Synthesis and Spontaneous Resolution by Crystallization of *R,S*-(±)-Dimethyl(1-methyl-2-oxo-2-phenylethyl)sulphonium Bromide. *X*-Ray Structure and Absolute Configuration of the *R*-Enantiomer

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R,S-(±)-Dimethyl(1-methyl-2-oxo-2-phenylethyl)sulphonium bromide (**3a**), obtained from 1-phenylpropanone by bromination with t-butyl bromide–dimethyl sulphoxide and further reaction with dimethyl sulphide, undergoes spontaneous resolution of its two enantiomers upon crystallization, as demonstrated by a single crystal *X*-ray analysis and assignment of absolute configuration (*R*).

Recently, we used t-butyl bromide–dimethyl sulphoxide as a mild brominating agent for phenols[1] and indoles.[2] We report now that the same reagent reacts with 1-phenylpropanone (**1a**) and 1-phenyl-2-methylpropanone (**1b**) [$Bu^tBr:Me_2SO$: ketone = 4:2:1 (molar ratio)] at 65 °C for 24 h to give the α-brominated derivatives (**2a**) (90% yield) and (**2b**) (70%). On treatment with dimethyl sulphide for 24 h, (**2a**) gives the corresponding dimethylsulphonium bromide (**3a**) (m.p. 129 °C, 80% yield), whereas (**2b**) does not react further. With acetophenone (**1c**), phenacyldimethylsulphonium bromide[3] (**3c**) is obtained directly (m.p. 132 °C, 90% yield) (see Scheme 1).

Both dimethylsulphonium salts (**3a,c**) were recrystallized from methanol–diethyl ether and characterised by ^1H n.m.r. spectroscopy[4] and *X*-ray crystallography.† Dimethyl(1-methyl-2-oxo-2-phenylethyl)sulphonium bromide (**3a**) crystallizes in the space group $P2_12_12_1$ (chiral) and to a single crystal manually sorted for *X*-ray analysis it was possible to assign the absolute configuration (*R*) by applying the Hamilton test.[5]

As the reaction was carried out under symmetrical conditions, a spontaneous resolution of the two enantiomers of (**3a**) must have occurred during crystallization. Although the phenomenon is known,[6] this is the first case, to our knowledge, of spontaneous resolution of a sulphonium salt.

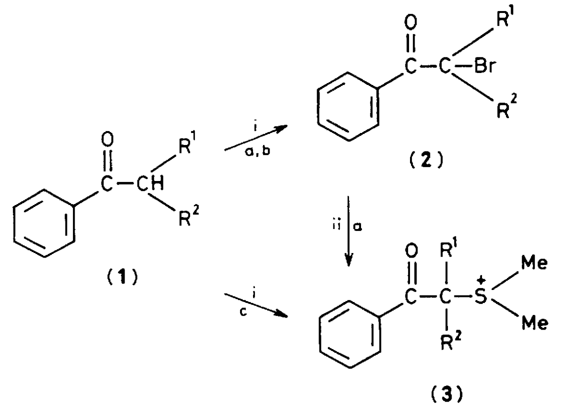
Crystal data: $C_{11}H_{15}BrOS{\cdot}H_2O$, $M = 293.2$, orthorhombic, space group $P2_12_12_1$, $a = 7.962(1)$, $b = 7.980(1)$, $c = 20.558(3)$ Å, $U = 1\,306.2$ Å^3, $Z = 4$, $D_c = 1.49$ g cm^{-3}, $F(000) = 1\,056$, Cu-K_α radiation, $\lambda = 1.54178$ Å, μ(Cu-K_α) = 59.9 cm^{-1}.

Data were measured to $2\theta_{max} = 140°$. A total of 1454 independent reflections were collected; of these, 1061 had $|F_o| > 2\sigma(|F_o|)$ and were treated as observed and used in the subsequent analysis. The crystal used was $0.56 \times 0.11 \times 0.05$ mm^3 in size. No absorption correction was applied. The structure was solved by the heavy atom method and refined by full matrix least-squares to R 0.0493 and R_w 0.0622 (observed reflections only; with unrefined isotropic hydrogen atoms).‡ The atomic scattering factors used in the calculations take into account the anomalous scattering effects.[7]

The absolute configuration, shown in Figure 1, was determined using the Hamilton[5] statistical test with calculated weighted R_w values for the two enantiomers. The resulting $R_w(S)$ 0.0628 and $R_w(R)$ 0.0622 for the two possible configurations around the chiral carbon atom C(8) showed that the *R* configuration with the lower R_w value has a probability of being correct at a significance level of *ca.* 0.005.

The sulphonium group has pyramidal geometry, with the sulphur atom lying 0.8 Å above the base of the pyramid defined by three bonded carbon atoms; the bonded distances involving the sulphur atom [S–C(8) 1.83(1); S–C(9) 1.83(1); S–C(10) 1.80(2) Å] are in agreement with literature values.[8]

The orientation of the methyl group, C(11), is defined by the torsion angles about C(7)–C(8) and C(8)–S [O(2)–C(7)–C(8)–C(11) 106.1(1.4); C(11)–C(8)–S–C(9) −66.3(1.0); C(11)–C(8)–S–C(10) 38.7(1.1)°] and the conformation around the C(8)–S bond is staggered. The phenyl ring is not coplanar with the carbonyl group and they share a dihedral angle of *ca.* 30 °.



Scheme 1. i, Me_2SO–Bu^tBr; ii, Me_2S; **a**, $R^1 = H$, $R^2 = Me$; **b**, $R^1 = R^2 = Me$; **c**, $R^1 = R^2 = H$.

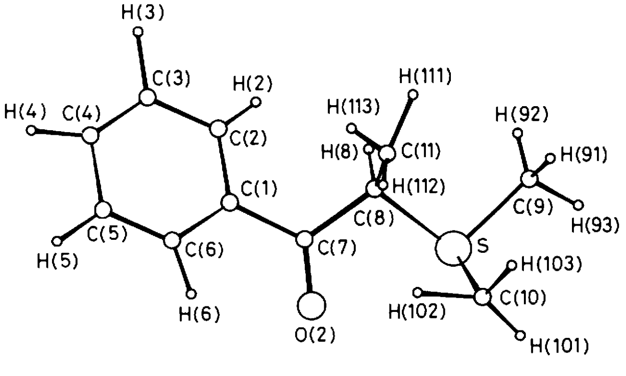


Figure 1. Projection of a molecule of compound (**3a**).

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† The structure determination of phenacyldimethylsulphonium bromide (**3c**) will be reported elsewhere.

‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

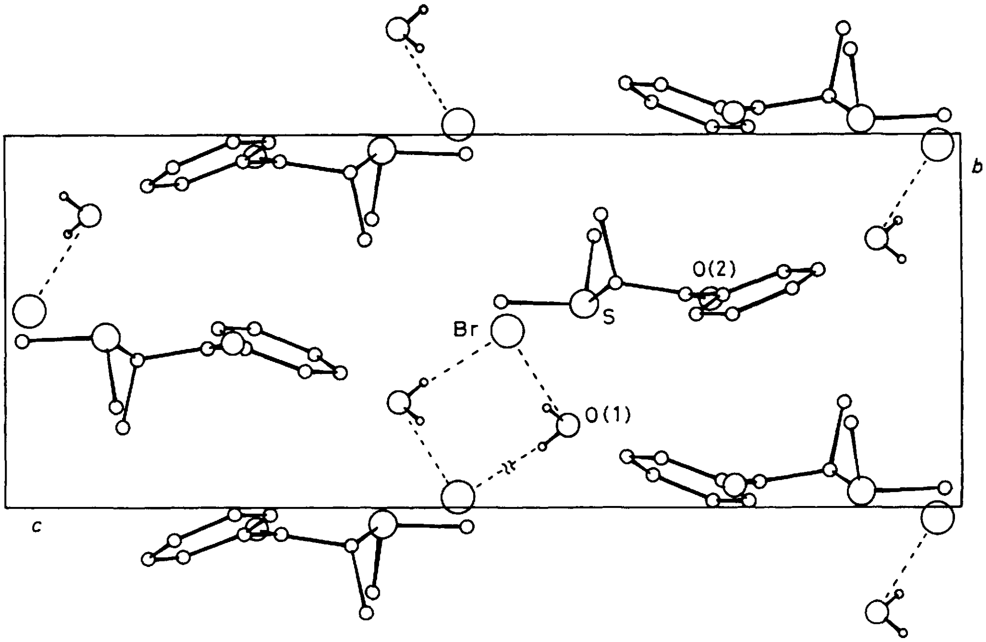

Figure 2. Projection of the structure of (**3a**) along the *a* axis.

The water molecules of crystallization are joined together by O–H • • • Br hydrogen bond interactions [3.27(1), 3.32(1) Å], and form a helical chain running along the *x* axis (Figure 2).

Sorted single crystals showed optical activity in the c.d. spectra {ellipticity [(+) or (−)] 2.4×10^4 deg cm^2 dmol^{-1} at λ_{max} 238 nm, in 95% EtOH}.

The occurrence of conglomerates is rarer than that of racemates[6] and of particular interest since the resolution does not require any optically active auxiliary agent, but occurs spontaneously during crystallization.

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