Isoxazolidines by Cycloadditions of *N*,α-Diphenyl Nitrone in the Benzo[*b*]thiophene *S*-Oxide and *SS*-Dioxide Series

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1,3-Dipolar cycloadditions of *N*,α-diphenyl nitrone have been investigated in the 2- or 3-substituted (methyl, phenyl, chloro, bromo, piperidino, acetyl) benzo[*b*]thiophene *S*-oxide and *SS*-dioxide series. The *S*-oxide and *SS*-dioxide derivatives show the same ability to form adducts. The 2,3-dihydrobenzo[*b*]-thieno[2,3-*d*]isoxazolidines are generally formed only as a single regioisomer, except in the case of 2-methyl dipolarophiles where both regioisomers are formed. The regioselectivity is discussed in terms of frontier orbital interactions on the basis of CNDO/S calculations and photoelectronic spectral ionization potentials. The nitrone, which has an elbow shape, could lead to the formation of diastereoisomers but in fact only the *trans*-isoxazolidines are formed. There is less stereoselectivity in the *S*-oxide series since we obtained only one adduct with the 3-methyl dipolarophiles but both *syn*- and *anti*-epimers with the 3-phenyl derivatives. The bromo derivatives do not lead to any adduct. *X*-Ray structures are presented for the two adducts corresponding to the addition of the nitrone to benzo[*b*]thiophene *SS*-dioxide and to the 2-methyl derivative.

In previous papers [1,2] the regioselective cycloaddition reactions of mesitonitrile oxide (linear structure) in the benzo[*b*]-thiophene *S*-oxide and *SS*-dioxide series have been reported. The use of *N*,α-diphenyl nitrone, which has an elbow shape,[3] would give more information about the stereochemical aspects of the cycloadditions since two types of regioisomers (I) and (II) are possible depending on whether the oxygen atom of the dipole is bonded to C(2) or C(3) of the benzo[*b*]-thiophene.

Moreover, for each regioisomer (I) or (II), there is *cis*/*trans* isomerism related to the position of 3-H of the dipole and the substituents R^2 and R^3 of the dipolarophile. The structure is *cis* when 3-H and R^2 are located on the same side of the isoxazolidine plane and *trans* in the other case (Figure). The *cis*/*trans* stereochemistry is related to two non-equivalent *endo and exo* approaches of the reactants.

On the other hand, as previously mentioned,[2] in the benzo[*b*]thiophene *S*-oxide series, cycloaddition may lead to two epimers *syn* or *anti*. The structure is *anti* when both the S–O bond and the R^2 substituent are located on one side of the benzo[*b*]thiophene plane (Figure), and *anti* in the opposite case. Three isomers may exist in the *S*-oxide series and so four diastereoisomers (*syn*/*anti*, *cis*/*trans*) may be formed for each regioisomer (I) and (II) thus leading to eight possible structures.

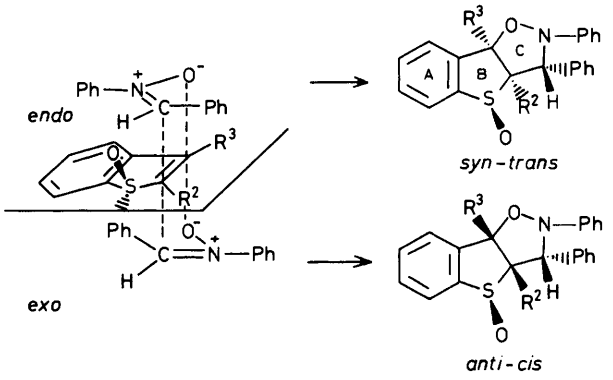


Figure *syn*/*anti* and *cis*/*trans* stereochemistry of the adducts

Results and Discussion

The results of the addition of the nitrone to 2- and 3-substituted benzo[*b*]thiophenes are given in Table 1.

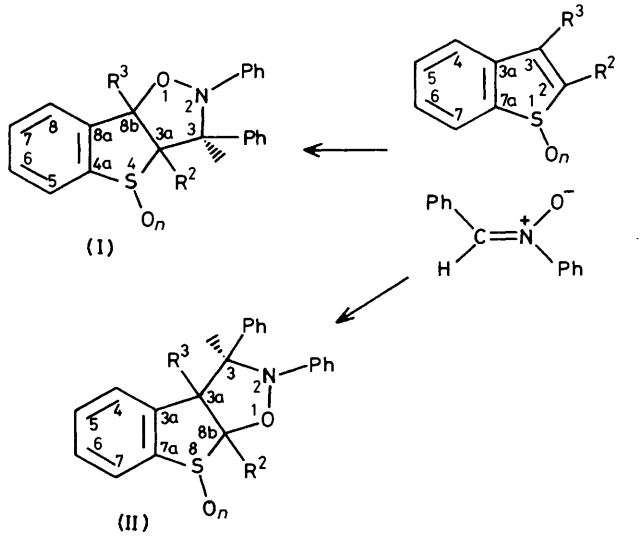
1,1-*Dioxobenzo*[b]*thiophene* (3) *and the* 3-*Methyl Derivative* (3b).—The nitrone reacted with (3) and (3b) in refluxing benzene to lead to one isoxazolidine in each case: respectively (4) (30 h; yield 85%) and (4b) (8 h; yield 55%). The ^{1}H n.m.r. spectrum of adduct (4b) (Table 2) shows two doublets for 3- and 3a-H that are consistent with a type (I) regioisomer [for type (II) two singlets would be observed]. The assignment of the 3a-H signal at high field (δ 4.10) and the 3-H signal at δ 5.50 was done on the basis of the results for the isoxazoline series [2] and taking into account the effect of the sulphone group.[4,5]

In the case of adduct (4), the corresponding spectrum shows a quartet at high field (δ 4.41 for 3a-H); this position is consistent with the α-effect of the sulphone group and so with structure (I). This conclusion was confirmed by an *X*-ray structure analysis. The effect of the 8b-methyl substituent previously observed [2] explains the difference between the chemical shifts for 3a-H in adduct (4b) (δ 4.10) and (4) (δ 4.41; Δδ 0.31). The chemical shifts for 3-H are closer than above (δ 0.11). 8b-H gives a low-field signal (δ 6.09) as for the isoxazoline series (δ 6.46).[2,6]

In the case of nitrones or nitronic esters reacting with polysubstituted ethylene derivatives [7,8] J_{trans} has a smaller value than J_{cis}.[9] Given this assumption, the coupling constants of adducts (4b) ($J_{3,3a}$ 3.5 Hz) and (4) ($J_{3,3a}$ 4 Hz) suggested a *trans*-structure.

In order to elucidate the complete structure of the cyclo-

Table 1. Experimental results in 4-oxo- and 4,4-dioxo-benzo[*b*]-thiophene series



Type I structure	Starting material R^2	Starting material R^3		Type II structure
t4-Oxo series (n = 1)				
(2aI)	CH_3	H	(1a)	(2aII)
syn-(2b)	H	CH_3	(1b)	
(2c)	CH_3	CH_3	(1c)	
(2e)	Br	H	(1e)	
syn-(2g), *anti*-(2g)	H	C_6H_5	(1g)	
4,4-Dioxo series (n = 2)				
(4)	H	H	(3)	
(4aI)	CH_3	H	(3a)	(4aII)
(4b)	H	CH_3	(3b)	
(4c)	CH_3	CH_3	(3c)	
(4d)	Cl	H	(3d)	
(4e)	Br	H	(3e)	
(4g)	H	C_6H_5	(3g)	
(4h)	H	piperidino	(3h)	
(4i)	H	CH_3CO	(3i)	

1-Oxobenzo[*b*]thiophene (1) cannot be isolated.[4] The 3-bromo-derivatives (1f), (3f) do not give any adduct.

Table 2. ^{1}H N.m.r. data of the adducts: sulphone series

Compd.	Chemical shifts δ: 3-Position	3a-Position	8b-Position
(4)	H, 5.39 (d) $J_{3,3a}$ 4 Hz	H, 4.41 (dd) $J_{3a,8b}$ 6 Hz, $J_{3,3a}$ 4 Hz	H, 6.09 (d) $J_{3a,8b}$ 6 Hz
(4aI)	H, 5.45 (s)	CH_3, 1.25 (s)	H, 5.56 (s)
(4aII)	H, 4.55 (d) $J_{3,3a}$ 6.5 Hz	H, 4.14 (d) $J_{3,3a}$ 6.5 Hz	CH_3, 2.00 (s) *
(4b)	H, 5.50 (d) $J_{3,3a}$ 3.5 Hz	H, 4.10 (d) $J_{3,3a}$ 3.5 Hz	CH_3, 2.02 (s)
(4c)	H, 5.52 (s)	CH_3, 1.26 (s)	CH_3, 1.73 (s)
(4d)	H, 5.67 (s)		H, 5.84 (s)
(4e)	H, 5.64 (s)		H, 6.00 (s)
(4g)	H, 5.37 (d) $J_{3,3a}$ 4.5 Hz	H, 4.41 (d) $J_{3,3a}$ 4.5 Hz	phenyl (m) 6.85—7.90
(4h)	H, 5.44 (d) $J_{3,3a}$ 5.5 Hz	H, 4.36 (d) $J_{3,3a}$ 5.5 Hz	piperidino (m) 1.5—2.90
(4i)	H, 5.19 (d) $J_{3,3a}$ 6 Hz	H, 4.83 (d) $J_{3,3a}$ 6 Hz	CH_3 acetyl (s) 2.83

* 8a-position.

Table 3. Characteristic *X*-ray data for adduct (4)

Dihedral angles (°)		Junction of heterocycles (°)	
H–C(3a)–C(8b)–H	18,5	H–C(3a)–C(8b)	113.7
S–C(3a)–C(8b)–C(8a)	16	C(3a)–C(8b)–H	115.6
H–C(3)–C(3a)–H	123.3	O–S–O′	118.2
H–C(3)–C(3a)–S	33		
Ph–C(3)–C(3a)–H	6.8		
C(3a)–C(3)–N–O(1)	37.3		
Ph–C(3)–N–Ph	86.9	Angles between rings (°)	
H–C(3)–N–Ph	30	A–B	5.15
O–S(4)–C(3a)–H	3.5	B–C	129

Table 4. ^{1}H N.m.r. data of the adducts: sulphoxide series

Compd.	Chemical shifts δ: 3-Position	3a-Position	8b-Position
(2aI)	H, 5.39 (s)	CH_3, 1.97 (s)	H, 5.34 (s)
(2aII)	H, 6.05 (d) $J_{3,3a}$ 2 Hz	H, 3.75 (d) $J_{3,3a}$ 2 Hz	CH_3, 2.13 (s) *
syn-(2b)	H, 5.65 (d) $J_{3,3a}$ 4 Hz	H, 5.34 (d) $J_{3,3a}$ 4 Hz	CH_3, 2.07 (s)
anti-(2b)	H, 5.03 (d) $J_{3,3a}$ 5 Hz	H, 4.10 (d) $J_{3,3a}$ 5 Hz	CH_3, 2.05 (s)
(2c)	H, 5.64 (s)	CH_3, 1.28 (s)	CH_3, 1.68 (s)
(2e)	H, 5.35 (s)		H, 5.96 (s)
syn-(2g)	H, 5.70 (d) $J_{3,3a}$ 4.5 Hz	H, 4.70 (d) $J_{3,3a}$ 4.5 Hz	phenyl (m) 6.9—8.0
anti-(2g)	H, 5.49 (d) $J_{3,3a}$ 2 Hz	H, 4.68 (d) $J_{3,3a}$ 2 Hz	phenyl (m) 7.1—8.0

* 8a-position.

adducts and to establish whether the approach was *endo* or *exo*, *X*-ray analysis of adduct (4) was carried out. The structure (Table 3) was confirmed as that of regioisomer (I), 3a- and 3-H are *trans* to each other (*endo*-approach), and 3a- and 8b-H are *cis*, in agreement with the *cis*-stereospecificity of the 1,3-dipolar cycloaddition reactions.[3,10]

1-Oxo-3-methylbenzo[b]thiophene (1b).—The addition of the nitrone with (1b) in refluxing benzene led to a single product *syn*-(2b) (yield 71%). Oxidation of this adduct at room temperature with *m*-chloroperbenzoic acid gave the corresponding sulphone derivative (4b): *syn*-(2b) and (4b) have the same '*trans*-(I)' stereochemistry.

The ^{1}H n.m.r. spectrum of adduct *syn*-(2b) (Table 4) shows two doublet signals with equal intensities at δ 4.34 and 5.65 ($J_{3,3a}$ 4 Hz). They were assigned respectively to 3a- and 3-H by analogy with the sulphone adduct [δ 4.10 and 5.50 ($J_{3,3a}$ 3.5 Hz)].

It was necessary to have the *anti*-(2b) epimer in order to assign the *syn* or *anti* position of the *S*-oxide in the *syn*-(2b) adduct. Since it was not possible to epimerize *syn*-(2b) either photochemically or chemically, *anti*-(2b) was obtained by reduction of *syn*-(2b) to the corresponding sulphide followed by oxidation resulting in a mixture of these two epimers (ratio 1 : 5). From the n.m.r. spectra, the minor isomer was identified as *syn*-(2b). The n.m.r. characteristics of the major oxidation product *anti*-(2b) are given in Table 4. The 3-H signal is found at higher field (δ 4.10) than the corresponding signal of adduct *syn*-(2b) (δ 4.35). However, the difference of chemical shifts between the *syn*- and *anti*-structures is in the same range in the isoxazoline series (Δδ 0.37 p.p.m.)[2] as in the present series (Δδ 0.25 p.p.m.).

1-Oxo- and 1,1-Dioxo-2-methylbenzo[b]*thiophene* (1a) *and*

(3a).—Heating a mixture of nitrone and dipolarophiles (1a) or (3a) in refluxing benzene for 15 days resulted in the formation of a mixture of regioisomers (I) and (II) in both cases. This result is evident from the multiplicity in the n.m.r. spectra (Tables 2 and 4). In the sulphone series, the major adduct (4a) has a type (I) structure. On the other hand, in the sulphoxide series, the major adduct (2a) is of type (II). The separation of these two isomers was difficult because of the low yields and also the number of decomposition products of the nitrone. In spite of these difficulties, from the value of the coupling constant ($J_{3,3a}$ 2 Hz), the *trans*-structure of the isoxazolidine ring in the major adduct (2aII) can be assumed. This was confirmed by the crystallographic data in Table 5.

1-*Oxo- and* 1,1-*Dioxo*-2,3-*dimethylbenzo*[b]*thiophenes* (1c) *and* (3c).—Heating a mixture of the nitrone and the *S*-dioxide dipolarophile (3c) in refluxing chloroform for 15 days resulted in the formation of only one adduct in low yield (7%), the isoxazolidine (4c). Similarly, starting from the sulphoxide (1c), the adduct (2c) was obtained in 4% yield. For these derivatives it is possible to assign structure (I) to adduct (4c) in agreement with the chemical shifts of (4c) and the reference adducts (4aI) and (4b) for 3-H and the 8b- and 3a-methyl group (Tables 2 and 4). No conclusion could be drawn as to the *cis*/*trans* structure of the isoxazolidine ring. In the same way, the analogy between the n.m.r. spectra of adducts (2c) and reference adducts (4b), (4aI), and *syn*- and *anti*-(2b) led to the same result [regioisomer (I)].

Reaction with 2-*Halogeno compounds*.—1,1-Dioxo-2-chlorobenzo[*b*]thiophene (3d) and the corresponding 2-bromo-substituted derivative (3e) reacted with the nitrone to give one adduct in each case, (4d and e) (yields 5 and 30%, respectively). Starting with the 1-oxo-2-bromo-derivative (1e), the isoxazolidine (2e) (16%) was obtained. The ^{1}H n.m.r. spectra of these three adducts are consistent with cycloaddition of type (I) in each case (Tables 2 and 4).

No adduct was detected by ^{1}H n.m.r. nor isolated by chromatography for the reaction of 3-bromo-compounds in refluxing chloroform for 15 days.

1-*Oxo and* 1,1-*Dioxo*-3-*phenylbenzo*[b]*thiophene* (1g) *and* (3g).—A mixture of (1g) and the nitrone heated in refluxing trichloroethylene for 10 days resulted in the formation of two diastereoisomers, *syn*- and *anti*-(2g). The yields were 58 and 4%, respectively (15 : 1 ratio). Under the same conditions (4g) is obtained from (3g) (yield 60%). From the ^{1}H n.m.r. spectra (Tables 2 and 4) *syn*- and *anti*-(2g) and (4g) have structure (I). Because of (i) the impossibility of epimerizing *syn*-(2g) and (ii) the low yield of *anti*-(2g) (to achieve oxidation of the mixture as we did for the methylated series), it was not possible to establish the nature of *cis*/*trans* or *syn*/*anti* isomerism by a chemical method. In the literature [7-9,11] the studies of isoxazolidine rings (configurations and conformations) show that the ^{1}H n.m.r. coupling constants J_{trans} are small. As for (4) and (4b), $J_{3,3a}$ of *syn*-(2g) (4.5 Hz) and *anti*-(2g) (2 Hz) are consistent with the *trans*-structure of the isoxazolidine rings and the two adducts are *syn*/*anti* epimers.

Comparison between the chemical shifts in Tables 2 and 4 shows similarities between *syn*-(2g) and *syn*-(2b), *anti*-(2g) and *anti*-(2b), and also (4g) (4.5 Hz) and (4b) (3.5 Hz). One has to note that the 8b-phenyl substituent should have no major interaction with 3-H (because of their position on opposite sides of the plane of the ring) while 3a-H is eclipsed by this group. Because of the analogy between the 3-methyl and 3-phenyl series the *trans-syn* structures can be suggested for adducts (4g) and *syn*-(2g).

1,1-*Dioxo*-3-*piperidino and* -3-*acetyl Derivatives* (3h) *and* (3i).—The mixture of (3h) and the nitrone heated in trichloroethylene for 40 h led to one adduct, (4h) (85%). In the same way, starting from (3i) a single adduct (4i) is obtained. The multiplicity of 3- and 3a-H n.m.r. signals (Table 4) is in accord with structure (I) for both adducts. In the ^{1}H n.m.r. spectrum of adducts (4 h and i) $J_{3,3a}$ values of 5.5 and 6 Hz, respectively, are in the range for J_{trans} (2.0—6.2 Hz in our series) and suggest a *trans*-structure for these adducts.

Kinetic Studies.—Dipolar cycloadditions are bimolecular reactions and the rate constants obtained under pseudo-molecular conditions for (3), (3b), and (1b) (excess of nitrone) are given in Table 6. The results are in accord with a consecutive kinetic scheme with the same reactivity for the *S*-oxide (1b) and *SS*-dioxide (3b), and a decrease in the reactivity due to a steric effect [12-14] for the compound with a 3-methyl group (k_{3b}/k_3 0.12).

Theoretical Approach.—MO calculations have been performed to explain the experimental results by determining the contribution of LUMO (dipole) – HOMO (benzothiophene sulphoxide) and LUMO (dipole) – HOMO (benzothiophene) to the total stabilization of the transition state.

Energies and atomic coefficients of the frontier orbitals from CNDO/S calculations [12,13,15,16] are reported in Table 7. The theoretical data concerning the occupied levels were confirmed by a photoelectron spectral study.[2] The HOMOs and LUMOs of the nitrone and of the sulphone derivatives are well separated. For the sulphoxides it is necessary to consider the two upper occupied levels, one of which is more located on the sulphoxide group.

Quantitatively the most stabilizing interaction occurs between the HOMO of the dipole and the LUMO of the dipolarophile. For the sulphone and the sulphoxides, however, the LUMO has two equivalent locations on C-2 and -3. Even in

Table 5. Characteristic *X*-ray data for adduct (4aI)

Dihedral angles (°)		Junction of heterocycles (°)	
H–C(8b)–C(3a)–CH_3	22.68	H–C(8b)–C(3a)	108.15
S–C(3a)–C(8b)–C(8a)	26.58	CH_3–C(3a)–C(8b)	113.67
H–C(3)–C(3a)–CH_3	−143.95	O–S–O′	117.58
C(3a)–C(3)–N–O(1)	4.50		
Ph–C(3)–N–Ph	−102.19	Angles between rings (°)	
H–C(3)–N–Ph	17.26	A–B	9.25
		B–C	79.26

Table 6. Rate constants for cycloaddition reactions

Dipolarophiles	$k_{disappearance}$	$k_{appearance}$	Adducts
(3)	8×10^{-4} l mol^{-1} s^{-1} ±6%	7×10^{-4} l mol^{-1} s^{-1} ±5%	(4)
(3b)	9.5×10^{-5} l mol^{-1} s^{-1} ±3.5%	9.5×10^{-5} l mol^{-1} s^{-1} ±2%	(4b)
(1b) *	9.5×10^{-5} l mol^{-1} s^{-1} ±7%		(2b)

* There is no $k_{appearance}$ value; it was difficult to follow the appearance of adduct (2b) in h.p.l.c.

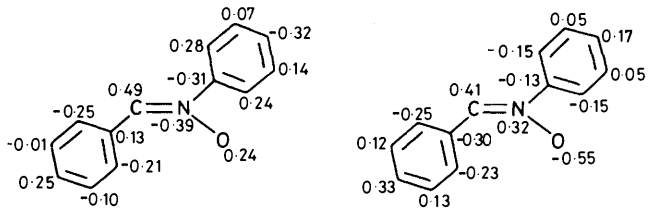
this case regioisomer (I) seems to be preferred because the dipole LUMO – dipolarophile HOMO interaction which has to be taken into account favours the transition state leading to that regioisomer.[18]

In order to check this hypothesis of HOMO – LUMO control according to the Sustmann [19] treatment, CNDO/S calculations were performed for mono- and di-methylated derivatives (Table 8). The data show regioisomer (II) to be favoured to some extent by the HOMO (dipole) – LUMO (dipolarophile) interaction [for example, 2-methylated derivatives (3a)] whereas HOMO (dipolarophile) – LUMO (dipole) interactions stabilize regioisomer (I) strongly [but less than for (3a)]. As a result the differences $\Delta(\Delta E)$ listed in Table 8 between stabilization energies for both approaches predict the formation of regioisomer (I) as a single adduct except for the 2-substituted derivative (3a). In that case a mixture of (I) and (II) is expected.

These calculations also apply to the sulphoxide derivatives since the HOMO controlling the regioselectivity has the same shape as the HOMO of the sulphone derivative. However, the calculation cannot explain the stereoselectivity and some other theoretical model is necessary for this purpose.

Table 7. Calculated frontier molecular orbitals by CNDO/S method (eigenvectors and eigenvalues)

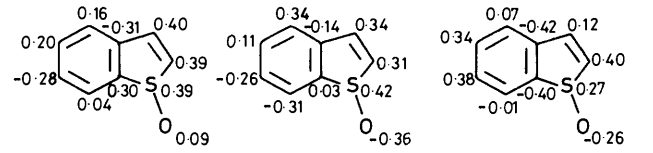
N,α-Diphenyl nitrone



E.i (e.v) 1·22 -9·14

I.P. (exp) 7·90

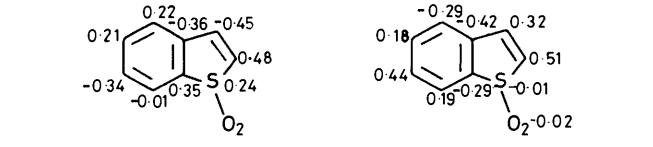
1-Oxobenzo[*b*]thiophene



E.i (e.v) -1·50 -10·86 -10·72

I.P. (exp)* 8·40 8·62

1,1-Dioxobenzo[*b*]thiophene



E.i (e.v) -1·69 -10·86

I.P (exp) 9·32

* 1-Oxo-2,3-dimethylbenzo[*b*]thiophene values.

Experimental

General Methods.—M.p.s are uncorrected. ^{1}H N.m.r. spectra were recorded in $CDCl_3$ on a Bruker WP 80. Mass spectra were determined on a CEC-110C instrument. I.r. spectra were obtained with a Perkin-Elmer 197 spectrophotomer.

Starting Materials.—*N*,α-Diphenyl nitrone was prepared according to standard procedures.[20] Sulphides, sulphoxides, and sulphones were prepared as previously described.[2] 3-Acetylbenzo[*b*]thiophene was synthesized by Farrar's procedure; [21] the corresponding sulphone (3i) was obtained by standard procedures.[22]

Additions to Sulphoxides.—Preparation of 8-*oxo*-8a-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[3,2-d]*isoxazolidine* (2aII). A solution of (1a) (1 g, 6 mmol) and *N*,α-diphenyl nitrone (2.9 g, 15 mmol) was refluxed in benzene (50 ml) for 15 days. The solution was concentrated and the residue chromatographed on a silica column using light petroleum–methylene chloride (9 : 1) as eluant. Compound (2aII) was obtained in 31% yield, m.p. 189 °C, *m/e* 361 (Found: C, 72.2; H, 5.3; N, 3.75. Calc. for $C_{22}H_{19}NO_2S$: C, 73.0; H, 5.25; N, 3.9%), ν 1 020—1 060 cm^{-1} (SO). The isomer 4-oxo-3a-methyl-2,3-diphenyl-2,3-dihydrobenzo[*b*]thieno[2,3-*d*]-isoxazolidine (2aI) was also obtained (4% yield, 0.08 g) but not crystallised, *m/e* 361.

Preparation of 4-*oxo*-8b-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-*d*]*isoxazolidine* syn-(2b). A solution of (1b) (1.5 g, 9 mmol) and *N*,α-diphenyl nitrone (3 g, 15 mmol) was refluxed in benzene (50 ml) for 27 h. The solution was concentrated and the residue crystallised (light petroleum–chloroform) giving compound *syn*-(2b) in 71% yield, m.p. 164 °C, *m/e* 361 (Found: C, 73.2; H, 5.1; N, 3.95%), ν 1 030—1 060 cm^{-1} (SO).

Preparation of 4-*oxo*-3a,8b-*dimethyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (2c). A solution of (1c) (0.18 g, 1 mmol) and *N*,α-diphenyl nitrone (1.8 g, 8 mmol) was refluxed in benzene (25 ml) for 15 days. The solution was concentrated and the residue chromatographed on silica t.l.c. using chloroform as eluant. Compound (2c) was obtained in 4% yield but not crystallised, *m/e* 375.

Preparation of 4-*oxo*-3a-*bromo*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (2e). A solution of (1e)

Table 8. C-2 and C-3 atomic coefficient (CNDO/S) of HOMO and LUMO of 1,1-dioxobenzo[*b*]thiophene derivatives and energy stabilization differences of the transition state

	$R^2 = R^3 = H$		R^2 = Me, R^3 = H		R^2 = H, R^3 = Me		$R^2 = R^3$ = Me	
	LUMO	HOMO	LUMO	HOMO	LUMO	HOMO	LUMO	HOMO
C-3	−0.45	0.32	−0.42	0.37	−0.42	0.35	−0.41	0.39
C-2	0.48	0.51	0.50	0.49	0.49	0.55	0.46	0.54
$10^3\Delta(\Delta E)\beta^2$ (eV)	4.1		0.7		7.1		3.9	

(0.23 g, 1 mmol) and *N*,α-diphenyl nitrone (1.8 g, 8 mmol) was refluxed in chloroform (25 ml) for 15 days. The solution was concentrated and the residue chromatographed on silica t.l.c. using chloroform as eluant. Compound (2e) was obtained in 16% yield, m.p. 96 °C, *m/e* 425 and 427 (Found: C, 58.55; H, 3.9; N, 2.2. Calc. for $C_{21}H_{16}BrNO_2S$: C, 59.1; H, 3.75; N, 2.3%), ν 1 060—1 070 cm^{-1} (SO).

Preparation of 4-*oxo*-2,3,8b-*triphenyl*-2,3-*dihydrobenzo*[b]-*thieno*[2,3-d]*isoxazolidine* syn- *and* anti-(2g). A solution of compound (1g) (0.23 g, 1 mmol) and *N*,α-diphenyl nitrone (1 g, 5 mmol) was refluxed in trichloroethylene (25 ml) for 10 days. The solution was concentrated and the residue chromatographed on silica t.l.c. using methylene chloride–acetone (24 : 1) as eluant. Compound *syn*-(2g) was obtained in 58% yield, m.p. 143 °C, *m/e* 423 (Found: C, 76.2; H, 5.1; N, 3.2. Calc. for $C_{27}H_{21}NO_2S$: C, 76.6; H, 4.95; N, 3.3%), ν 1 030—1 045 cm^{-1} (SO). The isomer *anti*-(2g) was also obtained (4%) but not crystallised, *m/e* 423.

Additions to Sulphones.—Preparation of 4,4-*dioxo*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-*d*]*isoxazolidine* (4). A solution of (3) (1.5 g, 9 mmol) and *N*,α-diphenyl nitrone (2.95 g, 15 mmol) was refluxed in benzene (50 ml) for 30 h. The solution was concentrated, and the residue chromatographed on silica column using light petroleum–methylene chloride (9 : 1) as eluant. Compound (4) was obtained in 85% yield, m.p. 175 °C, *m/e* 363 (Found: C, 63.3; H, 4.0; N, 4.85. Calc. for $C_{21}H_{17}NO_3S$: C, 63.15; H, 3.9; N, 4.9%), ν 1 150—1 310 cm^{-1} (SO_2).

Preparation of 4,4-*dioxo*-3a-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4aI). A solution of (3a) (1.08 g, 6 mmol) and *N*,α-diphenyl nitrone (3.5 g, 18 mmol) was refluxed in benzene (50 ml) during 13 h. The solution was concentrated and the residue chromatographed on a silica column using light petroleum–methylene chloride (9 : 1) as eluant. Compound (4aI) was obtained in 35% yield, m.p. 133 °C, *m/e* 377 (Found: C, 70.1; H, 5.1; N, 3.6. Calc. for $C_{22}H_{19}NO_3S$: C, 70.0; H, 5.05; N, 3.7%), ν 1 155—1 170 and 1 310 cm^{-1} (SO_2). The isomer 8,8-dioxo-8a-methyl-2,3-diphenyl-2,3-dihydrobenzo[*b*]thieno[3,2-*d*]isoxazolidine (4aII) was also obtained (3%) but not crystallised, ν 1 150—1 160 and 1 305 cm^{-1} (SO_2).

Preparation of 4,4-*dioxo*-8b-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4b). A solution of (3b) (1.8 g, 10 mmol) and *N*,α-diphenyl nitrone (0.6 g, 3 mmol) was refluxed in benzene (30 ml) for 8 h. The solution was concentrated and the residue chromatographed using light petroleum –methylene chloride (9 : 1) as eluant. Compound (4b) was obtained in 55% yield, m.p. 152 °C, *m/e* 377 (Found: C, 70.15; H, 5.2; N, 3.8%), ν 1 155—1 165 and 1 310 cm^{-1} (SO_2). Compound (4b) was also obtained by oxidation of *syn*-(2b) (0.08 g, 0.21 mmol) with *m*-chloroperbenzoic acid (0.04 g, 0.21 mmol) in chloroform (30 ml) at room temperature during 4 h.

Preparation of 4,4-*dioxo*-3a,8b-*dimethyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4c). A solution of (3c) (0.19 g, 1 mmol) and *N*,α-diphenyl nitrone (1 g, 5 mmol) in chloroform (25 ml) was refluxed for 15 days. After the usual work-up the residue was chromatographed on silica column using light petroleum–ether (9 : 1) as eluant. Compound (4c) was obtained in 7% yield but not crystallised, *m/e* 391, ν 1 150—1 160 and 1 305 cm^{-1} (SO_2).

Preparation of 4,4-*dioxo*-3a-*chloro*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4d). A solution of (3d) (0.2 g, 1 mmol) and *N*,α-diphenyl nitrone (1 g, 5 mmol) was refluxed in benzene (25 ml) for 15 days. After the usual work-up, the residue was chromatographed on silica t.l.c. using methylene chloride–acetone (19 : 1) as eluant. Compound (4d) was obtained in 5% yield but not crystallised, *m/e* 399 and 401.

Preparation of 4,4-*dioxo*-3a-*bromo*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4e). A solution of (3e) (0.245 g, 1 mmol) and *N*,α-diphenyl nitrone (1 g, 5 mmol) was refluxed in chloroform (25 ml) for 15 days. After the usual work-up the residue was chromatographed on silica t.l.c. using methylene chloride–light petroleum (86 : 14) as eluant. Compound (4e) was obtained in 30% yield, m.p. 151 °C, *m/e* 441 and 443 (Found: C, 57.1; H, 3.75; N, 3.25. Calc. for $C_{21}H_{16}BrNO_3S$: C, 57.1; H, 3.6; N, 3.1%), ν 1 160—1 165 and 1 325 cm^{-1} (SO_2).

Preparation of 4,4-*dioxo*-2,3,8b-*triphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4g). A solution of (3g) (0.17 g, 0.7 mmol) and *N*,α-diphenyl nitrone (0.36 g, 1.8 mmol) was refluxed in benzene (20 ml) for 2 days. After the usual work-up the residue was chromatographed on a silica column using light petroleum–methylene chloride (24 : 1) as eluant. Compound (4g) was obtained in 60% yield, m.p. 172 °C, *m/e* 439 (Found: C, 73.5; H, 4.8; N, 3.25. Calc. for $C_{27}H_{21}NO_3S$: C, 73.8; H, 4.8; N, 3.2%), ν 1 140—1 320 cm^{-1} (SO_2).

Preparation of 4,4-*dioxo*-8b-*piperidino*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4h). A solution of (3h) (1 g, 4 mmol) and *N*,α-diphenyl nitrone (1.57 g, 8 mmol) was refluxed in trichloroethylene (50 ml) for 2 days. After the usual work-up, the residue was chromatographed by silica t.l.c. using methylene chloride–acetone (99 : 1) as eluant. Compound (4h) was obtained in 85% yield, m.p. 134 °C, *m/e* 446 (Found: C, 69.5; H, 5.9; N, 6.1. Calc. for $C_{26}H_{26}N_2O_3S$: C, 69.9; H, 5.8; N, 6.25%), ν 1 185 and 1 310 cm^{-1} (SO_2).

Preparation of 4,4-*dioxo*-8b-*acetyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4i). A solution of (3i) (0.21 g, 1 mmol) and *N*,α-diphenyl nitrone (0.79 g, 4 mmol) was refluxed in benzene (25 ml) for 2 days. After the usual work-up, the residue was chromatographed on silica t.l.c. using methylene chloride–acetone (19 : 1) as eluant. Compound (4i) was obtained in 16% yield, m.p. 141 °C, *m/e* 405 (Found: C, 68.0; H, 4.8; N, 3.5. Calc. for $C_{23}H_{19}NO_4S$: C, 68.15; H, 4.7; N, 3.45%).

Catalytic deoxygenation of syn-(2b). Compound *anti*-(2b) (0.75 g, 2 mmol) and CoO–MoO_3 on Al_2O_3 catalyst (0.083 g) in benzene was heated (70 °C) under hydrogen pressure (10 bar) for 40 h. Two compounds were obtained after chromatography of the residue on silica using methylene chloride–light petroleum (3 : 2) as eluant.

(a) 8b-Methyl-2,3-diphenyl-2,3-dihydrobenzo[*b*]thieno-[2,3-d]isoxazolidine (68%) was not crystallised, *m/e* 345 (Found: C, 76.4; H, 5.55; N, 3.9. Calc. for $C_{22}H_{19}NOS$: C, 76.5; H, 5.5; N, 4.05%), δ 1.83 (3 H, s, 8b-CH_3), 4.18 (1 H, d, *J* 6.2 Hz, 3a-H), 4.65 (1 H, d, *J* 6.2 Hz, 3-H), and 6.9—8.0 (14 H, m, arom).

(b) 3-Methyl-2-(1-benzylphenylamino)benzo[*b*]thiophene (18%) was not crystallised, *m/e* 329 (Found: C, 80.1; H, 5.75; N, 4.3. Calc. for $C_{22}H_{19}NS$: C, 80.2; H, 5.8; N, 4.25%), δ 3.10—3.80 (1 H, s, amine), 4.33 (3 H, s, 3-CH_3), 6.60 (1 H, s), and 6.65—7.80 (14 H, m, arom), ν 3 420—3 504 cm^{-1} (NH).

Oxidation of 8b-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]-*thieno*[2,3-d]*isoxazolidine*. To a solution of the sulphide (0.08 g, 0.23 mmol) in chloroform (20 ml) at −10 °C was added over 30 min a solution of *m*-chloroperbenzoic acid (0.04 g, 0.23 mmol) and stirred during 5 h at the same temperature. After the usual work-up the residue was chromatographed on silica t.l.c. using chloroform–acetone (49 : 1) as eluant. Two compounds were obtained, *anti*-(2b) (44%) and *syn*-(2b) (9%).

4-*Oxo*-8b-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[*b*]*thieno*-[2,3-d]*isoxazolidine anti*-(2b). This had m.p. 142 °C, *m/e* 361 (Found: C, 73.0; H, 5.2; N, 3.8. Calc. for $C_{22}H_{19}NO_2S$: C,

73.1; H, 5.25; N, 3.9%), δ 2.05 (3 H, s, 8b-CH_3), 4.10 (1 H, d, *J* 5 Hz, 3a-H), 5.03 (1 H, d, *J* 5 Hz, 3-H), and 7.50—7.90 (14 H, m, arom), ν 1 025—1 050 cm^{-1} (SO).

Kinetic Studies.—In a refluxing chloroform solution of dipole, dipolarophile, and an internal standard, *i.e.* phenol, the following reactions were examined: (a) 1,1-dioxobenzo[*b*]thiophene (3) (0.018M), dipole (0.179M), phenol (0.640M); (b) 1,1-dioxo-3-methylbenzo[*b*]thiophene (3b) (0.016M), dipole (0.163M), phenol (0.035M); (c) 1-oxo-3-methylbenzo-[*b*]thiophene (1b) (0.016M), dipole (0.189M), phenol (0.078M). The reaction kinetics were carried out by analysing portions by h.p.l.c. with a u.v. detector at 270 nm for (3) and (3b) and 250 nm for (1b). The pseudo-first-order kinetic constants were determined by least-squares analysis, and the given values are the means of at least three runs with a precision of *ca.* 7%. The column type and the eluant used were respectively: for (3) and (3b) μ-Bondapak CN (Waters), cyclohexane 90%, methylene chloride 9.75%, propan-2-ol 0.25%; for (1b) μ-Bondapak CN (Waters), cyclohexane 80%, methylene chloride 19.5%, propan-2-ol 0.5%.

X-Ray Analysis and Structure Determination.—In each study a well formed crystal of dimensions 0.20 × 0.15 × 0.30 or 0.10 × 0.15 × 0.30 mm was mounted on a Syntex $P2_1$ autodiffractometer with Mo-K_α radiation (λ = 0.719 69 Å) with graphite monochromator. Automatic centring, indexing and least-squares routines were carried out to obtain the cell dimensions.

Structure determination of 4,4-*dioxo*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4). $C_{21}H_{17}NO_3S$, *M* = 363, *a* = 8.038(3), *b* = 14.880(8), *c* = 15.037(5) Å, β = 102.41(3)°, *V* = 1 756.5 Å^3, *Z* = 4, D_m 1.40 g cm^{-3}. The crystal was monoclinic, space group $P2_1/n$.

The structure was solved by MULTAN 78.[23] 2 585 Reflections were measured, only 2 021 of which had $I > 2.5\sigma(I)$. Lorentz and polarization corrections were applied to all reflections. The position of all non-hydrogen atoms were obtained from an *E*-map based on the solution with the highest combined figure of merit value and the lowest residual index. The structure was refined by full-matrix least-squares techniques with SHELX 76.[24] Two cycles of isotropic refinement converged at *R* = 0.10; the function minimized in the refinement was $\Sigma_w (F_o - F_c)^2$ where $w = 1/\sigma^2(F) + 0.001 F^2$. One cycle of anisotropic refinement reduced *R* to 0.074.

The hydrogen atoms were added to the model in geometrically ideal positions. The temperature factor for the hydrogen atoms was 6.50: final refinement led to convergence with *R* 0.053.

Structural details are in Supplementary Publication No. SUP 23733 (10 pp.).*

Structure determination of 4,4-*dioxo*-3a-*methyl*-2,3-*diphenyl*-2,3-*dihydrobenzo*[b]*thieno*[2,3-d]*isoxazolidine* (4aI). $C_{22}H_{19}NO_3S$, *M* = 377, *a* = 11.735(2), *b* = 10.322(2), *c* = 9.210(2) Å, α = 63.27(1)°, β = 101.59(1)°, γ = 110.71(1)°, *V* = 928.17 Å^3, *Z* = 2, D_m = 1.38 g cm^3, D_c 1.349 g cm^{-3}.

The crystal was triclinic, space group *P*1. *X*-Ray analysis were carried out as above: 2 756 reflections were measured, of which 2 021 had $I > 2.5\sigma(I)$. The structure was solved and refined as above and final refinement led to convergence with *R* 0.04. Structural details are in SUP 23733.

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* For details of Supplementary Publications see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 2*, 1984, Issue 1, p. xvii.