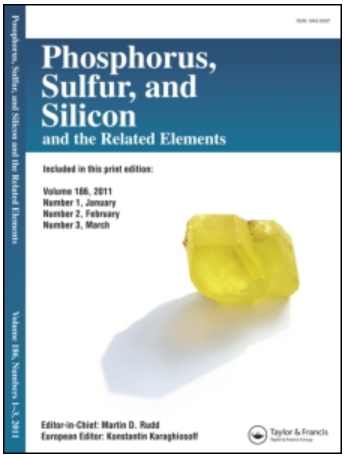

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Hydrolysis and Oxidation Products of the Chemical Warfare Agents 1,2-Bis[(2-chloroethyl)thio]ethane Q and 2,2'-Bis(2-chloroethylthio)diethyl Ether T

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HYDROLYSIS AND OXIDATION PRODUCTS OF THE CHEMICAL WARFARE AGENTS 1,2-BIS[(2-CHLOROETHYL)THIO]ETHANE Q AND 2,2′-BIS(2-CHLOROETHYLTHIO)DIETHYL ETHER T

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Syntheses of diols of structure $[HOCH_2CH_2S]_2(CH_2)_n$ *in 86–95% yield from the sodium salt of 2-mercaptoethanol and* $Br(CH_2)_nBr$ (n = *1 to 5) or in 60–90% yield from 2-chloroethanol and* $NaS(CH_2)_nSNa$ (n = *2 to 5) are described. The diol* $[HOCH_2CH_2SCH_2CH_2]_2O$ *was prepared in 82% yield from the sodium salt of 2-mercaptoethanol and* $[ClCH_2CH_2]_2O$*, and in 88% yield from 2-chloroethanol and* $[HSCH_2CH_2]_2O$*. Mono- and bis-sulfoxides and bis-sulfones of these species were prepared in generally high yield by treatment with an equivalent of* KIO_4 *in aqueous methanol, two equivalents of* $NaIO_4$ *in aqueous methanol, or four equivalents of* H_2O_2 *in trifluoroacetic acid respectively. The compounds are important analytical standards for investigating the fate of the chemical warfare agents sesquimustard Q and oxygen mustard T in environmental samples.*

Keywords: Chemical warfare agent; potassium periodate; sulfone; sulfoxide; sulfur mustard

Sulfur mustard H is a potent vesicant. It was used as a chemical warfare agent in World War I and has been stockpiled by several countries since. Its use during the Iran–Iraq conflict[1] renewed interest in it. Two analogues often feature in sulfur mustard mixtures: sesquimustard Q and oxygen mustard T (Scheme 1). They are more vesicant and persistent than sulfur mustard, but do not produce casualties by vapour action due to their lower volatility.

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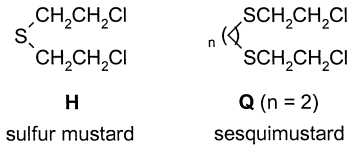
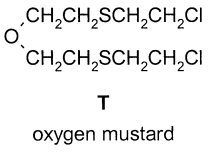




SCHEME 1

Sesquimustard[2,3] is five times more vesicant than sulfur mustard.[4] The HQ process, developed in the United Kingdom during World War II, involved treating a 15:85 mixture of 2-mercaptoethanol and thiodiglycol with hydrogen chloride. A 70:30 mixture of HQ resulted, having better vesicant properties than H alone. The skin damaging effect of bis(2-chloroethylsulfanyl)alkanes with one to ten methylene groups between the two sulfur atoms was also examined.[4] Vesicancy was maximal with an ethylene bridge (i.e., Q itself) and diminished with increasing bridge length. Compounds with one to five methylene groups in the bridge are more vesicant than sulfur mustard[4] and are important from the standpoint of chemical defence. Oxygen mustard[5] is 3.5 times more vesicant than sulfur mustard.[4] Thiodiglycol and gaseous hydrogen chloride at high temperature give a 60:40 mixture of sulfur mustard and a residue that contains T and related homologues.[6–8] The resulting HT mixture is a standard weapon fill.

The Chemical Weapons Convention[9] specifically lists a number of sulfur mustard homologues under Schedule 1 in the Annex of Chemicals considered a threat. These include Q, T, and analogues of structure $[ClCH_2CH_2S]_2(CH_2)_n$ where $n = 1$–5. Our laboratory, which supports the Organisation for the Prohibition of Chemical Weapons (OPCW), is required to be able to detect and identify the compounds and their degradation products in environmental samples. The Q analogue $[ClCH_2CH_2S]_2(CH_2)_5$ and its degradation product $[HOCH_2CH_2SO]_2(CH_2)_5$ were used as spiking compounds in the Sixth Official OPCW Proficiency Test. They were detected in soil and water samples respectively and their structures confirmed by the synthesis of analytical standards.

Degradation of sulfur mustard and its analogues occurs through hydrolysis and oxidation. Hydrolysis occurs through a cyclic episulfonium ion and results in stepwise replacement of the chlorine atoms by

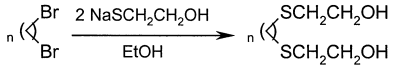
hydroxy groups. Oxidation of sulfur gives the sulfoxide and then the sulfone. These are stable and important forensic markers. Sulfur mustard has been studied for over a century and its degradation chemistry[10] is well characterized. Little is known about the fate of Q and T except that they behave like sulfur mustard in stagnant water,[11] sinking to the bottom and remaining hazardous for years. Hydrolysis pathways have not been elucidated in detail but appear to parallel those of sulfur mustard, the major products being the corresponding diols.[12,13]

Previous work from this laboratory described the preparation of various derivatives of sulfur mustard[14,15] for use in studies involving analysis[16,17] and metabolism.[18–20] This article describes the synthesis of Q and T diols and their sulfoxide and sulfone derivatives. Such compounds are likely to be present in contaminated soil samples or biological fluids, and are important reference compounds in support of the resolutions of the Chemical Weapons Convention. Although some of the diols have been reported before, their purity was dubious as they were made without the aid of modern chromatographic or analytical techniques. Syntheses of oxidation products have not been described. All products were prepared in over 98% purity and their structures confirmed by NMR and IR spectroscopy, and LC-MS.

RESULTS AND DISCUSSION

The Synthesis of Q Diols

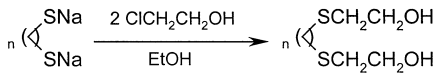
Diglycols **1a–e** having one to five methylene groups bridging the sulfur atoms were prepared in high yield by interaction of dibromoalkanes with two molar equivalents of 2-mercaptoethanol in alcoholic sodium ethoxide (Scheme 2). The method followed the early literature[2] although **1a** was obtained from dibromomethane (not dichloromethane)[4] and purification of the series was achieved by chromatography on silica gel (not distillation,[4] which gave impure specimens).



n = 1	**1a**	92%
2	**1b**	86%
3	**1c**	95%
4	**1d**	91%
5	**1e**	95%

SCHEME 2

Another route, reported only for the synthesis of **1b**,[15] involves treating the disodium salt of alkanedithiols with two molar equivalents of 2-chloroethanol in ethanol. This approach cannot be used for the simplest homologue as $HSCH_2SH$ is unavailable. We prepared diols **1b–e** from commercial dithiols in good yield (Scheme 3).



n = 2	**1b**	81%
3	**1c**	90%
4	**1d**	82%
5	**1e**	60%

SCHEME 3

An attempt to obtain compound **1a** by condensing 2-mercaptoethanol with formaldehyde, in the presence of concentrated sulfuric acid, did not give the desired product, but yielded a pale yellow liquid whose structure could not be resolved. Its LC-MS spectrum was consistent with the formula $HOC_2H_4SC_2H_4SCH_2SC_2H_4OH$, but conflicted with NMR data, which suggested extra hydrocarbon fragments. Diols **1a–e** are pale yellow liquids or low-melting white crystalline solids. 1,2-Bis(2-hydroxyethylsulfanyl)ethane **1b**, a major hydrolysis product of Q,[21] is a waxy white solid, soluble in water, ethanol, chloroform, and acetone, slightly soluble in ether, and insoluble in benzene or carbon tetrachloride. Analytical data appear in Table I.

The Synthesis of Q Diol Mono-Sulfoxides

Diols **1a-e** have two sulfur atoms and methods for obtaining the products of selective oxidation were sought. Conversion of sulfides to sulfoxides can be effected using an equimolar amount of aqueous sodium periodate at 0°C or at room temperature in a suitable cosolvent (e.g., methanol, ethanol, acetone, acetonitrile).[22,23] Sodium iodate forms as the byproduct. The system is mild and rarely results in overoxidation unless high temperatures are employed. In contrast, potassium periodate has not found much, if any, application in organic synthesis, which is surprising given its appreciably lower cost. This might arise partly from its lower aqueous solubility, which limits its use to heterogeneous systems (it is 25 times less soluble in water than sodium

TABLE I Data for Diols $(CH_2)_n(SC_2H_4OH)_2$ **1a–e** (NMR Data Measured in $CDCl_3$, R_f Values in 19:1 $CHCl_3$-MeOH)

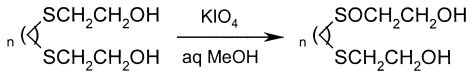
Compound	n	m.p. (°C)	Lit. m.p. (°C)	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)	IR ν (cm^{-1})
1a (R_f 0.10)	1	Liquid	18[4]	3.78 (4H, br dt, $J=6$, CH_2O), 3.76 (2H, s, SCH_2S), 3.67 (2H, t, $J=6$, OH), 2.85 (4H, t, $J=6$, SCH_2)	60.6 (CH_2OH), 35.3 (SCH_2S), 33.5 (SCH_2)	3392–3327 (br OH), 2951, 2918 and 2875 (CH_2), 2240, 1633, 1404 (OH), 1290, 1201, 1063, 1045, 1012, 912, 731
1b (R_f 0.15)	2	62–63	62[15]	3.76 (4H, t, $J=6$, CH_2O), 2.78 (4H, s, SCH_2CH_2S), 2.77 (4H, t, $J=6$, SCH_2), 2.47 (2H, br s, OH)	60.7 (CH_2OH), 35.3 (SCH_2CH_2S), 31.9 (SCH_2)	3356–3282 (br OH), 2956, 2931, 2920 and 2898 (CH_2), 2359, 2341, 1477, 1421, 1344, 1203, 1136, 1051, 1009, 690
1c (R_f 0.20)	3	Liquid	18[4]	3.74 (4H, br dt, $J=6$, CH_2O), 3.15 (2H, t, $J=6$, OH), 2.72 (4H, t, $J=6$, SCH_2), 2.66 (4H, t, $J=7$, $SC\underline{H}_2CH_2C\underline{H}_2S$), 1.88 (2H, quintet, $J=7$, CH_2)	60.4 (CH_2OH), 34.7 ($S\underline{C}H_2CH_2\underline{C}H_2S$), 30.2 ($CH_2$), 29 ($SCH_2$)	3388–3348 (br OH), 2949, 2920 and 2873 (CH_2), 1641, 1631, 1421, 1342, 1290, 1261, 1228, 1165, 1061, 1045, 1011, 943, 839
1d (R_f 0.15)	4	32–33	30[4]	3.73 (4H, t, $J=6$, CH_2O), 2.73 (4H, t, $J=6$, SCH_2), 2.56 (4H, complex m, $SC\underline{H}_2CH_2CH_2C\underline{H}_2S$), 2.43 (2H, br s, OH), 1.71 (4H, complex m, $SCH_2C\underline{H}_2C\underline{H}_2CH_2S$)	60.2 (CH_2OH), 35.1 ($S\underline{C}H_2CH_2CH_2\underline{C}H_2S$), 31.1 ($SCH_2$), 28.5 ($SCH_2\underline{C}H_2\underline{C}H_2CH_2S$)	3388–3350 (br OH), 2922 and 2868 (CH_2), 1450, 1421, 1282, 1227, 1200, 1045, 1009, 941, 820
1e (R_f 0.20)	5	33–34	30[4]	3.72 (4H, t, $J=6$, CH_2O), 2.73 (4H, t, $J=6$, SCH_2), 2.54 (4H, t, $J=7$, $SC\underline{H}_2CH_2CH_2CH_2C\underline{H}_2S$), 2.29 (2H, br s, OH), 1.62 (4H, quintet, $J=7$, $SCH_2C\underline{H}_2CH_2C\underline{H}_2CH_2S$), 1.52 (2H, complex m, CH_2)	60.2 (CH_2OH), 35.2 ($S\underline{C}H_2CH_2CH_2CH_2\underline{C}H_2S$), 31.4 ($SCH_2$), 29.1 ($SCH_2\underline{C}H_2CH_2\underline{C}H_2CH_2S$), 27.7 ($CH_2$)	3450–3327 (br OH), 2931, 2877, 2862, 2360, 2341, 2249, 1462, 1454, 1435, 1421, 1410, 1390, 1288, 1057, 1011, 910, 733, 648

TABLE II Data for Mono-Sulfoxides $HOC_2H_4S(CH_2)_nSOC_2H_4OH$ **2a–e** (NMR Data Measured in CD_3OD, R_f Values in 9:1 CH_2Cl_2-MeOH)

Compound	n	m.p. (°C)	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)	IR ν (cm^{-1})
2a (R_f 0.15)	1	Liquid	4.28 and 4.09 (2H, each d, $J=14$, SCH_2SO), 4.1 (2H, m, $SOCH_2CH_2OH$), 3.89 (2H, t, $J=6$, SCH_2CH_2OH), 3.27 and 3.09 (2H, each m, $SOCH_2$), 3.01 (2H, t, $J=6$, SCH_2)	62.5 (SCH_2CH_2OH), 55.8 ($SOCH_2CH_2OH$), 54.6 ($SOCH_2CH_2OH$), 54 (SCH_2SO), 36.8 (SCH_2CH_2OH)	3365 (br OH), 2918 (CH_2), 1655, 1400 (OH), 1290, 1063 (S=O), 1024 (C–O)
2b (R_f 0.10)	2	110–112	3.96 (2H, m, $SOCH_2CH_2OH$), 3.71 (2H, t, $J=6$, SCH_2CH_2OH), 3.2–2.9 (6H, complex m, $SCH_2CH_2SOCH_2$), 2.73 (2H, t, $J=6$, SCH_2CH_2OH)	62.4 (SCH_2CH_2OH), 55.8 ($SOCH_2CH_2OH$), 55.77 ($SOCH_2CH_2OH$), 53.4 (CH_2SO), 35 (SCH_2CH_2OH), 25.7 (SCH_2CH_2SO)	3390–3327 (br OH), 2920 and 2881 (CH_2), 1651, 1645, 1406 (OH), 1288, 1207, 1163, 1063 (S=O), 1024 (C–O), 995
2c (R_f 0.15)	3	Liquid	3.94 (2H, m, $SOCH_2CH_2OH$), 3.68 (2H, t, $J=7$, SCH_2CH_2OH), 3.02–2.93 (4H, complex m, CH_2SOCH_2), 2.73 (2H, m, $SCH_2CH_2CH_2SO$), 2.67 (2H, t, $J=7$, SCH_2CH_2OH), 2.06 (2H, m, $J=7$, CH_2)	62.4 (SCH_2CH_2OH), 55.8 ($SOCH_2CH_2OH$), 56 ($SOCH_2CH_2OH$), 51.7 (CH_2SO), 35 (SCH_2CH_2OH), 31.7 ($SCH_2CH_2CH_2SO$), 24 (CH_2)	3421–3271 (br OH), 2918 and 2875 (CH_2), 1649, 1402 (OH), 1363, 1290, 1111, 1063 (S=O), 1039 (C–O), 993
2d (R_f 0.15)	4	63–64	3.96 (2H, m, $SOCH_2CH_2OH$), 3.67 (2H, t, $J=7$, SCH_2CH_2OH), 3.05 and 2.97 (2H, each m, $SOCH_2CH_2OH$), 2.9 and 2.85 (2H, each m, CH_2SO), 2.64 (2H, t, $J=7$, SCH_2CH_2OH), 2.62 (2H, m, SCH_2), 1.88 (2H, m, $SCH_2CH_2CH_2CH_2SO$), 1.77 (2H, m, $SCH_2CH_2CH_2CH_2SO$)	62.5 (SCH_2CH_2OH), 55.9 ($SOCH_2CH_2OH$), 56 ($SOCH_2CH_2OH$), 52.6 (CH_2SO), 35.1 (SCH_2CH_2OH), 32.4 ($SCH_2CH_2CH_2CH_2SO$), 29.7 ($SCH_2CH_2CH_2CH_2SO$), 22.9 ($SCH_2CH_2CH_2CH_2SO$)	3420–3200 (br OH), 2918 (CH_2), 1652, 1448, 1436, 1354, 1300, 1259, 1236, 1201, 1178, 1126, 895, 858, 790, 750
2e (R_f 0.20)	5	70–71	3.96 (2H, m, $SOCH_2CH_2OH$), 3.66 (2H, t, $J=6$, SCH_2CH_2OH), 3.1–2.8 (6H, m, $CH_2CH_2CH_2SOCH_2$), 2.63 (2H, t, $J=6$, SCH_2CH_2OH), 2.58 (2H, m, SCH_2), 1.79 (2H, m, $SCH_2CH_2CH_2CH_2CH_2SO$), 1.59–1.65 (2H, m, SCH_2CH_2)	62.5 (SCH_2CH_2OH), 55.9 ($SOCH_2CH_2OH$), 56 ($SOCH_2CH_2OH$), 53 (CH_2SO), 35.2 (SCH_2CH_2OH), 32.6 (SCH_2), 30.4 (SCH_2CH_2), 28.8 ($SCH_2CH_2CH_2CH_2CH_2SO$), 22.4 (CH_2CH_2SO)	3310–3160 (br OH), 2954, 2933, 2924 and 2856 (CH_2), 1481, 1464, 1427, 1411, 1327, 1282, 1238, 1155, 1078, 1063 (S=O), 1043 (C–O), 1020, 985

periodate: solubilities at 25°C are 0.51 g KIO_4 and 12.62 g $NaIO_4$ per 100 g water).[24]

We found that a potassium periodate slurry in aqueous methanol oxidised diglycols **1a–e** to monosulfoxides **2a–e** at room temperature (Scheme 4). Thin-layer chromatograms of reaction mixtures suggested only trace amounts of the unwanted bis-sulfoxides. Work up was facile and involved removal of the inorganic material by filtration, removal of solvent and chromatography on silica gel. Mono-sulfoxides **2a–e** are viscous liquids or crystalline solids that exist as racemates. No attempt was made to resolve the enantiomers. Analytical details appear in Table II.



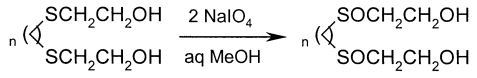
n = 1	**1a**	**2a**	80%
2	**1b**	**2b**	57%
3	**1c**	**2c**	52%
4	**1d**	**2d**	49%
5	**1e**	**2e**	54%

SCHEME 4

The lower reactivity of potassium periodate versus sodium periodate was demonstrated by treating 1,1-bis(2-hydroxyethylsulfanyl)methane **1a** with two molar equivalents of each and comparing the reaction rate. After 12 h, the former yielded mainly mono-sulfoxide, the latter mainly bis-sulfoxide. Oxidation of 1,3-bis(2-hydroxyethylsulfanyl)propane **1c** with a molar equivalent of potassium periodate or sodium periodate was also carried out under comparable conditions. The isolated yield of mono-sulfoxide **2c** was better from KIO_4 (52%) than from $NaIO_4$ (46%).

The Synthesis of Q Diol Bis-Sulfoxides

Treatment of diols **1a–e** with two molar equivalents of sodium periodate in aqueous methanol resulted in selective oxidation of both sulfur atoms and allowed the isolation of bis-sulfoxides **3a–e** (Scheme 5). They are white crystalline solids that exist as an enantiomeric pair and an achiral *meso* form; individual components were not separated. Analytical details appear in Table III.



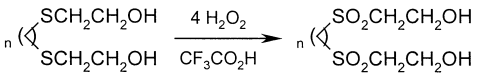
n = 1	**1a**	**3a**	79%
2	**1b**	**3b**	82%
3	**1c**	**3c**	55%
4	**1d**	**3d**	80%
5	**1e**	**3e**	61%

SCHEME 5

The synthesis of Q Diol Bis-Sulfones

The synthesis of sulfone derivatives of sulfur mustard and analogues often involves oxidation with hydrogen peroxide in glacial acetic acid.[25–27] This suffers the drawback that acetic acid can be difficult to remove from the product: prolonged drying under high vacuum is required. Replacement of glacial acetic acid (b.p. 118°C) with the more volatile trifluoroacetic acid (b.p. 72°C) overcomes this problem.

Treatment of diols **1a–e** with four molar equivalents of hydrogen peroxide in trifluoroacetic acid oxidised both sulfur atoms, when bridged by two or more methylene units, to the sulfone. 1,1-Bis(2-hydroxyethylsulfonyl)methane **4a** could not be obtained and gave a complex mixture of products arising from cleavage of the methylene bridge; the synthesis of geminal sulfones is known to be difficult.[28] Bis-sulfones **4b–e** were isolated in variable yield after chromatography as white solids (Scheme 6). Analytical details appear in Table IV. Our inability to prepare **4a** implies that it is unlikely to be found in environmental samples contaminated by sulfur mustard mixtures. Its synthesis was not pursued further.



n = 1	**1a**	**4a**	-
2	**1b**	**4b**	63%
3	**1c**	**4c**	10%
4	**1d**	**4d**	76%
5	**1e**	**4e**	26%

SCHEME 6

TABLE III Data for Bis-Sulfoxides $(CH_2)_n(SOC_2H_4OH)_2$ **3a–e** (NMR Data Measured in CD_3OD, R_f Values in 3:1 $CHCl_3$-MeOH)

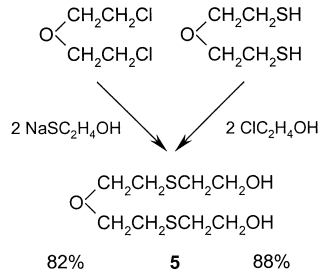
Compound	n	m.p. (°C)	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)	IR ν (cm^{-1})
3a (R_f 0.15)	1	79–81	4.0 (4H, complex m, CH_2OD), 3.35–3.11 (6H, complex m, $SOCH_2$)	56.9 (CH_2OD), 56.3 and 55.6 ($SOCH_2$)	3365, 2883, 1392, 1313, 1282, 1122, 1043, 999
3b (R_f 0.15)	2	113–115	4.05 (4H, m, CH_2OD), 3.43–3.05 (8H, m, CH_2SO)	56.1 and 56 (CH_2OD), 55.7 ($\underline{C}H_2CH_2OD$), 45.5 and 45.3 ($SOCH_2$)	3352, 2958, 2885, 2359, 2333, 1404, 1026, 995
3c (R_f 0.20)	3	84–87	3.97 (4H, m, CH_2OD), 3.1–2.8 (8H, m, CH_2SO), 2.28 (2H, m, CH_2)	55.9 and 56 (CH_2OD), 55.8 and 55.8 ($\underline{C}H_2CH_2OD$), 51.6 and 51.5 ($SOCH_2$), 18 and 17.8 (CH_2)	3348, 2918, 2910, 2881, 1448, 1417, 1406, 1034, 991
3d (R_f 0.15)	4	142–145	3.97 (4H, m, CH_2OD), 3.1–2.8 (8H, m, CH_2SO), 1.96 (4H, m, CH_2)	52.1 (CH_2OD), 52 ($\underline{C}H_2CH_2OD$), 48.6 ($SOCH_2$), 19 ($SOCH_2\underline{C}H_2$)	3255, 2908, 2765, 2519, 1973, 1466, 1408, 1340, 1103, 1078, 1039, 1022, 989
3e (R_f 0.20)	5	94–99	3.96 (4H, m, CH_2OD), 3.1–2.7 (8H, m, CH_2SO), 1.85 (4H, m, $SOCH_2C\underline{H}_2$), 1.67 (2H, m, CH_2)	55.9 ($\underline{C}H_2CH_2OD$), 52.7 ($SOCH_2$), 28.6 ($SOCH_2\underline{C}H_2$), 23.3 (CH_2)	3327, 2920, 2912, 2864, 2729, 1468, 1410, 1394, 1155, 1068, 1051, 1016, 973

TABLE IV Data for Bis-Sulfones $(CH_2)_n(SO_2C_2H_4OH)_2$ **4b–e** (NMR Data Measured in CD_3OD)

Compound	n	m.p. (°C)	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)	IR ν (cm^{-1})
4b	2	115–116	3.96 (4H, t, $J=6$, CH_2OD), 3.3 (4H, t, $J=6$, $SO_2C\underline{H}_2CH_2OD$), 3.61 (4H, s, SO_2CH_2)	58.1 (CH_2OD), 57.1 ($SO_2\underline{C}H_2CH_2OD$), 56.7 ($SO_2CH_2$)	3477–3433 (br OH), 3001, 2985, 2939 and 2900 (CH_2), 2727, 1475, 1414, 1327 (SO_2), 1280, 1184, 1113, 1068, 1002, 953, 856, 839
4c	3	152–153	4.02 (4H, t, $J=6$, CH_2OD), 3.3 (4H, t, $J=6$, $SO_2C\underline{H}_2CH_2OD$), 3.4 (4H, t, $J=7$, SO_2CH_2), 2.38 (2H, quintet, $J=7$, CH_2)	56.7 (CH_2OD), 56.7 ($SO_2\underline{C}H_2CH_2OD$), 58.3 ($SO_2CH_2$), 16.3 ($CH_2$)	3406 (br OH), 2995 and 2943 (CH_2), 1441, 1294, 1275, 1244, 1217, 1136 and 1124 (SO_2), 1065, 1045, 1026, 1011, 991, 742
4d	4	133–136	3.88 (4H, t, $J=6$, CH_2OD), 3.25–3.1 (8H, m, $CH_2SO_2CH_2$), 1.86 (4H, CH_2CH_2)	56.8 (CH_2O), 56.3 ($SO_2\underline{C}H_2CH_2OD$), 54.7 ($SO_2CH_2$), 21.9 ($CH_2$)	3479 (br OH), 2983, 2962 and 2933 (CH_2), 2723, 1635, 1481, 1427, 1398, 1309 (SO_2), 1263, 1234, 1174, 1122 (SO_2), 1068, 1022, 1001, 956, 848
4e	5	112–114	3.96 (4H, t, CH_2OD), 3.3 (4H, second order, AA'BB' system, $SO_2C\underline{H}_2CH_2OH$), 3.22 (4H, t, $J=7$, SO_2CH_2), 1.86 (4H, quintet, $J=7$, $SO_2CH_2C\underline{H}_2$), 1.61 (2H, m, CH_2)	56.8 (CH_2OD), 56.3 ($SO\underline{C}H_2CH_2OD$), 55 ($SO_2\underline{C}H_2$), 28.2 ($SO_2CH_2\underline{C}H_2$), 22.3 (CH_2)	3450–3303 (br OH), 2785, 2501 (br), 2243, 2220, 2139, 2071, 1946, 1678, 1392, 1205, 1122 (SO_2), 1092, 976, 823

The Synthesis of T Diol and Oxidation Products

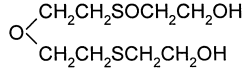
T diol **5**, from 2-chloroethyl ether and 2-mercaptoethanol in sodium ethoxide solution, was first reported in 1948 by Woodward[29] but no yield was given. This reaction was reinvestigated and we obtained the desired diol in 30% yield. The use of aqueous sodium hydroxide as base increased the yield to 82%. Diol **5** was isolated by chromatography on silica gel as a waxy white solid that melted between 31–32°C (in agreement with Woodward).[29] An alternative route from 2-mercaptoethyl ether gave the same compound in 88% yield (Scheme 7).



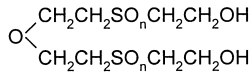
SCHEME 7

Mono-sulfoxide **6**, bis-sulfoxide **7**, and bis-sulfone **8** were prepared in 45%, 86%, and 58% yield, respectively, by employing the oxidising systems used for the Q derivatives (Figure 1). Analytical details appear in Table V.

In summary, the synthesis of six diols by two routes, from dihaloalkanes or alkanedithiols, has been studied. With the exception of 1,1-bis(2-hydroxyethylsulfanyl)methane, for which the former route is the only option, there is little advantage between the two routes in terms of yield. In the case of the Q derivatives, the former is more economical than the latter, as the starting dibromoalkanes are less expensive than



6



7 (n = 1) and **8** (n = 2)

FIGURE 1 T diol oxidation products.

TABLE V Data for T Diol **5** and Its Oxidation Products **6–8**

Compound	m.p (°C)	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)	IR ν (cm^{-1})
5[a]	31–32[b]	3.76 (4H, br dt, CH_2OH), 3.67 (4H, t, $J=6$, CH_2OCH_2), 3.13 (2H, br m, OH), 2.77 (8H, each t, $J=6$ and 6, CH_2SCH_2)	70.7 ($SCH_2\underline{C}H_2O$), 60.9 (CH_2OH), 35.8 ($S\underline{C}H_2CH_2OH$), 31.5 ($S\underline{C}H_2CH_2O$)	3421, 2927, 2871, 2252, 1410, 1390, 1109, 1059, 908, 735, 650
6[c]	Liquid	3.97 (2H, m, $SOCH_2C\underline{H}_2OD$), 3.88 (2H, m, $OC\underline{H}_2CH_2SO$), 3.69 (2H, t, $J=6$, CH_2O), 3.67 (2H, t, $J=7$, $SCH_2C\underline{H}_2OD$), 3.18/3.05 (2H, m, $SOC\underline{H}_2CH_2OD$), 3.15/3.02 (2H, m, $SOC\underline{H}_2CH_2OD$), 2.74 (2H, t, $J=6$ Hz, $SC\underline{H}_2CH_2O$), 2.69 (2H, t, $J=7$, $SC\underline{H}_2CH_2OD$)	72.2 ($SCH_2\underline{C}H_2O$), 64.2 ($O\underline{C}H_2CH_2SO$), 62.6 ($SCH_2\underline{C}H_2OD$), 56.3 ($SO\underline{C}H_2CH_2OD$), 55.9 ($SOCH_2\underline{C}H_2OD$), 53.5 ($OCH_2\underline{C}H_2SO$), 35.6 ($S\underline{C}H_2CH_2OD$), 32.4 ($S\underline{C}H_2CH_2O$)	3365, 2949, 2918, 2870, 1464, 1402, 1360, 1288, 1107, 1041, 995
7[c]	Liquid	3.96 (4H, m, CH_2OD), 3.93 (4H, m, CH_2O), 3.2/3.0 (4H, m, $DOCH_2C\underline{H}_2SO$), 3.05/2.95 (4H, m, $SOC\underline{H}_2CH_2O$)	64.4/64.5 (CH_2O), 55.9 (CH_2OD), 56.4 ($SO\underline{C}H_2CH_2OD$), 53.2/53.4 ($SO\underline{C}H_2CH_2O$)	3363, 2877, 1651, 1466, 1396, 1365, 1288, 1110, 1041, 995
8[c]	Liquid	3.93 (4H, t, $J=6$, CH_2OD), 3.88 (4H, t, $J=5$, CH_2OCH_2), 3.41 (4H, t, $J=6$, $SO_2C\underline{H}_2CH_2OD$), 3.3 (4H, t, $J=5$, $OCH_2C\underline{H}_2SO_2$)	65.7 ($SO_2CH_2\underline{C}H_2O$), 57.9 ($CH_2OD$), 56.8 ($SO_2\underline{C}H_2CH_2OD$), 55.6 ($SO_2\underline{C}H_2CH_2O$)	3406, 2927, 2891, 1392, 1313, 1281, 1122, 1065, 1007, 845, 725

[a] NMR data measured in $CDCl_3$.
[b] Literature[29] m.p. 32°C.
[c] NMR data measured in CD_3OD.

the corresponding alkanedithiols. Syntheses of pure compounds are described, updating those of 50 years ago. Selective methods to oxidation products also are outlined. These products are relevant to investigations involving the chemical warfare agents Q and T, and to analytical support for the Chemical Weapons Convention.

EXPERIMENTAL

Warning: 2-Chloroethyl ether is a potent alkylating agent and carcinogen and should only be used by trained personnel in an efficient fume cupboard. Reagents were purchased from Aldrich Ltd. (Gillingham, UK) and used as received. Anhydrous solvents were employed in all experiments. Thin layer chromatography plates, MK6F silica gel 60 Å (2.5 × 7.5 cm, layer thickness 250 μm), were obtained from Whatman (Maidstone, UK). Product spots were visualised with iodine vapor unless stated otherwise. Silica gel for flash chromatography was from BDH Laboratory Supplies (Poole, UK). NMR spectra were obtained on a JEOL Lambda 500 instrument (operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C spectra) or Lambda 300 instrument (operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C spectra) as solutions in $CDCl_3$ unless stated otherwise, with internal reference $SiMe_4$. Data are recorded as follows: chemical shifts in ppm from reference on the δ scale, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet; br = broad), coupling constant (*J*/Hz) and assignment. IR spectra were recorded as liquid films on a Nicolet SP210 instrument using Omnic software.

LC-MS of T and Q Hydrolysis and Oxidation Products

Compounds were analyzed as 10 μg/mL solutions in water. LC-MS was performed using a published method.[30] Brief details are as follows: A Hewlett-Packard LC system consisting of a model 1050 pump plus solvent conditioner was used. The system was fitted with a 150 × 2 mm internal diameter Columbus C_{18} column (Phenomenex). The mobile phase comprised 0.02 M ammonium formate in H_2O (solvent A) and 0.02 M ammonium formate in MeOH (solvent B). The elution gradient was 5% B (0–5 min) to 90% B (15–20 min) at a flow rate of 0.2 mL/min. Injections (10 μL) were made using a Rheodyne 9125 injector fitted with a 20 μL PEEK loop. The effluent was introduced into a Finnigan TSQ700 mass spectrometer operated in atmospheric pressure chemical ionisation mode. Source conditions: corona current 2 μA, vaporizer temperature 400°C, capillary temperature 150°C,

TABLE VI LC-MS Data for Q and T Hydrolysis and Oxidation Products

Compound	Structure	n	Number	MH^+ (m/z)	$M + NH_4^+$ (m/z)
Q diols	$(CH_2)_n(SCH_2CH_2OH)_2$	1	**1a**	169	186
		2	**1b**	183	200
		3	**1c**	197	214
		4	**1d**	211	228
		5	**1e**	225	242
Q mono-sulfoxides	$HOC_2H_4S(CH_2)_nSOC_2H_4OH$	1	**2a**	185	—
		2	**2b**	199	—
		3	**2c**	213	—
		4	**2d**	227	—
		5	**2e**	241	—
Q bis-sulfoxides	$(CH_2)_n(SOCH_2CH_2OH)_2$	1	**3a**	201	218
		2	**3b**	215	—
		3	**3c**	229	—
		4	**3d**	243	—
		5	**3e**	257	—
Q bis-sulfones	$(CH_2)_n(SO_2CH_2CH_2OH)_2$	2	**4b**	247	264
		3	**4c**	261	278
		4	**4d**	275	292
		5	**4e**	289	306
T derivatives	$O(CH_2CH_2SCH_2CH_2OH)_2$	—	**5**	227	244
	$HOC_2H_4S(CH_2)_2O(CH_2)_2SOC_2H_4OH$	—	**6**	243	—
	$O(CH_2CH_2SOCH_2CH_2OH)_2$	—	**7**	259	—
	$O(CH_2CH_2SO_2CH_2CH_2OH)_2$	—	**8**	291	308

sheath gas (nitrogen) 60 psi and auxiliary gas (nitrogen) flow meter reading 20. The source octapole (Q_0) was operated at an offset of −5 V.

Compounds gave a single major peak in the total ion chromatogram (Table VI). All produced protonated molecular ions (MH^+) and some the ammoniated ion ($M + NH_4^+$). The ion $M + NH_4^+$ constituted the base peak of the spectra obtained for sulfones.

The Synthesis of Bis(2-hydroxyethylsulfanyl)alkanes 1a–e

Procedures for 1,2-bis(2-hydroxyethylsulfanyl)ethane **1b** are given. Homologues were prepared on the same molar scale and purified by chromatography on silica gel eluting with 19:1 chloroform-methanol. Retention factors (R_f values) are given in Table I.

From 1,2-dibromoethane: Absolute ethanol (100 mL) and a magnetic flea were added to a 250 mL three-neck round-bottomed flask. The

centre neck was fitted with a double-surface water condenser and the side necks with stoppers. Sodium (4.6 g, 0.2 mol) in small pieces was added in portions to the stirred ethanol until all the metal had dissolved. 2-Mercaptoethanol (15.6 g, 0.2 mol) was added quickly. The reaction mixture warmed appreciably. 1,2-Dibromoethane (18.8 g, 0.1 mol) was added dropwise over 15 min from a pressure-equalising funnel. The mixture heated almost to the point of reflux and a white precipitate formed. After addition, the mixture was maintained at reflux for 1 h. After cooling, the precipitate was filtered through Celite and the solvent removed. Chromatography of the crude product, eluting with 19:1 chloroform-methanol, gave **1b** as a white solid (15.73 g, 86%).

From 1,2-ethanedithiol: Absolute ethanol (100 mL) and a magnetic flea were added to a 250 mL three-neck round-bottomed flask. The center neck was fitted with a double-surface water condenser and the side necks with stoppers. Sodium (4.6 g, 0.2 mol) in small pieces was added in portions to the stirred ethanol until all the metal had dissolved. Ethane-1,2-dithiol (9.4 g, 0.1 mol) was added in one portion. The mixture warmed slightly. 2-Chloroethanol (16.1 g, 0.2 mol) was added dropwise over 20 min from a pressure-equalizing funnel. The mixture heated almost to the point of reflux and a white precipitate formed. After addition, the mixture was maintained at reflux for 1 h. After cooling, the precipitate was filtered through Celite and the solvent removed. Chromatography of the crude product, eluting with 19:1 chloroform-methanol, gave **1b** as a white solid (14.66 g, 81%).

Attempted Synthesis of 1,1-Bis(2-hydroxyethylsulfanyl)-methane 1a Using Formaldehyde

A few drops of concentrated sulfuric acid (0.3–0.5 mL) were added to a stirred solution of 2-mercaptoethanol (15.6 g, 0.2 mol) and formaldehyde (8.11 g of 37% *w*/*w* formaldehyde in water, 0.1 mol). The mixture became very hot and almost boiled, and on standing gradually became cloudy. It was left to stand at room temperature for 24 h, made into a paste with anhydrous sodium sulfate and heated to 100°C for 2 h. After cooling to room temperature, water (150 mL) was added to dissolve most of the solid. The mixture was extracted with ether (4 × 50 mL) and the combined extracts dried (Na_2SO_4). Analysis by TLC using 19:1 chloroform-methanol showed a main spot (R_f 0.15) and some fainter faster-running spots. The drying agent was filtered off and the filtrate concentrated to a colorless liquid (11.74 g). Chromatography

on silica gel, eluting with the solvent system mentioned above, gave a yellow liquid (5.7 g). Its structure could not be determined with any confidence.

The Synthesis of 2-(Hydroxyethylsulfanyl) 2′-(Hydroxyethylsulfinyl) Alkanes 2a–e

Comparable procedures for mono-oxidation of 1,3-bis(2-hydroxyethylsulfanyl)propane **1c** with potassium periodate and sodium periodate are given. Homologues were prepared on the same molar scale using potassium periodate and purified by chromatography on silica gel, eluting with 9:1 dichloromethane-methanol. Retention factors are given in Table II.

Using potassium periodate: A solution of 1,3-bis(2-hydroxyethylsulfanyl)propane **1c** (3.92 g, 0.02 mol) in methanol (100 mL) and a magnetic flea were added to a 250 mL three-neck round-bottomed flask. The center neck was fitted with a double-surface water condenser, one of the side necks with a dropping funnel and the other with a stopper. A slurry of potassium periodate (4.6 g, 0.02 mol) in water (50 mL) was added dropwise over 5 min. The mixture warmed. After addition, stirring was continued for 2 h and the mixture left to stand for 12 h. Analysis by TLC, eluting with 9:1 dichloromethane-methanol, showed three compounds: starting material (R_f 0.6), an unidentified minor component (R_f 0.5, visualized poorly by iodine vapor), the desired mono-sulfoxide (R_f 0.2) and a minor spot for the bis-sulfoxide (R_f 0.05). The inorganic material was removed by filtration and the solvent removed from the filtrate to give a colorless liquid containing a little white solid (4.8 g). Chromatography of this on silica gel, eluting with 9:1 dichloromethane-methanol, gave **2c** as a viscous pale yellow liquid (2.2 g, 52%).

Using sodium periodate: A solution of 1,3-bis(2-hydroxyethylsulfanyl)propane **1c** (3.92 g, 0.02 mol) in methanol (100 mL) and a magnetic flea were added to a 250 mL three-neck round-bottomed flask. The center neck was fitted with a double-surface water condenser, one of the side necks with a dropping funnel and the other with a stopper. A solution of sodium periodate (4.28 g, 0.02 mol) in water (40 mL) was added dropwise over 40 min. The mixture became warm and a thick white precipitate was produced. After addition, stirring was continued for a further 3.5 h. Analysis of the reaction mixture by TLC, eluting with 9:1 dichloromethane-methanol, showed the presence of three compounds: starting material (R_f 0.5), the desired mono-sulfoxide (R_f 0.1) and a faint spot for the bis-sulfoxide (on the baseline). The inorganic material was removed by filtration and the solvent removed to

give a sticky white solid (4.6 g). Chromatography of this on silica gel, eluting with the solvent system mentioned before, gave pure **2c** (1.9 g, 46%).

The Synthesis of Bis(2-hydroxyethylsulfinyl)alkanes 3a–e

This general procedure is illustrated for the synthesis of 1,2-bis(2-hydroxyethylsulfinyl)ethane **3b**. A solution of sodium periodate (8.56 g, 0.04 mol) in water (40 mL) was added dropwise to a stirred solution of 1,2-bis(2-hydroxyethylsulfanyl)ethane **1b** (3.64 g, 0.02 mol) in methanol (100 mL). A white precipitate formed. After addition, the mixture was stirred at room temperature for 1 h. The precipitate was filtered off and the solvent removed. Chromatography of the residue on silica gel, eluting with 3:1 chloroform-methanol, gave **3b** as a white solid (3.52 g, 82%). M.p. 113–115°C.

The Synthesis of Bis(2-hydroxyethylsulfonyl)alkanes 4b–e

This general procedure is illustrated for the synthesis of 1,2-bis(2-hydroxyethylsulfonyl)ethane **4b**. A 100 mL two-neck round-bottomed flask was equipped with a magnetic flea, a double-surface water condenser and a dropping funnel. The flask was charged with a solution of 1,2-bis(2-hydroxyethylsulfanyl)ethane **1b** (3.64 g, 0.02 mol) in trifluoroacetic acid (20 mL). Hydrogen peroxide (10 mL of a 27.5% aqueous solution, 10% molar excess) was added in portions over 40 min. The temperature rose quickly, almost causing the solution to reflux. After addition, the mixture was heated under reflux for 90 min. The trifluoroacetic acid and water were removed using a rotary evaporator then an oil pump. Analysis of the residue by TLC in 12:1 chloroform-methanol, using a dilute solution of potassium permanganate in acetone as visualizing agent, showed the desired product (R_f 0.1) as a white spot on a pink background. Chromatography on silica gel, using the same solvent system, gave **4b** as a white solid (3.1 g, 63%).

2,2′-Bis(2-hydroxyethylsulfanyl)diethyl Ether 5

From 2-chloroethyl ether and NaOEt: 2-Mercaptoethanol (7.8 g, 0.1 mol) was added to a solution of sodium ethoxide prepared from sodium metal (2.3 g, 0.1 mol) and absolute ethanol (40 mL). 2-Chloroethyl ether (7.2 g, 0.05 mol) was added dropwise over 10 min. The mixture warmed up and turned cloudy. After addition, it was heated under reflux for 1 h. A thick precipitate of sodium chloride formed. The reaction mixture was filtered

through Celite, the precipitate rinsed with ethanol, and the solvent removed from the filtrate to leave a viscous yellow liquid. Anhydrous acetone (30 mL) was added to precipitate residual sodium chloride, which was removed by a second filtration through Celite. The filtrate was concentrated and the crude product distilled using a Kugelrohr apparatus to yield a yellow liquid that solidified on standing overnight (9.9 g). B.p. ~100°C/0.02 mmHg. The product was not pure by TLC analysis. Chromatography on silica gel, eluting with 19:1 chloroform-methanol, gave in order of elution: a small amount of an unidentified product (R_f 0.5), possibly a mono-dehydration product, the title compound (R_f 0.1), and 2-chloroethanol (R_f 0.05). Compound **5** was obtained as a white solid (3.44 g, 30%).

From 2-chloroethyl ether and NaOH: Sodium hydroxide pellets (8 g, 0.2 mol) were dissolved in water (8 mL) and absolute ethanol (65 mL). 2-Mercaptethanol (15.6 g, 0.2 mol) was added and the mixture stirred and heated to 45°C. 2-Chloroethyl ether (14.3 g, 0.1 mol) was added dropwise over 20 min. A white precipitate formed. After addition, the mixture was heated under reflux for 20 min, allowed to cool to room temperature and left for 12 h. Filtration through Celite and removal of solvent gave a yellow liquid (23.5 g). Chromatography on silica gel, eluting with 19:1 chloroform-methanol, gave pure compound **5** (18.58 g, 82%).

From 2-mercaptoethyl ether and NaOEt: A solution of sodium ethoxide was prepared by the addition of sodium metal (4.6 g, 0.2 mol) in small pieces to absolute ethanol (100 mL) with stirring. 2-Mercaptoethyl ether (13.8 g, 0.1 mol) was added. The mixture turned light yellow. 2-Chloroethanol (16.1 g, 0.2 mol) was added dropwise over 15 min. The mixture warmed up and sodium chloride precipitated. After addition, the mixture was heated under reflux for 1 h. The precipitate thickened. Filtration of the mixture through Celite and removal of solvent from the filtrate gave a pale yellow liquid. Chromatography on silica gel, eluting with 19:1 chloroform-methanol, gave pure compound **5** (19.89 g, 88%). R_f 0.1.

2-(Hydroxyethylsulfanyl) 2′-(hydroxyethylsulfinyl)diethyl Ether 6

A slurry of potassium periodate (2.3 g, 0.01 mol) in water (25 mL) was added over 5 min to a stirred solution of bis(2-hydroxyethylsulfanyl)ethyl ether **5** (2.26 g, 0.01 mol) in methanol (50 mL). The mixture warmed slightly. After addition, stirring was continued for a further 4 h with monitoring by TLC after 30, 90, 150, and 240 min. All TLC plates were similar and showed, after staining with

iodine vapor, significant starting material and mono-sulfoxide spots (R_f values 0.45 and 0.15), and a faint bis-sulfoxide spot (R_f 0.05). The intensity of the first two spots appeared to change in favor of the mono-sulfoxide as time elapsed. The mixture was filtered to remove inorganic material and the solvent removed from the filtrate to leave a viscous liquid containing some white solid (2.66 g). Chromatography on silica gel, eluting with 9:1 dichloromethane-methanol, gave compound **6** as a pale yellow liquid (1.09 g, 45%).

2,2′-Bis(2-hydroxyethylsulfinyl)diethyl Ether 7

A solution of sodium periodate (4.28 g, 0.02 mol) in water (40 mL) was added over 15 min to a stirred solution of bis(2-hydroxyethylsulfanyl)ethyl ether **5** (2.26 g, 0.01 mol) in methanol (80 mL). The mixture warmed up and a thick white precipitate formed. After stirring for a further 2 h, the mixture was analyzed by TLC using 3:1 chloroform-methanol. A very faint spot (R_f 0.8) for an unknown minor product, a faint spot for the starting material (R_f 0.5), and a spot of moderate intensity corresponding to the bis-sulfoxide (R_f 0.15) was observed. The mixture was left for 12 h at room temperature. Futher TLC analysis indicated no change. The precipitate was removed by filtration and the solvent removed to leave a white solid (3.1 g). Chromatography on silica gel, eluting with the solvent system mentioned before, gave compound **7** as a very viscous colourless liquid (2.22 g, 86%).

2,2′-Bis(2-hydroxyethylsulfonyl)diethyl Ether 8

A 50 mL two-neck round-bottomed flask was equipped with a magnetic flea, a double-surface water condenser and a dropping funnel. The flask was charged with a solution of bis(2-hydroxyethylsulfanyl)ethyl ether **5** (2.26 g, 0.01 mol) in trifluoroacetic acid (10 mL). Hydrogen peroxide (5 mL of a 27.5% aqueous solution, 1.1 molar equivalents) was added in six portions over 10 min. The oxidation is exothermic: the mixture heated to the point of reflux after half the peroxide had been added. After addition, the mixture was maintained under reflux for 60 min. Analysis by TLC was inconclusive. The trifluoroacetic acid and water were removed by rotary evaporation to give a syrup (3.67 g). Chromatography on silica gel, eluting with 9:1 dichloromethane-methanol, gave compound **8** as a very viscous colourless liquid (1.68 g, 58%).

REFERENCES

[1] R. M. Black, R. J. Clarke, R. W. Read, and M. T. J. Reid, *J. Chromatogr. A,* **662,** 301 (1994).

[2] G. M. Bennett and E. M. Whincop, *J. Chem. Soc*., **119,** 1860 (1921).
[3] G. M. Bennett, *J. Chem. Soc*., **121,** 2139 (1922).
[4] E. J. Gasson, H. McCombie, A. H. Williams, and F. N. Woodward, *J. Chem. Soc*., 44 (1948).
[5] J. S. H. Davies and A. E. Oxford, *J. Chem. Soc*., **119,** 224 (1931).
[6] E. M. Meade and R. C. G. Moggridge, *J. Chem. Soc*., 813 (1946).
[7] R. J. Charnock and R. C. G. Moggridge, *J. Chem. Soc*., 815 (1946).
[8] R. Brown and R. C. G. Moggridge, *J. Chem. Soc*., 816 (1946).
[9] Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction, Organisation for the Prohibition of Chemical Weapons (OPCW), The Hague (1994).
[10] N. B. Munro, S. S. Talmage, G. D. Griffin, et al., *Environ. Health Perspect.*, **107,** 933 (1999).
[11] M. Mazurek, Z. Witkiewicz, S. Popiel, and M. Sliwakowski, *J. Chromatogr. A*, **919,** 133 (2001).
[12] P. A. D'Agostino and L. R. Provost, *J. Chromatogr*., **645,** 283 (1993).
[13] P. A. D'Agostino, L. R. Provost, and J. R. Hancock, *J. Chromatogr. A*, **808,** 177 (1998).
[14] J. M. Harrison, *J. Labelled Comps. and Radiopharm*., **29,** 1175 (1991).
[15] R. M. Black, K. Brewster, J. M. Harrison, and N. Stansfield, *Phosphorus, Sulfur, and Silicon*, **71,** 31 (1992).
[16] R. M. Black, K. Brewster, R. J. Clarke, and J. M. Harrison, *Phosphorus, Sulfur, and Silicon*, **71,** 49 (1992).
[17] R. M. Black and R. W. Read, *J. Chromatogr. A*, **759,** 79 (1997).
[18] J. L. Hambrook, J. M. Harrison, D. J. Howells, and C. Schock, *Xenobiotica*, **22,** 65 (1992).
[19] R. M. Black, J. M. Harrison, and R. W. Read, *Xenobiotica*, **27,** 11 (1997).
[20] R. M. Black, R. J. Clarke, J. M. Harrison, and R. W. Read, *Xenobiotica*, **27,** 499 (1997).
[21] W. H. Stein, J. S. Fruton, and M. Bergmann, *J. Org. Chem*., **11,** 692 (1946).
[22] L. A. Paquette (ed.), *Encyclopedia of Reagents for Organic Synthesis* (John Wiley & Sons, Chichester, UK, 1995), vol. 7, p. 4613.
[23] G. H. Whitham, *Organosulfur Chemistry* (Oxford Chemistry Primers, Oxford University Press, 1995), number 33.
[24] A. E. Hill, *J. Am. Chem. Soc*., **50,** 2678 (1928).
[25] A. H. Ford-Moore, R. A. Peters, and R. W. Wakelin, *J. Chem. Soc.*, 1754 (1949).
[26] A. H. Ford-Moore, *J. Chem. Soc*., 2126 (1949).
[27] A. H. Ford-Moore, *J. Chem. Soc*., 2433 (1949).
[28] Y. Zhu and D. G. Drueckhammer, *Tetrahedron Lett.*, **43,** 1377 (2002).
[29] F. N. Woodward, *J. Chem. Soc*., 35 (1948).
[30] R. W. Read and R. M. Black, *J. Chromatogr. A*, **862,** 169 (1999).