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Anion reaction of 1,3-benzoxathiole-3-oxide with several electrophilic compounds☆

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Abstract—The reaction of benzoxathiole-3-oxide with LDA in THF or THF/hexane or THF/HMPA gave a carbanion which was reacted with methyl iodide, aromatic aldehydes or carbon dioxide. The conformational stability (α-diastereoselectivity) of the carbanion and the asymmetric induction due to the prochiral electrophiles (β-diastereoselectivity) was studied. The temperature and the solvent effects on the α- and β-diastereoselectivity are discussed.

1. Introduction

In the last years many researches have examined the regioselectivity of metallation reactions on several classes of compounds, such as alkylthio-, alkylamino-, alkoxybenzenes, 1,3-benzodioxoles and 1,3-benzoxathioles using butyllithium, LDA and superbases.[1–5] At present it seems interesting to extend the study to cyclic sulfoxides[6,7] such as 1,3-benzoxathiole-3-oxide to investigate the diasteroselectivity due to the nucleophile and the electrophile.

Earlier researches on the behaviour of enantiomerically pure molecules as benzylmethylsulfoxide, *tert*-butylbenzylsulfoxide, and similar substrates in the α-proton abstraction, showed high diastereoselectivity.[8–11] The extension of this study to the prochiral group of carbonyl compounds showed a poor asymmetric induction. However, when the reaction was performed on *tert*-butylbenzylsulfoxide with Zn^{++}[8] or on naphthylmethylsulfoxide,[12] dinaphtho-1,3-dithiepine-*S*-oxide[13,14] and *trans*-1,3-dithiane-1,3-dioxide[15,16] a good diastereoselectivity has been obtained.

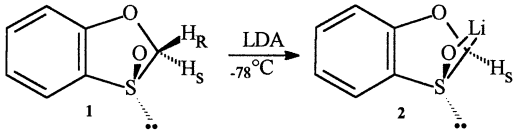
2. Results and discussion

In this paper the reactivity of the sulfinylcarbanion (**2**) obtained from 1,3-benzoxathiole-3-oxide towards electrophiles is described. Its formation is promoted by the acidity and overall by the co-ordination of the metal atom with the oxygen of the sulfoxide group (Scheme 1).[17]

Attempts to obtain **2** by means of alkyllithium reagents gave poor results because opening of the heterocyclic ring by an addition-elimination mechanism occurs together with the expected reaction.[18–19]

Thus LDA was then employed. In order to verify which of the two diastereotopic methylenic hydrogens was preferentially abstracted, the carbanion **2** was reacted with D_2O. The reactivity of the carbanion was tested by employing iodomethane, 4-substituted benzaldehydes and carbon dioxide (Scheme 2).

Identification of the methylenic protons was achieved by ^1H NMR spectroscopy in the presence of $[Eu(hfc)_3]$ as a complexing agent.[20–22] The spectra in $CDCl_3$ showed the signals of the methylenic protons of **1** as doublets (J=11.1 Hz) at 4.94 and 5.45 ppm. The downfield signal corresponds to the proton *cis* to the oxygen of the sulfoxide group as shown by experiments carried out with europium complex (Eu/**1** molar ratio=0.2). In fact, the proton at δ 5.45 ppm is shifted to 7.17 ppm, whereas the other signal



Scheme 1.

☆ Metallation Reactions: Part XXIX

Keywords: cyclic sulfoxide; metallation reactions; stereochemistry; aromatic aldehydes.

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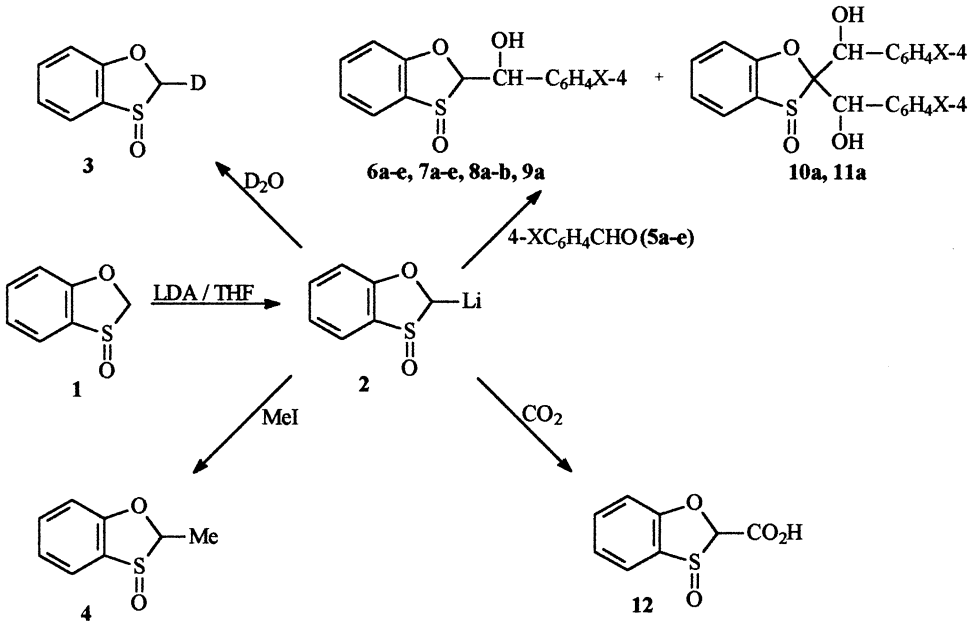


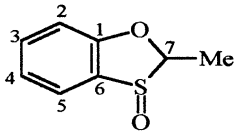
Scheme 2. **a**: X=OMe; **b**: X=Me; **c**: X=H; **d**: X=F; **e**: X=CF_3.

is shifted to a minor extent (see Table 1). By adding D_2O to the carbanionic intermediate compound **3** was obtained which showed the disappearance of the downfield proton. The deuterium exchange was 9:1 with respect to the *trans* proton. The reversal exchange of the deuterated derivative **3** with LDA in THF followed by reaction with H_2O increased the disappearance of the deuterium atom and a retention of configuration mechanism in the lithium–proton exchange has been supported.[7,9,17,23,24]

On the other hand, attack of iodomethane on **2**, produced under the same experimental conditions, occurred opposite to the lithium coordination side giving inversion of configuration.

The configuration of the 2-methyl derivative **4** was also assigned on the basis of the europium complexed proton shift. In ^1H NMR measurements on **4** and the europium complex, the H_7 is more deshielded than H_5 and this fact shows that hydrogen is *cis* with respect to the sulfoxide oxygen atom. This assignment was confirmed using the solvent shift method (Table 1).[25–27]

Table 1. Deshielding and shielding effects on the protons and the methyl group at C-7 and C-5 of compounds **1** and **4** (δ ppm)



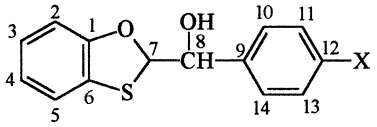
1 (Ss±Rs) $CDCl_3$			[(Eu(hfc)$_3$)/**1**(Ss±Rs)=0.2] $CDCl_3$			**1** C_6D_6		
H_{trans}	H_{cis}	H_5	H_{trans}	H_{cis}	H_5	H_{trans}	H_{cis}	H_5
4.899d	5.416d	7.816d	5.815dd	7.168dd	9.223dd	3.928d	4.889d	7.482d

Δ [(Eu(hfc)$_3$)/**1**(Ss±Rs)=0.2] − [**1**(Ss±Rs)] $CDCl_3$			**1** $\delta CDCl_3$-δC_6D_6		
H_{trans}	H_{cis}	H_5	H_{trans}	H_{cis}	H_5
0.916	1.752	1.406	0.971	0.526	0.334

4(7SSs±7RRs) $CDCl_3$			[Eu(hfc)$_3$/**4**(7SSs±7RRs)=0.2] $CDCl_3$			**4** C_6D_6		
CH_3	H_7	H_5	CH_3	H_7	H_5	CH_3	H_7	H_5
1.474d	5.577q	7.807d	1.973dd	7.364dq	8.703dd	0.782d	5.245q	7.436d

Δ [(Eu(hfc)$_3$)/**4**(7SSs±7RRs)=0.2] − [**4**(7SSs±7RRs)] $CDCl_3$			**4**$\delta CDCl_3$-δC_6D_6		
CH_3	H_7	H_5	CH_3	H_7	H_5
0.499	1.787	0.896	0.693	0.332	0.371

Table 2. ^{1}H and ^{13}C NMR Chemical shift (δ ppm) and coupling constants (J, Hz) of diastereomers **6–9**



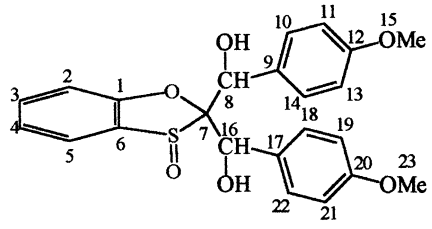
X	H-8		H-7		-OH		C-7
	δ	J	δ	J	δ	J	δ
6 [7R,8S,R_S+7S,8R,S_S]							
a	5.00	5.1	5.71	5.1	6.29	5.1	110.28
b	5.04	5.4	5.75	5.4	6.34	5.4	110.22
c	5.06	5.4	5.76	5.5	6.38	5.4	110.42
d	5.06	5.4	5.76	5.4	6.44	5.4	109.79
e	5.19	5.4	5.86	5.4	6.65	5.4	109.47
7 [7S,8S,S_S+7R,8R,R_S]							
a	5.28	4.5	5.75	4.5	6.18	4.5	109.07
b	5.34	4.2	5.78	4.2	6.20	4.2	108.98
c	5.40	5.4	5.81	5.5	6.26	5.4	110.42
d	5.42	5.4	5.80	5.4	6.30	5.4	108.57
e	5.62	5.4	5.89	5.4	6.41	5.4	108.14

X	H-8			H-7		-OH		C-7
	δ	J H_7-H_{OH}	J H_7-H_8	δ	J	δ	J	δ
8 [7R,8R,S_S+7S,8S,R_S]								
a	5.14	4.8	9.3	5.41	9.3	6.22	4.8	101.36
b	5.16	5.1	9.0	5.42	9.0	6.24	5.1	101.45
9 [7R,8S,S_S+7S,8R,R_S]								
a	5.07	5.1	9.6	5.39	9.6	6.52	5.1	100.74

By reaction of **2** with 4-substituted aromatic aldehydes **5a–e** the products **6a–e**, **7a–e**, **8ab**, **9a** were obtained. In particular from **5a** the structure of the obtained compounds **6a–9a** have been determined on the basis of NMR spectroscopy and by X-ray analysis. The configurations of the C-7 and C-8 stereogenic centres for compounds **6a**, **7a** and **9a** were determined and the assignment of the configuration to **8a** was made by default.

The structures of compounds **6b–e**, **7b–e** and **8b** were assigned by comparison of the NMR spectra with the analogous compounds **6a–8a**. In fact, the chemical shifts, as summarised in Table 2, are quite similar and attributable to an analogous chemical environment. The diastereomers in which the arylhydroxymethylenic groups are *cis* with respect to the sulfoxide oxygen atom show $J(H_7\text{-}H_8)$ coupling constants $\geq$ 9.0, values which are consistent with X-ray structures in which H-7 and H-8 are *anti-peri*-planar.

Table 3. ^{1}H Chemical shifts (δ ppm) of adducts **10a** and **11a**.



adducts	H-8	OH-8	H-16	OH-16
10a	5.21	5.65	5.51	6.26
11a	4.58	5.31	5.83	6.66

The assignment of the stereochemistry of the stereogenic centres of compound **11a** was made by comparing the NMR spectra date with compound **10a**, whose structure was established by X-ray analysis (see Table 3).

In Table 4 the molar fractions of adducts **6–9** obtained from the reaction of **2** with 4substituted benzaldehydes **5a–e** as electrophiles are listed.

In Tables 5 and 6 the solvent and temperature effects on the reaction of **2** with **5a** are summarised.

The diastereomers **6–9** were isolated by fractionate crystallization (see experimental section). The molar fractions (Table 4) were determined by HPLC analysis on the basis of calibration plots. The substituents of the aromatic moiety of aldehydes affected *facial* diastereoselectivity on the methylenic carbon of **1** (α at sulfoxide group) and in particular the electron-withdrawing substituted aldehydes **5d** and **5e** exclusively provided compounds in which the attack of the electrophiles occurred on the opposite side of the oxygen atom of the sulfoxide (**6d–e** and **7d–e**). On the other hand, electron-releasing substituents (particularly OMe) lowered the selectivity producing all diastereomers. The same substituents also reduced affected the diasteroselectivity on the prochiral group of aldehydes.

Independent of the electrophile, increasing solvent polarity scarcely influenced the facial diastereoselectivity on C-α, whilst, in the case of **5a** in the solvent mixture THF/HMPA, the sum of **6a** + **8a** achieved the highest molar fraction (0.85), indicating good attack on the same side of the carbonyl group for both sides of the α-carbanion. Moreover the increased solvent polarity also produced the disubstituted

Table 4. Product distribution for **2** + **5a–e** in THF in the range −72–−80°C

X-Φ-CHO	X	T°C	Molar fraction				Yield
			6	**7**	**8**	**9**	%[a]
5a	4-OMe	−72	0.46	0.34	0.08	0.12	84
		−80	0.45	0.28	0.11	0.16	91
5b	4-Me	−72	0.55	0.41	0.04	–	68
		−80	0.57	0.40	0.03	–	86
5c[b]	H	−72	0.58	0.42	–	–	56
		−80	0.50	0.50	–	–	59
5d[b]	4-F	−72	0.58	0.42	–	–	58
		−80	0.56	0.44	–	–	76
5e[b]	4-CF_3	−72	0.55	0.45	–	–	59
		−80	056	0.54	–	–	65

The LDA/sulfoxide ratio was usually 2.2. When the ratio was 1.2 the yields lowered (5–11%); in these cases unreacted **1** was recovered.
In the mixtures of the **2**+**5c–e** low amounts (5–6%) of bimetallation compounds (double abstraction of C2 protons) were identified.
[a] Determined by HPLC analyses.
[b] Runs carried out in solvent mixtures at higher polarity (THF/HMPA 1:5) showed analogous products distribution.

Table 5. Product distribution for **2** + **5a** in neat THF or in several solvent mixtures in the range −72–80°C

T°C	Solvent of **1**	Solvent of **5a**	10^3 mol/l **1**	LDA/**1**	Molar fraction **6a**	**7a**	**8a**	**9a**	Yield[a] %
−72	THF/HEX 1:2	THF/HEX 1:1	3.25	2.2	0.28	0.41	0.08	0.23	61
−72	THF	THF	3.25	2.2	0.47	0.33	0.08	0.12	84
−80	THF	THF	3.25	2.2	0.46	0.30	0.11	0.13	93
−76	THF	THF	6.49	1.5	0.53	0.20	0.17	0.10	87
−76	THF	THF/HMPA 2:1	3.25	2.2	0.65	0.18	0.12	0.04	98
−76	HMPA	THF	3.25	2.2	0.67	0.10	0.20	0.03	86
−76	THF	HMPA	3.25	2.2	0.67	0.12	0.18	0.03	92
−76	THF+ LiCl satur	THF	3.25	2.2	0.55	0.12	0.11	0.22	87
−76	THF	THF	3.25	2.2	0.35	0.15	0.22	0.13	97[b]
−76	THF	THF	3.25	2.2	0.34	0.11	0.17	0.17	92[c]
−72	THF/HMPA 2:1	THF/HMPA 2:1	3.25	2.2	0.56	0.41	0.02	0.01	48[d]

[a] Determined by HPLC analyses.
[b] Low amounts of electrophile almost simultaneously to sulfoxide were added. The bimetallate compounds **10a**, **11a** (yield 15%) were recovered.
[c] Simultaneous addition of the sulfoxide and the aldehyde. The bimetallate compounds **10a**, **11a** (yield 18%) were recovered.
[d] The yield is low because unreacted sulfoxide was recovered.

Table 6. Product distribution for **2** + **5a** in neat THF or in several solvent mixtures in the range −72−−80°C as sum of the selectivity on the α- and β-carbons

T°C	Solvent of **1**	Solvent of **5a**	10^3 mol/l **1**	LDA/**1**	Molar fraction **6a**+**7a**	**8a**+**9a**	**6a**+**8a**	**7a**+**9a**	Yield %[a]
−72	THF/HEX 1:2	THF/HEX 1:1	3.25	2.2	0.69	0.31	0.36	0.64	61.6
−72	THF	THF	3.25	2.2	0.80	0.20	0.55	0.45	84.3
−80	THF	THF	3.25	2.2	0.76	0.24	0.57	0.43	93.4
−76	THF	THF	6.49	1.5	0.73	0.27	0.70	0.30	87.6
−76	THF	THF/HMPA 2:1	3.25	2.2	0.83	0.17	0.78	0.22	98.2
−76	HMPA	THF	3.25	2.2	0.77	0.23	0.87	0.13	86.7
−76	THF	HMPA	3.25	2.2	0.79	0.21	0.85	0.15	92.8
−76	THF+LiCl satur	THF	3.25	2.2	0.67	0.33	0.66	0.34	87.5
−76	THF	THF	3.25	2.2	0.50	0.50	0.57	0.43	97.6[b]
−76	THF	THF	3.25	2.2	0.45	0.55	0.51	0.49	92.2[c]
−72	THF/HMPA 2:1	THF/HMPA 2:1	3.25	2.2	0.97	0.03	0.58	0.42	48.9[d]

[a] Determined by HPLC analyses.
[b] Low amounts of electrophile almost simultaneously to sulfoxide were added. The bimetallate compounds **10a**, **11a** (yield 15%) were recovered.
[c] Simultaneous addition of the sulfoxide and the aldehyde. The bimetallated compounds **10a**, **11a** (yield 18%) were recovered.
[d] The yield is low because unreacted sulfoxide was recovered.

products. Particularly using **5a**, compounds **10a** and **11a** were obtained and their formation was increased from 5% to 15% when the sulfoxide and the aldehyde were added simultaneously to the LDA solution. When **1** and **5d** or **5e** were added simultaneously to LDA solution neither mono- nor disubstituted compound was formed. The selectivity of **9a** increased when the reaction was carried out in THF-LiCl saturated solution (see Table 5).

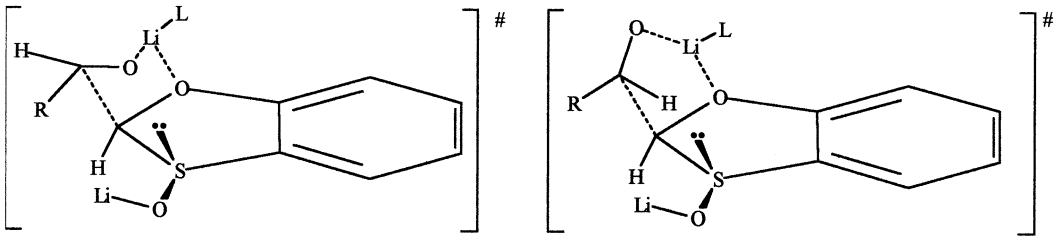
On the basis of the literature reports on open chain or conformationally flexible cyclic sulfoxides,[8,12,17,28,29] reaction **2** with 4-substituted benzaldehydes, adducts rising from the attack on the same side of oxygen atom of SO group would been expected. The cited literature reports indicate that the stereoselectivity on the α carbon and on the C=O group is ruled under kinetic control. The reactions of **2** with **5c–e** provided exclusive attack on the opposite side of the SO group, while with the electrophiles **5a–b** adducts arising from both types of attack were produced (see Table 4). In all cases the majority of attack is opposite to the SO group.

When attack occurs on the opposite side, coordination of the carbonyl oxygen with the lithium cation is not geometrically available and adducts prevalently arise from direct interaction of **2** with the C=O group.

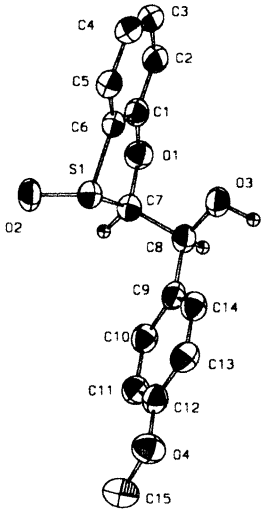
Experiments on the adducts stability carried out under the same metallation conditions had not pointed out any product interconversion and in the case of **5a** the adducts distribution, at various reaction conversions, remained substantially unchanged. It is likely enough that amongst the hypothetical transition states producing the adducts **6a** and **7a** there are some involving the interaction of the lithium cation with the benzoxathiole and aldehyde oxygen atoms (Scheme 3).

Finally, it can be pointed out that notwithstanding the reaction stereoselectivity is not high the stereoisomer **6a** has been isolated as pure at 95–96% by treatment of the reaction mixture with diethyl ether, in which the other diastereoisomers are soluble.

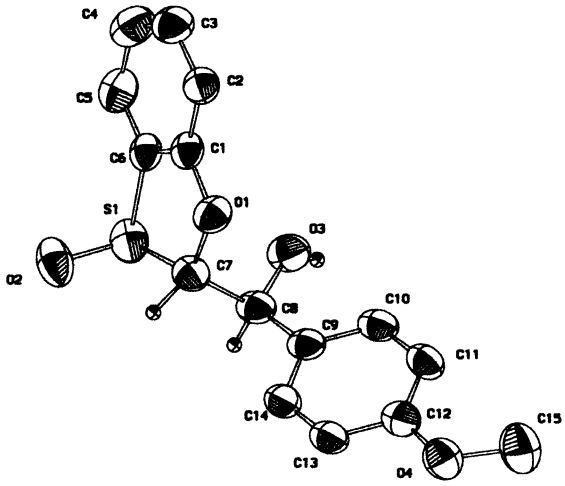
The stereochemical assignment to the carboxylic acid **12**, obtained by reaction with carbon dioxide, was made on the basis both of the ^{1}H NMR (OH signal undetectable) and IR spectroscopy (very broad signal for OH) meaning a strong intramolecular hydrogen bond with the sulfoxide oxygen atom.



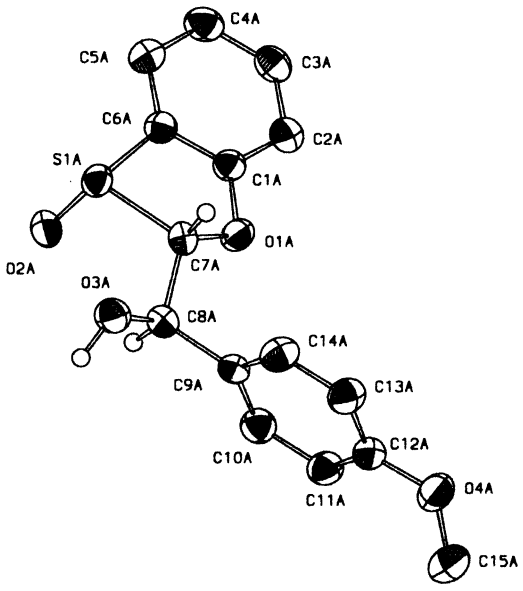
Scheme 3. T.S.



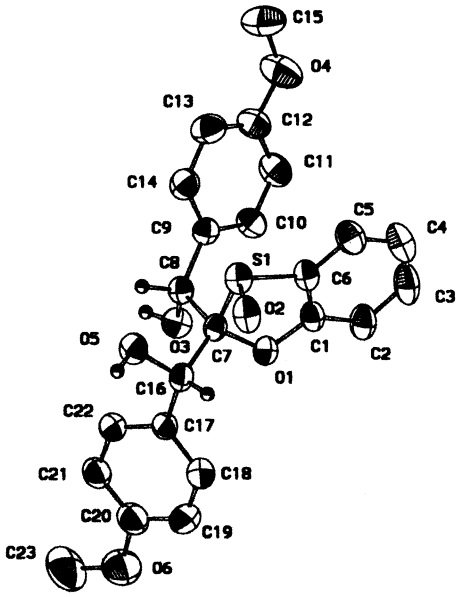
6a 7R, 8S, RS



7a 7S, 8S, SS



9a 7S, 8R, RS



10a 7s, 8R, 16S, SS

Figure 1. X-ray structures of compounds **6a**,**7a**, **9a**, **10a**.

3. Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer with tetramethylsilane as internal reference; δ values are given in ppm and J values in Hz. MS spectra were recorded at 70 eV with a Hewlett–Packard 5989A MS spectrometer using the direct insertion probe (DIP) method. IR spectra were recorded with a Nicolet FT-IR 210 spectrophotometer. Microanalyses were carried out on a Carlo Erba model 1106 Elemental Analyzer. Analytical TLC plates and silica gel (230–400 mesh) were purchased from Merck. Flash chromatographies were performed on silica gel 60, 0.04–0.063 mm (Fluka). Melting points were determined with a Kofler hot stage microscope and are uncorrected.

In order to determine yields and the molar fractions HPLC analyses were performed by Waters 600 HPLC instrument employing a Spherisorb-CN normal phase column of 250 mm length and 4.6 mm i.d., hexane/isopropanol (75:25) as eluant (1 mL/min). The UV detector was positioned at λ_{max}. All determinations were carried out on the basis of calibration plots on the pure compounds.

3.1. Materials

Reagents grade reagents and solvents were used. All the reagents were purchased from Aldrich Chemical Co. Solutions of butillithium in hexane were purchased from Aldrich Chemical Co. and were analyzed by the Gilman double titration method.[30] Solutions of LDA in tetrahydrofuran were prepared by literature methods.[31] All solvents were dried and purified using standard techniques. Petroleum ether (bp 40–70°C) was used for chromatography.

3.2. X-Ray structures determination[†]

X-ray crystal structures of the substituted benzaldehyde adducts **6a**, **7a**, **9a** and **10a** were obtained and are shown in Fig. 1.

The stereochemistry at the chiral atoms of the adducts obtained by the crystals structure determinations are referred at one of the enantiomers. Of course, the space groups all being centrosymmetric, the configurations of the other enantiomers are also present.

3.2.1. (±)1,3-Benzoxathiole-3(2*H*)-oxide (1). To a vigorously stirred solution of 1,3-benzoxathiole[32] (10 g, 72 mmol) and dichloromethane (80 mL) 3-chloroperbenzoic acid (15 g, 75 mmol) was gradually added at −10°C. After the addition was complete, the reaction mixture was stirred at room temperature overnight. The 3-chlorobenzoic acid was filtered and the organic layer was washed with 10% aqueous sodium bicarbonate, water and dried (Na_2SO_4). After evaporation of the solvent in vacuo, the sulfoxide was crystallized from 1:1 THF/hexane. White crystals, yield 60%, mp 103–104°C. IR (nujol, cm^{-1}): 1586, 1305, 1274, 1125, 1039, 998; ^{1}H NMR ($CDCl_3$): δ 4.84 (d, 1H, H_7 (*trans*), J=11.1), 5.34 (d, 1H, H_7 (*cis*), J=11.1), 7.05 (t, 1H, H_4, J=7.8), 7.09 (d, 1H, H_2, J=7.8), 7.43 (t, 1H, H_3, J=7.8), 7.75 (d, 1H, H_5, J=7.8). ^{13}C NMR ($CDCl_3$): δ 90.50 (t, C_2), 112.83 (d, C_9), 122.60 (d, C_7), 126.88 (d, C_6), 129.27 (d, C_5), 134.56 (s, C_8), 159.39 (s, C_4). EI-MS, *m/z*: 154 (37%, M^+), 138 (4%, M^+-O), 137 (9%, M^+-OH), 124 (43%, M^+-CH_2O), 109 (7%, $C_6H_4SH^+$), 96 (100%, $C_5H_4S^+$), 95 (8%, $C_5H_3S^+$), 70 (17.5%, $C_3H_3S^+$). Anal. calcd for $C_7H_6O_2S$: C, 54.53; H, 3.92; S, 20.79. Found: C, 54.93; H, 4.01; S, 20.52.

3.2.2. General Method for the Condensation between 2-Lithiated 1,3-Benzoxathiole-3(2*H*)-oxide and Electrophiles. To a stirred solution of LDA (8.7 mmol) in dry THF (15 mL) cooled at −78°C, a solution of **1** (3.47 mmol) in dry THF (12 mL) was added dropwise. After stirring for 10 min at the same temperature, a solution of the electrophile (namely D_2O or MeI or 4-substituted benzaldehydes) (5.0 mmol) in dry THF (6 mL) was added. The stirring was continued for further 15 min and the reaction was quenched at −78°C with aqueous saturated NH_4Cl, extracted with diethyl ether, and dried (Na_2SO_4), filtered and the solvent removed in vacuo.

When D_2O was employed as electrophile, the reaction mixture was worked up in the same manner above described and analyzed by GC–MS. By means of *m/z* 154 and *m/z* 155 peaks intensity the percentage of the deuterated compounds was determined as 63%. Moreover by ^{1}H NMR analysis the diastereomers ratio was determined on the basis of the intensity of the methylenic protons signals (*cis/trans*=9/1).

By addition of diethyl ether to the crude reaction mixtures obtained by using 4-substituted benzaldehydes the crystalline compounds (one or more) were isolated and then identified. When mixtures of less soluble adducts have been obtained a further separation was carried out by flash-chromatography on a Merck silica gel 43–60 μm, eluting with diethyl ether/petroleum ether. Analogous separations have been performed to obtain the remaining compounds from the mother liquids.

When the carbon dioxide was employed as electrophile, the metallated mixture of **1** was poured into ca. 100 g of crushed solid CO_2. After 12 h the residue was treated with 10% aqueous sodium bicarbonate and then with diethyl ether. The alkali layer was separated, washed with diethyl ether, and then acidified with cold concentrated hydrochloric acid, extracted with diethyl ether, dried (Na_2SO_4), and concentrated.

In order to increase the reactions diastereoselectivity different temperatures and solvent mixtures were used. Solvents, yields and molar fractions of the diastereomers from the reactions with **5a–e** were summarised in the Tables 4–6.

When the reactions were performed by adding an equimolar amount of **5a** and **1** onto the LDA, the **10a** and **11a** (total yield 18%) were also obtained.

In this manner the following compounds, as racemic mixture, were isolated and characterized:

[†] Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB IEZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers CCDC 171400–171403.

3.2.3. (2*R*,R_S+2*S*,S_S)-2-Methyl-1,3-benzoxathiole-3(2*H*)-oxide (4). Yellow liquid, yield 66%; flash-chromatography (3:7 diethyl ether/petroleum ether); n_D^{17}=1.576, IR (nujol, cm^{-1}): 1587, 1308, 1281, 1119, 1042, 1000; ^1H NMR ($CDCl_3$): δ 1.47 (d, 3H, CH_3 *J*=6.6), 5.58 (q, 1H, H_7, *J*=6.6), 7.10 (t, 1H, H_4, *J*=8.1), 7.12 (d, 1H, H_2, *J*=8.1), 7.50 (t, 1H, H_3, *J*=8.1), 7.81 (d, 1H, H_5, *J*=8.1). ^{13}C NMR ($CDCl_3$): δ: 15.61 (q, *C*H_3), 101.15 (d, C_7), 113.50 (d, C_2), δ 122.67 (d, C_4), 127.86 (d, C_5), 129.56 (d, C_6), 134.91 (s, C_3), 159.71 (s, C_1). EIMS, *m/z*: 168 (26%, M^+), 152 (2.5%, M^+-O), 137 (11%, M^+-O-CH_3), 126 (16%, $C_6H_4OHSH^+$), 124 (32%, M^+-CH_2O), 109 (2%, $C_6H_4SH^+$), 96 (100%, $C_5H_4S^+$), 95 (10%, $C_5H_3S^+$), 70 (23%, $C_3H_3S^+$), Anal. calcd for $C_8H_8O_2S$: C, 57.14; H, 4.79; S, 19.06. Found: C, 57.49; H, 4.70; S, 18.82.

3.2.4. (2*R*,R_S)-2-[(1*S*)-1-Hydroxy-1-(4-methoxyphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (6a). This product was isolated by fractionated precipitation with diethyl ether; white crystals mp 202–203°C; IR (nujol, cm^{-1}): 3358 (OH),1607, 1582, 1510, 11240, 1100, 1027, 1016, 1005; ^1H NMR (DMSO-d_6): δ 3.89 (s, 3H, OCH_3), 5.00 (t, 1H, H_8, *J*=5.1), 5.71 (d, 1H, H_7, *J*=5.1), 6.29 (d, 1H, OH, *J*=5.1), 7.08 (d, 2H, H_{11}-H_{13}, *J*=8.4), 7.29 (t, 1H, H_4, *J*=8.4), 7.35 (d, 1H, H_2, *J*=8.4), 7.54 (d, 2H, H_{10}-H_{14}, *J*=8.4), 7.74 (t, 1H, H_3, *J*=8.4), 8.06 (d, 1H, H_5, *J*=8.4); ^{13}C NMR (DMSO-d_6): δ 55.21 (q, O*C*H_3), 70.68 (d, C_8), 110.27 (d, C_7), 112.83 (d, C_2), 113.83 (d, C_{11}-C_{13}), 122.59 (d, C_4), 127.67 (d, C_5), 128.18 (d, C_{10}-C_{14}), 129.20 (s, C_6), 131.86 (s, C_9), 134.88 (d, C_3), 159.12 (s, C_{12}), 160.51 (s, C_1). EI-MS, DIP, *m/z*: 290 (0.3%, M^+), 274 (0.7%, M^+-O), 273 (2%, M^+-OH), 272 (2.5%, M^+-H_2O), 244 (1.5%, M^+-H_2O-CO), 243 (3%, M^+-H_2O-CO-H), 150 (42%, $CH_3OC_6H_4COHCH_2^+$), 149 (99% $CH_2OC_6H_4$-$COHCH_2^+$), 138 (19%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 135 (45%, $CH_3OC_6H_4CO^+$,), 121 (65%, $CH_3OC_6H_4CH_2^+$), 109 (24%, $C_6H_4SH^+$), 107 (10%, $CH_3OC_6H_4^+$), 94 (18%, C_6H_5OH), 92 (9%, C_6H_4O), 77 (47%, $C_6H_5^+$), 65 (19%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86; S, 11.04. Found: C, 61.70; H, 4.98; S, 10.79.

3.2.5. (2*S*,S_S)-2-[(1*S*)-1-Hydroxy-1-(4-methoxyphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (7a). Flash-chromatography (4:1 diethyl ether/petroleum ether); white crystals mp 121–122°C. IR (nujol, cm^{-1}): 3340 (OH) 1608, 1585, 1511, 1243, 1102, 1030, 1008; ^1H NMR (DMSO-d_6): δ 3.82 (s, 3H, OCH_3), 5.28 (t, 1H, H_8, *J*=4.5), 5.74 (d, 1H, H_7, *J*=4.5), 6.18 (d, 1H, OH, *J*=4.5), 6.96 (d, 2H, H_{11}-H_{13}, *J*=8.7), 7.22 (t, 1H, H_4, *J*=8.1), 7.30 (d, 1H, H_2, *J*=8.1), 7.45 (d, 2H, H_{10}-H_{14}, *J*=8.7), 7.66 (t, 1H, H_3, *J*=8.1), 7.96 (d, 1H, H_5, *J*=8.1). ^{13}C NMR (DMSO-d_6): δ: 55.21 (q, OCH_3), 70.80 (d, C_8), 109.07 (d, C_7), 112.68 (d, C_2), 113.44 (d, C_{11}-C_{13}), 122.37 (d, C_4), 127.38 (d, C_5), 128.79 (d, C_{10}-C_{14}), 129.42 (s, C_6), 131.72 (s, C_9), 134.73 (d, C_8), 159.71 (s, C_{12}), 160.92 (s, C_1). EI-MS, DIP, *m/z*: 290 (1%, M^+), 274 (2%, M^+-O), 273 (3%, M^+-OH), 272 (6%, M^+-H_2O), 244 (2.5%, M^+-H_2O-CO), 243 (6.5%, M^+-H_2O-CO-H), 150 (39%, $CH_3OC_6H_4COHCH_2^+$), 149 (89.5%, $CH_2OC_6H_4COHCH_2^+$), 138 (27%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 135 (57%, $CH_3OC_6H_4CO^+$), 121 (62%, $CH_3OC_6H_4CH_2^+$), 109 (31%, $C_6H_4SH^+$), 107 (14%, $CH_3OC_6H_4^+$), 92 (16%, $C_6H_4O^+$.), 77 (60%, $C_6H_5^+$), 65 (30%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86; S, 11.04. Found: C, 61.85; H, 4.89; S, 10.99.

3.2.6. (2*R*,S_S)-2-[(1*R*)-1-Hydroxy-1-(4-methoxyphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (8a). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 159–160°C. IR (nujol, cm^{-1}): 3339 (OH),1610, 1585, 1511, 1235, 1064, 1052, 1027, 1013; ^1H NMR (DMSO-d_6): δ 3.90 (s, 3H, OCH_3), 5.14 (dd, 1H, H_8, *J*=4.8, *J*=9.3), 5.41 (d, 1H, H_7, *J*=9.3), 6.22 (d, 1H, OH, *J*=4.8), 7.10 (d, 2H, H_{11}-H_{13}, *J*=8.7), 7.32 (t, 1H, H_4, *J*=7.8), 7.47 (d, 1H, H_2, *J*=7.8), 7.60 (d, 2H, H_{10}-H_{14}, *J*=8.7), 7.76 (t, 1H, H_3, *J*=7.8), 8.06 (d, 1H, H_5, *J*=7.8). ^{13}C NMR (DMSO-d_6): δ55.27 (q, O*C*H_3),68.97 (d, C_8), 101.36 (d, C_7), 113.20 (d, C_2), 113.82 (d, C_{11}-C_{13}), 123.04 (d, C_4), 127.89 (d, C_5), 129.05 (d, C_{10}-C_{14}), 130.90 (s, C_6), 132.20 (s, C_9) 135.08 (d, C_8), 159.47 (s, C_{12}), 159.98 (s, C_1). EI-MS, DIP, *m/z*: 290 (11%, M^+), 274 (3%, M^+-O), 273 (9%, M^+-OH), 272 (8%, M^+-H_2O), 244 (1%, M^+-H_2O-CO), 243 (2.5%, M^+-H_2O-CO-H), 150 (17%, $CH_3OC_6H_4$-$COHCH_2^+$), 149 (14%, $CH_2OC_6H_4COHCH_2^+$), 138 (14%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 135 (43%, $CH_3OC_6H_4CO^+$), 121 (23.5%, $CH_3OC_6H_4CH_2^+$), 109 (15%, $C_6H_4SH^+$), 107 (9%, $CH_3OC_6H_4^+$), 92 (9%, $C_6H_4O^+$), 77 (29%, $C_6H_5^+$), 65 (14%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86; S, 11.04. Found: C, 62.10; H, 4.85; S, 11.01.

3.2.7. (2*S*,R_S)-2-[(1*R*)-1-Hydroxy-1-(4-methoxyphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (9a). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 186–188°C. IR (nujol, cm^{-1}): 3308 (OH) 1610, 1587, 1512, 1247, 1066, 1025, 1002; ^1H NMR (DMSO-d_6): δ 3.92 (s, 3H, OCH_3), 5.07(dd, 1H, H_8, *J*=5.1, *J*=9.6), 5.39 (d, 1H, H_7, *J*=9.6), 6.52 (d, 1H, OH, *J*=5.1), 7.10 (d, 2H, H_{11}-H_{13}, *J*=8.7), 7.26 (d, 1H, H_4, *J*=8.1), 7.32 (t, 1H, H_2, *J*=8.1), 7.68 (d, 2H, H_{10}-H_{14}, *J*=8.7), 7.68 (t, 1H, H_3, *J*=8.1), 8.17 (d, 1H, H_5, *J*=8.1). ^{13}C NMR (DMSO-d_6): δ 55.26 (q, O*C*H_3), 66.85 (d, C_8), 100.74 (d, C_7), 113.20 (d, C_2), 113.87 (d, C_{11}-C_{13}), 123.10 (d, C_4), 128.136 (d, C_5), 129.07 (d, C_{10}-C_{14}), 130.86 (s, C_6), 132.85 (s, C_9) 134.87 (d, C_3), 159.34 (s, C_{12}), 159.89 (s, C_1). EI-MS, DIP, *m/z*: 290 (3%, M^+), 274 (1%, M^+-O), 273 (4%,M^+-OH), 272 (5.5%, M^+-H_2O), 244 (1%, M^+-H_2O-CO,), 243 (2%, M^+-H_2O-CO-H), 150 (12.5%, $CH_3OC_6H_4COHCH_2^+$), 149 (12%, $CH_2OC_6H_4COHCH_2^+$), 138 (17%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 135 (43%, $CH_3OC_6H_4CO^+$), 121 (19%, $CH_3OC_6H_4CH_2^+$), 109 (16%, $C_6H_4SH^+$), 107 (9%, $CH_3OC_6H_4^+$), 92 (11.5%, $C_6H_4O^+$), 77 (34%, $C_6H_5^+$), 65 (19%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86; S, 10.95.

3.2.8. (2*R*,R_S)-2-[(1*S*)-1-Hydroxy-1-(4-methylphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (6b). Flash-chromatography (7:3 diethyl ether/petroleum ether), white crystals mp 200–202°C. IR (nujol, cm^{-1}): 3339 (OH), 1587, 1268, 1224, 1127, 1098, 1026, 1008; ^1H NMR (DMSO-d_6): δ 2.45 (s, 3H, CH_3), 5.04 (t, 1H, H_8, *J*=5.4), 5.74 (d, 1H, H_7, *J*=5.4), 6.34 (d, 1H, OH, *J*=5.4), 7.30 (t, 1H, H_4, *J*=8.4), 7.35 (d, 2H, H_{11}-H_{13}, *J*=8.1), 7.36 (d, 1H, H_2, *J*=8.4), 7.53 (d, 2H, H_{10}-H_{14}, *J*=8.1), 7.72 (t, 1H, H_3,

J=8.4), 8.08 (d, 1H, H_5, J=8.4). ^{13}C NMR (DMSO-d_6): δ 20.88 (q, CH_3), 70.88 (d, C_8), 110.22 (d, C_7), 112.78 (d, C_2), 122.55 (d, C_4) 126.82 (d, C_{11}-C_{13}), 127.66 (d, C_5), 128.98 (d, C_{10}-C_{14}), 129.23 (s, C_6), 134.81 (d, C_3), 136.70 (s, C_{12}), 137.26 (s, C_9), 160.48 (s, C_1). EI-MS, DIP, *m/z*: 274 (3%, M^+), 258 (1%, M^+-O), 257 (3%, M^+-OH), 256 (2%, M^+-H_2O), 228 (1%, M^+-H_2O-CO), 227 (3%, M^+-H_2O-CO-H), 226 (2%, M^+-SO), 149 (2%, $CH_3C_6H_4COHCHO^+$), 138 (18%, $C_6H_4OSCH_2^+$), 137 (68%, $C_6H_4OSCH^+$), 134 (50%, $CH_3C_6H_4COHCH_2^+$), 133 (93%, $CH_2C_6H_4COHCH_2^+$), 126 (11%, $C_6H_4OHSH^+$), 125 (8%, $C_6H_4OHS^+$), 121 (36% $CH_3C_6H_4CHOH^+$), 119 (45%, $CH_2C_6H_4COH^+$), 109 (9.5%, $C_6H_4SH^+$), 105 (100%, $CH_3C_6H_4CH_2^+$), 96 (17%, $C_5H_4S^+$), 93 (31%, $C_6H_5O^+$), 91 (58%, $CH_3C_6H_4^+$), 77 (46%, $C_6H_5^+$), 65 (37%, $C_5H_5^+$), Anal. calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.55; H, 4.92; S, 11.52

3.2.9. (2*S*,S_S)-2-[(1*S*)-1-Hydroxy-1-(4-methylphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (7b). Flash-chromatography (7:3 diethyl ether/petroleum ether), white crystals mp 175–177°C. IR (nujol, cm^{-1}): 3321(OH), 1585, 1264, 1224, 1137, 1092, 1015; ^{1}H NMR (DMSO-d_6): δ 2.37 (s, 3H, CH_3), 5.34 (t, 1H, H_8, J=4.2), 5.78 (d, 1H, H_7, J=4.2), 6.20 (d, 1H, OH, J=4.2), 7.23 (d, 2H, H_{11}-H_{13}, J=8.1), 7.29 (t, 1H, H_4, J=7.5), 7.33 (d, 1H, H_2, J=7.5), 7.44 (d, 2H, H_{10}-H_{14}, J=8.1), 7.66 (t, 1H, H_3, J=7.5), 7.97 (d, 1H, H_5, J=7.5). ^{13}C NMR (DMSO-d_6): δ 20.89 (q, CH_3), 70.88 (d, C_{11}), 108.98 (d, C_7), 112.61 (d, C_2), 122.29(d, C_4) 126.81 (d, C_{11}-C_{13}), 127.33 (d, C_5), 128.57 (d, C_{10}-C_{14}), 129.43 (s, C_6), 134.65 (d, C_3), 136.78 (s, C_{12}), 136.93 (s, C_9), 160.81 (s, C_1). EI-MS, DIP, *m/z*: 274 (2%, M^+), 258 (1%, M^+-O), 257 (3%, M^+-OH,), 256 (2%, M^+-H_2O), 228 (1.5%, M^+-H_2O-CO), 227 (3%, M^+-H_2O-CO-H), 226 (2%, M^+-SO), 149 (2%,$CH_3C_6H_4COHCHO^+$), 138 (19%, $C_6H_4OSCH_2^+$), 137 (72.5%, $C_6H_4OSCH^+$), 134 (55%, $CH_3C_6H_4COHCH_2^+$), 133 (89.5%, $CH_2C_6H_4COHCH_2^+$), 126 (12%, $C_6H_4OHSH^+$), 125 (7%, $C_6H_4OHS^+$), 121 (40%, $CH_3C_6H_4CHOH^+$), 119 (47%, $CH_2C_6H_4COH^+$), 109 (10.5%, $C_6H_4SH^+$), 105 (100%, $CH_3C_6H_4CH_2^+$), 96 (13%, $C_5H_4S^+$), 93 (35%, $C_6H_5O^+$), 91 (55%, $CH_3C_6H_4^+$), 77 (43%, $C_6H_5^+$), 65 (36%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.49; H, 5.06; S, 11.75

3.2.10. (2*R*,S_S)-2-[(1*R*)-1-Hydroxy-1-(4-methylphenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (8b). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 160–162°C. IR (nujol, cm^{-1}): 3319 (OH), 1592, 1272, 1235, 1130, 1100, 1015, 1002. ^{1}H NMR (DMSO-d_6): δ 2.46 (s, 3H, CH_3), 5.16 (dd, 1H, H_8, J=5.1, J=9.0), 5.42 (d, 1H, H_7, J=9.0), 6.24 (d, 1H, OH, J=5.1), 7.33 (t, 1H, H_4, J=8.1), 7.35 (d, 2H, H_{11}-H_{13}, J=8.1), 7.48 (d, 1H, H_2, J=8.1), 7.57 (d, 2H, H_{10}-H_{14}, J=8.1), 7.77 (t, 1H, H_3, J=8.1), 8.07 (d, 1H, H_5, J=8.1). ^{13}C NMR (DMSO-d_6): δ 20.78 (q, CH_3), 70.05 (d, C_8), 101.45 (d, C_7), 112.54 (d, C_2), 122.24 (d, C_4) 126.86 (d, C_{11}-C_{13}), 127.64 (d, C_5), 128.93 (d, C_{10}-C_{14}), 129.63 (s, C_6), 134.95 (d, C_3), 136.35 (s, C_{12}), 137.02 (s, C_9), 160.26 (s, C_1). EI-MS,DIP, *m/z*: 274 (7%, M^+), 258 (2%, M^+-O), 257 (4.5%, M^+-OH,), 256 (2%, M^+-H_2O,), 228 (1.5%, M^+-H_2O-CO,), 227 (4%, M^+-H_2O-CO-H), 226 (3%, M^+-SO), 149 (3%, $CH_3C_6H_4COHCHO^+$), 138 (20%, $C_6H_4OSCH_2^+$), 137 (70%, $C_6H_4OSCH^+$), 134 (48%, $CH_3C_6H_4COHCH_2^+$), 133 (90.5%, $CH_2C_6H_4COHCH_2^+$), 126 (12.5%, $C_6H_4OHSH^+$), 125 (9%, $C_6H_4OHS^+$), 121 (37.5%, $CH_3C_6H_4CHOH^+$), 119 (45%, $CH_2C_6H_4COH^+$), 109 (9%, $C_6H_4SH^+$), 105 (100%, $CH_3C_6H_4CH_2^+$), 96 (13%, $C_5H_4S^+$), 93 (30.5%, $C_6H_5O^+$), 91 (57%, $CH_3C_6H_4^+$), 77 (46%, $C_6H_5^+$), 65 (39%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.65; H, 5.09; S, 11.64

3.2.11. (2*R*,R_S)-2-[(1*S*)-1-Hydroxy-1-(phenyl)methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (6c). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 175–177°C. IR (nujol, cm^{-1}): 3385 (OH), 1587, 1273, 1221, 1127, 1102, 1027, 1016; ^{1}H NMR (DMSO-d_6): δ 5.06 (t, 1H, H_8, J=5.4), 5.76 (d, 1H, H_7, J=5.5), 6.38 (d, 1H, OH, J=5.4), 7.30 (t, 1H, H_4, J=8.1), 7.36 (d, 1H, H_2, J=8.1), 7.48 (t, 1H, H_{12}, J=7.2), 7.53 (t, 2H, H_{11}-H_{13}, J=7.2), 7.63 (d, 2H, H_{10}-H_{14}, J=7.2), 7.72 (t, 1H, H_3, J=8.1), 8.07 (d, 1H, H_5, J=8.1). ^{13}C NMR (DMSO-d_6): δ 71.44 (d, C_8), 110.42 (d, C_7), 113.29 (d, C_2), 123.24 (d, C_4), 127.29 (dm, C_{11}-C_{13}), 128.07 (d, C_5), 128.71 (s, C_{12}), 128.99 (d, C_{10}-C_{14}), 129.14 (s, C_6), 135.61 (d, C_3), 139.73 (s, C_9) 160.95 (s, C_1). EI-MS, DIP, *m/z*: 260 (8%, M^+), 244 (2%, M^+-O), 243 (7%, M^+-OH), 242 (11%, M^+-H_2O), 214 (3%, M^+-H_2O-CO), 213 (6.5%, M^+-H_2O-CO-H,), 212 (9%, M^+-SO), 154 (5%, $C_6H_4OSOCH_2^+$), 150 (8%, $C_6H_5CHCSO^+$), 149 (26.5%, $C_6H_5C_2CSO^+$), 141 (28%, $C_6H_4SO_2H^+$), 138 (23%, $C_6H_4OSCH_2^+$), 137 (93%, $C_6H_4OSCH^+$), 126 (22%, $C_6H_4SHOH^+$), 125 (15%, $C_6H_4SOH^+$), 121 (19%, $C_6H_4SCH^+$), 120 (51%, $C_6H_5C_2H_2OH^+$), 119 (43%, $C_6H_5C_2HOH^+$) 109 (15%, $C_6H_4SH^+$), 107 (27%, $C_6H_5CHOH^+$), 105 (59%, $C_6H_5CO^+$), 96 (22%, $C_5H_4S^+$), 92 (13%, $C_7H_8^+$), 91 (100%, $C_7H_7^+$), 79 (33%, $C_6H_7^+$), 77 (63.5%, $C_6H_5^+$), 65 (32%, $C_5H_5^+$), 51 (28%, $C_4H_3^+$). Anal. calcd for $C_{14}H_{12}O_3S$: C, 64.60; H, 4.65; S, 12.32. Found: C, 64.37; H, 4.49; S, 12.01.

3.2.12. (2*S*,S_S)-2-[(1*S*)-1-Hydroxy-1-(phenyl)methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (7c). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 158–160°C. IR (nujol, cm^{-1}): 3352 (OH) 1591, 1271, 1066, 1053, 1000; ^{1}H NMR (DMSO-d_6): δ 5.40 (t, 1H, H_8, J=3.9), 5.81 (d, 1H, H_7, J=3.9), 6.48 (d, 1H, OH, J=3.9), 7.21 (t, 1H, H_4, J=7.5), 7.30 (d, 1H, H_2, J=7.5), 7.37 (t, 1H, H_{12}, J=7.8), 7.40 (t, 2H, H_{11}-H_{13}, J=7.2), 7.54 (d, 2H, H_{10}-H_{14}, J=7.8), 7.65 (t, 1H, H_3, J=7.5), 7.96 (d, 1H, H_5, J=7.5). ^{13}C NMR (DMSO-d_6): δ 71.16 (d, C_8), 108.79 (d, C_7), 112.57 (d, C_2), 122.29 (d, C_4), 126.80 (dm, C_{11}-C_{13}), 127.25 (d, C_5), 127.78 (s, C_{12}), 127.95 (d, C_{10}-C_{14}), 129.41 (s, C_6), 134.63 (d, C_3), 139.66 (s, C_9), 160.79 (s, C_1). EI-MS, DIP, *m/z*: 260 (9%, M^+), 244 (2%, M^+-O), 243 (6%, M^+-OH), 242 (11%, M^+-H_2O), 214 (3%, M^+-H_2O-CO), 213 (6%, M^+-H_2O-CO-H), 212 (8%, M^+-SO), 154 (93%, $C_6H_4OSOCH_2^+$), 149 (20%, $C_6H_5C_2CSO^+$), 141 (26%, $C_6H_4SO_2H^+$), 138 (20%, $C_6H_4OSCH_2^+$), 137 (74.5%, $C_6H_4OSCH^+$), 126 (21.5%, $C_6H_4SHOH^+$), 125 (14%, $C_6H_4SOH^+$), 121 (7%, $C_6H_4SCH^+$), 120 (47%, $C_6H_5C_2H_2OH^+$), 119 (39%, C_6H_5-C_2HOH^+), 109 (11%, $C_6H_4SH^+$), 107 (25%, $C_6H_5CHOH^+$), 105 (56%, C_6H_5CO), 97 (16%, $C_5H_5S^+$), 96 (31%, $C_5H_4S^+$), 92 (13%, $C_7H_8^+$), 91 (100%, $C_7H_7^+$), 79 (34%, $C_6H_7^+$), 77 (60%, $C_6H_5^+$), 65 (33%, $C_5H_5^+$), 51 (30%, $C_4H_3^+$). Anal. calcd for $C_{14}H_{12}O_3S$: C, 64.60; H, 4.65; S, 12.32. Found:C, 64.58; H, 4.57; S, 12.25.

3.2.13. (2*R*,R_S)-2-[(1*S*)-1-Hydroxy-1-(4-fluorophenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (6d). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 191–193°C. IR (nujol, cm^{-1}): 3339 (OH),1601, 1589, 1507, 1270, 1209, 1113, 1031, 1010; ^{1}H NMR (DMSO-d_6), δ: 5.01 (t, 1H, H_8, J=5.4), 5.76 (d, 1H, H_7, J=5.4), 6.44 (d, 1H, OH, J=5.4), 7.30 (t, 1H, H_4, J=7.8), 7.35 (t, 2H, H_{11}-H_{13}, J=8.2), 7.35 (d, 1H, H_2, J=7.8) 7.66 (t, 2H, H_{10}-H_{14}, J=8.2), 7.72 (t, 1H, H_3, J=7.8), 8.07 (d, 1H, H_5, J=7.8). ^{13}C NMR (DMSO-d_6), δ: 70.27 (d, C_8), 109.79 (d, C_7), 112.82 (d, C_2), 115.17 (dd, C_{11}-C_{13}, $^2J_{HF=}$21.2), 122.62 (d, C_4), 127.69 (d, C_5), 129.00 (dm, C_{10}-C_{14}, $^3J_{HF=}$8.47), 129.06 (s, C_6), 134.88 (d, C_3), 135.88 (d, C_9, $^4J_{HF=}$3.1), 160.41 (s, C_1), 161.89 (d, C_{12}, $^1J_{HF=}$242.2). EI-MS, DIP, *m/z*: 278 (1%, M^+), 262 (1.%, M^+-O), 261 (1%, M^+-OH), 260 (1%, M^+-H_2O), 231 (1%, M^+-H_2O-CO-H), 230 (1%, M^+-SO), 141 (15%, $C_6H_4SOOH^+$), 138 (34%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 126 (15%, $C_6H_4SHOH^+$), 125 (29%, $FC_6H_4CHOH^+$), 123 (30%, $FC_6H_4CO^+$), 109 (81%, $C_6H_4SH^+$), 97 (34.5%, $C_5H_4SH^+$), 96 (26%, $C_5H_4S^+$), 95 (26%, $FC_6H_5^+$), 83 (11%, $FC_5H_4^+$), 77 (20%, $C_6H_5^+$), 65 (17.5%, $C_5H_5^+$), 51 (17%, $C_5H_5^+$). Anal. calcd for $C_{14}H_{11}FO_3S$: C, 60.42; H, 3.98; S, 11.52. Found: C, 60.31; H, 4.10; S, 11.24.

3.2.14. (2*S*,S_S)-2-[(1*S*)-1-Hydroxy-1-(4-fluorophenyl)-methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (7d). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 184–187°C. IR (nujol, cm^{-1}): 3320(OH), 1603, 1590, 1214, 1115, 1086, 1002; ^{1}H NMR (DMSO-d_6), δ: 5.24 (t, 1H, H_8, J=4.5), 5.80 (d, 1H, H_7, J=4.5), 6.30 (d, 1H, OH, J=4.5), 7.23 (t, 1H, H_4, J=7.8), 7.35 (t, 2H, H_{11}-H_{13}, J=8.4), 7.36 (d, 1H, H_2, J=7.8), 7.56 (t, 1H, H_3, J=7.8), 7.66 (t, 2H, H_{10}-H_{14}, J=8.4), 7.97 (d, 1H, H_5, J=7.8). ^{13}C NMR (DMSO-d_6), δ: 70.53 (d, C_8), 108.57 (d, C_7), 112.60 (d, C_2), 114.76 (dd, C_{11}-C_{13}, $^2J_{HF=}$21.2), 122.37 (d, C_4), 127.30 (d, C_5), 128.85 (dm, C_{10}-C_{14}, $^3J_{HF=}$8.47), 129.41 (s, C_6), 134.71 (d, C_3), 135.91 (d, C_9, $^4J_{HF=}$3.1), 160.31 (s, C_1), 161.73 (d, C_{12}, $^1J_{HF=}$241.9). EI-MS, DIP, *m/z*: 278 (7%, M^+), 262 (2%, M^+-O), 261 (5.5%, M^+-OH), 260 (6%, M^+-H_2O), 231 (5%, M^+-H_2O-CO-H), 230 (5%, M^+-SO), 141 (19%, $C_6H_4SOOH^+$), 138 (43%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 126 (19%, $C_6H_4SHOH^+$), 125 (33%, $FC_6H_4CHOH^+$), 123 (32%, $FC_6H_4CO^+$), 109 (87%, $C_6H_4SH^+$), 97 (36%, $C_5H_4SH^+$), 96 (26%, $C_5H_4S^+$), 95 (25%, $FC_6H_5^+$), 83 (10%, $FC_5H_4^+$), 77 (18.5%, $C_6H_5^+$), 65 (14%, $C_5H_5^+$), 51 (13.5%, $C_5H_5^+$). Anal. calcd for $C_{14}H_{11}FO_3S$: C, 60.42; H, 3.98; S, 11.52. Found:C, 60.36; H, 4.03; S, 11.40.

3.2.15. (2*R*,R_S)-2-[(1*S*)-1-Hydroxy-1-(4-trifluoromethyl-phenyl)methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (6e). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 220–222°C. IR (nujol, cm^{-1}): 3307 (OH), 1617, 1587, 1459, 1171, 1109, 1097, 1064, 1030, 1015; ^{1}H NMR (DMSO-d_6), δ: 5.19 (t, 1H, H_8, J=5.4), 5.86 (d, 1H, H_7, J=5.4), 6.65 (d, 1H, OH, J=5.4), 7.31 (t, 1H, H_4, J=7.8), 7.38 (d, 1H, H_2, J=7.8), 7.73 (t, 1H, H_3, J=7.8), 7.89 (q, 4H, H_{11}-H_{13}-H_{10}-H_{14}), 8.10 (d, 1H, H_5 J=7.8). ^{13}C NMR (DMSO-d_6), δ: 70.43 (d, C_8), 109.47 (d, C_7), 112.90 (d, C_2), 122.75 (d, C_4), 124.35 (qd, CF_3, $^1J_{HF=}$270.2), 125.30 (d, C_{11}-C_{13}), 127.74 (d, C_5), 127.85 (d, C_{10}-C_{14}), 128.72 (d, C_{12}, $^2J_{HF=}$31.5), 129.08 (s, C_6), 135.98 (d, C_3), 144.51 (s, C_9), 160.44 (s, C_1). EI-MS, DIP, *m/z*: 328 (12%, M^+), 312 (2%, M^+-O), 311 (4%, M^+-OH,), 310 (6%, M^+-H_2O), 309 (4%, M^+-F), 281 (8%, M^+-H_2O-CO-H), 280 (7%, M^+-SO), 188 (10%, $CF_3C_6H_4COHCH_2^+$), 175 (20%, $CF_3C_6H_4$-$CHOH^+$), 174 (12.5%, $CF_3C_6H_4COH^+$), 173 (48%, CF_3-$C_6H_4CO^+$), 159 (17%, $CF_3C_6H_4CH_2^+$), 145 (39%, CF_3-$C_6H_4^+$), 141 (50%, $C_6H_4OHSO^+$), 138 (13%, C_6H_4OS-CH_2^+), 137 (100%, $C_6H_4OSCH^+$), 127 (33%, $CF_2C_6H_5^+$), 126 (27%, $C_6H_4SHOH^+$), 125 (24%, $C_6H_4SOH^+$),113 (14%, $CF_2C_5H_3^+$), 109 (21%, $C_6H_4SH^+$), 97 (22%, $C_5H_4SH^+$), 96 (31%, $C_5H_4S^+$), 95 (15%, $CFC_5H_4^+$), 77 (14%, $C_6H_5^+$), 70 (11%, CF_3H^+), 69 (17%, CF_3^+), 65 (23%, $C_5H_5^+$), 51 (17%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{11}F_3O_2S$: C, 54.87; H, 3.29; S, 9.77. Found:C, 54.90; H, 3.52; S, 9.38.

3.2.16. (2*S*,S_S)-2-[(1*S*)-1-Hydroxy-1-(4-trifluoromethyl-phenyl)methyl]-1,3-benzoxathiole-3-(2*H*)-oxide (7e). Flash-chromatography (3:2 diethyl ether/petroleum ether), white crystals mp 137–138°C. IR (nujol, cm^{-1}): 3285(OH),1618, 1588, 1458, 1160, 1129, 1119, 1096, 1066, 1027, 1115, 1003; ^{1}H NMR (DMSO-d_6): δ 5.62 (t, 1H, H_8, J=3.9), 5.89 (d, 1H, H_7, J=3.3), 6.41 (d, 1H, OH, J=4.8), 7.23 (t, 1H, H_4, J=8.1), 7.29 (d, 1H, H_2, J=8.1), 7.66 (t, 1H, H_3, J=8.1), 7.90 (s, 4H, H_{11}-H_{13}-H_{10}-H_{14}), 8.00 (d, 1H, H_5 J=8.1). ^{13}C NMR (DMSO-d_6): δ 70.78 (d, C_8), 108.14 (d, C_7), 112.55 (d, C_2), 122.38 (d, C_4), 124.33 (qd, CF_3, $^1J_{HF=}$270.6), 124.89 (d, C_{11}-C_{13}), 127.29 (d, C_5), 127.58 (d, C_{10}-C_{14}), 128.33 (d, C_{12}, $^2J_{HF=}$31.8), 129.55 (s, C_5), 134.71 (d, C_3), 144.77 (s, C_9), 160.01 (s, C_1). EI-MS, DIP, *m/z*: 328 (8%, M^+), 312 (1%, M^+-O), 311 (2%, M^+-OH), 310 (4%, M^+-H_2O), 309 (3%, M^+-F), 281 (5%, M^+-H_2O-CO-H), 280 (6%, M^+-SO), 188 (8%, $CF_3C_6H_4COHCH_2^+$), 175 (17%, $CF_3C_6H_4CHOH^+$), 174 (10%, $CF_3C_6H_4COH^+$), 173 (37%, $CF_3C_6H_4CO^+$), 159 (15%, $CF_3C_6H_4CH_2^+$), 145 (31%, $CF_3C_6H_4^+$), 141 (56%, $C_6H_4OHSO^+$), 138 (12%, $C_6H_4OSCH_2^+$), 137 (100%, $C_6H_4OSCH^+$), 127 (25%, $CF_2C_6H_5^+$), 126 (25%, $C_6H_4SHOH^+$), 125 (22%, $C_6H_4SOH^+$), 113 (14%, $CF_2C_5H_3^+$), 109 (19%, $C_6H_4SH^+$), 97 (18%, $C_5H_4SH^+$), 96 (31%, $C_5H_4S^+$), 95 (12%, $CFC_5H_4^+$), 77 (11%, $C_6H_5^+$), 70 (9.5%, CF_3H^+), 69 (14%, CF_3^+), 65 (21%, $C_5H_5^+$), 51 (13%, $C_5H_5^+$). Anal. calcd for $C_{15}H_{11}F_3O_2S$: C, 54.87; H, 3.29; S, 9.77. Found: C, 54.78; H, 3.28; S, 9.55.

3.2.17. (2*R*,S_S)-1,3-Benzoxathiole-3-oxido-2-carboxylic Acid (12). Yield 60%; crystallized from 1:1 aqueous EtOH, white crystals mp 148–149°C. IR (nujol, cm^{-1}): 2845 broad (OH), 1727 (C=O), 1578, 1416, 1274, 1249, 1217, 1129, 1068, 1054, 1000. ^{1}H NMR (DMSO-d_6): δ 6.60 (s, 1H, H_7), 7.37 (t, 1H, H_4, J=7.8), 7.54 (d, 2H, H_2, J=7.8), 7.80 (t, 1H, H_3, J=7.8), 8.17 (d, 1H, H_5, J=7.8). ^{13}C NMR (DMSO-d_6): δ 100.31 (d, C_7), 113.50 (d, C_2), 123.47 (d, C_4), 127.93 (d, C_5), 129.31 (d, C_6), 135.70 (s, C_3), 160.52 (s, C_1), 165.53 (s, C=O). EI-MS, DIP, *m/z*: 198 (17%, M^+), 182 (2%, M^+-O), 154 (23.5%, M^+-CO_2), 137 (67%, M^+-CO_2-OH), 126 (58%, $C_6H_4OHSH^+$), 124 (37%, $C_6H_4OS^+$), 109 (11%, $C_6H_4SH^+$), 97 (71%, $C_5H_5S^+$), 96 (100, $C_5H_4S^+$), 70 (43%, $C_3H_3S^+$). Anal. calcd for $C_8H_6O_4S$: C, 48.48; H, 3.05; S, 16.18; Found: C, 48.70; H, 3.08; S, 16.36.

3.2.18. (2*S*,S_S)-(2*E*)-2-[(1*R*)-1-Hydroxy-1-(4-methoxyphenyl)methyl]-2-[(1′*S*)-1′-hydroxy-1′-(4-methoxyphenyl)methyl]-1,3-benzoxathiole-3(2*H*)-oxide (10a). Flash-chromatography (1:1 diethyl ether/petroleum ether), white crystals mp 186–187°C. IR (nujol, cm^{-1}): 3360, broad (OH), 1611, 1583, 1511, 1251, 1171, 1058, 998;; ^1H NMR (DMSO-d_6): δ 3.75 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 5.21 (sbr, 1H, H_8), 5.51 (sbr, 1H, H_{16}), 5.65 (sbr, 1H, OH), 6.26 (sbr, 1H, OH), 6.74 (d, 2H, H_{11}-H_{13}, J=8.7 Hz), 6.96 (d, 2H, H_{19}-H_{21}, J=8.7 Hz), 7.02 (t, 1H, H_4, J=7.6), 7.18 (d, 1H, H_2, J=7.6 Hz), 7.32 (d, 2H, H_{14}-H_{10}, J=8.7 Hz), 7.54 (t, 1H, H_3, J=7.6 Hz), 7.58 (d, 2H, H_{22}-H_{18}, J=8.7 Hz), 7.60 (d, 1H, H_5, J=7.6 Hz). ^{13}C NMR (DMSO-d_6): δ 55.15 (q, (OCH_3), 68.90(d, C_8), 71.46 (d, C_{16}), 109.08 (d, C_7), 112.38 (d, C_2), 112.55 (d, C_{11}-C_{13}), 112.78 (d, C_{19}-C_{21}), 121.85(d, C_4), 127.04 (d, C_5), 128.73 (s, C_6), 129.62 (d, C_{22}-C_{18}), 130.14 (d, C_{14}-C_{10}), 130.72 (s, C_9), 132.95 (s, C_{17}), 134.18 (d, C_3), 158.44 (s, C_{12}), 158.78 (s, C_{20}), 161.34 (s, C_1). EI-MS, DIP, *m/z*: 410 (0.2%, M^+-O), 409 (1%, M^+-OH), 408 (2%, M^+-H_2O), 273 (44%, M^+-$CH_3OC_6H_4CHO$-OH), 272 (16%, M^+-$CH_3OC_6H_4CHO$-H_2O), 256 (21%, M^+-$CH_3OC_6H_4CHO$-O-H_2O), 244 (6%, M^+-$CH_3OC_6H_4CHO$-H_2O-CO), 243 (12%, M^+-$CH_3OC_6H_4CHO$-H_2O-CO-H), 137 (100%, C_6H_4OS-CH^+), 136 (41%, $CH_3OC_6H_4CHO^+$), 135 (97%, CH_3O-$C_6H_4CO^+$), 121 (9%, $CH_3OC_6H_4CH_2^+$), 109 (18%, $C_6H_4SH^+$), 107 (19%, $CH_3OC_6H_4^+$), 94 (11%, $C_6H_5OH^+$), 92 (18.3%, $C_6H_4O^+$), 77 (53%, $C_6H_5^+$), 65 (18%, $C_5H_5^+$). Anal. calcd for $C_{23}H_{22}O_6S$: C, 64.77; H, 5.19; S, 7.52. Found: C, 64.12; H, 5.53; S, 7.27.

3.2.19. (2*R*,S_S)-(2*Z*)-2-[(1*S*)-1-Hydroxy-1-(4-methoxyphenyl)methyl]-2-[(1′*R*)-1′-hydroxy-1′-(4-methoxyphenyl)methyl]-1,3-benzoxathiole-3(2*H*)-oxide (11a). Flash-chromatography (1:1 diethyl ether/petroleum ether), white crystals mp 194–195°C. IR (nujol, cm^{-1}): 3365 and 3455 (OH), 1610, 1585, 1511, 1247, 1172, 1086, 1030; ^1H NMR (DMSO-d_6): δ 3.66 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.58 (d, 1H, H_8, J=3.6 Hz), 5.83 (d, 1H, H_{16}, J=3.2 Hz), 5.31 (d, 1H, OH, J=3.2 Hz), 6.66 (d, 1H, OH, J=3.6 Hz), 6.69 (d, 2H, H_{11}-H_{13}, J=8.4 Hz), 7.06 (t, 1H, H_4, J=7.6), 7.12 (d, 2H, H_{14}-H_{10}, J=8.4 Hz), 7.16 (d, 2H, H_{19}-H_{21}, J=8.8 Hz), 7.16 (d, 1H, H_2, J=7.6 Hz), 7.52 (t, 1H, H_3, J=7.6 Hz), 7.69 (d, 2H, H_{22}-H_{18}, J=8.8 Hz), 7.73 (d, 1H, H_5, J=7.6 Hz). ^{13}C NMR (DMSO-d_6): δ 55.06 (q, OCH_3), 55.25 (q, OCH_3), 71.80 (d, C_8), 72.39 (d, C_{16}), 109.33 (d, C_7), 112.50 (d, C_2), 112.81 (d, C_{11}-C_{13}), 113.46 (d, C_{19}-C_{21}), 122.17 (d, C_4), 127.22 (d, C_5), 127.40 (s, C_6), 128.60 (d, C_{22}-C_{18}), 129.56 (s, C_9), 129.80 (d, C_{14}-C_{10}), 130.35 (s, C_{17}), 134.72 (d, C_3), 158.87 (s, C_{12}), 159.22 (s, C_{20}), 160.07 (s, C_1). EI-MS, DIP, *m/z*: 410 (0.1%, M^+-O), 409 (0.4%, M^+-OH), 408 (1%, M^+-H_2O), 290 (0.3%, M^+-$CH_3OC_6H_4CHO$), 273 (65%, M^+-$CH_3OC_6H_4CHO$-OH), 272 (17%, M^+-$CH_3OC_6H_4CHO$-H_2O), 256 (9%, M^+-$CH_3OC_6H_4CHO$-O-H_2O), 244 (7.5%, M^+-$CH_3OC_6H_4CHO$-H_2O-CO), 243 (12.5%, M^+-$CH_3OC_6H_4CHO$-H_2O-CO-H), 137 (100%, $C_6H_4OSCH^+$), 136 (45%, $CH_3OC_6H_4CHO^+$), 135 (83%, $CH_3OC_6H_4CO^+$), 121 (7%, $CH_3OC_6H_4CH_2^+$), 109 (16%, $C_6H_4SH^+$), 107 (17%, $CH_3OC_6H_4^+$), 94 (10%, $C_6H_5OH^+$), 92 (18%, $C_6H_4O^+$), 77 (51%, $C_6H_5^+$), 65 (17%, $C_5H_5^+$). Anal. calcd for $C_{23}H_{22}O_6S$: C, 64.77; H, 5.19; S, 7.52. Found: C, 64.07; H, 5.41; S, 7.34.

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