Syntheses of Sulfinylmethyl Ethers and Conversion of these into Halomethyl and Acyloxymethyl Ethers

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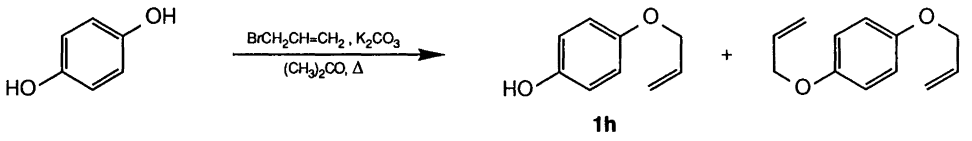
Halomethyl ethers can be prepared from sulfinyl ethers by cleavage of the carbon–sulfur bond with thionyl chloride, acetyl chloride or trimethylsilyl halides. In the presence of alkenyl groups in the substrate, acetyl chloride is the reagent of choice. Trifluoroacetic anhydride reacts in the same manner to form the trifluoroacetoxymethyl ether. With acetic anhydride, catalysis by methanesulfonic acid was required. At elevated temperatures in the presence of sodium acetate the products were formed by the Pummerer rearrangement.

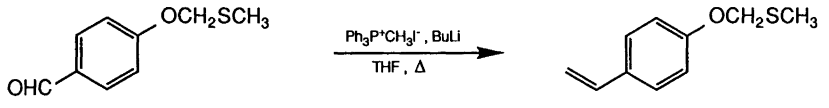
α-Halo and α-acyl ethers are important synthons for the introduction of oxa-alkyl side-chains into heterocyclic systems of biological interest.[1] In previous reports we have shown that α-halo ethers can be made by cleavage of *O,S*-acetals with sulfuryl chloride or with bromine.[2] The method, however, is limited to substrates without an olefinic bond since the halogenating agent, or the methanesulfenyl halide which is formed as one of the products in the desired reaction, will add to the olefinic bond. This report describes work with other cleavage agents, some with reduced activity towards the olefines.

The polarization and the reactivity of the carbon–sulfur bonds of the sulfides have been increased by oxidation to the corresponding sulfoxides **3**. The starting materials **1** (Scheme 2) were commercially available except for 4-allyloxyphenol (**1h**) (Scheme 1), which was made by alkylation of hydroquinone with allyl bromide under alkaline conditions.

The *O,S*-acetals **2** were prepared by a reaction



1h



2d **2f**

Scheme 1.

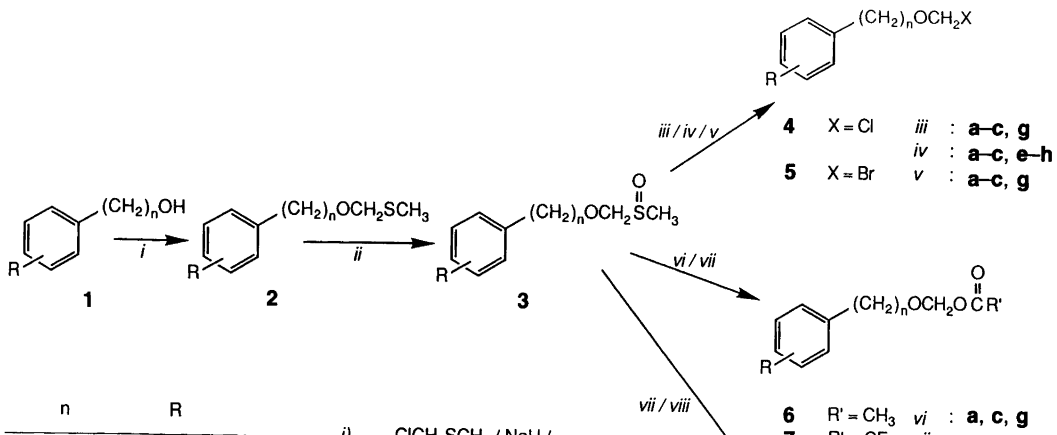
between chloromethyl methyl sulfide and the respective sodium olate, either in 1,2-dimethoxyethane (DME)[3] or in DMF when preliminary experiments had shown that reactions in DMF gave the better yield. The 4-vinylphenyloxy derivative **2f** was prepared from the corresponding 4-formyl derivative **2d** by a Wittig reaction using methyltriphenylphosphonium iodide and butyllithium.

Oxidation of the sulfides **2** to the sulfoxides **3** proceeded smoothly using *m*-chloroperbenzoic acid (MCPBA) in dichloromethane at 0 °C. Some α-alkoxy sulfoxides have been reported to rearrange very easily,[4] but all the sulfoxides **3** were stable compounds which could be stored for months without significant decomposition.

The carbon–sulfur bond in the sulfoxides **3** was cleaved on treatment with trimethylsilyl bromide (TMS-Br) at 0 °C, the product being the desired bromomethyl ethers **5**. Products arising from a Pummerer rearrangement, were not seen. The course of this reaction parallels the finding that α-alkoxy sulfoxides react with TMS-cyanide to yield the corresponding α-alkoxy cyanides, even in the presence of an olefinic bond.[5] The sulfoxide substrates **3** with an olefinic bond, however, gave complex products in reaction with TMS-Br. The major product (ca. 50 %) was the sulfide **2** which was formed by deoxygenation of the sulfoxide. Deoxygenation has also been reported for reactions between TMS halides and sulfoxides without an α-alkoxy function, together with the formation of Pummerer rearrangement products.[6,7] TMS-Cl was less satisfactory than the bromide in the desired halogenating reaction. The benzyl derivative **3b**, however, readily gave the desired reaction with formation of **4b**.

The sulfoxides **3** react with thionyl chloride to form the corresponding chloromethyl ethers **4**. The vinyl group in **3f**, however, was involved in adduct formation (^{1}H NMR). The cleavage of the alkoxy sulfoxides has its analogy in reactions of thio analogues, i.e. α-alkylthio sulfoxides, which are cleaved by thionyl chloride or acyl chlorides to form the corresponding α-chloro sulfides.[8]

The sulfoxides **3** were also readily cleaved in the desired fashion by acetyl chloride. An important feature is that an olefinic bond is not



	n	R
a	0	4-Br
b	1	4-Br
c	0	4-CH_3CO
d	0	4-CHO
e	0	2-CH_2=$CHCH_2$
f	0	4-CH_2=CH
g	0	4-CH_3O
h	0	4-CH_2=$CHCH_2O$

i) $ClCH_2SCH_3$ / NaH / NaI / DME or DMF
ii) MCPBA / CH_2Cl_2
iii) $SOCl_2$ / CH_2Cl_2
iv) CH_3COCl / CH_2Cl_2
v) TMS-Br / CH_2Cl_2
vi) $(CH_3CO)_2O$ / H^+
vii) $(CF_3CO)_2O$ / CH_2Cl_2
viii) $(CH_3CO)_2O$ / $CH_3CO_2^-$

Scheme 2.

affected under the reaction conditions, as seen in the selective formation of the vinyl derivatives **4e,f** and **h**. Presumably the reaction occurs by initial acetylation of the sulfinyl oxygen and subsequent nucleophilic displacement of the sulfinyl moiety at the acetal carbon. The acetic methanesulfinic anhydride, in contrast to the methanesulfinyl halides generated in the above reactions, does not attack olefinic bonds under the conditions used in the reactions. Based on this rationalization for the course of the reaction, and on the absence of a Pummerer rearrangement product, it appeared likely that the sulfoxides **3** would react with carboxylic acid anhydrides to form acyloxymethyl ethers, e.g. **6**. Accordingly, compounds **3** were found to react with acetic anhydride in the presence of catalytic amounts of methanesulfonic acid to give the acetoxymethyl ethers **6** in 60–76% yield. The strong acid was required for the reaction to proceed. With trifluoroacetic anhydride, which presumably contains small amounts of free acid, the cleavage reaction proceeds readily at 0°C (30 min) with formation of **7a** and **7g** as the major products, the minor products corresponding to **8a** and **8g** being formed by the Pummerer rearrangement. Substrates with an olefinic substituent gave ill-defined products. The substrate **3c** with the electron withdrawing acetyl group formed the major product by Pummerer rearrangement. The change in the balance between the two possible courses for the reaction is in accordance with a report stating that Pummerer rearrangements are promoted by increasing electron-withdrawing effects.[9]

The course of the reaction between the sulfoxides **3** and acetic anhydride could also be changed. When this reagent was used at elevated temperatures in the presence of sodium acetate the Pummerer rearrangement was responsible for the major products **9**, the minor products (18–20%) from **3a** and **3c** being identified as the corresponding phenyl acetates. In all cases of the Pummerer rearrangement the methyl group was oxidized in preference to the aryloxymethyl group. These findings parallel results from metallation studies, which show that 2-methylthiotetrahydrofuran is lithiated on the methyl carbon[10] and that 1,3-oxathiane-3,3-dioxide is monometallated at C-4.[11] Assuming a carbanion-like intermediate in the Pummerer rearrangement,[12] selective reaction at the terminal methyl group is not unexpected.

Experimental

The ^{1}H NMR spectra were recorded at 60 MHz or at 300 MHz, and the ^{13}C NMR spectra at 75 MHz. The mass spectra under electron impact conditions (MS) were recorded at 70 eV ionizing voltage. Isobutane was used for chemical ionization MS (CI); the spectra are presented as *m/z* (% rel. int.).

4-Allyloxyphenol (**1h**).[13] Allyl bromide (121.0 g, 1.00 mol) was added dropwise with stirring during 15 min to a mixture of hydroquinone (110.1 g, 1.00 mol) and potassium carbonate (138.2 g, 1.00 mol) in acetone (400 ml), the mixture heated under reflux for 5 h, filtered, the filtrate and acetone washings of the solid evaporated and the residue stirred with 1 M NaOH (300 ml). Extraction with diethyl ether (3×100 ml) removed the 1,4-diallyloxybenzene. Neutralization of the aqueous solution using 6 M HCl, followed by extraction with diethyl ether (3 × 100 ml) and evaporation of the washed and dried ($MgSO_4$) ether solution gave an oily material which was distilled; yield 40.8 g (27%), b.p. 104–108°C/0.1 mmHg, m.p. 42°C (Et_2O). Anal. $C_9H_{10}O_2$: C, H. ^{1}H NMR ($CDCl_3$): δ 4.44 (2 H, m, *J* 5.4, 1.5 and 1.5 Hz, OCH_2), 5.24 [1 H, m, *J* 10.5, 1.5 and 1.5 Hz, $=CH_2$ (*trans*)], 5.36 [1 H, m, *J* 17.3, 1.5 and 1.5 Hz, $=CH_2$ (*cis*)], 6.01 (1 H, m, *J* 17.4, 10.4 and 5.4 Hz, =CH−), 6.7–6.8 (4 H, m, Ar), 6.90 (bs, OH). ^{13}C NMR ($CDCl_3$): δ 69.8 (OCH_2), 116.0, 149.7, 152.3 (Ar), 117.7 ($=CH_2$), 133.3 (=CH−). MS: 150 (4, *M*), 111 (6), 110 (100), 109 (17), 108 (7), 82 (14), 81 (24).

Characterization of 1,4-diallyloxybenzene. The ether extracts from the preparation of **1h** were evaporated and the residue recrystallized from pentane; yield 40.0 g, m.p. 36°C. Anal. $C_{12}H_{14}O_2$: C, H. ^{1}H NMR ($CDCl_3$): δ 4.45 (4 H, d, *J* 5.1 Hz, 2×OCH_2), 5.24 [2 H, d, *J* 10.5 Hz, 2 × $=CH_2$ (*trans*)], 5.37 [2 H, d, *J* 17.1 Hz, 2 × $=CH_2$ (*cis*)], 6.03 (2 H, m, *J* 17.4, 10.5 and 5.1 Hz, 2×=CH−), 6.83 (4 H, s, Ar). ^{13}C NMR ($CDCl_3$): δ 69.4 (OCH_2), 115.7, 152.9 (Ar), 117.3 ($=CH_2$), 133.6 (=CH−). MS: 190 (12, *M*), 150 (2), 149 (25), 109 (3), 81 (2), 41 (100).

General procedure for the preparation of methylthiomethyl ethers (**2**).[3] Sodium hydride dispersion

in liquid paraffin (80%, 22 mmol) and sodium iodide (20 mmol) were added successively to a solution of the phenol (20 mmol) in 1,2-dimethoxyethane (20 ml) at 4°C, and the mixture was stirred for 30 min before chloromethyl methyl sulfide (20 mmol) was added. The resultant mixture was allowed to reach ambient temperature and was stirred for 6 h; the volume was reduced to 1/3 at reduced pressure, the residue poured onto ice-water, the mixture extracted with diethyl ether, the washed and dried ($MgSO_4$) ether solution evaporated and the residue purified by distillation.

4-Bromophenyl methylthiomethyl ether (**2a**).[14] Yield 58%, b.p. 80°C/0.05 mmHg. Anal. C_8H_9BrOS: C, H. ^1H NMR ($CDCl_3$): δ 2.19 (SCH_3), 5.06 (OCH_2S), 6.7–7.4 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 14.4 (SCH_3), 72.4 (OCH_2S), 113.9, 117.7, 132.2, 155.9 (Ar). MS: 234/232 (4/4, *M*), 157 (2), 155 (2), 76 (3), 75 (3), 62 (4), 61 (100).

4-Bromobenzyl methylthiomethyl ether (**2b**). Yield 85%, b.p. 90–92°C/0.05 mmHg. Anal. $C_9H_{11}BrOS$: C, H. ^1H NMR ($CDCl_3$): δ 2.16 (SCH_3), 4.55 (CH_2), 4.66 (CH_2), 7.1–7.5 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 13.9 (SCH_3), 68.4 (CH_2), 74.3 (CH_2), 121.4, 129.4, 131.2, 136.3 (Ar). MS: 248/246 (3/3, *M*), 218 (9), 216 (9), 200 (18), 198 (18), 185 (16), 171 (95), 169 (100), 90 (34), 61 (33).

4-Acetylphenyl methylthiomethyl ether (**2c**).[14] Yield 65%, b.p. 108–110°C/0.01 mmHg. Anal. $C_{10}H_{12}O_2S$: C, H. ^1H NMR ($CDCl_3$): δ 2.27 (SCH_3), 2.57 (CH_3CO), 5.21 (OCH_2S), 6.9–8.0 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 14.7 (SCH_3), 26.4 (CH_3CO), 72.3 (OCH_2S), 115.4, 130.5, 131.1, 160.9 (Ar), 196.7 (CH_3CO). MS: 196 (6, *M*), 91 (2), 77 (2), 76 (3), 63 (6), 62 (4), 61 (100).

4-Formylphenyl methylthiomethyl ether (**2d**). Yield 70%, b.p. 109–112°C/0.05 mmHg. Anal. $C_9H_{10}O_2S$: C, H. ^1H NMR ($CDCl_3$): δ 2.25 (SCH_3), 5.21 (OCH_2S), 7.0–7.9 (4 H, m, Ar), 9.88 (CHO). ^{13}C NMR ($CDCl_3$): δ 14.6 (SCH_3), 72.2 (OCH_2S), 115.7, 130.3, 131.5, 161.7 (Ar), 190.3 (CHO). MS: 182 (4, *M*), 121 (2), 105 (2), 77 (5), 76 (3), 65 (4), 62 (4), 61 (100).

2-Allylphenyl methylthiomethyl ether (**2e**). The crude product was purified by flash chromatography on silica gel using hexane/EtOAc (20:1) for elution; yield 54%, colourless liquid. Anal. $C_{11}H_{14}OS$: C, H. ^1H NMR ($CDCl_3$): δ 2.24 (SCH_3), 3.41 (2 H, d, *J* 6.6 Hz, Ar-CH_2), 5.04 [1 H, m, *J* 10.7 and 1.5 Hz, $=CH_2$ (*trans*)], 5.05 [1 H, m, *J* 16.7 and 1.5 Hz, $=CH_2$ (*cis*)], 5.15 (OCH_2S), 5.99 (1 H, m, *J* 16.6, 10.7 and 6.6 Hz, =CH−), 6.8–7.2 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 14.7 (SCH_3), 34.3 (Ar-CH_2), 72.4 (OCH_2S), 113.1, 121.6, 127.1, 129.7, 130.2, 154.7 (Ar), 115.5 ($=CH_2$), 136.9 (=CH−). MS: 194 (0, *M*), 147 (2), 133 (9), 131 (5), 115 (5), 77 (7), 63 (8), 61 (100).

Methylthiomethyl 4-vinylphenyl ether (**2f**) *by Wittig reaction.* Butyllithium (1.6 M in hexane; 48 ml, 77 mmol) was added dropwise during 15 min with stirring to methyltriphenylphosphonium iodide (31.12 g, 77 mmol) in dry THF (80 ml) under N_2 at 0°C. The mixture was stirred at ambient temperature for 30 min before 4-formylphenyl methylthiomethyl ether (**2d**) (12.75 g, 70 mmol) in dry THF (20 ml) was added dropwise during 5 min to the deep red solution. The mixture was stirred at 60°C for 2 h and poured onto water (200 ml); the resulting mixture was extracted with diethyl ether (3×100 ml), the washed and dried ($MgSO_4$) ether solution evaporated, the residue stirred with diethyl ether, the filtered ether extracts evaporated, the residue extracted with hexane, the filtered solution evaporated and the residue distilled; yield 73%, b.p. 84°C/0.05 mmHg. Anal. $C_{10}H_{12}OS$: C, H. ^1H NMR ($CDCl_3$): δ 2.21 (SCH_3), 5.09 (OCH_2S), 5.12 [1 H, dd, *J* 11.7 and 2.1 Hz, $=CH_2$ (*trans*)], 5.60 [1 H, dd, *J* 17.7 and 2.1 Hz, $=CH_2$ (*cis*)], 6.64 (1 H, dd, *J* 17.7 and 11.7 Hz, =CH−), 6.8–7.4 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 14.5 (SCH_3), 72.4 (OCH_2S), 112.1 ($=CH_2$), 115.9, 127.3, 131.4, 156.7 (Ar), 136.1 (=CH−). MS: 180 (11, *M*), 103 (3), 91 (3), 77 (6), 65 (4), 63 (6), 62 (4), 61 (100).

4-Methoxyphenyl methylthiomethyl ether (**2g**). Yield 52%, b.p. 90–92°C/0.1 mmHg. Anal. $C_9H_{12}O_2S$: C, H. ^{1}NMR ($CDCl_3$): δ 2.22 (SCH_3), 3.75 (OCH_3), 5.08 (OCH_2S), 6.8–7.0 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 14.5 (SCH_3), 55.5 (OCH_3), 73.3 (OCH_2S), 114.4, 117.2, 150.6,

154.4 (Ar). MS: 184 (13, *M*), 123 (6), 95 (4), 92 (4), 77 (5), 64 (5), 63 (8), 61 (100).

4-Allyloxyphenyl methylthiomethyl ether (**2h**). *N,N*-dimethylformamide was used instead of 1,2-dimethoxyethane; the crude product was purified by flash chromatography on silica gel using hexane/EtOAc (20:1) for elution; yield 58%, colourless liquid. Anal. $C_{11}H_{14}O_2S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.24 (SCH_3), 4.49 (2 H, m, *J* 5.4, 1.5 and 1.5 Hz, OCH_2C), 5.10 (2 H, s, OCH_2S), 5.27 [1 H, m, *J* 10.5, 1.5 and 1.5 Hz, $=CH_2$ (*trans*)], 5.40 (1 H, m, *J* 17.3, 1.5 and 1.5 Hz, $=CH_2$ (*cis*)], 6.04 (1 H, m, *J* 17.3, 10.5 and 5.4 Hz, =CH−), 6.8–8.0 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 14.5 (SCH_3), 69.4 (OCH_2C), 73.5 (OCH_2S), 115.7, 117.4, 151.1, 153.7 (Ar), 117.5 ($=CH_2$), 133.5 (=CH−). MS: 210 (7, *M*), 109 (2), 64 (5), 63 (9), 61 (100).

General procedure for the preparation of aryl and benzyl methylsulfinylmethyl ethers (**3**). *m*-Chloroperbenzoic acid (10.5 mmol) was added to a solution of the aryl or benzyl methylthiomethyl ether **2** (10.0 mmol) in dichloromethane (50 ml) at 0 °C. The mixture was stirred for 10 min, shaken with saturated sodium bisulfite solution and then with sodium bicarbonate solution before the dried ($MgSO_4$) solution was evaporated to leave the crude product, which was further purified as described below for each compound.

4-Bromophenyl methylsulfinylmethyl ether (**3a**). Compound **3a** was obtained from **2a** and was purified by flash chromatography on silica gel using acetonitrile for elution; yield 86%, m.p. 85 °C (EtOAc). Anal. $C_8H_9BrO_2S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.70 (SCH_3), 4.93 (1 H, d, *J* 10.5 Hz, H_A, OCH_2S), 4.98 (1 H, d, *J* 10.5 Hz, H_B, OCH_2S), 6.9–7.5 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 35.5 (SCH_3), 84.2 (OCH_2S), 115.1, 117.2, 132.3, 156.3 (Ar). MS: 250/248 (3/3, *M*), 187 (98), 185 (100), 157 (82), 155 (77), 78 (21), 77 (18), 61 (16).

4-Bromobenzyl methylsulfinylmethyl ether (**3b**). Compound **3b** was obtained from **2b** and was purified by recrystallization from diethyl ether/hexane (1:1); yield 80%, m.p. 44–45 °C. Anal. $C_9H_{11}BrO_2S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.57 (SCH_3), 4.44 (1 H, d, *J* 10.8 Hz, H_A, CH_2'), 4.51 (1 H, d, *J* 10.8 Hz, H_B, CH_2'), 4.76 (1 H, d, *J* 11.7 Hz, H_A, CH_2''), 4.83 (1 H, d, *J* 12.0 Hz, H_B, CH_2''), 7.1–7.5 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 34.8 (SCH_3), 74.2 (CH_2), 86.4 (CH_2), 122.0, 129.3, 131.4, 135.1 (Ar). MS (CI): 265/263 (16/16, *M*+1), 235 (57), 233 (57), 171 (91), 170 (10), 169 (100), 155 (13), 91 (21).

4-Acetylphenyl methylsulfinylmethyl ether (**3c**). Compound **3c** was obtained from **2c** and was purified by flash chromatography on silica gel using acetonitrile for elution; yield 69%, m.p. 110–114 °C (EtOAc). Anal. $C_{10}H_{12}O_3S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.55 (CH_3CO), 2.72 (SCH_3), 5.07 (OCH_2S), 7.0–7.8 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 26.3 (CH_3CO), 35.5 (SCH_3), 83.6 (OCH_2S), 114.9, 130.3, 131.7, 160.8 (Ar), 196.1 (CH_3CO). MS: 212 (1, *M*), 150 (10), 149 (100), 119 (45), 107 (16), 91 (50), 77 (17), 61 (13).

2-Allylphenyl methylsulfinylmethyl ether (**3e**). Compound **3e** was obtained from **2e** and was purified by flash chromatography on silica gel using acetonitrile for elution; yield 84%, m.p. 34–38 °C (Et_2O/hexane). Anal. $C_{11}H_{14}O_2S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.62 (SCH_3), 3.40 (2 H, dd, *J* 6.5 and 1.5 Hz, Ar-CH_2), 4.87 (1 H, d, *J* 10.2 Hz, H_A, OCH_2S), 4.98 (1 H, d, *J* 10.2 Hz, H_B, OCH_2S), 5.01 [1 H, m, *J* 16.9, 1.8 and 1.5 Hz, $=CH_2$ (*cis*)], 5.04 [1 H, m, *J* 10.1, 1.8 and 1.5 Hz, $=CH_2$ (*trans*)], 5.95 (1 H, m, *J* 16.8, 10.2 and 6.6 Hz, =CH−), 6.9–7.3 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 34.1 (Ar-CH_2), 35.6 (SCH_3), 84.5 (OCH_2S), 113.1, 122.8, 127.6, 129.1, 130.4, 155.2 (Ar), 115.8 ($=CH_2$), 136.4 (=CH−). MS: 210 (0, *M*), 147 (62), 115 (57), 107 (24), 91 (100), 77 (20), 61 (25).

Methylsulfinylmethyl 4-vinylphenyl ether (**3f**). Compound **3f** was prepared from **2f** and was purified by flash chromatography on silica gel using acetonitrile/EtOAc (1:1) for elution; yield 80%, m.p. 48 °C (Et_2O). Anal. $C_{10}H_{12}O_2S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.66 (SCH_3), 4.87 (1 H, d, *J* 10.2 Hz, H_A, OCH_2S), 5.00 (1 H, d, *J* 9.9 Hz, H_B, OCH_2S), 5.18 [1 H, d, *J* 11.1 Hz, $=CH_2$ (*trans*)], 5.64 (1 H, d, *J* 17.4 Hz, $=CH_2$ (*cis*)], 6.65 (1 H, dd, *J* 17.4 and 11.1 Hz, =CH−), 6.9–7.4 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 35.5 (SCH_3), 84.1 (OCH_2S), 112.8 ($=CH_2$), 115.4, 127.3, 132.4, 156.8 (Ar), 135.5 (=CH−). MS: 196 (5, *M*), 133 (90), 105 (24), 103 (100), 102 (14), 77 (55), 61 (15).

4-Methoxyphenyl methylsulfinylmethyl ether (**3g**). Compound **3g** was obtained from **2g** and was purified by flash chromatography on silica gel using acetonitrile for elution; yield 89 %, m.p. 32–35 °C (Et_2O). Anal. $C_9H_{12}O_3S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.68 (SCH_3), 3.78 (OCH_3), 4.82 (1 H, d, *J* 10.2 Hz, H_A, OCH_2S), 4.98 (1 H, d, *J* 10.2 Hz, H_B, OCH_2S), 6.8–7.0 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 35.7 (SCH_3), 55.7 (OCH_3), 85.7 (OCH_2S), 114.9, 117.1, 151.7, 155.6 (Ar). MS: 200 (5, *M*), 138 (8), 137 (100), 123 (6), 109 (26), 107 (51), 92 (32), 77 (58), 64 (17), 63 (14), 61 (23).

4-Allyloxyphenyl methylsulfinylmethyl ether (**3h**). Compound **3h** was obtained from **2h** and was purified by flash chromatography on silica gel using acetonitrile for elution; yield 87 %, m.p. 42–43 °C (Et_2O). Anal. $C_{11}H_{14}O_3S$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.68 (SCH_3), 4.50 (2 H, m, *J* 5.4, 1.5 and 1.5 Hz, OCH_2C), 4.83 (1 H, d, *J* 10.2 Hz, H_A, OCH_2S), 4.98 (1 H, d, *J* 10.2 Hz, H_B, OCH_2S), 5.28 [1 H, m, *J* 10.5, 1.5 and 1.5 Hz, $=CH_2$ (*trans*)], 5.40 [1 H, m, *J* 17.3, 1.5 and 1.5 Hz, $=CH_2$ (*cis*)], 6.04 (1 H, m, *J* 17.4, 10.5 and 5.4 Hz, =CH−), 6.8–7.1 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 35.7 (SCH_3), 69.4 (OCH_2C), 85.6 (OCH_2S), 115.8, 117.0, 151.7, 154.5 (Ar), 117.7 ($=CH_2$), 133.2 (=CH−). MS: 226 (2, *M*), 163 (50), 103 (6), 79 (24), 77 (12), 66 (6), 64 (20), 63 (17), 61 (22), 55 (10), 41 (100).

General procedure for the preparation of chloromethyl ethers (**4**) *using thionyl chloride.* A solution of thionyl chloride (5.5 mmol) in dry dichloromethane (5 ml) was added dropwise during 5 min to a solution of the aryl or benzyl methylsulfinylmethyl ether (**3**) (5.0 mmol) in dichloromethane (5 ml) under N_2 at 0 °C, the mixture stirred at ambient temperature for 1.5 h, and the solution evaporated at reduced pressure.

4-Bromophenyl chloromethyl ether (**4a**).[15] Compound **4a** was obtained from **3a** and was purified by distillation; yield 62 %, b.p. 70 °C/0.05 mmHg. ^{1}H NMR ($CDCl_3$): δ 5.95 (OCH_2Cl), 6.9–7.6 (4 H, m, Ar). MS: 224/222/220 (25/100/76, *M*), 187 (69), 185 (71), 173 (51), 171 (54), 157 (38), 155 (30), 145 (42), 143 (42), 43 (97), 40 (82).

4-Bromobenzyl chloromethyl ether (**4b**). Compound **4b** was obtained from **3b** and was purified by distillation; yield 73 %, b.p. 70 °C/0.05 mmHg. ^{1}H NMR ($CDCl_3$): δ 4.74 ($ArCH_2O$), 5.49 (OCH_2Cl), 7.2–7.8 (4 H, m, Ar). MS: 238/236/234 (4/17/13, *M*), 208 (1), 206 (4), 204 (3), 171 (98), 169 (100), 91 (14), 90 (36), 89 (31).

4-Acetylphenyl chloromethyl ether (**4c**).[2a,16] Compound **4c** was obtained from **3c** and was purified by distillation; yield 60 %. MS: 186/184 (9/27, *M*), 171 (32), 169 (100), 149 (21), 143 (2), 141 (6), 121 (16), 119 (8), 92 (13), 77 (23).

Chloromethyl 4-methoxyphenyl ether (**4g**).[15] Compound **4g** was obtained from **3g** and was purified by distillation; yield 65 %, b.p. 42–44 °C/0.01 mmHg. ^{1}H NMR ($CDCl_3$): δ 3.75 (OCH_3), 5.82 (OCH_2Cl), 6.7–7.2 (4 H, m, Ar). MS: 174/172 (10/30, *M*), 137 (19), 124 (26), 123 (100), 107 (8), 95 (23).

General procedure for the preparation of chloromethyl ethers (**4**) *using acetyl chloride.* Acetyl chloride (5.5 mmol) was added dropwise during 5 min to a solution of the aryl or benzyl methylsulfinylmethyl ether (**3**) (5.0 mmol) in dry dichloromethane (10 ml) under N_2 at 0 °C, the mixture stirred at ambient temperature for 2.5 h, the solution evaporated at reduced pressure and the residue allowed to stand under the vacuum from an oil pump for 1 h.

4-Bromophenyl chloromethyl ether (**4a**).[15] Compound **4a** was obtained from **3a** (4.98 g, 20.0 mmol). The crude product was purified by distillation; yield 3.31 g, 75 %, b.p. 93–96 °C/0.2 mmHg.

4-Bromobenzyl chloromethyl ether (**4b**). Compound **4b** was obtained from **3b**. The crude product was not further purified; yield 80 %.

4-Acetylphenyl chloromethyl ether (**4c**).[2a,16] Compound **4c** was obtained from **3c**. The crude product was not further purified; yield 96 %.

2-Allylphenyl chloromethyl ether (**4e**). Compound **4e** was obtained from **3e**. The crude product was not further purified; yield 80 %. ^{1}H NMR ($CDCl_3$): δ 3.2–3.5 (2 H, m, *J* 6 Hz, $ArCH_2$),

4.8–5.3 (2 H, m, $=CH_2$), 5.7–6.4 (1 H, m, =CH–), 5.90 (2 H, s, OCH_2Cl), 6.7–7.4 (4 H, m, Ar).

Chloromethyl 4-vinylphenyl ether (**4f**). Compound **4f** was obtained from **3f** and was purified by rapid distillation in a "Kugelrohr" apparatus (80 °C/0.05 mmHg). Part of the crude product polymerized on heating. The yield of distilled product was 20 %. ^{1} NMR ($CDCl_3$): δ 5.1–5.9 (2 H, m, $=CH_2$), 5.94 (OCH_2Cl), 6.5–7.0 (1 H, m, =CH–), 7.0–7.6 (4 H, m, Ar). MS: 170/168 (4/11, *M*), 133 (13), 120 (11), 119 (19), 103 (14), 91 (15), 77 (15), 63 (11), 61 (100).

Chloromethyl 4-methoxyphenyl ether (**4g**).[15] Compound **4g** was obtained from **3g**. The crude product was not further purified; yield 90 %.

4-Allyloxyphenyl chloromethyl ether (**4h**). Compound **4h** was obtained from **3h**. The crude product was not further purified; yield 70 %. ^{1}H NMR ($CDCl_3$): δ 4.3–4.6 (2 H, m, *J* 5 Hz, OCH_2C), 5.1–5.6 (2 H, m, $=CH_2$), 5.7–6.4 (1 H, m, =CH–), 5.80 (2 H, s, OCH_2Cl), 6.7–7.2 (4 H, m, Ar).

General procedure for the preparation of bromomethyl ethers (**5**). A solution of trimethylbromosilane (6.0 mmol) in dry dichloromethane (5 ml) was added dropwise during 5 min to a solution of the aryl or benzyl methylsulfinylmethyl ether (**3**) (5.0 mmol) in dichloromethane (5 ml) under N_2 at 0 °C, the mixture stirred at ambient temperature for 2 h, the solvent distilled off and the residue left under the vacuum from an oil pump for 5 h before further purification.

Bromomethyl 4-bromophenyl ether (**5a**). Compound **5a** was obtained from **3a** and was purified by recrystallization from hexane; yield 69 %, m.p. 65 °C. ^{1}H NMR ($CDCl_3$): δ 6.04 (OCH_2Br), 6.9–7.7 (4 H, m, Ar). MS: 268/266/264 (6/18/14, *M*), 187 (93), 185 (100), 157 (47), 155 (44), 76 (31), 75 (31).

4-Bromobenzyl bromomethyl ether (**5b**). Compound **5b** was obtained from **3b** and was purified by rapid distillation in an "Kugelrohr" apparatus (110 °C/0.05 mmHg). Part of the material decomposed on heating. The yield of pure material was 38 % (yield of crude product 70 %). ^{1}H NMR ($CDCl_3$): δ 4.67 (OCH_2Ar), 5.72 (OCH_2Br), 7.1–7.7 (4 H, m, Ar). MS: 282/280/278 (1.0/2.5/1.2, *M*), 201 (5), 199 (5), 172 (7), 171 (95), 170 (8), 169 (100), 90 (38), 89 (28).

4-Acetylphenyl bromomethyl ether (**5c**). Compound **5c** was obtained from **3c**. The crude product was not purified; yield 75 %, colourless liquid. ^{1}H NMR ($CDCl_3$): δ 2.60 (CH_3CO), 6.07 (OCH_2Br), 7.1–8.2 (4 H, m, Ar). MS: 230/228 (21/21, *M*), 215 (52), 213 (55), 149 (68), 121 (86), 93 (28), 91 (34), 76 (39), 65 (32), 50 (42), 43 (100).

Bromomethyl 4-methoxyphenyl ether (**5g**). Compound **5g** was obtained from **3g** and was purified by rapid distillation (b.p. 46 °C/0.05 mmHg). Part of the material decomposed on heating. The yield of pure material was 41 % (yield of crude product 85 %). ^{1}H NMR ($CDCl_3$): δ 3.79 (OCH_3), 5.98 (OCH_2Br), 6.7–7.2 (4 H, m, Ar). MS: 218/216 (2/2, *M*), 137 (15), 124 (51), 109 (61), 82 (31), 81 (37), 80 (33), 53 (38), 45 (52), 43 (100).

General procedure for the preparation of acyloxymethyl ethers (**6**). One drop of methanesulfonic acid was added to a solution of the aryl methylsulfinylmethyl ether (**3**) (2.5 mmol) in acetic anhydride (2.5 ml) at ambient temperature under N_2 and the mixture was stirred for 12 h at 25 °C (**4c** was stirred at 40 °C); the solution was evaporated at reduced pressure, diethyl ether (20 ml) and methanol (1 ml) were added, and the mixture was stirred for 1 h. The solution was washed with saturated sodium bicarbonate solution, and the dried ($MgSO_4$) solution was evaporated at reduced pressure. The crude product was purified as described below for each compound.

4-Bromophenyloxymethyl acetate (**6a**). Compound **6a** was obtained from **3a** and was purified by flash chromatography on silica gel using dichloromethane/pentane (1:1) for elution; yield 76 %, colourless liquid. ^{1}H NMR ($CDCl_3$): δ 2.11 (CH_3CO), 5.73 (OCH_2O), 6.7–7.6 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 20.8 (CH_3CO), 85.3 (OCH_2O), 115.1, 117.9, 132.4, 155.9 (Ar), 169.7 (CH_3CO). MS: 246/244 (14/14, *M*), 216 (11), 214 (11), 187 (15), 185 (15), 174 (99), 172 (100), 63 (11), 43 (92). Mol. wt.: obs. 243.9725, calc. for $C_8H_9BrO_3$ 243.9735.

4-Acetylphenyloxymethyl acetate (**6c**). Compound **6c** was obtained from **3c** and was purified by flash chromatography on silica gel using hexane/ethyl acetate (2:3) for elution; yield 67%, m.p. 73°C (Et_2O/pentane). Anal. $C_{11}H_{12}O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.13 (CH_3CO_2), 2.57 (CH_3COAr), 5.71 (OCH_2O), 6.9–8.1 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 20.8 (CH_3CO_2), 26.3 (CH_3COAr), 84.6 (OCH_2O), 115.5, 130.5, 132.0, 160.4 (Ar), 169.6 (CH_3CO_2), 196.6 (CH_3COAr). MS: 208 (5, *M*), 178 (20), 149 (12), 136 (35), 123 (6), 121 (81), 119 (8), 43 (100).

4-Methoxyphenyloxymethyl acetate (**6g**). Compound **6g** was obtained from **3g** and was purified by flash chromatography on silica gel using hexane/EtOAc (2:1) for elution; yield 76%, colourless liquid. Anal. $C_{10}H_{12}O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.07 (CH_3CO), 3.72 (CH_3O), 5.67 (OCH_2O), 6.6–7.1 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 21.2 (CH_3CO), 55.8 (CH_3O), 86.8 (OCH_2O), 114.7, 117.5, 150.9, 155.3 (Ar), 170.0 (CH_3CO), MS: 196 (15, *M*), 137 (15), 125 (8), 124 (100), 109 (31), 107 (5).

General procedure for the reaction between aryl methylsulfinylmethyl ether (**3**) *and trifluoroacetic anhydride.* Trifluoroacetic anhydride (4.4 mmol) was added dropwise during 5 min to a solution of the aryl methylsulfinylmethyl ether (**3**) (4.0 mmol) in dry dichloromethane (8 ml) under N_2 at 0°C. The mixture was stirred for 30 min at 0°C and evaporated to dryness. The crude product was purified as described below for each compound.

4-Bromophenyloxymethyl trifluoroacetate (**7a**). Compound **7a** was obtained from **3a** and was purified by chromatography on silica gel using trichloromethane for elution; yield 83%, colourless liquid. Anal. $C_9H_6BrF_3O_3$: C, H. ^{1}H NMR ($CDCl_3$): δ 5.92 (OCH_2O), 6.9–7.5 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 88.6 (OCH_2O), 114.3 (q, *J* 284 Hz, CF_3CO), 116.6, 118.2, 132.8, 155.3 (Ar), 156.5 (q, *J* 44 Hz, CF_3CO). MS: 300/298 (45/45, *M*), 270 (54), 268 (55), 173 (25), 171 (25), 75 (29), 69 (100).

4-Methoxyphenyloxymethyl trifluoroacetate (**7g**). Compound **7g** was obtained from **3g** and was purified by flash chromatography on silica gel using dichloromethane for elution; yield 58%, colourless liquid. Anal. $C_{10}H_9F_3O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 3.78 (OCH_3), 5.88 (OCH_2O), 6.8–7.1 (4 H, m, Ar). ^{13}C NMR ($CDCl_3$): δ 55.3 (OCH_3), 89.9 (OCH_2O), 113.9 (q, *J* 283 Hz, CF_3CO), 114.4, 117.8, 149.8, 155.7 (Ar), 156.1 (q, *J* 43 Hz, CF_3CO). MS: 250 (36, *M*), 220 (19), 137 (17), 124 (10), 123 (100), 95 (16).

[(4-Acetylphenyloxymethyl)thio]methyl trifluoroacetate (**8c**). Compound **8c** was obtained from **3c** and was purified by flash chromatography on silica gel using hexane/EtOAc (3:2) for elution; yield 50%, colourless liquid. ^{1}H NMR ($(CD_3)_2CO$): δ 2.52 (CH_3CO), 5.57 (CH_2), 5.73 (CH_2), 6.9–8.1 (4 H, m, Ar). MS: 308 (24, *M*), 173 (100), 149 (34), 143 (34), 127 (23), 121 (34), 99 (22).

General procedure for the preparation of [(aryloxymethyl)thio]methyl acetates (**9**). The aryl methylsulfinylmethyl ether (**3**) (1.0 mmol) in acetic anhydride (1 ml) with sodium acetate (0.1 mmol) was stirred for 3 h at 140°C. The solution was evaporated at reduced pressure, diethyl ether (20 ml) and methanol (1 ml) were added to the residue and the mixture was stirred for 1 h. The washed (saturated sodium bicarbonate solution) and dried ($MgSO_4$) ether solution was evaporated to leave the crude product, which was purified as described below for each compound.

[(4-Bromophenyloxymethyl)thio]methyl acetate (**9a**). Compound **9a** was obtained from **3a** and was purified by flash chromatography on silica gel using hexane/EtOAc (4:1) for elution, yield 64%; colourless liquid. Anal. $C_{10}H_{11}BrO_3S$: C, H. ^{1}H NMR (acetone-d_6): δ 2.03 (CH_3CO), 5.29 (CH_2), 5.44 (CH_2), 6.9–7.5 (4 H, m, Ar). ^{13}C NMR (acetone-d_6): δ 20.9 (CH_3CO), 64.9 (CH_2), 70.7 (CH_2), 114.4, 119.1, 133.1, 157.0 (Ar), 170.7 (CH_3CO). MS: 292/290 (3/3, *M*), 187 (3), 185 (3), 174 (26), 172 (26), 119 (75), 89 (38), 76 (8), 75 (8), 73 (29), 63 (8), 50 (8), 43 (100). The reaction also gave 4-bromophenyl acetate (20%) which was identified by comparision with an authentic sample.[17]

[(4-Acetylphenyloxymethyl)thio]methyl acetate (**9c**). Compound **9c** was obtained from **3c** and was purified by flash chromatography on silica gel using hexane/EtOAc (2:1) for elution; yield 78%, colourless liquid. Anal. $C_{12}H_{14}O_4S$: C, H. ^{1}H NMR (acetone-d_6): δ 2.03 (CH_3CO_2), 2.53 (CH_3COAr), 5.31 (CH_2), 5.51 (CH_2), 7.0–8.0

(4 H, m, Ar). ^{13}C NMR (acetone-d_6): δ 20.9 (CH_3CO_2), 26.5 (CH_3COAr), 64.9 (CH_2), 70.4 (CH_2), 116.4, 131.1, 132.2, 161.4 (Ar), 170.6 (CH_3CO_2), 196.4 (CH_3COAr). MS: 254 (2, *M*), 136 (13), 121 (43), 120 (4), 119 (71), 91 (5), 89 (36), 43 (100). The reaction also gave 4-acetylphenyl acetate (18 %) which was identified by comparision with an authentic sample.[18]

[(4-Methoxyphenyloxymethyl)thio]methyl acetate (**9g**). Compound **9g** was obtained from **3g** and was purified by flash chromatography on silica gel using hexane/EtoAc (2:1) for elution; yield 83 %, colourless liquid. ^{1}H NMR (acetone-d_6): δ 2.02 (CH_3CO), 3.73 (CH_3O), 5.26 (CH_2), 5.34 (CH_2), 6.8–7.0 (4 H, m, Ar). ^{13}C NMR (acetone-d_6): δ 20.8 (CH_3CO), 55.8 (CH_3O), 64.7 (CH_2), 71.3 (CH_2), 115.3, 118.3, 151.5, 155.8 (Ar), 170.6 (CH_3CO). MS: 242 (12, *M*), 182 (3), 137 (9), 124 (100), 123 (10), 119 (46), 109 (31), 89 (23), 43 (74). Mol. wt.: obs. 242.0623, calc. for $C_{11}H_{14}O_4S$ 242.0613.

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