Synthesis, Stereochemistry, and Rearrangement of Thioxanthen-10-io-(bismethoxycarbonyl)methanides and their 9-Alkyl Derivatives [1]

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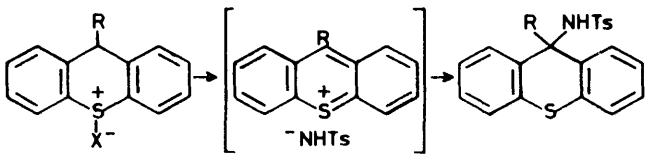
Thioxanthen-10-io- and 2,4-dimethylthioxanthen-10-io-(bismethoxycarbonyl)methanides and their 9-alkyl derivatives were synthesised by the reaction of the corresponding thioxanthens with bismethoxycarbonylcarbene generated thermally from dimethyl diazomalonate in the presence of copper(II) sulphate. The stereochemistry of the ylides was determined by examination of the n.m.r. spectra and by *X*-ray analysis of *trans*-9-ethyl-2,4-dimethylthioxanthen-10-io(bismethoxycarbonyl)methanide. Refluxing the sulphonium ylides in toluene in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) caused rearrangement to the corresponding 9-(bismethoxycarbonylmethyl)thioxanthens with the exception of the 9-isopropyl derivative, which was stable even in refluxing xylene. The mechanism of the rearrangement is discussed.

THIOXANTHEN *N*-TOSYLSULPHIMIDES (1) undergo base-catalysed rearrangement to 9-(*N*-tosylamido)thioxanthens (5) by way of a mechanism which involves thioxanthylium ions (4).[2-5] Thioxanthen 10-oxides (2) are known to be relatively stable under basic conditions. It appeared to be of interest to see if the iso-electronic sulphonium ylides (3) would undergo a similar rearrangement. We now report the synthesis, stereochemistry, and base-catalysed rearrangement of thioxanthen-10-io(bismethoxycarbonyl)methanides and their 9-alkyl derivatives.

Synthesis.—The thioxanthenio(bismethoxycarbonyl)-methanides (7a—g) were prepared in 60—84% yields by heating the thioxanthen (6a—g) at 90 °C for 4 h with dimethyl diazomalonate in the presence of anhydrous copper(II) sulphate, under conditions analogous to those reported by Ando *et al.*[6] 9-Methyl- (6b), 9-ethyl- (6c), and 9-isopropyl-thioxanthens (6d) and 9-ethyl-2,4-dimethylthioxanthen (6g) gave exclusively *trans*-isomers of the sulphonium ylides (7b—d and g). The only exception to this was (6f) which gave a mixture of *trans*- (7f) and *cis*- (8f) isomers in *ca.* 3 : 1 ratio. This mixture



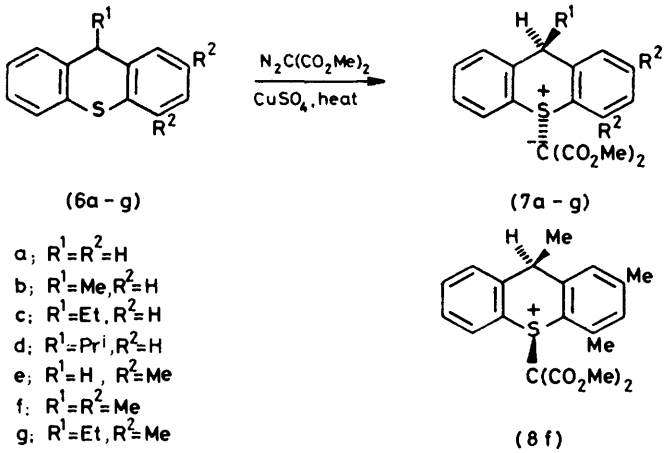
(1) X = NTs (4) (5)
(2) X = O
(3) X = CR′ R″

SCHEME 1

could not be separated by the conventional means. It should be noted that (7b—d) did not thermally epimerise: when solutions of (7b—d) in toluene were refluxed for 3 h, pure samples of (7b—d) were recovered unchanged. The exclusive or predominant formation of the more stable *trans*-isomers (7b—d, f, g) may reflect the high reaction temperature (high temperature may cause *cis–trans* isomerisation [7]) and bulk of the reagent.

Irradiation of a solution of dimethyl diazomalonate and (6b) in benzene in a Pyrex tube with a high-pressure mercury lamp [6] also gave (7b) but in low yield.

The structures of (7a—g) were apparent from the spectroscopic data. The mass spectra of the ylides showed the molecular ion peak [with the exception of

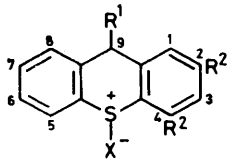


SCHEME 2

(7d)] and important fragment ions due to $[M - OCH_3]^+$, $[M - CH(CO_2CH_3)_2]^+$, and $[M - CR(CO_2CH_3)_2]^+$. The i.r. spectra showed a broad carbonyl band at 1 640—1 660 cm^{-1}. Further confirmation of these structures and stereochemistry was obtained from careful examination of the n.m.r. spectra (see later).

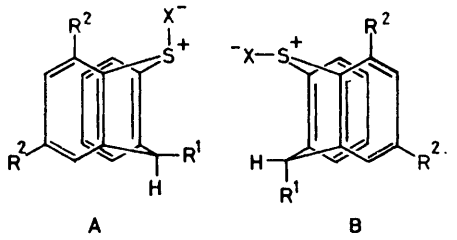
Stereochemistry.—The 9-H protons of (7a) appear as an AB quartet at δ 4.00 and 4.28 with *J* 17.5 Hz, the upper doublet (axial proton) of which is slightly broadened due to allylic coupling with the 1-H and 8-H protons, as anticipated.[8] The chemical shifts of the 9-H proton and 9-alkyl group of (7b—d) are closer to those of the *trans*-isomers of the corresponding sulphoxides [8,9] and *N*-tosylsulphimides [3] rather than to those of the *cis*-isomers (see Table 1). These observations define not only the *trans*-stereochemistry of (7b—d), but also the preferred conformation of (7a—d) which has the bismethoxycarbonylmethyl group equatorial

(conformer A). If the bismethoxycarbonylmethyl group were in the axial position, the chemical shifts of the axial 9-H proton or 9-alkyl group would be greatly affected due to anisotropy of the carbonyl group. This was demonstrated by the n.m.r. spectrum of (7e) in which the broadened (axial) 9-H proton signal (δ 5.03) is shifted *ca.* 1 p.p.m. to lower field than that of (7a) (δ 4.00). Apparently the bismethoxycarbonylmethyl group occupies an axial position in (7e) to avoid steric interaction with the 4-methyl group. However, this steric interaction appears to be not large enough to govern the conformation of 9-alkyl derivatives such as (7f) and (7g). The chemical shifts for both the 9-H and 9-methyl or methylene protons of (7f) and (7g) are closer to those of (7b)



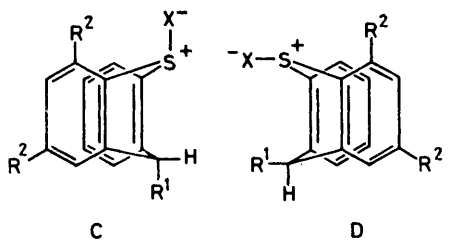
(1a–g), X = NTs

(7a–g), (8f), X = $C(CO_2Me)_2$



A B

trans - isomer



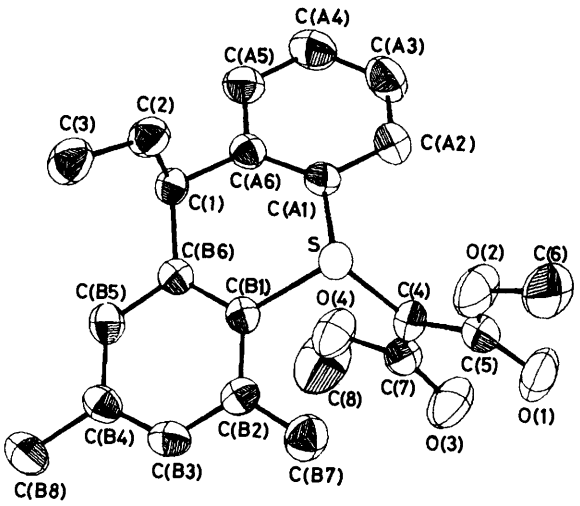
C D

cis - isomer

SCHEME 3

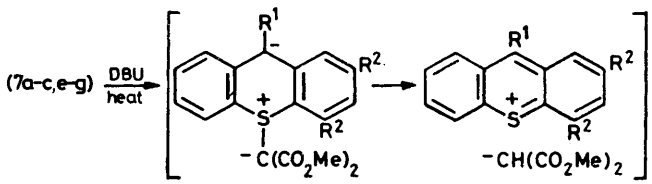
and (7c) (conformer A), but not to those of either isomers of the sulphimides (1f) and (1g) (conformer D for the *cis*- and conformer B for the *trans*-isomer) (see Table 1), suggesting that the bismethoxycarbonylmethyl group is equatorial (conformer A). This stereochemical assignment was finally confirmed by an *X*-ray analysis of (7g). The preferred conformation of (8f) (conformer C or D) is not clear at the present stage.

Crystal Structure of (7g).—The molecular structure of (7g) is illustrated in the Figure. The six-membered heterocyclic ring has a boat conformation; the deviations of the sulphur atom and C-9 atom from planarity

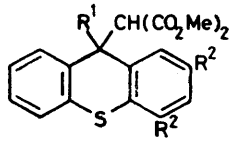


Perspective ORTEP drawing of compound (7g)

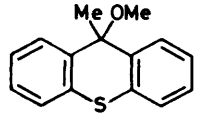
of the best plane were 0.35 and 0.42 Å, respectively. The 9-ethyl group occupies an axial and the *S*-bismethoxycarbonylmethyl group an equatorial position. The latter is oriented almost perpendicularly to the folded thioxanthen molecule. The dihedral angle between the least-squares planes of the two benzene



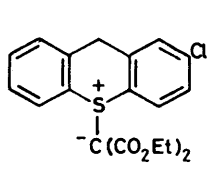
(8) (9)



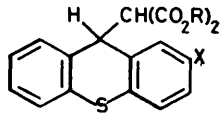
(10a-c,e-g)



(11)



(12)



(13) R = Et, X = H

(14) R = Et X = Cl

(15) R = Me, X = Cl

SCHEME 4

rings is 151.6°, which is the largest among the known thioxanthen derivatives.[10]

Base-catalysed Rearrangement.—Previously we noted that treatment of thioxanthen *N*-tosylsulphimide with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene at room temperature undergoes rearrangement to 9-(*N*-tosylamido)thioxanthen.[2] The sulphonium ylides (7a) and (7e) were stable under the same conditions, but on refluxing in toluene in the presence of DBU, (7a, e) were converted into the rearranged products (10a, e) in 81 and 85% yields, respectively. No rearrangement took place in the absence of DBU; when a toluene solution of (7a) was refluxed for 3 h, (7a) was recovered unchanged. Similarly the 9-alkyl congeners (7b, c) and (7f *,g) were transformed in this temperature range to (10b, c) and (10f, g) in good yields, respectively. The structures of the rearranged products (10a—c, e—g) were easily confirmed by spectral evidence (see Experimental section).

This rearrangement was found to be markedly affected by the solvent used. Thus, heating (7a) and DBU in dimethylformamide at 145 °C gave (10a) and thioxanthone † in 14 and 34% yields, respectively. When heated in methanol in the presence of DBU at 150 °C in a sealed tube (7b) gave exclusively 9-methoxy-9-methylthioxanthen (11) in 61% yield. If the reaction was carried out on a mixture of (7a) and 2-chlorothioxanthen-10-io(bisethoxycarbonyl)methanide (12) (prepared by the reaction of 2-chlorothioxanthen with diethyl diazomalonate) in toluene in the presence of DBU, no crossover products were formed, only (10a) and (14) being obtained. However, the same mixture, upon heating with DBU in dimethylformamide at 145 °C, afforded four possible products [(10a) : (13) = 1.5 : 1 and (14) : (15) = 2 : 1 (n.m.r.)], along with thioxanthone and 2-chlorothioxanthone. That bismethoxycarbonylcarbene [12] is not involved in this rearrangement was demonstrated by the fact that no adduct was formed when the reaction of (7a) was carried out in refluxing toluene in the presence of cyclo-octene.

A mechanistic rationalisation would involve an initial formation of the carbanions (8) which induce sulphur–carbon cleavage to give thioxanthylium ions (9), followed by intra- or inter-molecular recombination to give (10) or (11) depending on the degree of dissociation of the ions in the solvent used. The formation of (8), at least in methanol, was demonstrated by isolation of the 9-deuterio-derivative of (7b) after stirring (7b) in methan-[^{2}H]ol containing DBU at room temperature.

The 9-isopropyl derivative (7d) was remarkably stable and withstood prolonged refluxing (25 h) even in xylene, although the solution darkened gradually; refluxing in mesitylene resulted only in the decomposition of (7d). No characterisable product was isolated. Non-bonding interaction between the bulky 9-isopropyl group and *peri*-hydrogens in the transition state leading to the thioxanthylium ion (8; R^1 = Pr^i, R^2 = H) may be responsible for the low reactivity of (7d).

TABLE 1

N.m.r. spectra for thioxanthen-10-io(bismethoxycarbonyl)methanides (7a—g) and the corresponding *N*-tosylsulphimides (in $CDCl_3$)

Compd.	X	R^1	R^2	Preferred conformation	Chemical shift 9-H	Chemical shift 9-R^1
(7a)	$C(CO_2Me)_2$	H	H	*eq*-X	4.00,[a] 4.28 (AB q)	
(1a)	NTs	H	H	*eq*-X	3.88,[a] 4.32 (AB q)	
(7b)	$C(CO_2Me)_2$	Me	H	A	4.39 (q)	1.51 (d)
cis-(1b)	NTs	Me	H	C	3.86 (q)	1.90 (d)
trans-(1b)	NTs	Me	H	A	4.35 (q)	1.43 (d)
(7c)	$C(CO_2Me)_2$	Et	H	A	4.09 (t)	1.85 (m), 0.92 (t)
cis-(1c)	NTs	Et	H	D	3.80 (t)	2.28 (m), 1.04 (t)
trans-(1c)	NTs	Et	H	A	4.06 (t)	1.69 (m), 0.87 (t)
(7d)	$C(CO_2Me)_2$	i-Pr	H	A	3.62 (d)	1.85 (m), 0.85 (d)
trans-(1d)	NTs	i-Pr	H	A	3.72 (d)	1.75 (m), 0.82 (d)
(7e)	$C(CO_2Me)_2$	H	Me	*ax*-X	3.96, 5.03 [a] (AB q)	
(1e)	NTs	H	Me	*ax*-X	3.86, 4.80 [a] (AB q)	
(8f)	$C(CO_2Me)_2$	Me	Me	C or D	4.11 (q)	1.99 (d)
(7f)	$C(CO_2Me)_2$	Me	Me	A	4.39 (q)	1.39 (d)
cis-(1f)	NTs	Me	Me	D	4.15 (q)	1.89 (d)
trans-(1f)	NTs	Me	Me	B	5.14 (q)	1.89 (d)
(7g)	$C(CO_2Me)_2$	Et	Me	A	4.13 (q)	1.68 (m), 0.69 (t)
cis-(1g)	NTs	Et	Me	D	3.78 (q)	2.35 (m), 0.98 (t)
trans-(1g)	NTs	Et	Me	B	4.51 (q)	2.02 (m), 1.00 (t)

[a] Broadened by allylic coupling with 1-H and 8-H. This was confirmed by decoupling experiments.

EXPERIMENTAL

N.m.r. spectra were determined with a Hitachi R-20A spectrometer (tetramethylsilane as internal standard). I.r. spectra were recorded with a Hitachi EPI-G2 spectrophotometer. Column chromatography was carried out on

* A mixture of (7f) and (8f) (*ca.* 3 : 1) was used.

† The mechanism for the formation of thioxanthone is not clear. The possibility that 9-hydroxythioxanthen, formed from the possible intermediate thioxanthylium ion (9; R^1 = R^2 = H) and water, disproportionates to give thioxanthone and thioxanthen [11] is eliminated by the fact that the latter was not observed in the reaction mixture.

Merck silica gel. Mass spectra were obtained with a Hitachi RMU-6E with a direct inlet system operating at 70 eV.

General Procedure for the Preparation of Thioxanthenio(bismethoxycarbonyl)methanides (7).—According to the procedure of Ando *et al.*,[6] a mixture of a thioxanthen (2.2 mmol), dimethyl diazomalonate (400 mg, 2.5 mmol), and anhydrous copper(II) sulphate (15 mg) was heated at 90 °C for 4 h. After cooling, $CHCl_3$ (15 ml) was added to the reaction mixture and the mixture was filtered and concentrated. The residual oil was chromatographed on silica gel [benzene–EtOAc (2 : 1 v/v)]. *Thioxanthen-10-io(bismethoxycarbonyl)methanide* (7a) (66%) had m.p. 199—200 °C (from benzene–n-hexane) (Found: C, 65.9; H, 4.95. $C_{18}H_{16}O_4S$ requires C, 65.83; H, 4.91%); $\nu_{max.}$ ($CHCl_3$) 1 650 cm^{-1}; δ ($CDCl_3$) 7.3—7.8 (8 H, m, aromatic), 4.28, 4.00 (1 H each, ABq, *J* 17.5 Hz, 9-H), and 3.60 (6 H, s, 2 × OCH_3); *m/e* 328 (M^+, 0.8%), 297 (4.1), and 197 (100); trans-9-*methylthioxanthen*-10-*io*(*bismethoxycarbonyl*)*methanide* (7b) (84%) had m.p. 175—176 °C [from benzene–light petroleum (b.p. 40—60 °C)] (Found: C, 66.55; H, 5.25. $C_{19}H_{18}O_4S$ requires C, 66.64; H, 5.30%); $\nu_{max.}$ ($CHCl_3$) 1 650 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (8 H, m, aromatic), 4.39 (1 H, q, *J* 7 Hz, 9-H), 3.59 (6 H, s, 2 × OCH_3), and 1.51 (3 H, d, *J* 7 Hz, 9-CH_3); *m/e* 342 (M^+, 0.9%), 311 (4.7), 211 (100), and 197 (30); trans-9-*ethylthioxanthen*-10-*io*(*bismethoxycarbonyl*)*methanide* (7c) (76%) had m.p. 178—179 °C (from EtOAc–di-isopropyl ether) (Found: C, 66.95; H, 5.65. $C_{20}H_{20}O_4S$ requires C, 67.39; H, 5.66%); $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1}; δ ($CDCl_3$) 7.3—7.9 (8 H, m, aromatic), 4.09 (1 H, t, *J* 7.5 Hz, 9-H), 3.59 (6 H, s, 2 × OCH_3), 1.85 (2 H, m, 9-CH_2CH_3), and 0.92 (3 H, t, *J* 6.5 Hz, 9-CH_2CH_3); *m/e* 356 (M^+, 0.3%), 325 (5.5), 225 (100), and 197 (48); trans-9-*isopropylthioxanthen*-10-*io*(*bismethoxycarbonyl*)*methanide* (7d) (72%) had m.p. 163—164.5 °C (from EtOAc–isopropyl ether) (Found: C, 67.65; H, 5.95. $C_{21}H_{22}O_4S$ requires C, 68.08; H, 6.00%); $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (8 H, m, aromatic), 3.62 (1 H, d, *J* 8 Hz, 9-H), 3.82 (3 H, s, OCH_3), 3.26 (3 H, s, OCH_3), 1.85 [1 H, m, 9-$CH(CH_3)_2$], and 0.85 [6 H, d, *J* 7 Hz, 9-$CH(CH_3)_2$]; *m/e* 339 (5.2%), 239 (95), and 197 (100) (the molecular ion peak was not observed); 2,4-*dimethylthioxanthen*-10-*io*(*bismethoxycarbonyl*)*methanide* (7e) (64%) had m.p. 187.5—190 °C (from benzene–n-hexane) (Found: C, 67.3; H, 5.6. $C_{20}H_{20}O_4S$ requires C, 67.40; H, 5.66%); $\nu_{max.}$ ($CHCl_3$) 1 640 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (4 H, m, aromatic), 7.01 (2 H, brs, aromatic), 5.03, 3.96 (1 H each, AB q, *J* 20 Hz, 9-H), 3.67 (6 H, s, 2 × OCH_3), 2.54 (3 H, s, 2- or 4-CH_3), and 2.33 (3 H, s, 4- or 2-CH_3); *m/e* 356 (M^+, 2.3%), 325 (4.5), 225 (100), and 211 (9.5); cis- (8f) *and* trans-2,4,9-*trimethylthioxanthen*-10-*io*(*bismethoxycarbonyl*)*methanide* (7f) (60%) formed an inseparable mixture in a ratio of *ca.* 1 : 3 (n.m.r.), m.p. 156—158 °C (from EtOAc) (Found: C, 67.7; H, 6.0. $C_{21}H_{22}O_4S$ requires C, 68.08; H, 5.99%); $\nu_{max.}$ ($CHCl_3$) 1 640 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (4 H, m, aromatic), 6.73 and 6.84 (1 H each, br s, aromatic), 4.39 and 4.11 (1 H, q, *ca.* 3 : 1, *J* 7.5 Hz, 9-H), 3.56 and 3.64 (6 H, s, *ca.* 3 : 1, 2 × OCH_3), 2.50 (3 H, s, 2- or 4-CH_3), 2.33 (3 H, s, 4- or 2-CH_3), and 1.99, 1.39 (3 H, d, *ca.* 3 : 1, *J* 7.5 Hz, 9-CH_3); trans-9-*ethyl*-2,4-*dimethylthioxanthen*-10-*io*(*bismethoxycarbonyl*)*methanide* (7g) (76%) had m.p. 169—170 °C (from EtOAc) (Found: C, 68.7; H, 6.25. $C_{22}H_{24}O_4S$ requires C, 68.73; H, 6.29%); $\nu_{max.}$ ($CHCl_3$) 1 650 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (4 H, m, aromatic), 6.97 and 7.07 (1 H each, br s, aromatic), 4.13 (1 H, t, *J* 7 Hz, 9-H), 3.54 (6 H, s, 2 × OCH_3), 2.33 (3 H, s, 2- or 4-CH_3), 2.50 (3 H, s, 4- or 2-CH_3), 1.68 (2 H, m, 9-CH_2CH_3), and 0.69 (3 H, t, *J* 8 Hz, 9-CH_2CH_3); *m/e* 384 (M^+, 2.4%), 353 (4.5), 253 (98), and 225 (100).

Photolysis of Dimethyl Diazomalonate in the Presence of (6b).—A solution of (6b) (100 mg, 0.47 mmol) and dimethyl diazomalonate (80 mg, 0.55 mmol) in benzene (20 ml) was irradiated in a Pyrex vessel with a high-pressure mercury lamp for 24 h. The reaction mixture was concentrated and the residue was chromatographed on silica gel. Elution with benzene–EtOAc (2 : 1) gave (7b) (10 mg, 6%) as the only characterisable product.

X-Ray Analysis of Compound (7g).—*Crystal data.* $C_{22}H_{24}O_4S$, M = 384.5. Monoclinic, a = 14.635 (10), b = 9.964 (5), c = 15.877 (9) Å, β = 106.80 (5)°, U = 1994.1 Å^3, Z = 4, D_c = 1.28 g cm^{-3}. Space group $P2_1/n$. Mo-K_α radiation, λ = 0.7107 Å, μ(Mo-K_α) = 1.9 cm^{-1}.

Data collection. A crystal, *ca.* 0.2 × 0.4 × 0.4 mm, was mounted on a Syntex R_3 four-circle automated diffractometer. The cell dimensions were refined by the least-squares method, using 20 reflexions measured on the diffractometer with graphite-monochromated Mo-$K\alpha$ radiation. Intensity data were collected on the diffractometer with the same radiation using an ω–2θ scanning technique within 2θ less than 45°. Three reference reflexions monitored periodically showed no significant intensity fluctuations during the course of data collection. A total of 2 206 independent reflexions were used for the structure analysis. Intensities were corrected for Lorentz and polarisation factors, but not for absorption.

Structure determination and refinement. The structure was solved by direct methods (MULTAN method [13]). The positional co-ordinates were refined by the block-diagonal least-squares method, using anisotropic temperature factors for all the non-hydrogen atoms and isotropic ones for hydrogen atoms. The final R-value was 0.041. The atomic scattering factors were taken from 'International Tables for X-ray Crystallography.' [14] Bond lengths and bond angles are listed in Tables 2 and 3. Observed and calculated structure factors, atomic co-ordinates, and thermal parameters are listed in Supplementary Publication No. SUP 22907 (16 pp.).*

TABLE 2

Bond lengths (in Å) with estimated standard deviations in parentheses

S–C(A1)	1.792(3)	C(A6)–C(1)	1.507(4)
S–C(B1)	1.805(3)	C(B1)–C(B2)	1.413(5)
S–C(4)	1.722(3)	C(B1)–C(B6)	1.395(4)
O(1)–C(5)	1.208(4)	C(B2)–C(B3)	1.387(5)
O(2)–C(5)	1.363(4)	C(B2)–C(B7)	1.507(5)
O(2)–C(6)	1.447(5)	C(B3)–C(B4)	1.394(4)
O(3)–C(7)	1.217(4)	C(B4)–C(B5)	1.376(5)
O(4)–C(7)	1.359(4)	C(B4)–C(B8)	1.514(5)
O(4)–C(8)	1.413(4)	C(B5)–C(B6)	1.397(4)
C(A1)–C(A2)	1.393(5)	C(B6)–C(1)	1.509(4)
C(A1)–C(A6)	1.387(4)	C(1)–C(2)	1.548(4)
C(A2)–C(A3)	1.380(5)	C(2)–C(3)	1.519(5)
C(A3)–C(A4)	1.375(5)	C(4)–C(5)	1.446(4)
C(A4)–C(A5)	1.386(5)	C(4)–C(7)	1.439(5)
C(A5)–C(A6)	1.403(5)		

9-Bismethoxycarbonylmethylthioxanthen (10a).—(a) *In Toluene.* A solution of (7a) (150 mg, 0.46 mmol) and DBU (70 mg, 0.46 mmol) in toluene (4 ml) was refluxed for 3 h. After cooling, the reaction mixture was washed with 10% HCl and H_2O, dried ($MgSO_4$), and concentrated. The

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residual solid was recrystallised from EtOH to give (10a) (121 mg, 81%) as colourless needles, m.p. 110.5—111 °C (lit.,[15] 113 °C); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 730 cm^{-1}; δ ($CDCl_3$) 7.1—7.6 (8 H, m, aromatic), 4.93 and 4.20 [1 H each, ABq, *J* 11 Hz, $CH(CO_2CH_3)_2$ and 9-H, respectively], and 3.48 (6 H, s, 2 × OCH_3).

(b) *In DMF.* A solution of (7a) (100 mg, 0.30 mmol) and DBU (48 mg, 0.31 mmol) in DMF (3 ml) was heated at 145 °C for 3 h. After cooling, the reaction mixture was concentrated, diluted with $CHCl_3$, and washed with 10% HCl and H_2O, dried ($MgSO_4$), and concentrated. The residual oil was chromatographed on silica gel (benzene as eluant) to give (10a) (14 mg, 14%) and thioxanthone (22 mg, 34%).

9-Bismethoxycarbonylmethyl-9-methylthioxanthen (10b).—A solution of (7b) (100 mg, 0.29 mmol) and DBU (45 mg, 0.30 mmol) in toluene (3 ml) was refluxed for 5 h. Work-up as described above gave (10b) (71 mg, 71%) as *scales*, m.p. 85—86 °C (Found: C, 66.55; H, 5.3. $C_{19}H_{18}O_4S$ requires C, 66.64; H, 5.30%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 725 cm^{-1}; δ ($CDCl_3$) 7.1—7.7 (8 H, m, aromatic), 4.90 [1 H, s, $CH(CO_2CH_3)_2$], 3.33 (6 H, s, 2 × OCH_3), and 2.32 (3 H, s, 9-CH_3).

TABLE 3

Bond angles (°) with estimated standard deviations in parentheses

C(A1)–S–C(B1)	102.4(1)	C(B2)–C(B3)–C(B4)	122.4(3)
C(A1)–S–C(4)	105.4(2)	C(B3)–C(B4)–C(B5)	118.0(3)
C(B1)–S–C(4)	108.2(2)	C(B3)–C(B4)–C(B8)	120.3(3)
C(5)–O(2)–C(6)	116.7(3)	C(B5)–C(B4)–C(B8)	121.7(3)
C(7)–O(4)–C(8)	116.5(3)	C(B4)–C(B5)–C(B6)	122.9(3)
S–C(A1)–C(A2)	115.7(2)	C(B1)–C(B6)–C(B5)	117.1(3)
S–C(A1)–C(A6)	122.3(2)	C(B1)–C(B6)–C(1)	123.6(3)
C(A2)–C(A1)–C(A6)	122.0(3)	C(B5)–C(B6)–C(1)	119.0(3)
C(A1)–C(A2)–C(A3)	118.6(3)	C(A6)–C(1)–C(B6)	114.3(3)
C(A2)–C(A3)–C(A4)	120.9(4)	C(A6)–C(1)–C(2)	108.4(2)
C(A3)–C(A4)–C(A5)	120.3(3)	C(B6)–C(1)–C(2)	111.9(2)
C(A4)–C(A5)–C(A6)	120.4(3)	C(1)–C(2)–C(3)	115.6(3)
C(A1)–C(A6)–C(A5)	117.9(3)	S–C(4)–C(5)	117.2(2)
C(A1)–C(A6)–C(1)	122.1(3)	S–C(4)–C(7)	121.8(2)
C(A5)–C(A6)–C(1)	119.9(3)	C(5)–C(4)–C(7)	121.0(3)
S–C(B1)–C(B2)	118.2(2)	O(1)–C(5)–O(2)	121.7(3)
S–C(B1)–C(B6)	119.8(2)	O(1)–C(5)–C(4)	127.1(3)
C(B2)–C(B1)–C(B6)	122.0(3)	O(2)–C(5)–C(4)	111.3(3)
C(B1)–C(B2)–C(B3)	117.3(3)	O(3)–C(7)–O(4)	121.4(3)
C(B1)–C(B2)–C(B7)	124.4(3)	O(3)–C(7)–C(4)	127.2(3)
C(B3)–C(B2)–C(B7)	118.3(3)	O(4)–C(7)–C(4)	111.4(3)

9-Bismethoxycarbonylmethyl-9-ethylthioxanthen (10c).—A solution of (7c) (150 mg, 0.42 mmol) and DBU (65 mg, 0.42 mmol) in toluene (4 ml) was refluxed for 18 h and work-up gave (10c) (93 mg, 62%) as *needles*, m.p. 146—147 °C (Found: 67.35; H, 5.7. $C_{20}H_{20}O_4S$ requires C, 67.39; H, 5.66%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 725 cm^{-1}; δ ($CDCl_3$) 7.2—7.7 (8 H, m, aromatic), 4.48 [1 H, s, $CH(CO_2CH_3)_2$], 3.32 (6 H, s, 2 × OCH_3), 3.12 (2 H, q, *J* 7.0 Hz, 9-CH_2CH_3), and 1.03 (3 H, t, *J* 7.0 Hz, 9-CH_2CH_3).

9-Bismethoxycarbonylmethyl-2,4-dimethylthioxanthen (10e).—A solution of (7e) (150 mg, 0.42 mmol) and DBU (60 mg, 0.40 mmol) in toluene (10 ml) was refluxed for 3 h. Work-up gave (10e) (127 mg, 85%) as *crystals*, m.p. 114—114.5 °C (from MeOH) (Found: C, 67.25; H, 5.65. $C_{20}H_{20}O_4S$ requires C, 67.40; H, 5.66%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 730 cm^{-1}; δ ($CDCl_3$) 6.8—7.5 (6 H, m, aromatic), 4.78 and 4.14 [1 H each, AB q, *J* 11.5 Hz, $CH(CO_2CH_3)_2$ and 9-H, respectively], 3.46 (3 H, s, OCH_3), 3.43 (3 H, s, OCH_3), 2.39 (3 H, s, 2- or 4-CH_3), and 2.28 (3 H, s, 4- or 2-CH_3).

9-Bismethoxycarbonylmethyl-2,4,9-trimethylthioxanthen (10f).—A solution of (7f) [150 mg as a mixture of (7f) and (8f), 0.41 mmol] and DBU (60 mg, 0.40 mmol) in toluene (10 ml) was refluxed for 2 h and work-up gave (10f) (103 mg, 70%) as *needles*, m.p. 96.5—97 °C (from MeOH) (Found: C, 68.0; H, 5.95. $C_{21}H_{22}O_4S$ requires C, 68.08; H, 5.99%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 730 cm^{-1}; δ ($CDCl_3$) 6.8—7.1 (6 H, m, aromatic), 4.90 [1 H, s, $CH(CO_2CH_3)_2$], 3.34 (3 H, s, OCH_3), 3.32 (3 H, s, OCH_3), 2.42 (3 H, s, 2- or 4-CH_3), and 2.32 (6 H, s, 4- or 2-CH_3 and 9-CH_3).

9-Bismethoxycarbonyl-9-ethyl-2,4-dimethylthioxanthen (10 g).—A solution of (7g) (150 mg, 0.39 mmol) and DBU (50 mg, 0.40 mmol) in toluene (10 ml) was refluxed for 3.5 h. Work-up gave (10 g) (98 mg, 65%) as *crystals*, m.p. 162—163 °C (from MeOH) (Found: C, 68.55; H, 6.35. $C_{22}H_{24}O_4S$ requires C, 68.73; H, 6.29%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 730 cm^{-1}; δ ($CDCl_3$) 6.9—7.5 (6 H, m, aromatic), 4.46 [1 H, s, $CH(CO_2CH_3)_2$], 3.30 (6 H, s, 2 × OCH_3), 3.08 (2 H, q, *J* 7.2 Hz, 9-CH_2CH_3), 2.40 (3 H, s, 2- or 4-CH_3), 2.32 (3 H, s, 4- or 2-CH_3), and 1.02 (3 H, t, *J* 7.2 Hz, 9-CH_2CH_3).

Reaction of (7b) *with DBU in Methanol.*—A solution of (7b) (30 mg, 0.09 mmol) and DBU (15 mg, 0.1 mmol) in MeOH (1 ml) was heated in a sealed tube at 150 °C for 6 h. After cooling, the reaction mixture was concentrated, diluted with 10% HCl, and extracted with $CHCl_3$. The extract was washed with H_2O, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [benzene–EtOAc (5 : 1 v/v) as eluant] to give 9-methoxy-9-methylthioxanthene (11) (13 mg) as *needles*, m.p. 120—121 °C (lit.,[3] 120—121 °C).

2-Chlorothioxanthen-10-io(bisethoxycarbonyl)methanide (12).—By using a similar procedure to that described for the preparation of (7a), compound (12) (456 mg, 78%) was obtained from 2-chlorothioxanthen (350 mg, 1.5 mmol) and diethyl diazomalonate (300 mg, 1.6 mmol) as *crystals*, m.p. 164—166 °C (from benzene–n-hexane) (Found: C, 61.75; H, 4.9. $C_{20}H_{19}ClO_4S$ requires C, 61.45; H, 4.90%); $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (7 H, m, aromatic), 4.20 and 3.90 (1 H, each AB q, *J* 18 Hz, 9-H), 4.01 (4 H, q, *J* 7.5 Hz, OCH_2CH_3), and 1.02 (6 H, t, *J* 7.5 Hz, OCH_2CH_3).

9-Bisethoxycarbonylmethylthioxanthen (13).—Treatment of (6a) (100 mg, 0.51 mmol) with diethyl diazomalonate (110 mg, 0.60 mmol) in the presence of anhydrous copper(II) sulphate (5 mg) as described for the preparation of (7a), gave *thioxanthen-10-io(bisethoxycarbonyl)methanide* (132 mg, 73%) as *needles*, m.p. 187—188 °C (from benzene–n-hexane) (Found: C, 67.7; H, 5.65. $C_{20}H_{20}O_4S$ requires C, 67.39; H, 5.66%); $\nu_{max.}$ ($CHCl_3$) 1 650 cm^{-1}; δ ($CDCl_3$) 7.2—7.8 (8 H, m, aromatic), 4.25 (1 H, a part of AB q, *J* 18 Hz, one of 9-H; the signal for another 9-H was masked by those of the ethoxy-methylene protons), 4.00 (5 H, q, *J* 7.5 Hz, 2 × OCH_2CH_3 and one of 9-H), and 1.00 (6 H, t, *J* 7.5 Hz, 2 × OCH_2CH_3). A solution of this methanide (150 mg, 0.42 mmol) and DBU (65 mg, 0.42 mmol) in toluene (4 ml) was refluxed for 3 h. Work-up gave (13) (118 mg, 79%) as *needles*, m.p. 69—70.5 °C (from MeOH) (lit.,[15] 69—70 °C); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 725 cm^{-1}; δ ($CDCl_3$) 7.0—7.5 (8 H, m, aromatic), 4.85 and 4.12 [1 H each, AB q, *J* 12 Hz, $CH(CO_2CH_3)_2$ and 9-H, respectively], 3.91 (4 H, q, *J* 7.5 Hz, 2 × OCH_2CH_3), and 1.02 (6 H, t, *J* 7.5 Hz, 2 × OCH_2CH_3).

9-Bisethoxycarbonylmethyl-2-chlorothioxanthen (14).—By using a similar procedure to that described for the preparation of (10a), compound (14) (115 mg, 77%) was obtained from (12) (150 mg, 0.38 mmol) as *needles*, m.p. 121.5—122 °C (from MeOH) (Found: C, 61.6; H, 4.85. $C_{20}H_{19}$-

ClO_4S requires C, 61.45; H, 4.90%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 725 cm^{-1}; δ ($CDCl_3$) 7.0—7.5 (7 H, m, aromatic), 4.85 and 4.13 [1 H each, AB q, *J* 12 Hz, $CH(CO_2C_2H_5)_2$ and 9-H, respectively], 3.98 (2 H, q, *J* 7.5 Hz, OCH_2CH_3), 3.91 (2 H, q, *J* 7.5 Hz, OCH_2CH_3), 1.10 (3 H, t, *J* 7.5 Hz, OCH_2CH_3), and 1.02 (3 H, t, *J* 7.5 Hz, OCH_2CH_3).

9-Bismethoxycarbonylmethyl-2-chlorothioxanthen (15).—Treatment of 2-chlorothioxanthen (350 mg, 1.5 mmol) with dimethyl diazomalonate (250 mg, 1.6 mmol) in the presence of copper(II) sulphate (10 mg) gave *2-chlorothioxanthen-10-io(bismethoxycarbonyl)methanide* (400 mg, 73%) as *needles*, m.p. 183.5—185 °C (from benzene–n-hexane) (Found: C, 59.7; H, 4.2. $C_{18}H_{15}ClO_4S$ requires C, 59.58; H, 4.17%); $\nu_{max.}$ ($CHCl_3$) 1 650 cm^{-1}; δ ($CDCl_3$) 7.2—7.7 (7 H, m, aromatic), 4.25 and 3.88 (1 H each, AB q, *J* 18 Hz, 9-H), and 3.60 (6 H, s, 2 × OCH_3). By using a similar procedure to that described for the preparation of (10a), compound (15) (113 mg, 75%) was obtained from the above methanide as *needles* (150 mg, 0.41 mmol), m.p. 118—119 °C (from EtOH) (Found: C, 59.75; H, 4.2 $C_{18}H_{15}ClO_4S$ requires C, 59.58; H, 4.17%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 730 cm^{-1}; δ ($CDCl_3$) 7.0—7.5 (7 H, m, aromatic), 4.85 and 4.15 [1 H each, AB q, *J* 11 Hz, $CH(CO_2CH_3)_2$ and 9-H, respectively], 3.52 (3 H, s, OCH_3), and 3.45 (3 H, s, OCH_3).

Deuterium Exchange of (7b) *in Methan*[^{2}H]*ol.*—A solution of (7b) (50 mg, 0.15 mmol) and DBU (20 mg, 0.14 mmol) in methan[^{2}H]ol (2 ml) was set aside at room temperature for 4 h. The reaction mixture was then concentrated and the residue chromatographed on silica gel [benzene–EtOAc (2 : 1 v/v) as eluant] to give 9-methyl[9-^{2}H]thioxanthen-10-io(bismethoxycarbonyl)methanide (48 mg), m.p. 175—176 °C [from benzene–light petroleum (b.p. 40—60 °C)]; δ ($CDCl_3$) 7.2—7.8 (8 H, m, aromatic), 3.55 (6 H, s, 2 × OCH_3), and 1.50 (3 H, s, 9-CH_3).

Crossover Experiments.—(a) *In toluene.* A solution of (7a) (84 mg, 0.26 mmol) and (12) (100 mg, 0.26 mmol) in toluene (5 ml) containing DBU (80 mg, 0.52 mmol) was refluxed for 3 h. After cooling the reaction mixture was washed with 10% HCl and H_2O, dried ($MgSO_4$), and concentrated. The residual oil was chromatographed on silica gel (benzene as eluant) to give (10a) (62 mg, 74%) and (14) (79 mg, 79%). The n.m.r. spectrum of the crude mixture showed that no crossover products were formed.

(b) *In DMF.* A solution of (7a) (84 mg, 0.26 mmol) and (12) (100 mg, 0.26 mmol) in DMF (5 ml) containing DBU (80 mg, 0.52 mmol) was heated at 145 °C for 3 h. After cooling the reaction mixture was concentrated. The residue was diluted with $CHCl_3$ and washed with 10% HCl and H_2O, dried ($MgSO_4$), and concentrated. The residual oil was chromatographed on silica gel with benzene to give a mixture of (10a) and (13) (10 mg) in the ratio 1.5 : 1 (n.m.r.) and a mixture of (14) and (15) (13 mg) in the ratio 2 : 1 (n.m.r.) along with thioxanthone (20 mg) and 2-chlorothioxanthone (21 mg).

[0/571 *Received*, 17*th April*, 1980]

REFERENCES

[1] Preliminary communication, Y. Tamura, C. Mukai, and M. Ikeda, *Heterocycles*, 1979, **12**, 1179.
[2] Y. Tamura, Y. Nishikawa, K. Sumoto, M. Ikeda, M. Murase, and M. Kise, *J. Org. Chem.*, 1977, **42**, 3226.
[3] Y. Tamura, Y. Nishikawa, C. Mukai, K. Sumoto, M. Ikeda, and M. Kise, *J. Org. Chem.*, 1979, **44**, 1684.
[4] Y. Tamura, C. Mukai, Y. Nishikawa, and M. Ikeda, *J. Org. Chem.*, 1979, **44**, 3296.
[5] Y. Tamura, C. Mukai, N. Nakajima, and M. Ikeda, *J. Org. Chem.*, 1980, **45**, 2972.
[6] W. Ando, T. Yagihara, S. Tozune, I. Imai, J. Suzuki, T. Toyama, S. Nakaido, and T. Migita, *J. Org. Chem.*, 1972, **37**, 1721.
[7] D. Darwish and R. L. Tomilson, *J. Amer. Chem. Soc.*, 1968, **90**, 5938.
[8] A. L. Ternay, jun., L. Ens, J. Herrmann, and S. Evans, *J. Org. Chem.*, 1969, **34**, 940.
[9] S. A. Evans and A. L. Ternay, jun., *J. Org. Chem.*, 1975, **40**, 2993; 1978, **43**, 5026.
[10] S. S. C. Chu, *Acta Cryst.*, 1975, **B31**, 1082 and references cited therein.
[11] D. W. Chasar, A. L. Ternay, jun., L. Hushes, H. J. Shine, and S. A. Evans, *J. Org. Chem.*, 1975, **40**, 1737.
[12] R. J. Gillespie, A. E. A. Porter, and W. E. Willmott, *J.C.S. Chem. Comm.*, 1978, 85.
[13] G. Mermain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.
[14] 'International Tables for *X*-ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. IV, p. 71.
[15] I. Okabayashi and K. Okochi, *J. Pharm. Soc. Japan*, 1966, **86**, 828.