# Absolute Configuration of Ethylmethylpropylsulphonium Ion determined by Chemical Correlation with (4*S*,6*S*)-4-Ethyl-6-methyl-2-oxo-1,4-oxathianium Ion [1]

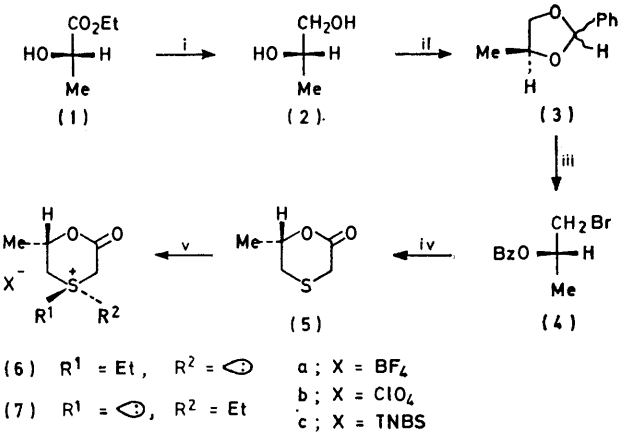
By **Ebbe Kelstrup**, Department of Organic Chemistry, The Technical University of Denmark, 2800 Lyngby, Denmark

The (4*S*,6*S*)- and (4*R*,6*S*)-4-ethyl-6-methyl-2-oxo-1,4-oxathianium ions (6) and (7) have been synthesized from ethyl (*S*)-lactate (1) and the *trans*-isomer (6) has been chemically degraded to (+)-methylethylpropylsulphonium ion (16). Control experiments served to ascertain that the sulphur centre retains its chirality virtually unimpaired under the reaction conditions employed. Consequently, dextrorotatory (16) possesses (*S*)-configuration. The optical rotation and thermodynamic parameters for pyramidal inversion of (*S*)-(16), produced by resolution of racemic (16), compared satisfactorily with those of (*S*)-(16) resulting from chemical degradation of (6).

SULPHONIUM ions with three carbon atoms attached to sulphur were first resolved at the turn of the century.[2] Much later, their optical stability and mechanisms of their racemization were studied, notably by Darwish and his co-workers.[3,4] Sulphonium ions normally racemize by pyramidal inversion, their optical stability being dependent upon the degree of steric compression in the ground state.[3,4] Thus, optically active triarylsulphonium ions have so far not been produced, and diarylalkylsulphonium ions racemize fairly readily in solution.[4] In 1971, Andersen [5] reported the conversion of sulphoxides of known absolute configuration into optically active aryldialkylsulphonium ions by reaction with dialkylcadmium reagents. This reaction was subsequently shown to proceed predominantly by *inversion* in the case of cyclic aryl alkyl sulphoxides.[6] By analogy, the absolute configurations of several aryldialkylsulphonium ions were inferred.[6,7] In 1975, the absolute configuration of the formally simplest trialkylsulphonium ion, *viz.* the methylethylpropylsulphonium ion, was established in this laboratory by chemical correlation with (*S*)-lactic acid through the intermediacy of (4*S*,6*S*)-4-ethyl-6-methyl-2-oxo-1,4-oxathianium ion, the relative configuration of which was established by single crystal *X*-ray anylysis [1] and by a combination of chemical and n.m.r. spectroscopic methods.[8]

## RESULTS AND DISCUSSION

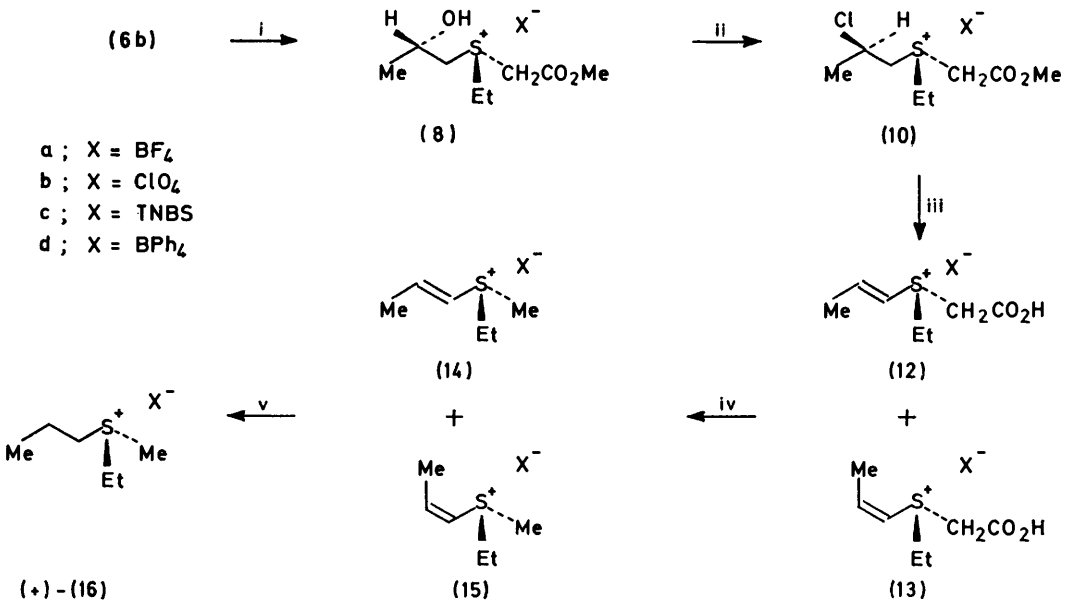
The (4*S*,6*S*)- and (4*R*,6*S*)-4-ethyl-6-methyl-2-oxo-1,4-oxathianium ions, (6) and (7), were synthesized as shown in Scheme 1. Optically active propane-1,2-diol (2) is usually produced by reduction of lactic acid derivatives.[9-11] In the present work, the conversion of the acetal mixture (3) into the bromobenzoate (4) was modelled after known reactions in the carbohydrate series.[12] The lactone (5), easily purified, presumably to a high degree of optical purity, on ethylation gave a *ca.* 1 : 1 mixture of (6) and (7), isolated as a mixture of their 2,4,6-trinitrobenzenesulphonate ($TNBS^-$) salts, from which homogeneous (6c) was obtained and subsequently converted into (6b). The mother liquors, after ion-exchange, afforded the salt (7b). The transformation of (6b) into methylethylpropylsulphonium ion is summarized in Scheme 2. Though experimentally unproven, the second step is assumed to proceed with inversion. Ester hydrolysis and elimination were carried out in one step to give a 2.5 : 1 mixture of the *trans*- and *cis*-propenylsulphonium salts (12) and (13). Decarboxylation of thetins under mild conditions was reported in 1959 by Burness,[13] a reaction optimized in the present work to proceed smoothly at 56 °C when (14) and




SCHEME 1 Reagents: i, $LiAlH_4$, THF; ii, PhCHO, TsOH, $C_6H_6$; iii, *N*-bromosuccinimide, $CCl_4$, $BaCO_3$, ***hν***, heat; iv, (a) $HS{\cdot}CH_2CO_2H$, NaOMe, MeOH, (b) HCl, (c) IR 120/$H^+$–resin; v, $Et_3O^+BF_4^-$, $CH_2Cl_2$

(15), in an unchanged ratio, were produced in less than 10 min. The first three steps in the sequence involve sulphonium ions containing two chiral centres. Even when the reaction conditions would not, *a priori*, be expected to affect the sulphur centre, independent evidence was sought. Thus, the two first steps were checked by analyzing the compositions of the diastereoisomers (8)—(9) and (10)—(11), in the racemic sequences starting from $(6a)_{rac}$[8] and $(7b)_{rac}$[8] (Scheme 3). The analyses were performed on the tetraphenylborate salts, $(8d)_{rac}$—$(11d)_{rac}$, by an $^1H$ n.m.r. technique. Only with this anion [14] was sufficient anisochronism between the diastereoisomers obtained. Virtually homogeneous hydroxy-esters, (8) and (9), were obtained from the lactones, (6) and (7), respectively, whereas the reactions of the former with thionyl chloride proceed less stereospecifically. Thus, $(6a)_{rac}$ and $(7b)_{rac}$ both afforded

mixtures, containing >80% of $(10)_{rac}$ and $(11)_{rac}$ respectively. Similar controls were made in the actual degradation of optically active (6b). The third step proceeded in >80% yield within <2 min at ambient temperature, conditions which can hardly affect the stereochemical integrity of the sulphur centre in view of the known, reasonably high barriers to pyramidal inversion of sulphonium ylides.[15-17] The methylethylpropylsulphonium salt (16c) obtained exhibited a low specific rotation, $[\alpha]_D^{20}$ +1.08 (*c* 19.4, acetonitrile). It underwent thermal racemization with only negligible




SCHEME 2 The configuration at the chlorine-bearing carbon in (10) has not been proven. Reagents: i, (a) NaOMe, MeOH (2 min), (b) HCl; ii, $Bu_4N^+Cl^-$, $SOCl_2$, $MeNO_2$; iii, (a) NaOH (2 min), (b) HCl; iv, (a) X = Cl→$ClO_4$, (b) $Bu_3N$, $Me_2CO$, heat, (c) HCl; v, (a) $H_2$, Pd–C, MeOH, 144 atm, (b) $H^+TNBS^-$

decomposition at two temperatures, permitting the determination of the reasonable [3] thermodynamic parameters for pyramidal inversion: $\Delta G^{\ddagger}$ (50 °C) 26.5 kcal mol$^{-1}$, $\Delta H^{\ddagger}$ 27.3 kcal mol$^{-1}$, and $\Delta S^{\ddagger}$ +2.4 eu. The specific rotation {$[\alpha]_D^{25}$ +1.14° (*c* 17.6, acetonitrile)} and the parameters for pyramidal inversion [$\Delta G^{\ddagger}$ (50 °C) 26 kcal mol$^{-1}$, $\Delta H^{\ddagger}$ 27 kcal mol$^{-1}$, and $\Delta S^{\ddagger}$ +1 eu], determined for a specimen of (16c) obtained by resolution of racemic (16) with α-bromo-π-camphorsulphonic acid followed by anion exchange, compared satisfactorily with the above data.

In conclusion, the methylethylpropylsulphonium ion (+)-(16) possesses (*S*)-configuration whereas no evidence is available as to the optical purity of the salt (16c).

## EXPERIMENTAL

Elemental analyses were carried out commercially or by Mr. G. Cornali and his staff. $^1$H n.m.r. spectra were determined on a Bruker HXE-90 (mostly CW mode, only a few spectra in the FT mode) spectrometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter.

(S)-2-*Benzoyloxy*-1-*bromopropane* (4).[12]—(*S*)-Propane-1,2-diol (2), b.p. 86—87° at 9 mmHg, $[\alpha]_D^{20}$ +20.9° (*c* 7.8, water) (lit.,[9] $[\alpha]_D^{20}$ +20.7°), was prepared from ethyl (*S*)-lactate (1), $[\alpha]_D^{26}$ −10.8° (neat), essentially as described by Gombos *et al.*[10] The diol was treated with excess of benzaldehyde in benzene with toluene-*p*-sulphonic acid as catalyst and azeotropic removal of water to give a mixture of *trans*- and *cis*-4-methyl-2-phenyl-1,3-dioxolans (3) in 89% yield. The $^1$H n.m.r. spectrum of the product, b.p. 110—114 °C at 15 mmHg, disclosed a 42 : 58 *trans* : *cis* ratio.[18]

The mixture (3) (30.0 g) was added to a suspension of *N*-bromosuccinimide (39.2 g) and $BaCO_3$ (23.9 g) in $CCl_4$ (250 ml). The stirred reaction mixture was refluxed, exposed to electric light (250 W) for 30 min, and was then cooled and filtered. The filter cake was thoroughly washed with ether, and the combined washings and filtrate washed with $NaHSO_3$ and $NaHCO_3$ solutions, dried ($MgSO_4$), and concentrated. The residual oil, 88%, [determined by $^1$H n.m.r. spectroscopy (acetonitrile as internal standard, methylene chloride as solvent)] was used directly in the next step. In several preparations, yields varied from 78—88%. In the $^1$H n.m.r. spectrum 7—10% of the isomer, 1-benzoyloxy-2-bromopropane, could be detected. $^1$H N.m.r. data for both isomers have been reported.[19]

(S)-6-*Methyl*-2-*oxo*-1,4-*oxathian* (5).—(*S*)-2-Benzoyloxy-1-bromopropane (4) (97 mmol) was evaporated twice with methanol to remove traces of other solvents. The residue, in methanol (50 ml), was added to a cooled suspension of disodium mercaptoacetate [from mercaptoacetic acid (9.82 g) and sodium methoxide (190 mmol)] in methanol (120 ml). The mixture was stirred at 20 °C for 30 min and then refluxed for 15 min. More sodium methoxide (33 mmol, in methanol) was added, and after reflux for another 30 min the solution remained strongly alkaline (pH > 11). The residue obtained after cooling and concentration was dissolved in water and quickly extracted with ether (3 ×). The ether solutions were washed with water and discarded. The combined water phases were acidified with concentrated hydrochloric acid (30 ml) and extracted with ether (3 ×). The aqueous solution was saturated with sodium

chloride and extracted continously with ether overnight and discarded after controlling the pH-value (pH < 3). The combined ether extracts were worked-up as described for racemic (5).[8] Crude (5) was purified by column chromatography (100 g; Merck 60 $PF_{254}$ silica gel, deactivated with 5 ml of water; benzene–ethyl acetate, 3 : 1). Of three 50 ml fractions containing (5) (detected by u.v. light) two were combined and concentrated to reveal (n.m.r.) 75—80% lactone, the remainder being benzoic acid and unidentified impurities.

At −78 °C, (5) crystallized from ether (20 ml). Four recrystallizations at −78 °C (ether; 4 × 20 ml) gave the pure *oxathian* (5) [4.98 g, 39% from (4)], $[\alpha]_D^{20}$ −211.7° (*c* 7.2, acetone). The sample of highest optical purity had m.p. 38—39.5 °C, $[\alpha]_D^{20}$ −212.9° (*c* 7.2, acetone) (Found: C, 45.3; H, 6.0; S, 24.2. $C_5H_8O_2S$ requires C, 45.5; H, 6.1; S, 24.3%). Higher yields (40—45%) were obtained in other preparations, but results were inconsistent. Most likely, an alternative procedure *via* (*S*)-(−)-1,2-epoxypropane,[9] analogous to that employed for the preparation of racemic (5),[8] would be advantageous.

(4S,6S)-4-*Ethyl*-6-*methyl*-2-*oxo*-1,4-*oxathianium* 2,4,6-*Trinitrobenzenesulphonate* (6c).—The lactone (5) (4.98 g, $[\alpha]_D^{20}$ −211.7°) and triethyloxonium tetrafluoroborate (7.18 g) were stirred in dry acetonitrile (30 ml) at room temperature for 3 h. The solution was concentrated and the residue dissolved in acetonitrile (6 ml) and cooled. Addition of ice-cold 2,4,6-trinitrobenzenesulphonic acid ($TNBS^-H^+$, tetrahydrate, 9.0 g) in methanol (30 ml), cooling, and scratching caused crystallization. Ethyl acetate (30 ml) was added and the suspension filtered; the precipitate was washed with ice-cold methanol (20 ml), ethyl acetate (20 ml), and ether to yield, after drying *in vacuo*, a mixture of (6c) and (7c) [8.65 g, 51% from (5)]. $^1$H N.m.r. revealed a slight preponderance of (6c). The mixture was dissolved in formic acid (10 ml). A few crystals of pure (6c) were added, immediately followed by acetic acid (60 ml). The flask was stoppered and left for 5 min. Filtration, washing with acetic acid (3 × 20 ml), then thoroughly with ether, and drying *in vacuo* over solid NaOH gave (6c) (3.78 g), containing *ca.* 10% of (7c). The filtrate and washings from this first recrystallization were used for the preparation of (7b) (see below). Crude (6c) (above) was dissolved in formic acid (7 ml) and filtered through Celite (1—2 g). Addition of acetic acid (42 ml) and work-up as above gave the *oxathianium salt* (6c) [3.10 g, 18% from (5)], $[\alpha]_D^{20}$ −66.4° (*c* 1.4, acetonitrile) (Found: C, 34.0; H, 3.5; N, 9.1; S, 14.2. $C_{13}H_{15}N_3O_{11}S_2$ requires C, 34.4; H, 3.3; N, 9.3; S, 14.1%). $^1$H N.m.r. indicated <5% contamination with (7c). The above purification procedure should be strictly followed, as (6c) and (7c) possess about equal solubility, the separation achieved being due to unequal rates of crystallization.

(4S,6S)-4-*Ethyl*-6-*methyl*-2-*oxo*-1,4-*oxathianium Perchlorate* (6b).—Sodium perchlorate (monohydrate, 1.15 g) and (6c) (3.10 g) were dissolved in acetonitrile containing formic acid and the solution was concentrated. The residue was extracted with nitromethane (total 40 ml) and the extract filtered and concentrated. The resulting mixture of oil and crystals was extracted again with nitromethane (total 11 ml), and the extract was filtered and concentrated to an oil, soluble in nitromethane. Trituration with ethyl acetate and inoculation with pure (6b) resulted in crystallization. Filtration and washing with ethyl acetate and ether gave crude (6b) (1.61 g, 90%). Recrystallization from acetone (10 ml) and ethyl acetate (10 ml) gave the homogeneous, slightly hygroscopic *perchlorate* (6b) [1.30 g, 73% from (6c)], m.p. 105.5—107 °C, $[\alpha]_D^{20}$ −116.5° (*c* 1.5, acetonitrile) (Found: C, 32.2; H, 5.0; Cl, 13.2; S, 12.0. $C_7H_{13}ClO_6S$ requires C, 32.2; H, 5.0; Cl, 13.6; S, 12.3).

(4R,6S)-4-*Ethyl*-6-*methyl*-2-*oxo*-1,4-*oxathianium Perchlorate* (7b).—The filtrate and washings from the first recrystallization of (6c) were combined and diluted with a large volume of ether to form a precipitate. Filtration, thorough washing with ether, and drying *in vacuo*, gave a 1 : 3 ratio (n.m.r.) of (6c) : (7c). Attempts to obtain pure (7c) by recrystallization of this product from acetic and formic acid were abortive. Ion-exchange to the perchlorates was carried out as described for (6b) using the mixture (*ca.* 3.06 g) and sodium perchlorate (monohydrate, 1.14 g). The crude (7b) (1.55 g) obtained was recrystallized from acetonitrile (5 ml)–ethyl acetate (10 ml) to yield the pure *perchlorate* (7b) [1.32 g, 13% from (5)], m.p. 162.5—164.5 °C, $[\alpha]_D^{20}$ −145.1° (*c* 1.6, acetonitrile) (Found: C, 32.3, H, 5.0; S, 12.2. $C_7H_{13}ClO_6S$ requires C, 32.3; H, 5.0; 12.3%).

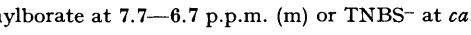
*Degradation of* (6b) *to* (16c).—*Ring opening.* A solution of (6b) (2.87 g, $[\alpha]_D^{20}$ −115.6°) in acetonitrile (10 ml) was

TABLE 1

$^1$H N.m.r. (90 MHz) data [a] of acyclic sulphonium salts

| | $\delta_1$ [b] | $\delta_2$ | $\delta_3$ | $\delta_4$ | $\delta_5$ | $\delta_6$ | $\delta_{(Z)}$ | $\delta_{(R)}$ | $J_{11}$ | $J_{12}$ | $J_{23}$ | $J_{45}$ | $J_{66}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (8d) [c] | 1.79(m) | 3.40(m) | 0.89(d) | 2.19(q) | 0.86(t) | 2.52(s) | 1.44(d) | 3.73(s) | 13.8 | 3.3 | 7 | 7 | |
| | 1.88(m) | | | | | | | | | 9.2 | | | |
| (9d) [c] | 1.78(m) | 3.34(m) | 0.90(d) | 2.09(d) | 0.84(t) | 2.62(d) | 1.39(s) | 3.73(s) | 13.5 | 3.3 | 6.5 | 7.5 | 18 |
| | 1.96(m) | | | | | 2.72(d) | | | | 8.6 | | | |
| (10d) [c] | 3.83(d) | 4.60(m) | 1.66(d) | 3.48(q) | 1.43(t) | 4.47(s) | | 3.80(s) | 14.5 | 6.5 | 6.5 | 7.3 | 16.8 |
| (11d) [c] | 3.68(m) | 4.63(m) | 1.63(d) | 3.42(q) | 1.42(t) | 4.43(d) | | 3.80(s) | | 9.9 | 6.5 | 7.5 | |
| | 3.87(m) | | | | | 4.53(d) | | | | 3.0 | | | |
| (12c) [c,d] | 6.31(m) | 7.27(m) | 2.14(dd) | 3.62(q) | 1.53(t) | 4.49(s) | | | | 15.3 | 7.3 | 7.3 | |
| (14c) [c,d] | 6.17(m) | 7.12(m) | 2.10(dd) | 3.39(m) | 1.49(t) | 2.98(s) | | | | 15.0 | 7.0 | 7.5 | |
| (16c) [c] | 1.84(m) | ~3.4(m) | 1.18(t) | ~3.4(m) | 1.56(t) | 2.91(s) | | | | 8 | 7 | 7.5 | |
| (17d) [c,d] | 5.99(m) | | 1.95(dd) | 3.16(q) | 1.24(t) | 4.00(s) | | 3.78(s) | | 15.3 | 7.0 | 7.3 | |

[a] δ in p.p.m. downfield from internal $Me_4Si$; *J* in Hz; s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. For methylene groups, δ and *J* values on the same line correspond to each other, *e.g.* for (8d) the C-1 proton at 1.79 p.p.m. couples to the C-2 proton with $J_{12}$ 3.3 Hz. AB and ABX sub-systems have been calculated where appropriate. Otherwise, δ and *J* have been read directly from the spectra. [b] The δ-values signify the chemical shifts of the protons at the carbon atoms, numbered as follows:



Anion tetraphenylborate at 7.7—6.7 p.p.m. (m) or $TNBS^-$ at *ca.* 8.7 p.p.m. (s). [d] $J_{13}$(allylic coupling) 1.5 Hz.

added over 1 min with stirring at room temperature to sodium methoxide (1.61 mmol) in methanol (30 ml). After 1 min, aqueous HCl (*ca.* 2.3 mmol) was added and the solution diluted to 50.0 ml with methanol. Most of this solution (47.0 ml) was concentrated; the residue was concentrated with and then extracted with acetonitrile. The extract was concentrated and the resulting oil evaporated twice with nitromethane to give (8b) as an oil. The balance (3.0 ml) of the above methanol solution was concentrated and dissolved in water. Addition of sodium tetraphenylborate (304 mg) gave a precipitate, which was washed with water and dried *in vacuo* to yield crude (8d) [310 mg, 92% from (6b)], <5% (9d) (n.m.r.). Recrystallization of racemic (8d) from methylene chloride–benzene (5 : 4) gave *ethyl*-(RS)-2-*hydroxypropyl*(*methoxycarbonyl*)-*methyl*-(SR)-*sulphonium tetraphenylborate* (8d) [<6% (9d)] (Found: C, 74.8; H, 7.2; S, 6.4. $C_{32}H_{37}BO_3S$ requires C, 75.0; H, 7.3; S, 6.3%); $^1$H n.m.r. analysis, 48 mg in deuteriochloroform–methylene chloride (500 μl; 3 : 2). Similarly the (RS),(RS)-*isomer* (9d), slightly contaminated (< 6%) with (8d), was characterized (Found: C, 75.0; H, 7.2; S, 6.5. $C_{32}H_{37}BO_3S$ requires C, 75.0; H, 7.3; S, 6.3%); $^1$H n.m.r., 46 mg in the same mixture as above. (8d) and (9d) were easily distinguished in the $\overset{+}{S}$–$CH_2CO$ region of the $^1$H n.m.r. spectrum; mixtures may be analyzed with an accuracy better than ±5%.

*Reaction of* (8b) *with thionyl chloride.* Crude (8b) (*ca.* 10 mmol), tetrabutylammonium chloride (*ca.* 10.6 mmol), and thionyl chloride (5 ml) in nitromethane (40 ml) were stirred at room temperature for 5 min. The mixture was concentrated at 35—38 °C and the residue kept at 41—42 °C for 5 min *in vacuo*. The remaining oil was dissolved in a little cold MeCN and ice cold water (5—10 ml) added. The resulting two-phase system was extracted with $CHCl_3$ (6 × 10 ml) and the aqueous phase concentrated. The residue was dissolved in MeOH to a volume of 50.0 ml. Most of this solution (47.0 ml) was concentrated giving (10) (X = Cl) as an oil. The balance (3.0 ml) was concentrated and the residue dissolved in water. Crude (10d) [223 mg, 70% from (6b)] precipitated on addition of $NaB(C_6H_5)_4$ (310 mg). The product was electrically charged and difficult to handle. $^1$H N.m.r. disclosed a content of 15—20% (11d). Analogously, $(10d)_{rac}$ was obtained from the lactone $(6a)_{rac}$; Three recrystallization from acetone–ether (1 : 4) gave nearly homogeneous (RS)-2-*chloropropylethyl*(*methoxycarbonyl*)*methyl*-(RS)-*sulphonium tetraphenylborate* $(10d)_{rac}$, m.p. 124—125 °C (Found: C, 72.0; H, 6.6; Cl, 6.6; S, 6.0. $C_{32}H_{36}BClO_2S$ requires C, 72.4; H, 6.8; Cl, 6.7; S, 6.0%); $^1$H n.m.r., 42 mg in 400 μl of $[^2H_6]$acetone. Racemic (11d), from the lactone $(7b)_{rac}$, was more soluble than $(10d)_{rac}$. Consequently, the sample analyzed contained $(10d)_{rac}$ and $(11d)_{rac}$ in the ratio *ca.* 1 : 2 (Found: C, 72.4; H, 6.9; Cl, 6.8; S, 6.1%); $^1$H n.m.r. [another sample, containing relatively more of $(11d)_{rac}$], 45 mg in 400 μl of $[^2H_6]$acetone. (10d) and (11d) were distinguishable in the $CH_3CH_2\overset{+}{S}$ and $CH_3CH_2\overset{+}{S}$ regions of the $^1$H n.m.r. spectrum, but quantitative analyses of mixtures were difficult.

*Reaction of* (10; X = Cl) *with sodium hydroxide.* Sodium hydroxide (1.21 g) in water (15 ml) was added, during 15 s with stirring at room temperature, to a solution of (10; X = Cl) (*ca.* 7.8 mmol) in water (15 ml) to give a strongly alkaline solution. After another 105 s, the still alkaline mixture was quickly acidified with conc. HCl (3.0 ml) and concentrated. The residue was evaporated several times with MeOH and finally dissolved in ethanol. Addition of $NaClO_4 \cdot H_2O$ in MeCN caused NaCl to precipitate. Filtration and concentration gave a residue from which NaCl and excess of $NaClO_4$ were mostly removed by extractions with MeCN and $MeNO_2$. Finally, evaporations with MeCN (2 ×) and acetone produced (12b) and (13b) [2.5 : 1 (n.m.r.)] as an oil, ready for the next step. Racemic (12c) was characterized as below.

*Decarboxylation of* (12b) *and* (13b). A solution of (12b) and (13b) (*ca.* 7.7 mmol) and tri-n-butylamine (2.7 g) in acetone (40 ml) was stirred and refluxed for 10 min. Cooling and concentration gave a residue, from which most of the amine was removed by three washings with ether. The residue was taken up in dilute HCl and the solution extracted with $CHCl_3$ (5 × 10 ml). The aqueous phase was concentrated and the resulting oil was evaporated and extracted with $CH_3CN$. Concentration of the extract and two evaporations of the residue with methanol gave (14) and (15) [2.5 : 1 (n.m.r.)], X = $ClO_4$ and/or Cl, as an oil ready for hydrogenation. Racemic (14c) was characterized (see below).

*Hydrogenation of* [(14) *and* (15); X = Cl]. An oily mixture of the salts (14) and (15) (*ca.* 4.9 mmol) and palladium–charcoal (5%; 990 mg) in MeOH (50 ml) were treated with hydrogen (*ca.* 144 atm) for 3 h at ambient temperature. The reaction mixture was filtered and concentrated to give a residue which was suspended in ethanol (10 ml). Addition of $TNBS^-H^+,4H_2O$ (2.53 g) gave a precipitate which redissolved on heating. Cooling, filtration, and washing of the precipitate with ice-cold ethanol (2—5 ml) and ether produced (S)-*ethylmethylpropylsulphonium* 2,4,6-*trimitrobenzoate* (16c) [1.69 g, 42% from (6b)], $[\alpha]_D^{20}$ +0.95° (*c* 17.7, MeCN). Three recrystallizations from water (16, 14, and 13 ml) gave 1.16 g of product which was dissolved in $CH_3CN$. Filtration, evaporation, and recrystallization of the residue from acetone–ethyl acetate (1 : 2; 36 ml) gave 1.09 g, $[\alpha]_D^{20}$ +1.08° (*c* 19.4, MeCN). After more than ten half-lives at 65 °C in acetonitrile, $[\alpha]_D^{20}$ was 0.00° (Found: C, 35.0; H, 4.2; N, 10.2; S, 15.5. $C_{12}H_{17}N_3O_9S_2$ requires C, 35.0; H, 4.2; N, 10.2; S, 15.6%).

Thermal racemization at 50.0 and 65.0 °C in acetonitrile was carried out. Rotations were corrected for residual rotations after at least six half-lives. First order kinetics were assumed and $k_1$ determined as the slope of a plot of [log $(\alpha_0/\alpha)$]/0.434 3 *vs.* time. Graphical and least squares analysis gave comparable results. Integrals ($^1$H n.m.r.) of the cation and anion were correct within ±5% before and after racemization. Furthermore, when racemic (16c) in acetonitrile was kept at 50.0 °C for 168 h, or at 65.0 °C for 72 h, 94—95% of (16c), recrystallized once from ethanol, was recovered. Results:

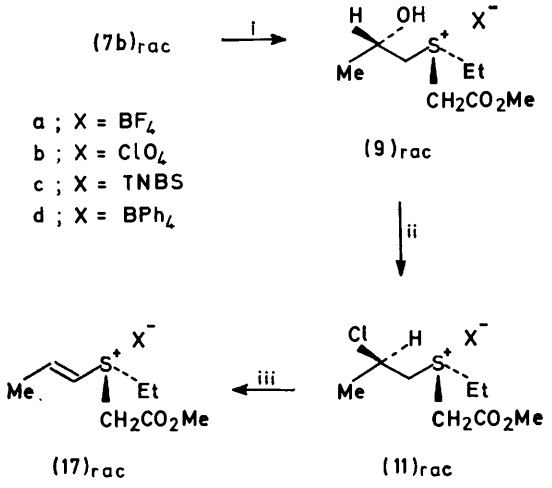
(i) 50.0 °C. The rotation of a solution of (*S*)-(16c) (0.50M) in acetonitrile (Merck, spectroscopic grade) containing a small amount of perchloric acid (*ca.* 0.02M) at 50.0 °C was followed. From the data, $k_\alpha^{50} = 1.66 \times 10^{-5}$ s$^{-1}$ ($T_{0.5}$ 695 min) was determined.

(ii) 65.0 °C. Similarly, (*S*)-(16c) (0.47M) in acetonitrile with perchloric acid (*ca.* 0.02M) was racemized giving $k_\alpha^{65} = 1.13 \times 10^{-4}$ s$^{-1}$ ($T_{0.5}$ 102 min).

Noting $k_i = 0.5 \times k_\alpha$, the following thermodynamic parameters were calculated: $\Delta H^\ddagger$ 27.3 kcal mol$^{-1}$, $\Delta G^\ddagger$ (50 °C) 26.5 kcal mol$^{-1}$, and $\Delta S^\ddagger$ +2.4 eu.

*Characterization of the salts* $(12d)_{rac}$, $(14d)_{rac}$, *and* $(17d)_{rac}$. (i) $(17d)_{rac}$. A mixture of $(10)_{rac}$ and $(11)_{rac}$ (X = Cl,

mostly $(11)_{rac}$, *ca.* 1.5 mmol total), trifluoroethanol (200 μl), and tributylamine (400 μl) in dry acetonitrile (3 ml) was stirred (homogeneous solution) for 10 min at room temperature. Concentrated hydrochloric acid (200 μl) was added, the mixture was concentrated, and the residue was dissolved in dilute hydrochloric acid and extracted with chloroform (5 × 5 ml). The aqueous phase on concentration gave an oil containing a mixture of (17) and its *cis*-isomer [*ca.* 2 : 1, respectively, (n.m.r.)]. An aqueous solution of this oil was neutralized (pH 6—7, pH >7 should be avoided) with solid sodium bicarbonate and sodium tetraphenylborate (616 mg) was added to give a precipitate. Coagulation was promoted by addition of some aqueous sodium chloride, and the suspension was filtered. Washing with water and ether, and drying *in vacuo* gave a mixture of $(17d)_{rac}$ and its *cis*-isomer (572 mg, about 77%). Two recrystallizations from acetone–ether (1 : 2) gave homogeneous *ethyl(methoxycarbonyl)methylprop*-1-*enylsulphonium*




SCHEME 3 All compounds are racemic, but only one enantiomer is shown. Reagents: i, (a) NaOMe, MeOH (2 min), (b) HCl; ii, $Bu_4N^+Cl^-$, $SOCl_2$, $MeNO_2$; iii, (a) $NBu_3$, $CF_3CH_2OH$, MeCN, (b) HCl

*tetraphenylborate* $(17d)_{rac}$, m.p. 142—143 °C (Found: C, 77.5; H, 6.9; S, 6.5. $C_{32}H_{35}BO_2S$ requires C, 77.7; H, 7.1; S, 6.5%); $^1H$ n.m.r., 41 mg in 400 μl of $CD_3CN$.

(iv) $(12c)_{rac}$. A solution of $(17d)_{rac}$ (250 mg) and tetrabutylammonium perchlorate (190 mg) in acetone was concentrated and the residue was extracted with water. The aqueous solution was concentrated and the resulting oil was treated with sodium hydroxide (1N; 6 ml) for 5 min at room temperature. Addition of dilute hydrochloric acid (1N; 7 ml) and concentration of the strongly acidic solution gave a residue which was dissolved in water (3 ml). Filtration and addition of $TNBS^-H^+,4H_2O$ (398 mg) gave a precipitate, which was washed with water (1 ml) and ether, and dried to yield crude $(12c)_{rac}$ [217 mg, 87% from $(17d)_{rac}$]. Recrystallization from MeCN (1 ml) and ethyl acetate (3 ml) gave pure *carboxymethylethylprop*-1-*enylsulphonium* 2,4,6-*trinitrobenzoate* $(12c)_{rac}$ (161 mg), m.p. 142.5—143.5 °C (Found: C, 34.6; H, 3.2; N, 9.3; S, 14.1. $C_{13}H_{15}N_3O_{11}S_2$ requires C, 34.40 H, 3.3: N, 9.3: S, 14.1%); $^1H$ n.m.r., 42 mg in trifluoroacetic acid–$CD_3CN$ (500 μl; 4 : 1).

(iii) $(14c)_{rac}$. Pure $(17d)_{rac}$ (383 mg) was converted into $(12b)_{rac}$ as described above. This oil was concentrated and extracted with acetonitrile. The extract was evaporated and the residue concentrated once with acetone. Decarboxylation was carried out as described above for the mixture of optically active (12b) and (13b) to give $(14)_{rac}$, which was dissolved in ethanol (5 ml). Addition of $TNBS^-H^+\cdot4H_2O$ (355 mg) caused precipitation of $(14c)_{rac}$ [264 mg, 83% from $(17d)_{rac}$]. Recrystallization from acetone (3 ml) and ethyl acetate (6 ml) gave 215 mg of homogeneous *ethylmethylprop*-1-*enylsulphonium* 2,4,6-*trinitrobenzoate* $(14c)_{rac}$, m.p. 136—137 °C (Found: C, 35.4; H, 3.7; N, 10.4; S, 15.5. $C_{12}H_{15}N_3O_9S_2$ requires C, 35.2; H, 3.7; N, 10.3; S, 15.7%); $^1H$ n.m.r., 42 mg in trifluoroacetic acid–$CD_3CN$ (500 μl; 4 : 1).

*Resolution of Racemic* (16).—Methyl propyl sulphide (5.86 g) and triethyloxonium tetrafluoroborate (13 g) in dry $CH_2Cl_2$ (50 ml) were stirred in an ice-bath for 15 min and at ambient temperature overnight. The clear solution was concentrated and an aqueous solution of the resulting oil was extracted with $CHCl_3$ and neutralized with ion-exchange resin (Amberlite IR4B, amine form). Evaporation gave $(16a)_{rac}$ as an oil.

Addition of $TNBS^-H^+\cdot4H_2O$ to a solution in ethanol of $(16a)_{rac}$ caused precipitation of $(16c)_{rac}$. Recrystallizations from water (several times) and then ethyl acetate–acetone produced homogeneous $(16c)_{rac}$, m.p. 134—135 °C; $^1H$ n.m.r., 49 mg in $CF_3CO_2H$–$CD_3CN$ (500 μl; 4 : 1).

The salt $(16a)_{rac}$ (an oil containing maximum 26 mmol) was converted into the chloride by ion-exchange in water (Amberlite IRA 400, chloride, *ca.* 135 mmol). Titration with standard silver nitrate indicated 21.5 mmol of [$(16)_{rac}$; X = Cl] (83% from methyl propyl sulphide). [$(16)_{rac}$; X = Cl] (20.6 mmol) and silver oxide (3.54 g) in water were stirred for 10 min and then filtered. Addition of ammonium α-bromo-π-camphorsulphonate (6.76 g) gave a clear solution which was then concentrated. The residue was evaporated with mixtures of acetone and $CHCl_3$ until soluble in $CHCl_3$ alone. The solution in $CHCl_3$ was filtered and concentrated. The residue was dissolved in a little acetone, and the α-bromo-π-camphorsulphonate of (16) (highly hygroscopic at this stage) crystallized on addition of dry ether. The mixture was recrystallized seven times from acetone and ether. A small sample was withdrawn from each crystallization and some of it converted into (+)-(16c) by precipitation with $TNBS^-H^+\cdot4H_2O$. The α-bromo-π-camphorsulphonate of (16) (250—300 mg) and $TNBS^-H^+\cdot4H_2O$ (270—300 mg) in ethanol (3 ml) gave a precipitate, which mostly dissolved on short heating until near the b.p. Cooling, filtration, and careful washing with a little ice-cold ethanol (2 ×) and with ether gave yields >93% of (+)-(16c) in most cases. Physical data are presented in Table 2. The reliability of the rotations was checked by thermal racemization of (+)-(16c) derived from crystallization no. 5. The rotation $[\alpha]_D^{20}$ −0.02° (*c* 20, acetonitrile) was measured after 9—10 half-lives at 65.0 °C. This residual rotation is small but probably significant. The rotation of (+)-ammonium α-bromo-π-camphorsulphonate is strongly positive {$[\alpha]_D^{20}$ +88.0 (*c* 14.0, water)}. Samples of (+)-(16c) derived from crystallizations 4, 6, 7, and 8 (see Table 2) were recovered (884 mg) and recrystallized six times from water (9, 8, 7, 6, 5, and 4.5 ml; yields were 82—86%) to give (+)-(16c) (321 mg), $[\alpha]_D^{25}$ +1.14° (*c* 17.6, acetonitrile). The rotation was also determined after the first ($[\alpha]_D^{25}$ +0.85°) and third ($[\alpha]_D^{25}$ +1.06°) recrystallization. The solid phase (KBr) i.r. spectra of the samples of the α-bromo-π-camphorsulphonates of (16) in Table 2 showed no significant differences; the same applied to the solution

TABLE 2

Resolution of ethylmethylpropylsulphonium α-bromo-π-camphorsulphonate

| Recryst. no. | $Me_2CO$/ml $Et_2O$/ml | Yield [a]/g (%) | M.p./°C | Yield of (+)-(16c) (%) | $[\alpha]_D^{25}$ | c(g/100 ml, MeCN) |
|---|---|---|---|---|---|---|
| 0 | | ⩽8.84 | 93—99 | 83.5 | +0.068 | 17.8 |
| 1 | 20<br>30 | 5.67 (67) | 104.5—107 | 91 | +0.237 | 17.7 |
| 2 | 20<br>30 | 4.09 (77) | 108—109 | 94 | +0.430 | 19.1 |
| 3 | 10<br>10 | 3.13 (84) | 108.5—110 | 94.5 | +0.565 | 18.1 |
| 4 | 10<br>10 | 2.24 (80) | 111—112.5 | 93 | +0.755 | 19.0 |
| 5 | 8<br>5 | 1.62 (85) | 111—112 | 94 | +0.841 | 20.1 |
| 6 | 8<br>4 | 1.01 (78) | 112.5—113.5 | 93 | +0.965 | 18.6 |
| 7 | 8<br>4 | 0.46 (67) | 112—113 | 93.5 | +1.034 | 20.7 |

[a] All weights shown are before withdrawal of samples (0.32—0.38 g) for conversion to (+)(16c).

$^1$H n.m.r. spectra. Thermal racemization experiments were carried out on (+)-(16c) at 50.0 and 65.0 °C as described above, but without addition perchloric acid. Determination of the rates $k_\alpha^{50}$ $1.8 \times 10^{-5}$ $s^{-1}$ and $k_\alpha^{65}$ $1.20 \times 10^{-4}$ $s^{-1}$ allowed calculation of $\Delta G^\ddagger(50°)$ 26 kcal $mol^{-1}$, $\Delta H^\ddagger$ 27 kcal $mol^{-1}$, and $\Delta S^\ddagger$ +1 eu.

Sincere thanks are due to Professor A. Kjaer for his help with the manuscript.

[8/427 *Received*, 9*th March*, 1978]

REFERENCES

[1] Preliminary communication, E. Kelstrup, A. Kjaer, S. Abrahamsson, and B. Dahlén, *J.C.S. Chem. Comm.*, 1975, 629.
[2] S. Smiles, *J. Chem. Soc.*, 1900, **77**, 1174; W. J. Pope and S. J. Peachey, *ibid.*, 1900, **77**, 1072.
[3] D. Darwish, *Mech. React. Sulfur Compd.*, 1968, **3**, 33.
[4] D. Darwish and C. E. Scott, *Canad. J. Chem.*, 1973, **51**, 3647.
[5] K. K. Andersen, *J.C.S. Chem. Comm.*, 1971, 1051.
[6] K. K. Andersen, R. L. Caret, and I. Karup-Nielsen, *J. Amer. Chem. Soc.*, 1974, **96**, 8026.
[7] K. K. Andersen, R. L. Caret, and D. L. Ladd, *J. Org. Chem.*, 1976, **41**, 3096.
[8] E. Kelstrup, *J.C.S. Perkin I*, preceeding paper.
[9] B. T. Golding, D. R. Hall, and S. Sakrikar, *J.C.S. Perkin I*, 1973, 1214.
[10] J. Gombos, E. Haslinger, and U. Schmidt, *Chem. Ber.*, 1976, **109**, 2645.
[11] C. Melchiorre, *Chem. Ind.*, 1976, 218.
[12] S. Hanessian and N. R. Plessas, *J. Org. Chem.*, 1969, **34**, 1035.
[13] D. M. Burness, *J. Org. Chem.*, 1959, **24**, 849.
[14] G. P. Schiemenz and H. P. Hansen, *Angew. Chem.*, 1973, **85**, 404.
[15] B. M. Trost and R. F. Hammen, *J. Amer. Chem. Soc.*, 1973, **95**, 962.
[16] D. Darwish and R. L. Tomilson, *J. Amer. Chem. Soc.*, 1968, **90**, 5938.
[17] D. M. Roush and C. H. Heathcock, *J. Amer. Chem. Soc.*, 1977, **99**, 2337.
[18] T. D. Inch and N. Williams, *J. Chem. Soc.* (*C*), 1970, 263.
[19] Y. Kamiya and S. Takemura, *Chem. Pharm. Bull.*, 1974, **22**, 201.