.73; H, 4.56; N, 3.40.

3-Chloro-*N*-(2-fluorophenyl)-5,6-dimethoxybenzo[*b*]thiophene-2-carboxamide (**8b**).

A mixture of 1.80 g (6.18 mmoles) of carbonyl chloride **6** [12,13] and 0.69 g (6.21 mmoles) of 2-fluoroaniline (**9**) in 40 ml of benzene was heated under reflux for 4 hours. The mixture was evaporated to dryness *in vacuo* and the solid residue was recrystallized from benzene to afford 1.97 g (5.39 mmoles, 87%) of **8b** as colorless prisms, mp 237-239°; ir (potassium bromide): 3407 (NH stretching), 2942, 2836 (aliphatic CH stretching), 1653 (C=O stretching), 1293 (C-O stretching of ArO), 1031 (C-O stretching of OCH_3); ^{1}H nmr (deuteriochloroform): 55°, δ 3.96, 3.99 (2 s, 6H, 2 OCH_3), 7.03-7.34 (m, 5H, ArH), 8.37-8.57 (m, 1H, H3'), 9.13 (br s, 1H, NH).

Anal. Calcd. for $C_{17}H_{13}ClFNO_3S$: C, 55.82; H, 3.58; N, 3.83; S, 8.77. Found: C, 55.82; H, 3.57; N, 3.81; S, 8.63.

3-Chloro-5,6-methylenedioxy-*N*-phenylbenzo[*b*]thiophene-2-carboxamide (**8c**).

This compound was prepared from **10** (2.75 g, 10 mmoles) [12,13] and aniline (**11**) (0.9 ml, 10 mmoles) in 85 ml of benzene and 1.4 ml of triethylamine in a manner similar to that described for the synthesis of **8a**, and 2.5 g (7.54 mmoles, 75%) of **8c** was

obtained after recrystallization from water as a beige solid, mp 198-199°; ir (potassium bromide): 3350 (NH stretching), 1635 (C=O stretching); ^{1}H nmr (DMSO-d_6): δ 6.19 (s, 2H, CH_2), 7.33 (s, 1H, H7), 7.44 (m, 5H, ArH), 7.66 (s, 1H, H4), 10.3 (br s, 1H, NH).

Anal. Calcd. for $C_{16}H_{10}ClNO_3S$: C, 57.92; H, 3.04; N, 4.22; S, 9.66. Found: C, 57.84; H, 3.04; N, 4.21; S, 9.65.

3-Chloro-*N*-(2-fluorophenyl)-5,6-methylenedioxybenzo[*b*]thiophene-2-carboxamide (**8d**).

A mixture of 2.22 g (8.07 mmoles) of carbonyl chloride **10** [12,13], 0.90 g (8.10 mmoles) of 2-fluoroaniline (**9**) and 50 ml of benzene was heated under reflux for 4 hours. After cooling the precipitate was collected by filtration and recrystallized from benzene to give 2.55 g (7.29 mmoles, 90%) of **8d** as colorless fine needles, mp 218-220°; ir (potassium bromide): 3394 (NH stretching), 3081 (aromatic CH stretching), 2911 (aliphatic CH stretching), 1661 (C=O stretching), 1288 (C-O stretching of ArO), 1037 (C-O stretching of O-CH_2); ^{1}H nmr (DMSO-d_6): 100°, δ 6.15 (s, 2H, CH_2), 7.16-7.34 (m, 4H, H4′, H5′, H6′ and H7 as a singlet at 7.28), 7.56 (s, 1H, H4), 7.79-7.99 (m, 1H, H3′), 9.60 (br s, 1H, NH).

Anal. Calcd. for $C_{16}H_9ClFNO_3S$: C, 54.94; H, 2.59; N, 4.00; S, 9.17. Found: C, 55.06; H, 2.45; N, 3.94; S, 9.09.

2,3,9,10-Tetramethoxy[1]benzothieno[2,3-*c*]quinolin-6(5*H*)-one (**12a**).

A mixture of 0.5 g (1.2 mmoles) of amide **8a** and 0.2 ml of triethylamine in 500 ml of acetone was irradiated with a 450 watt Hanovia medium pressure mercury vapor lamp for 5 hours. A slow stream of air was passed through the solution during the course of the reaction. The solid was collected by filtration, washed with water and acetone and dried to give 0.26 g (0.70 mmole, 58%) of **12a** as a beige solid, mp >280°; ir (potassium bromide): 3299 (NH stretching); ^{1}H nmr (DMSO-d_6): δ 3.88 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.14 (s, 1H, H4), 7.72 (s, 1H, H8), 7.95 (s, 1H, H1), 8.05 (s, 1H, H11). This compound was used without further purification in the next reaction due to its low solubility.

4-Fluoro-9,10-dimethoxy[1]benzothieno[2,3-*c*]quinolin-6(5*H*)-one (**12b**).

A mixture of 0.5 g (1.37 mmoles) of carboxamide **8b**, 56 mg of triethylamine, and 500 ml of benzene was irradiated with a 450 watt Hanovia medium pressure mercury lamp for 4 hours. A slow stream of air was passed through the solution during the course of the reaction. The solid was collected by filtration and washed with water to give 0.39 g (1.18 mmoles, 86%) of lactam **12b**, mp >280°; ir (potassium bromide): 3137 (NH stretching), 1653 (C=O stretching), 1260 (C-O stretching of ArO), 1026 (C-O stretching of OCH_3); ^{1}H nmr (DMSO-d_6): 140°, δ 3.96, 4.01 (2 s, 6H, 2 OCH_3), 7.28-7.43 (m, 2H, H2 and H3), 7.69 (s, 1H, H8), 8.05 (s, 1H, H11), 8.34 (m, 1H, H1). This compound was used without further purification in the next reaction due to its low solubility.

9,10-Methylenedioxy[1]benzothieno[2,3-*c*]quinolin-6(5*H*)-one (**12c**).

This compound was prepared from **8c** (0.5 g, 1.5 mmoles) and triethylamine (0.2 ml) and 500 ml of benzene in a manner similar to that described for the synthesis of **12a**, and 0.26 g (0.88 mmole, 59%) of **12c** as a beige powder was obtained, mp >300°; ir (potassium bromide): 3435 (NH stretching), 1671 (C=O stretching); ^{1}H nmr (DMSO-d_6): 120°, δ 6.17 (s, 2H, OCH_2O), 7.30-7.63 (m, 4H, ArH), 8.20 (s, 1H, H11), 8.50-8.59 (m, 1H, H1). This compound was used without further purification in the next reaction due to its low solubility.

4-Fluoro-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinolin-6(5*H*)-one (**12d**).

A mixture of 0.50 g (1.43 mmoles) of **8d**, 0.15 g of triethylamine, and 500 ml of benzene was irradiated with a 450 watt Hanovia medium pressure mercury lamp for 4 hours. A slow stream of air was passed through the solution during the course of the reaction. The solid was collected by filtration and washed with water to give 0.44 g (1.40 mmoles, 98%) of lactam **12d**, mp >300°; ir (potassium bromide): 3132 (NH stretching), 2983, 2911, 2836 (aliphatic CH stretching), 1635 (C=O stretching), 1245 (C-O stretching of ArO), 1039 (C-O stretching of OCH_2); ^{1}H nmr (DMSO-d_6): 160°, δ 6.15 (s, 2H, CH_2), 7.22-7.46 (m, 2H, H2 and H3), 7.57 (s, 1H, H8), 8.09 (s, 1H, H1), 8.10-8.35 (m, 1H, H1). This compound was used without further purification in the next reaction due to its low solubility.

6-Chloro-2,3,9,10-tetramethoxy[1]benzothieno[2,3-*c*]quinoline (**13a**).

A mixture of 4.0 g (10.8 mmoles) of lactam **12a**, 1.5 ml of triethylamine and 50 ml of phosphorus oxychloride was heated under reflux for 12 hours. The reaction mixture was evaporated to dryness *in vacuo* and ice-water was added with caution. The solid was collected by filtration and dried. The solid was recrystallized from benzene to give 3.35 g (8.5 mmoles, 79%) of **13a** as an off-white solid, mp 269-271° dec; Beilstein test positive; ir (potassium bromide): 1558, 774, 668, 601; ^{1}H nmr (deuteriochloroform): δ 3.99 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 7.26 (s, 1H, H4), 7.39 (s, 1H), 7.61 (s, 1H), 7.70 (s, 1H).

Anal. Calcd. for $C_{19}H_{16}ClNO_4S$: C, 58.54; H, 4.14; N, 3.59. Found: C, 58.53; H, 4.22; N, 3.72.

6-Chloro-4-fluoro-9,10-dimethoxy[1]benzothieno[2,3-*c*]quinoline (**13b**).

A mixture of 1.06 g (3.22 mmoles) of **12b** and 30 ml of phosphorus oxychloride was heated at 110-120° for 4 hours. After cooling the mixture was poured into 350 ml of ice-water very slowly and carefully with stirring. The solid was collected by filtration and recrystallized from benzene to yield 1.00 g (2.88 mmoles, 89%) of **13b** as colorless crystals, mp 275-276°; ir (potassium bromide): 3070 (aromatic CH stretching), 2998, 2936, 2836 (aliphatic CH stretching), 1383 (CH bending of CH_3), 1273 (C-O stretching of ArO), 1031 (C-O stretching of OCH_3); ^{1}H nmr (DMSO-d_6): 120°, δ 3.99, 4.05 (2 s, 6H, 2 OCH_3), 7.43-8.04 (m, 3H, H2, H3 and H8 as a singlet at 7.73), 8.19 (s, 1H, H11), 8.65 (dt, $J_{1,2}$ = 8.5 Hz, $J_{1,3}$ = $J_{1,F}$ = 1.0 Hz, 1H, H1).

Anal. Calcd. for $C_{17}H_{11}ClFNO_2S$: C, 58.71; H, 3.19; N, 4.03; S, 9.22. Found: C, 58.84; H, 3.11; N, 4.05; S, 9.21.

6-Chloro-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinoline (**13c**).

This compound was prepared from **12c** (2.2 g, 7.4 mmoles), triethylamine (0.9 ml) and phosphorus oxychloride (30 ml) in a manner similar to that described for the synthesis of **13a**, and 0.9 g (2.9 mmoles, 39%) of **13c** was obtained after recrystallization from benzene as thin needles, mp 276-278°; ir (potassium bromide): 1561, 1491, 840, 743; ^{1}H nmr (DMSO-d_6): δ 6.25 (s, 2H, CH_2), 7.78 (s, 1H, H8), 7.81 (m, 2H, H2 and H3), 8.12 (m, 1H, H4), 8.42 (s, 1H, H11), 8.93 (m, 1H, H1).

Anal. Calcd. for $C_{16}H_8ClNO_2S$: C, 61.25; H, 2.57; N, 4.46. Found: C, 61.50; H, 2.71; N, 4.46.

6-Chloro-4-fluoro-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinoline (**13d**).

A mixture of 1.58 g (5.04 mmoles) of **12d** and 30 ml of phosphorus oxychloride was heated at 110-120° for 4 hours. After cooling the mixture was poured into 400 ml of ice-water very slowly and carefully with stirring. The solid was collected by filtration and recrystallized from benzene to afford 1.12 g (3.38 mmoles, 67%) of **13d** as colorless crystals, mp >310°; ir (potassium bromide): 3091 (aromatic CH stretching), 2924 (aliphatic CH stretching), 1288 (C-O stretching of ArO), 1029 (C-O stretching of OCH_2); ^1H nmr (DMSO-d_6): 140°, δ 6.23 (s, 2H, CH_2), 7.48-7.90 (m, 3H, H2, H3 and H8 as a singlet at 7.74), 8.33 (s, 1H, H11), 8.69 (m, 1H, H1).

Anal. Calcd. for $C_{16}H_7ClFNO_2S$: C, 57.92; H, 2.13; N, 4.22; S, 9.67. Found: C, 58.01; H, 1.97; N, 4.22; S, 9.50.

2,3,9,10-Tetramethoxy[1]benzothieno[2,3-*c*]quinoline (**14a**).

A solution of 0.2 g (0.51 mmole) of **13a**, 0.1 g of 10% Pd-C, 29 mg of potassium hydroxide, 100 ml of benzene and 100 ml of methanol was hydrogenated at atmospheric pressure at room temperature for 3 days. The catalyst was removed by filtration through a Celite pad and the filtrate was evaporated to dryness *in vacuo*. The solid was recrystallized from benzene to give 0.125 g (0.35 mmole, 69%) of **14a** as colorless needles, mp 245-247° dec; Beilstein test negative; ^1H nmr (deuteriochloroform); δ 4.04 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 4.11 (s, 3H, OCH_3), 4.14 (s, 3H, OCH_3), 7.38 (s, 1H, H4), 7.60 (s, 1H, H8), 7.91 (s, 1H, H1 or H11), 7.98 (s, 1H, H11 or H1), 9.08 (s, 1H, H6); ^{13}C nmr (deuteriochloroform): δ 55.74, 55.89, 55.95, 56.11, 101.38, 104.67, 106.97, 109.77, 119.75, 127.80, 131.39, 134.67, 135.04, 142.26, 143.05, 148.14, 149.69, 150.22, 150.28.

Anal. Calcd. for $C_{19}H_{17}NO_4S$: C, 64.21; H, 4.82; N, 3.94. Found: C, 64.12; H, 4.93; N, 4.18.

4-Fluoro-9,10-dimethoxy[1]benzothieno[2,3-*c*]quinoline (**14b**).

A mixture of 0.96 g (2.76 mmoles) of **13b**, 0.155 g (2.76 mmoles) of potassium hydroxide, 0.1 g of 10% Pd-C, 150 ml of benzene and 150 ml of methanol was hydrogenated at room temperature under atmospheric pressure until the uptake of hydrogen ceased. The mixture was filtered and the filtrate was evaporated to dryness *in vacuo*. The residual solid was recrystallized from benzene to give 0.63 g (2.01 mmoles, 73%) of **14b** as colorless fine needles, mp 224-225°; ir (potassium bromide): 3073, 3055 (aromatic CH stretching), 2983, 2898, 2818 (aliphatic CH stretching), 1368 (CH bending of CH_3), 1270 (C-O stretching of ArO), 1026 (C-O stretching of OCH_3); ^1H nmr (deuteriochloroform): δ 4.04, 4.11 (2 s, 6H, 2 OCH_3), 7.32-7.77 (m, 3H, H2, H3 and H8 as a singlet at 7.41), 8.05 (s, 1H, H11), 8.43 (dt, $J_{1,2}$ = 8.1 Hz, $J_{1,3}$ = $J_{1,F}$ = 1.5 Hz, H1), 9.28 (s, 1H, H6).

Anal. Calcd. for $C_{17}H_{12}FNO_2S$: C, 65.16; H, 3.86; N, 4.47; S, 10.23. Found: C, 65.21; H, 4.00; N, 4.39; S, 10.36.

9,10-Methylenedioxy[1]benzothieno[2,3-*c*]quinoline (**14c**).

This compound was prepared from **13c** (0.25 g, 0.8 mmole), 10% Pd-C (0.1 g), potassium hydroxide (50 mg), benzene (100 ml) and methanol (100 ml) in a manner similar to that described for the synthesis of **14a**, and 0.18 g (0.58 mmole, 72%) of **14c** was obtained after recrystallization from 1:1 hexane-benzene mixture, mp 248-250°; ir (potassium bromide): 1540, 1499, 931, 748; ^1H nmr (deuteriochloroform): 360 MHz, δ 6.16 (s, 2H, CH_2), 7.38 (s, 1H, H8), 7.74 (m, 2H, H2 and H3), 8.20 (s, 1H, H11), 8.29 (dd, $J_{3,4}$ = 8.3 Hz, $J_{2,4}$ = 1.9 Hz, 1H, H4), 8.72 (dd, $J_{1,2}$ = 7.6 Hz, $J_{1,3}$ = 1.9 Hz, 1H, H1), 9.26 (s, 1H, H6).

Anal. Calcd. for $C_{16}H_9NO_2S$: C, 68.80; H, 3.25; N, 5.01. Found: C, 68.88; H, 3.23; N, 5.06.

4-Fluoro-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinoline (**14d**).

A mixture of 1.09 g (3.29 mmoles) of **13d**, 0.184 g (3.29 mmoles) of potassium hydroxide, 0.10 g of 10% Pd-C, 450 ml of benzene, and 250 ml of methanol was hydrogenated at atmospheric pressure at room temperature until the uptake of hydrogen ceased. The mixture was filtered and the filtrate was evaporated to dryness *in vacuo*. The residual solid was recrystallized from benzene to give 0.75 g (2.52 mmoles, 77%) of **14d** as yellow crystals, mp 298-299° dec; ir (potassium bromide): 3091 (aromatic CH stretching), 2998, 2916 (aliphatic CH stretching), 1273 (C-O stretching of ArO), 1029 (C-O stretching of OCH_2); ^1H nmr (DMSO-d_6): 150°, δ 6.21 (s, 2H, CH_2), 7.32-7.86 (m, 3H, H2, H3 and H8 as a singlet at 7.71), 8.34 (s, 1H, H11), 8.67 (ddd, $J_{1,2}$ = 8.2 Hz, $J_{1,3}$ = 1.3 Hz, $J_{1,F}$ = 0.9 Hz, H1), 9.38 (s, 1H, H6).

Anal. Calcd. for $C_{16}H_8FNO_2S$: C, 64.64; H, 2.71; N, 4.71; S, 10.79. Found: C, 64.48; H, 2.70; N, 4.69; S, 10.61.

2,3,9,10-Tetramethoxy-5-methyl[1]benzothieno[2,3-*c*]quinolinium Iodide (**5a**).

A mixture of 0.11 g (0.31 mmole) of **14a** and 1.2 g (8.47 mmoles) of iodomethane in 50 ml of benzene was heated under reflux in a sealed reaction vessel for 12 hours. After cooling the solid was collected by filtration and recrystallized from methanol to give 0.1 g (0.20 mmole, 65%) of **5a** as orange crystals, mp 280-282° dec; ir (potassium bromide): 1532, 1275, 820; ^1H nmr (DMSO-d_6): 115°, δ 4.03 (s, 3H, OCH_3), 4.10 (s, 3H, OCH_3), 4.17 (s, 3H, OCH_3), 4.23 (s, 3H, OCH_3), 4.62 (s, 1H, N-CH_3), 7.76 (s, 1H, H4), 7.98 (s, 1H, H8), 8.31 (s, 1H, H1 or H11), 8.36 (s, 1H, H11 or H1), 9.81 (s, 1H, H6).

Anal. Calcd. for $C_{20}H_{20}INO_4S \cdot H_2O$: C, 46.61; H, 4.30; N, 2.72. Found: C, 46.82; H, 4.54; N, 2.71.

4-Fluoro-9,10-dimethoxy-5-methyl[1]benzothieno[2,3-*c*]quinolinium Iodide (**5b**).

A mixture of 0.60 g (1.91 mmoles) of **14b**, 2 ml of iodomethane, and 60 ml of benzene was heated at 110-120° in a sealed reaction vessel for 24 hours. After cooling the orange precipitate was collected by filtration and recrystallized from methanol to afford 0.82 g (1.80 mmoles, 94%) of the quaternary salt **5b** as orange crystals, mp 231-233° dec; ir (potassium bromide): 3050 (aromatic CH stretching), 2970, 2942 (aliphatic CH stretching), 1368 (CH bending of CH_3), 1278 (C-O stretching of ArO), 1031 (C-O stretching of OCH_3); ^1H nmr (DMSO-d_6): 120°, δ 4.04, 4.10 (2 s, 6H, 2 OCH_3), 4.77 (d, J_{F,CH_3} = 9.2 Hz, 3H, N-CH_3), 7.96-8.20 (m, 3H, H2, H3 and H8 as a singlet at 8.06), 8.33 (s, 1H, H11), 9.07 (m, 1H, H1), 10.11 (s, 1H, H6).

Anal. Calcd. for $C_{18}H_{15}FINO_2S$: C, 47.48; H, 3.32; N, 3.08; S, 7.04. Found: C, 47.28; H, 3.24; N, 3.07; S, 7.19.

5-Methyl-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinolinium Iodide (**5c**).

This compound was prepared from **14c** (0.12 g, 0.43 mmole), iodomethane (2.4 g, 16.9 mmoles) and 50 ml of benzene in a manner similar to that described for the synthesis of **5a**, and 0.11 g (0.26 mmole, 61%) of **5c** was obtained after recrystallization from

methanol, mp >300°; ir (potassium bromide): 1604, 1532, 941, 753; ^{1}H nmr (DMSO-d_6): 110°, δ 4.65 (s, 3H, CH_3), 6.35 (s, 2H, OCH_2O), 7.97 (s, 1H, H8), 8.12-8.50 (m, 2H, H2 and H3), 8.63-8.61 (m, 1H, H4), 8.64 (s, 1H, H11), 10.10 (s, 1H, H6).

Anal. Calcd. for $C_{17}H_{12}INO_2S$: C, 48.47; H, 2.84; N, 3.32. Found: C, 48.54; H, 2.96; N, 3.27.

4-Fluoro-5-methyl-9,10-methylenedioxy[1]benzothieno[2,3-*c*]quinolinium Iodide (**5d**).

A mixture of 0.69 g (2.32 mmoles) of **14d**, 2 ml of iodomethane and 80 ml of benzene was heated at 110-120° in a sealed reaction vessel for 24 hours. After cooling the solid was collected by filtration and recrystallized from methanol to yield 0.36 g (0.82 mmole, 35%) of the quaternary salt **5d** as yellow crystals, mp 298-300° dec; ir (potassium bromide): 3093, 3021 (aromatic CH stretching), 2885 (aliphatic CH stretching), 1275 (C–O stretching of ArO), 1036 (C–O stretching of OCH_2); ^{1}H nmr (DMSO-d_6): 110°, δ 4.77 (d, J_{F,CH_3} = 9.5 Hz, 3H, CH_3), 6.36 (s, 2H, CH_2), 7.95-8.13 (m, 3H, H2, H3 and H8 as a singlet at 8.00), 8.59 (s, 1H, H11), 9.03-9.13 (m, 1H, H1), 10.08 (s, 1H, H6).

Anal. Calcd. for $C_{17}H_{11}FINO_2S$: C, 46.48; H, 2.52; N, 3.19; S, 7.30. Found: C, 46.45; H, 2.77; N, 3.19; S, 7.47.

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