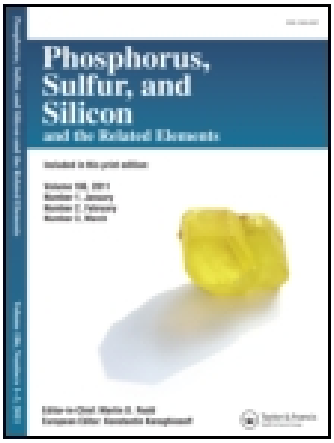

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Synthesis, Spectroscopic Analysis, and In-Vitro Antimicrobial Evaluation of some Tetrahydrobenzo[a]Xanthene-11-Thiones

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SYNTHESIS, SPECTROSCOPIC ANALYSIS, AND IN-VITRO ANTIMICROBIAL EVALUATION OF SOME TETRAHYDROBENZO[a]XANTHENE-11-THIONES

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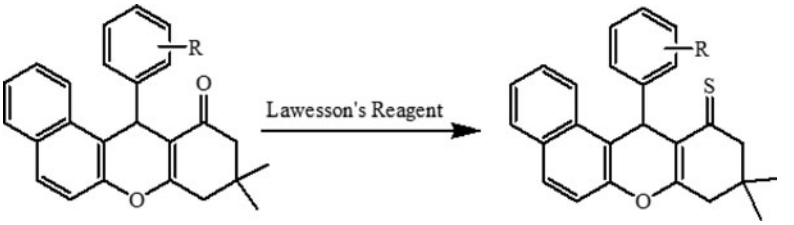
GRAPHICAL ABSTRACT



Abstract *A series of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thiones were synthesized by the reaction of substituted 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones with Lawesson's Reagent in toluene under standard reaction conditions. All synthesized compounds were characterized by IR, NMR (^{1}H and ^{13}C), and mass spectra. Moreover, 2D-NMR (HOMOCOSY, HSQC, and HMBC) studies were also performed for compound* ***10b****. The synthesized compounds were also screened for their antibacterial activities.*

[Supplementary materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfer, and Silicon and the Related Elements for the following free supplemental files: Additional figures.]

Keywords Lawesson reagent; xanthene-11-thiones; 2D-NMR; antibacterial activity

INTRODUCTION

Xanthenes, one of the most widely distributed classes of natural compounds, and benzoxanthenes constitute an important class of biologically active heterocycles; thus, their synthesis has received great attention in medicinal and pharmaceutical chemistry. They have antibacterial, anti-inflammatory, antiviral, and anticancer activities.[1–4] Xanthene-based compounds serve as antagonists for paralyzing the action of zoxalamine, in photodynamic therapy (PDT), and as antagonists for drug-resistant leukemia lines.[5–7] In addition, their

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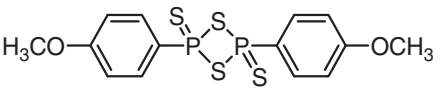
derivatives can be used as dyes, pH-sensitive fluorescent materials for the visualization of biomolecular assemblies, agricultural bactericides, and in laser technologies.[8–12].

Organosulfur compounds occupy a uniquely important place in synthetic organic chemistry due to their rich and versatile chemistry.[13] Furthermore, they are of widespread interest because of their ubiquitous biological activities and rich photochemistry.[14,15] These compounds are usually synthesized using thionation, which converts a carbonyl group to thiocarbonyl. The larger and less electronegative sulfur atom, relative to oxygen, might alter the hydrogen bonding ability and/or induce conformational changes in the modified molecule. In addition, these derivatives can be used as intermediates for further transformations due to the increased reactivity of the thione function. Lawesson's Reagent (**1**, LR) is the most efficient and broadly utilized reagent in this transformation.[16]



1 (1)

In the course of a program devoted to the synthesis of new heterocyclic scaffolds of bioactive compounds, here we proposed the synthetic strategy for 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thiones. The synthesized compounds were characterized by IR, NMR (^{1}H and ^{13}C), and also tested for antibacterial activities. 2D-NMR (HOMOCOSY, HSQC, and HMBC) spectroscopic studies of compound **10b** were also performed for the unambiguous assignment of signals.

RESULTS AND DISCUSSION

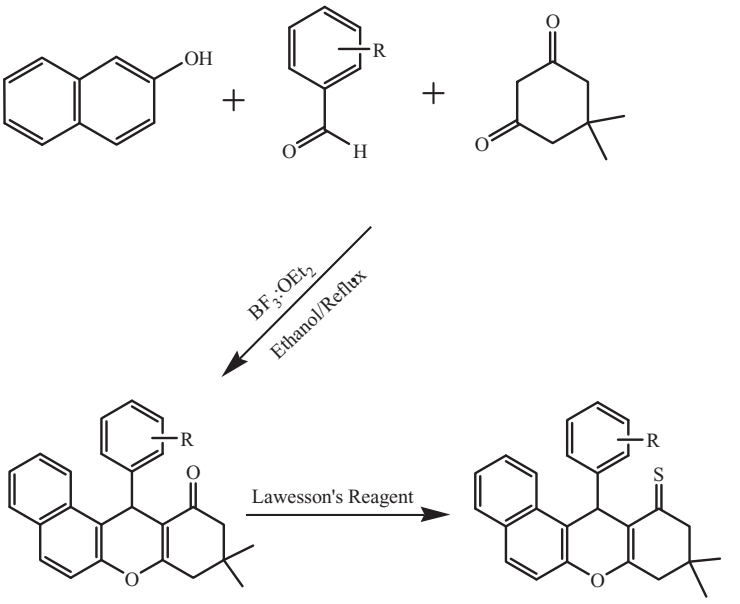
Chemistry

The synthetic route to the target compounds is outlined in Scheme 1. Starting compounds (12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones) **1a–10a** were prepared by the synthetic procedure described earlier.[17]

Thionation of the parent compounds **1a–10a** was achieved with LR. The respective 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones **1a–10a** were refluxed with Lawesson's Reagent in toluene for 45 min to afford the purple color solid 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thiones **1b**–**10b**. The synthesized compounds were characterized by IR and NMR spectra as well as mass spectrometry. Spectroscopic data are listed in the Experimental Section. They are in accordance with the assigned structures.

IR Spectroscopic Analysis of Compounds 1b–10b

Since the C═S bond is not as strongly polar as the C═O bond, the absorption band is not very intense and appears in the low-frequency region of the spectrum. The compounds **1b–10b** also showed a moderate intense band in the region 1210–1225 cm^{-1} characteristic of thiocarbonyl (C═S) stretching frequencies. The disappearance of the carbonyl (C═O) stretching frequency and the appearance of new stretching band around 1225 cm^{-1} characteristic for a thiocarbonyl (C═S) group evidences the formation of thioketones.



1b; R = H, **2b;** R = 2-Cl, **3b;** R = 3-Br, **4b;** R = 3-OCH_3 , **5b;** R = 4-Cl, **6b;** R = 4-F, **7b;** R = 4-OCH_3, **8b;** R = 4-CH_3, **9b;** R = 3-OCH_3-4-OH, **10b;** R = 3-OC_2H_5-4-OH

Scheme 1 Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thiones **1b–10b**.

^{1}H NMR Spectroscopic Analysis of Compound 10b

Compound **10b** (Figure 1 with spectroscopic numbering) was chosen as a representative compound and the ^{1}H NMR spectral analysis is presented here in detail. The ^{1}H NMR spectrum of **10b** is shown in Figure 2. For **10b**, 2D-NMR (HOMOCOSY, HSQC, and HMBC) spectra were also recorded for the unambiguous assignment of signals. Aromatic protons appear in the region 6.70–8.22 ppm. In the lower frequency region of the spectrum, there are two sharp singlets at 1.00 and 1.14 ppm (each with three proton integrals) due to methyl protons. The two doublets at 2.85 and 3.00 ppm are assigned to methylene protons at C-10 adjacent to the thiocarbonyl group [AB system, C=C–CH_aH_b, $\delta_{2.85}$ (d, J = 17.0 Hz, 1H) and $\delta_{3.00}$ (d, J = 17.0 Hz, 1H)].[18] Likewise, the other methylene protons at C-8 appeared as two doublets at 2.62 and 2.67 ppm. [AB system, C(=S)CH_aCH_b, $\delta_{2.62}$ (d, J = 18.5 Hz, 1H) and $\delta_{2.67}$ (d, J = 18.5 Hz, 1H)]. The benzylic proton at C-12 resonates at 6.27 ppm as a singlet. Methyl protons of the ethoxy group appeared as a triplet with three-proton integration at 1.42 ppm (J = 7.0 Hz). The remaining signals due to substituents in aromatic ring (ethoxy and hydroxyl) are observed in normal region.

^{13}C NMR Spectroscopic Analysis of Compound 10b

The ^{13}C NMR spectrum of **10b** is shown in Figure 3. The signal at higher frequency region of 230.7 ppm is assigned to the thiocarbonyl (C=S) carbon atom. In the up-field region three signals were observed at 14.9, 26.3, and 28.9 ppm. These were assigned to the two methyl carbons attached to C-9 and ethoxy methyl carbon respectively. Methylene carbon signals appear at 61.2 and 43.0 ppm[17] and the signal at 61.2 ppm is assigned to

Table 1 Correlations in the HOMOCOSY, HSQC, and HMBC spectra of compound **10b** (δ, ppm)

Signal in the ^{1}H spectrum	Correlations in the HOMOCOSY spectrum	Correlations in the HSQC spectrum	Correlations in the HMBC spectrum
1.00 (s, 3H, CH_3)	—	26.3	61.2, 42.9, 33.0, 28.9
1.14 (s, 3H, CH_3')	—	28.9	61.2, 42.9, 33.0, 26.3
1.42 (t, 3H, $OCH_2C\underline{H}_3$)	4.08–4.11	14.8	64.4
2.62 (d, 1H, H-8a)	2.67	42.9	161.2, 124.4, 61.2, 33.0, 26.3
2.67 (d, 1H, H-8b)	2.62	42.9	161.2, 124.4, 61.2, 33.0, 26.3
2.70 (d, 1H, H-10a)	3.00	61.2	230.7, 124.4, 42.9, 33.1, 26.3
3.00 (d, 1H, H-10b)	2.70	61.2	230.7, 124.4, 42.9, 33.1, 26.3
4.08–4.11 (q, 2H, OCH_2)	1.42	64.4	14.8
5.52 (s, 1H, Ar-OH)	—	—	—
6.27 (s, 1H, H-12)	—	37.2	230.7, 161.2, 113.5–146.9
6.71 (d, 1H, H-17)	6.76	113.9	144.9, 136.3
6.76 (dd, H, H-18)	7.11, 6.71	121.7	143.9, 113.9
7.11 (d, 1H, H-14)	6.76	113.5	144.9, 133.9, 121.7
7.38 (d, 1H, H-5)	7.77	116.8	146.8, 131.7, 118.8
7.43 (t, 1H, H-2)	7.81, 7.52	125.0	131.7, 123.6
7.52 (t, 1H, H-3)	8.21, 7.43	126.9	128.6, 128.5, 131.2, 116.8
7.77 (d, 1H, H-6)	7.38	128.5	146.8, 131.2
7.81 (d, 1H, H-4)	7.43	128.6	131.2, 128.6, 128.5
8.21 (d, 1H, H-1)	7.52	123.6	131.7, 131.2, 125.0, 118.8

the methylene carbon in α-position to the thiocarbonyl group (C-10). Shielding differences between methylene carbons are about 18 ppm and this clearly exemplifies a drift of electron density from C-10 toward the electron deficient thiocarbonyl carbon. The methylene carbon C-12 is slightly deshielded and observed at 37.2 ppm. The C-9 carbon signal appeared at 28.9 ppm.

The individual assignment of the proton and carbon signals for **10b** was achieved by use of HOMOCOSY, HSQC, and HMBC spectroscopic measurements, and the observed

Table 2 Comparison of ^{1}H and ^{13}C chemical shift values of compounds **10a** and **10b**

Carbon numbering	**10a**	**10b**
C-8	2.54 (s, 2H), 41.4	2.62 (d, 1H), 2.67 (d, 1H), 42.9
C-9	32.2	33.1
C-10	2.25 (d, 1H), 2.30 (d, 1H), 50.9	2.84 (d, 1H), 3.00 (d, 1H), 61.2
C-11	197.1	230.7
C-12	5.62 (s, 1H), 34.1	6.27 (s, 1H), 37.2
CH_3 at C-9	0.96 (s, 3H), 27.1	1.00 (s, 3H), 26.3
CH_3 at C-9	1.10 (s, 3H), 29.3	1.14 (s, 3H), 28.9

Table 3 Antimicrobial activities of **1b–10b** determined by the disk diffusion method (zone of inhibition in mm) at 10 μg/mL in Muller–Hinton agar

Compounds	B. cereus	S. aureus	P. aeruginosa	S. typhi
1b	9	12	7	9
2b	12	12	8	7
3b	11	11	—	8
4b	9	10	—	15
5b	8	12	—	8
6b	13	11	9	10
7b	8	11	8	7
8b	8	15	10	10
9b	12	9	7	8
10b	13	14	16	13
Control (ampicillin)	15.8	17.5	15	16.5

correlations are given in Table 1. The HMBC spectrum of **10b** is shown in Figure 4 and its mass spectrum is shown in Figure 5.

Thionation results in a shift of the ^{1}H and ^{13}C signals toward the higher frequency region. The reason for deshielding is the strong C═S anisotropy compared with the parent ketones **1a–10a**. The extent of deshielding is very high in magnitude for the α-methylene protons and carbons (C-10). The C-10 methylene protons are deshielded to around 0.9 ppm and the corresponding carbon is deshielded to ~10 ppm. The trend is similar for the C-12 benzylic protons and carbons and the chemical shift differences or shielding differences for **10a** and **10b** given in Table 2.

Antibacterial Evaluation

All synthesized 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thiones **1b–10b** were tested for their in vitro antibacterial activity against *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Salmonella typhi*. The antibacterial potency of the tested compounds in 10 μg/mL was compared with the standard drug ampicillin (10 μg/mL). The zone of inhibition is summarized in Table 3.

The biological results suggest that products **1b–10b** exhibit mild to good inhibitory effect against most of the tested microbes. Compound **4b** was found to have good inhibitory effect on *Salmonella typhi*, *Staphylococcus aureus*, and *Bacillus cereus*. Compounds **6b** and **10b** are found to have good inhibitory effect against *Bacillus cereus* and *Staphylococcus aureus*. Most of the compounds have mild inhibitory activity against *P. aeruginosa* at the tested concentration level of 10 μg/mL. The studies thus confirm the potential biological activity and consequently the utility of these derivatives as potent drug sources.

CONCLUSION

We have carried out the synthesis of a series of 12-aryl-8,9,10,12-tetrahydrobenzo [a]xanthene-11-thiones (**1b–10b**) from 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones (**1a–10a**) using Lawesson's Reagent. Compound **10b** shows potential biological activity against all tested bacterial strains compared with other compounds **1b–9b**. The synthesized compounds are of interest as they are therapeutically noteworthy and useful building blocks for further transformations.

EXPERIMENTAL

Chemistry

Melting points (mp) were determined in open capillaries and are uncorrected. IR spectra were recorded on an Avatar Nicholet FT-IR spectrophotometer (range 4000–400 cm^{-1}) as KBr pellets. ^1H NMR spectra were recorded on a Bruker AMX-400 spectrometer operating at 400.23 MHz and a Bruker AVIII 500 MHz spectrometer operating at 500.3 MHz using $CDCl_3$ as solvent and TMS as internal reference. ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer operating at 100.63 MHz and Bruker AVIII 500 MHz spectrometer operating at 125.75 MHz. Mass spectra were recorded on a JEOL GC MATE II spectrometer.

By employing the literature precedent,[17] all parent 12-aryl-8,9,10,12-tetrahydrobenzo [a]xanthene-11-ones **1a–10a** were prepared by the condensation of appropriate aldehydes with dimedone and 2-naphthol using $BF_3{\cdot}OEt_2$ as catalyst.

General Procedure for the Preparation of 1b–10b

Lawesson's Reagent (2.5 mmol) was added to a solution of the parent ketone **1a–10a** (1 mmol) in toluene (15 mL). The reaction mixture was refluxed for 45 min. After the completion of the reaction, the solvent was removed and the residue was subjected to column chromatography (CH_2Cl_2:MeOH, 98:2) to afford **1b–10b** as purple color solids.

9,9-Dimethyl-12-phenyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (1b). Purple crystals; yield: 78%; mp 106–108 °C; IR: 3063, 3019, 2964, 2925, 2849, 1651, 1595, 1374, 1225; ^1H NMR (400 MHz) δ: 7.01–8.19 (m, Ar-H, 11H), 6.29 (s, 1H), 2.95 (d, 1H, $J = 16.8$ Hz), 2.82 (d, 1H, $J = 16.8$ Hz), 2.67 (d, 1H, $J = 18.4$ Hz), 2.61 (d, 1H, $J = 18.0$), 1.11 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz) δ: 230.5, 161.3, 146.9, 144.1, 131.6, 131.2, 129.2, 128.7, 128.5, 128.2, 127.9, 127.0, 126.2, 125.0, 124.2, 123.7, 123.6, 118.7, 117.3, 116.8, 61.1, 42.9, 37.7, 33.1, 29.7, 28.8, 26.4.

12-(2-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (2b). Purple crystals; yield: 80%; mp 150–152 °C; IR: 3057, 3002, 2953, 2923, 2854, 1630, 1578, 1370, 1220; ^1H NMR (400 MHz) δ: 8.43–6.95 (m, Ar-H, 10H), 6.42 (s, 1H), 2.95 (d, 1H, $J = 16.8$ Hz), 2.83 (d, 1H, $J = 16.8$ Hz), 2.69 (d, 1H, $J = 18.0$ Hz), 2.62 (d, 1H, $J = 18.0$ Hz), 1.12 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz) δ: 230.6, 161.9, 147.3, 140.6, 133.8, 133.2, 131.5, 130.6, 130.5, 129.1, 128.5, 127.8, 126.2, 124.9, 124.2, 122.7, 117.0, 116.8, 61.5, 43.0, 37.3, 32.9, 28.8, 26.5; MS (EI 70 eV): *m/z* 368.5 (100), 404.3 (M^+, 16).

12-(3-Bromophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (3b). Purple crystals; yield: 84%; mp 136–138 °C; IR: 3066, 2956, 2923, 1632, 1584, 1369, 1219; ^1H NMR (400MHz) δ: 8.17–7.03 (m, Ar-H, 10H), 6.31 (s, 1H), 2.99 (d, 1H, $J = 17.0$ Hz), 2.85 (d, 1H, $J = 16.5$ Hz), 2.71 (d, 1H, $J = 18.0$ Hz), 2.64 (d, 1H, $J = 18.0$ Hz), 1.46 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz) δ: 230.3, 161.5, 146.9, 146.3, 132.1, 131.7, 131.0, 129.4, 129.1, 128.6, 128.1, 127.2, 125.2, 123.5, 123.3, 122.2, 117.8, 116.9, 61.1, 42.9, 37.5, 33.2, 28.8, 26.4; MS (EI 70 eV): *m/z* 248.9(60), 449.8(M^++1, 12).

9,9-Dimethyl-12-(3-methoxyphenyl)-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (4b). Purple crystals; yield: 82%; mp 158–160 °C; IR: 3067, 3008, 2958, 2922, 2852, 1647, 1374, 1225; ^1H NMR (400MHz) δ: 8.23–7.01 (m, Ar-H, 10H), 6.31 (s, 1H), 2.98 (d, 1H, $J = 18.0$ Hz), 2.84 (d, 1H, $J = 17.2$ Hz), 2.67 (d, 1H, $J = 18.0$ Hz), 2.63 (d,

1H, $J = 18.0$ Hz), 1.14 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz) δ: 230.5, 161.4, 159.2, 146.8, 145.7, 131.6, 131.2, 128.8, 128.7, 128.5, 127.1, 125.1, 124.0, 123.6, 121.8, 118.5, 116.8, 115.6, 111.1, 61.1, 55.1, 42.9, 37.6, 33.1, 28.8, 26.48; MS (EI 70 eV): *m*/*z* 269.5 (100), 399.5 (M^+, 5).

12-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (5b). Purple crystals; yield: 82%; mp 164–166 °C; IR: 3059, 2922, 2853, 1628, 1375, 1221; ^{1}H NMR (400 MHz, ppm) δ: 8.11–7.09 (m, Ar-H, 10H), 6.27 (s, 1H), 2.95 (d, 1H, $J = 16.8$ Hz), 2.81 (d, 1H, $J = 16.8$ Hz), 2.66 (d, 1H, $J = 18.0$ Hz), 2.60 (d, 1H, $J = 18.0$ Hz), 1.11 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (125 MHz) δ: 230.5, 161.5, 146.8, 142.6, 131.9, 131.6, 130.9, 130.6, 128.9, 128.6, 128.1, 127.2, 125.2, 123.7, 123.3, 118.1, 116.8, 61.0, 42.9, 37.2, 33.1, 28.9, 26.3.

9,9-Dimethyl-12-(4-fluorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (6b). Purple crystals; yield: 84%; mp 120–122 °C; IR: 3065, 2956, 2923, 2858, 1627, 1583, 1506, 1224; ^{1}H NMR (400 MHz) δ: 8.19–6.34 (m, Ar-H, 10H), 3.01 (d, 1H, $J = 16.4$ Hz), 2.85 (d, 1H, $J = 16.8$ Hz), 2.69 (d, 1H, $J = 19.2$ Hz), 2.63 (d, 1H, $J = 20.0$ Hz), 1.15 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz) δ: 230.5, 162.3, 161.4, 159.9, 146.8, 140.0, 140.0, 131.6, 131.0, 130.8, 130.7, 129.0, 128.6, 127.2, 125.2, 123.9, 123.4, 118.4, 116.9, 114.9, 114.6, 61.1, 42.9, 37.0, 34.8, 33.1, 30.9, 28.9, 27.0,26.3.

9,9-Dimethyl-12-(4-methoxyphenyl)-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (7b). Purple crystals; yield: 80%; mp 180–182 °C; IR: 3073, 3024, 2956, 2925, 2860, 1607, 1579, 1508, 1250, 1220, 1183; ^{1}H NMR (400 MHz) δ: 8.19–6.89 (m, Ar-H, 10H), 6.24 (s, 1H), 3.66 (s, 3H), 2.95 (d, 1H, $J = 16.8$ Hz), 2.81 (d, 1H, $J = 16.8$ Hz), 2.66 (d, 1H, $J = 18.8$ Hz), 2.59 (d, 1H, $J = 17.6$ Hz), 1.11 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (125 MHz) δ: 230.6, 161.2, 157.7, 146.8, 136.5, 131.6, 131.1, 130.2, 128.6, 128.5, 127.0, 125.0, 124.3, 123.6, 118.9, 116.8, 113.3, 61.1, 55.0, 42.9, 36.9, 33.1, 28.9, 26.4.

9,9-Dimethyl-12-(4-tolyl)-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thione (8b). Purple crystals; yield: 79%; mp 140–142 °C; IR: 3079, 3013, 2956, 2920, 2856, 1605, 1579, 1368, 1221, 1185; ^{1}H NMR (500 MHz) δ: 8.18–6.66 (m, Ar-H, 10H), 6.28 (s, 1H), 2.97 (d, 1H, $J = 16.5$ Hz), 2.85 (d, 1H, $J = 16.5$ Hz), 2.69 (d, 1H, $J = 20.0$ Hz), 2.64 (d, 1H, $J = 16.5$ Hz), 2.2 (s, 3H), 1.14 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz) δ: 230.5, 161.2, 146.8, 141.2, 135.6, 131.6, 131.2, 129.1, 128.6, 128.5, 128.4, 126.9, 124.9, 124.3, 123.6, 118.9, 116.8, 61.1, 42.9, 37.3, 33.1, 29.2, 28.8, 26.5, 20.9.

9,9-Dimethyl-12-(4-hydroxy-3-methoxyphenyl)-8,9,10,12-tetrahydrobenzo[a] xanthene-11-thione (9b). Purple crystals; yield: 78%; mp 158–160 °C; IR: 3501, 3063, 2923, 2853, 1612, 1578, 1512, 1371, 1268; ^{1}H NMR (400 MHz) δ: 8.21–6.68 (m, Ar-H, 9H), 6.27 (s, 1H), 5.45 (s, 1H), 3.85 (s, 3H), 3.02 (d, 1H, $J = 16.8$ Hz), 2.84 (d, 1H, $J = 16.8$ Hz), 2.63 (d, 1H, $J = 18.4$ Hz), 2.58 (d, 1H, $J = 18.4$ Hz), 1.14 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz) δ: 230.7, 161.3, 146.8, 145.8, 143.8, 136.4, 131.7, 131.2, 128.6, 128.5, 127.0, 125.1, 124.4, 123.6, 121.9, 118.8, 116.8, 113.9, 112.5, 61.2, 55.9, 42.9, 37.2, 33.1, 28.9, 26.3; MS (EI 70 eV): *m*/*z* 135.4 (100), 418.2 (M^++2, 18).

9,9-Dimethyl-12-(3-ethoxy-4-hydroxyphenyl)-8,9,10,12-tetrahydrobenzo[a] xanthene-11-thione (10b). Purple crystals; yield: 79%; mp 144–146 °C; IR: 3526, 3433, 3062, 2957, 2922, 2871, 1611, 1582, 1511, 1368, 1266, 1217, 1184; ^{1}H NMR (500 MHz) δ: 8.22–6.70 (m, Ar-H, 9H), 6.27 (s, 1H), 5.52 (s, 1H), 4.11–4.08 (m, 2H), 3.00 (d, 1H, $J = 17.0$ Hz), 2.85 (d, 1H, $J = 17.0$ Hz), 2.67 (d, 1H, $J = 18.5$ Hz), 2.62 (d, 1H, $J = 18.5$ Hz), 1.42 (t, 3H, $J = 7$ Hz), 1.14 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz) δ: 230.7, 161.2, 146.8, 144.9, 143.9, 136.3, 131.7, 131.2, 128.6, 128.5, 126.9, 125.0, 124.5, 123.6, 121.7,

118.8, 116.8, 113.9, 113.5, 64.4, 61.2, 42.9, 37.2, 33.1, 28.9, 26.3, 14.8; MS (EI 70 eV): *m*/*z* 146.9 (80), 429.5 (M^+, 18).

Microbiological Screening

Antimicrobial activity tests were carried out against *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Salmonella typhi* strains using the disc diffusion method. The in vitro activities of the compounds were tested in Muller–Hinton agar (Hi-Media, Mumbai) for bacteria by the zone of inhibition method.[19] While this manuscript was under review, Khurana et. al.[20] reported the synthesis and biocidal evaluation of a series of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-thiones. The antibacterial potency of the tested compounds in 10 μg/mL was compared with the standard drug ampicillin (10 μg/mL). Microbial suspensions were prepared in sterile saline (0.85% NaCl) with an optical density conforming to the McFarland standard 0.5 [150 $\times$ 106 colony-forming units (CFU)/mL)]. All stock solutions of the tested compounds were dissolved in dimethyl sulfoxide (DMSO). It was found that DMSO at the final concentration had no influence on the growth of the tested microorganisms.

Discs impregnated with known concentrations of the tested compounds were placed on a Muller–Hinton agar plate that had been inoculated or seeded uniformly over the entire plate with a culture of the bacterium to be tested. The plate was incubated for 18–24 h at 37 °C. Followed by incubation, the diameter of the zones of inhibition of growth (including the 6-mm diameter of the disc itself) was measured and compared with the standard drug.

Supplementary Data

Figures 1–5 are available in the Supplemental Materials.

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