Synthesis of Unsaturated Chloromethyl Ethers

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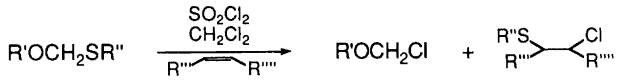
Alkenyl or alkynyl chloromethyl ethers have been prepared from *O,S*-acetals by reaction with sulfuryl chloride in the presence of cyclohexene or a styrene as a trapping reagent for the sulfenyl halide which is formed in the reaction. Chloromethyl phenyl ethers, where the benzene ring carries substituents containing alkenyl or alkynyl functions, are likewise prepared from the corresponding *O,S*-acetals and sulfuryl chloride in the presence of a trapping reagent.

α-Halo ethers can be prepared by cleavage of *O,S*-acetals with chlorine, sulfuryl chloride or bromine.[1] The method is finding general use.[2]

During the cleavage reaction of *O,S*-acetals with sulfuryl chloride to form the α-chloro ether an equivalent amount of the respective sulfenyl chloride is also formed. The latter, very often methanesulfenyl chloride from a methylthio group, is removed by distillation. When the substrate contains an alkenyl or alkynyl function, however, the sulfenyl halide may react rapidly with the unsaturated function to form an adduct. This behaviour was originally observed in alkynes. Therefore, a trapping agent for the sulfenyl chloride was required which did not interfere with the halogenating agent. Olefins have been found to be useful trapping agents because of rapid reaction with sulfenyl chlorides[3] and little interference with sulfuryl chloride.[4] Typically, when the *O,S*-acetals **1a–1c** are reacted with sulfuryl chloride at 0 °C in the presence of 1.1 mole equivalents of cyclohexene as the trapping agent no addition to the triple bond is observed in the formation of the chloromethyl ethers **2**.



1a–i **2** **3**

	R'	R''	R''', R''''
1a	$TBDMSOCH_2C{\equiv}CCH_2$	CH_3	$-(CH_2)_4-$
1b	$AcOCH_2C{\equiv}CCH_2$	CH_3	H, 4-BrC_6H_4
1c	$AcOCH_2C{\equiv}CCH_2$	4-ClC_6H_4	$-(CH_2)_4-$
1d	*cis*-$TBDMSOCH_2CH{=}CHCH_2$	CH_3	H, 4-BrC_6H_4
1e	*cis*-$AcOCH_2CH{=}CHCH_2$	CH_3	H, 4-BrC_6H_4
1f	4-$H_2C{=}CHC_6H_4$	CH_3	$-(CH_2)_4-$
1g	2-$H_2C{=}CHCH_2C_6H_4$	CH_3	$-(CH_2)_4-$
1h	4-$H_2C{=}CHCH_2OCH_2C_6H_4$	CH_3	$-(CH_2)_4-$
1i	4-$HC{\equiv}CCH_2OCH_2C_6H_4$	CH_3	$-(CH_2)_4-$

Scheme 1.

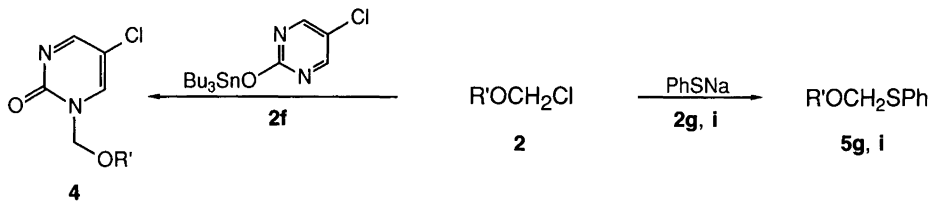
The chloromethyl ether **2b**, which was formed from **1b**, and the cyclohexene adduct with methanesulfenyl chloride had similar boiling points which made it difficult to separate these products by distillation. Substituted styrenes were therefore tried as trapping agents. The adduct between 4-bromostyrene and methanesulfenyl chloride had a sufficiently high boiling point for the chloromethyl ether to be isolated by distillation. The sulfenyl chloride adduct can also be made less volatile by increasing the size of the *S*-substituent, e.g. from the methyl group to an aryl group, as seen with the O,S-acetal **1c**.

Alkenes, in general, add sulfenyl chlorides more readily than do the corresponding alkynes, and *cis*-alkenes are more reactive than *trans*-alkenes.[3] In the reaction of **1d** and **1e** with sulfuryl chloride, the sulfenyl chloride was trapped as a cyclohexene adduct or as a 4-bromostyrene adduct; styrenes are reported to be highly reactive towards sulfenyl chlorides.[3b]

In the absence of an acid-sensitive substituent, chloromethyl ethers of unsaturated alcohols such as propargyl or allyl alcohol can be prepared from the reaction between the alcohol, paraformaldehyde and hydrochloric acid.[5] The *O,S*-acetals **1a–e** contain an acid-sensitive substituent which survives the cleavage reaction by sulfuryl chloride in the formation of the chloromethyl ethers **2a–e**.

Aromatic halomethyl ethers are generally not available by direct halomethylation of phenols because of preferential electrophilic substitution in the activated aromatic ring.[6] We have reported previously that halogen cleavage reactions of *O,S*-acetals prepared from a phenol will yield the corresponding aryl chloromethyl ether.[1a] Additional alkene or alkyne substituents in the aromatic moiety may cause side-reactions such as adduct formation with the sulfenyl halide. One way around this problem has been found using acetyl chloride to cleave the sulfoxide derivative of the *O,S*-acetal.[7]

In the sulfuryl chloride cleavage of **1f-i** cyclohexene was an efficient trapping agent for methanesulfenyl chloride. Especially noteworthy in this series of reactions is the for-



Scheme 2.

mation of the chloromethyl styryl ether **2f** since 4-methoxystyrene, which corresponds to **1f/2f** in electronic activation, is reported to add 2,4-dinitrobenzenesulfenyl chloride ca. 60 times more rapidly than cyclohexene.[8]

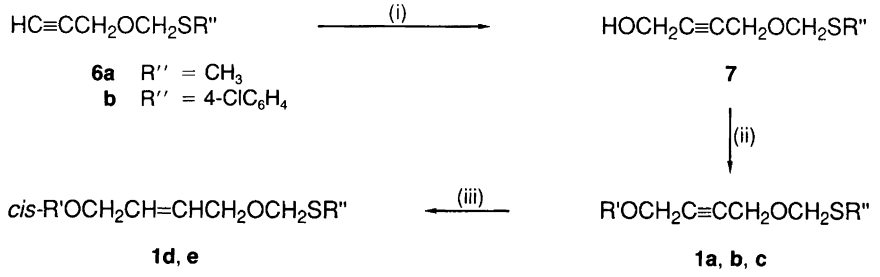
Sulfenyl chlorides are classified as soft electrophiles,[9] and hence one might expect reaction of the sulfenyl chloride with the softer part of the *O,S*-acetal, to give carbon–sulfur cleavage as is the case with sulfuryl chloride. Treating 4-bromophenyl methylthiomethyl ether with half an equivalent of sulfuryl chloride, gave only the corresponding α-chloro ether together with dimethyl disulfide. However, reaction of the unsaturated *O,S*-acetal **1g** with half an equivalent of sulfuryl chloride, gave ca. 50 % α-chloro ether and partial saturation of the olefin function. This indicates that methanesulfenyl chloride, in contrast with sulfuryl chloride, reacts with the unsaturated function in preference to the *O,S*-acetal function.

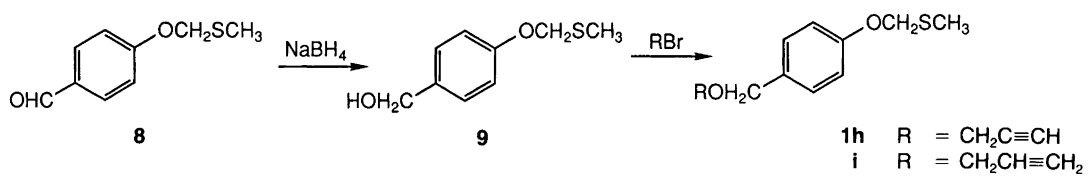
The chloromethyl aryl ethers **2f–i** are unstable. The allyloxy derivative **2h**, however, was isolated by distillation from a 1:1 mixture with 1-chloro-2-methylthiocyclohexane (**3**), the co-product in the reaction. The other aryl chloromethyl ethers, in the presence of **3**, were treated directly with added nucleophiles. The chloromethyl styryl ether **2f** gave the *N*-alkylated pyrimidinone **4** when treated with 5-chloro-2-tributylstannyloxypyrimidine.[10] The reaction mixtures containing **2g** and **2h**, reacted readily with sodium thiophenolate to form the corresponding *O,S*-acetals **5g** and **5h** in good overall yields. The high reactivity of the chloromethyl ethers **2** excluded significant product formation from the co-product **3** in these reactions.

The *O,S*-acetals **1a–c** were prepared from propargyl alcohol. The alcohol was *O*-alkylated by means of chloromethyl methyl sulfide,[7,11] lithiated on the terminal acetylenic carbon atom and hydroxymethylated by means of paraformaldehyde,[12] and finally the alcohol was silylated by means of *tert*-butyldimethylsilyl chloride (TBDMS-Cl)[13] or esterified.[14] The *cis*-alkenes **1d** and **1e** were prepared by partial hydrogenation of the corresponding alkynes **1a** and **1b** over a poisoned palladium catalyst.[15] The *O,S*-acetals **1h** and **1i** were prepared from 4-formylphenyl methylthiomethyl ether **8**[7] by standard procedures.

Experimental

The ^1H NMR spectra were recorded in $CDCl_3$ at 300 MHz, the ^{13}C NMR spectra in $CDCl_3$ at 75 MHz. The mass spectra under electron-impact conditions (MS) were recorded at 70 eV ionizing voltage. Isobutane was used for





Scheme 3.

chemical ionization [MS (CI)]; the spectra are presented as *m/z* (% rel. int).

4-tert-Butyldimethylsilyloxy-2-butynyl methylthiomethyl ether (**1a**). A solution of 4-methylthiomethoxy-2-butyn-1-ol (10.2 mmol), *tert*-butyldimethylchlorosilane (11.3 mmol), triethylamine (12.3 mmol), and 4-*N*,*N*-dimethylaminopyridine (0.4 mmol) in dichloromethane (15 ml) was stirred under N_2 at ambient temperature for 40 min. The solution was then evaporated and the residue dissolved in diethyl ether, and the ether solution was treated with activated charcoal, filtered and evaporated to leave the crude product which was purified by distillation; yield 97%, b.p. 90–91 °C/0.08 mmHg. Anal. $C_{12}H_{24}O_2SSi$: C, H. ^{1}H NMR: δ 0.07 [6 H, s, $(CH_3)_2Si$], 0.86 [9 H, s, $(CH_3)_3C$], 2.07 (3 H, s, SCH_3), 4.26–4.30 (4 H, m, 2 × $\equiv CCH_2$), 4.68 (2 H, s, CH_2S). ^{13}C NMR: δ −5.5 [$(CH_3)_2Si$], 13.5 (SCH_3), 17.8 [$C(CH_3)_3$], 25.4 [$(CH_3)_3C$], 51.3 ($\equiv CCH_2$), 53.9 ($\equiv CCH_2$), 73.0 (CH_2S), 79.7 (≡C), 84.8 (≡C). MS (CI): 261 (10, *M*+1), 215 (10), 213 (12), 203 (34), 184 (11), 183 (70), 173 (39), 129 (100).

4-Acetoxy-2-butynyl methylthiomethyl ether (**1b**). A solution of 4-methylthiomethoxy-2-butyn-1-ol (56 mmol) and 4-*N*,*N*-dimethylaminopyridine (10 mmol) in pyridine (225 mmol) and acetic anhydride (112 mmol) was stirred at ambient temperature for 20 h under N_2. Methanol (50 ml) was added, the solution was stirred for 1 h and 1 M HCl (100 ml) added. The mixture was extracted with diethyl ether (3 × 100 ml), the ether extracts washed with 1 M HCl (3 × 50 ml) and saturated aqueous $NaHCO_3$ (3 × 50 ml), dried ($MgSO_4$) and evaporated to leave the crude product which was purified by distillation; yield 67%, b.p. 68–70 °C/0.01 mmHg. Anal. $C_8H_{12}O_3S$: C, H. ^{1}H NMR: δ 2.10 (3 H, s, CH_3CO), 2.14 (3 H, s, SCH_3), 4.32 (2 H, t, *J* 1.8 Hz, $\equiv CCH_2$), 4.72 (2 H, t, *J* 1.8 Hz, $\equiv CCH_2$), 4.72 (2 H, s, CH_2S). ^{13}C NMR: δ 14.0 (SCH_3), 20.7 (CH_3CO), 52.2 ($\equiv CCH_2$), 54.4 ($\equiv CCH_2$), 73.8 (CH_2S), 80.6 (≡C), 82.2 (≡C), 170.0 (CO). MS (CI): 189 (2, *M*+1), 173 (2), 171 (5), 159 (2), 158 (6), 147 (15), 129 (70), 111 (100).

4-Acetoxy-2-butynyl 4-chlorophenylthiomethyl ether (**1c**). Compound **1c** was obtained from 4-chlorophenylthiomethoxy-2-butyn-1-ol using the procedure described for the preparation of **1b**. The crude product was purified by flash chromatography on silica gel eluting with pentane–ethyl acetate 5:2; yield 96%, colourless liquid. Anal. $C_{13}H_{13}ClO_3S$: C, H. ^{1}H NMR: δ 2.10 (3 H, s, CH_3CO), 4.39 (2 H, t, *J* 1.8 Hz, $\equiv CCH_2$), 4.71 (2 H, t, *J* 1.8 Hz, $\equiv CCH_2$), 5.06 (2 H, s, CH_2S), 7.2–7.4 (4 H, m, Ar). ^{13}C NMR: δ 20.5 (CH_3CO), 51.9 ($\equiv CCH_2$), 54.6 ($\equiv CCH_2$), 73.9 (CH_2S), 80.9 (≡C), 81.4 (≡C), 128.9, 131,2, 132.8, 133.6 (Ar), 169.9 (CO). MS: 286/284 (2/5, *M*), 159 (2), 157 (4), 146 (1), 145 (2), 144 (2), 143 (4), 141 (2), 111 (71), 108 (5) 43 (100).

cis-*4-tert-Butyldimethylsilyloxy-2-butenyl methylthiomethyl ether* (**1d**). A solution of 4-*tert*-butyldimethysilyloxy-2-butynyl methylthiomethyl ether (3.85 mmol), 5% palladium on barium sulfate (2% weight), and quinoline (2% weight) in methanol (16 ml) was hydrogenated at 50 psi for 19 h. The mixture was centrifuged and the supernatant was evaporated to leave the crude product which was purified by distillation; yield 83%, b.p. 60–62 °C/0.01 mmHg. Anal. $C_{12}H_{26}O_2SSi$: C, H. ^{1}H NMR: δ 0.07 [6 H, s, $(CH_3)Si$], 0.87 [9 H, s $(CH_3)C$], 2.13 (3 H, s, CH_3S), 4.10–4.15 (2 H, m, *J* 6.6 and 1.2 Hz, $CH_2C=$), 4.23–4.27 (2 H, m, *J* 6.0 and 1.2 Hz, $CH_2C=$), 4.61 (2 H, s, CH_2S), 5.50–5.60 (1 H, m, *J* 11.4, 6.6 and 1.2 Hz, =CH–), 5.65–5.75 (1 H, m, *J* 11.2, 6.0 and 1.2 Hz, =CH–). ^{13}C NMR: δ −5.3 [$(CH_3)_2Si$], 13.8 (SCH_3), 18.2 [$(CH_3)_3C$], 25.8 [$(CH_3)_3C$], 59.4 ($CH_2C=$), 63.0 ($CH_2C=$), 74.3 (CH_2S), 125.7 (=CH–), 135.3 (=CH–). MS: 143 (5), 127 (9), 113 (3), 105 (10), 75 (18), 73 (21), 61 (100).

cis-*4-Acetoxy-2-butenyl methylthiomethyl ether* (**1e**). Compound **1e** was prepared from 4-acetoxy-2-butynyl methylthiomethyl ether using the same procedure as for the preparation of **1d**; yield 79%, b.p. 60–62 °C/0.01 mmHg. Anal. $C_8H_{14}O_3S$: C, H. ^{1}H NMR: δ 2.07 (3 H, s, SCH_3), 2.15 (3 H, s, CH_3CO), 4.19 (2 H, d, *J* 5.1 Hz, $=CCH_2$), 4.64 (2 H, s, SCH_2), 4.67 (2 H, d, *J* 5.4 Hz, $=CCH_2$), 5.68–5.82 (2 H, m, 2 × =CH–). ^{13}C NMR: δ 13.6 (SCH_3), 20.6 (CH_3CO), 60.0 ($=CCH_2$), 62.6 ($=CCH_2$), 74.3 (CH_2S), 127.1 (=CH–), 129.7 (=CH–), 170.4 (CO). MS (CI): 191 (15, *M*+1), 143 (15), 131 (43), 129 (5), 114 (5), 113 (100).

Methylthiomethyl 4-styryl ether (**1f**).[7]

2-Allylphenyl methylthiomethyl ether (**1g**).[7]

4-Allyloxymethylphenyl methylthiomethyl ether (**1h**). Sodium hydride (80% in paraffin; 40 mmol) was added to a solution of 4-hydroxymethylphenyl methylthiomethyl ether (20 mmol) in DMF (20 ml) at 0 °C, the mixture was stirred for 30 min, and a solution of allyl bromide (20 mmol) in DMF (20 ml) was added dropwise at 0 °C over 10 min. The mixture was stirred at ambient temperature for 2 h before the solvent was evaporated under reduced pressure. The residual material was poured into saturated aqueous NH_4Cl (100 ml) and extracted with diethyl ether (3 × 50 ml). The ether extracts were dried ($MgSO_4$) and evaporated to leave the crude product which was purified by flash chromatography on silica gel eluting with hexane–ethyl acetate 10:1; yield 60%, colourless liquid. Anal. $C_{12}H_{16}O_2S$: C, H, ^{1}H NMR: δ 2.23 (3 H, s, SCH_3), 4.00 (2 H, m, *J* 5.7, 1.5, and 1.5 Hz, $CH_2C=$), 4.45 (2 H, s, CH_2Ar), 5.13 (2 H, s, CH_2S), 5.19 [1 H, m, *J* 10.5, 1.5, and 1.5 Hz, $=CH_2$ (*trans*)], 5.29 [1 H, m, *J* 17.3, 1.5 and 1.5 Hz, CH_2 (*cis*)], 5.94 (1 H, m, *J* 17.3, 10.5 and 5.7 Hz, =CH–), 6.9–7.3 (4 H, m, Ar). ^{13}C NMR: δ 14.3 (SCH_3), 70.7 (CH_2), 71.5 (CH_2), 72.3 (CH_2), 115.7, 129.0, 131.4, 156.4 (Ar), 116.8 ($=CH_2$), 134.6 (=CH–). MS: 224 (9, *M*), 177 (1), 176 (1), 167 (1), 153 (1), 147 (3), 107 (3), 61 (100).

4-Propargyloxymethylphenyl methylthiomethyl ether (**1i**). Compound **1i** was obtained from 4-hydroxymethylphenyl methylthiomethyl ether and propargyl bromide using the procedure described for the preparation of **1h**. The crude product was purified by flash chromatography on silica gel eluting with pentane–ethyl acetate 3:1; yield 62%, colourless liquid. Anal. $C_{12}H_{14}O_2S$: C, H. ^{1}H NMR: δ 2.22 (3 H, s, SCH_3), 2.47 (1 H, t, *J* 2.4 Hz, ≡CH), 4.13 (2 H, d, *J* 2.4 Hz, ≡CCH_2), 4.53 (2 H, s, CH_2Ar), 5.12 (2 H, s, CH_2S), 6.9–7.3 (4 H, m, Ar). ^{13}C NMR: δ 14.3 (SCH_3), 56.5 (CH_2C≡), 70.8 (CH_2), 72.2 (CH_2), 74.3 (C≡CH), 79.5 (≡CH), 115.7, 129.4, 130.3, 156.6 (Ar). MS: 222 (6, *M*), 175 (1), 166 (1), 153 (1), 145 (1), 107 (1), 89 (3), 61 (100).

General procedure for the preparation of the chloromethyl ethers (**2**). A solution of sulfuryl chloride (5.0 mmol) in dichloromethane (5 ml) was added dropwise with stirring at 0 °C to a solution of the *O,S*-acetal **1** (5.0 mmol) and cyclohexene (5.25 mmol) or 4-bromostyrene (5.00 mmol) in dichloromethane (5 ml). The solution was stirred at ambient temperature under N_2 for 1 h and the solvent was evaporated to leave the crude product which was purified by distillation.

4-tert-*Butyldimethylsilyloxy-2-butynyl chloromethyl ether* (**2a**). Compound **2a** was obtained from **1a** in the presence of cyclohexene. Yield 77%, b.p. 80–88 °C/0.01 mmHg. Anal. $C_{11}H_{21}ClO_2Si$: C, H. ^{1}H NMR: δ 0.08 [6 H, s, $(CH_3)_2Si$], 0.87 [9 H, s, $(CH_3)_3C$], 4.35 (4 H, m, 2 × ≡CCH_2), 5.54 (2 H, s, CH_2Cl). ^{13}C NMR: δ −5.3 [$(CH_3)_2Si$], 18.0 [$(CH_3)_3C$], 25.6 [$(CH_3)_3C$], 51.4 (≡CCH_2), 54.3 (≡CCH_2), 79.8 (CH_2Cl), 79.9 (≡C), 85.0 (≡C). MS (CI): 251/249 (1/2, *M*+1), 213 (16), 203 (15), 185 (16), 184 (16), 183 (100), 173 (12), 169 (16), 161 (10), 159 (13), 145 (20).

4-Acetoxy-2-butynyl chloromethyl ether (**2b**): Method A. Compound **2b** was obtained from **1b** in the presence of 4-bromostyrene. Yield 57%, b.p. 62 °C/0.05 mmHg. Anal. $C_7H_9ClO_3$: C, H. ^{1}H NMR: δ 2.11 (3 H, s, CH_3), 4.43 (2 H, t, *J* 1.8 Hz, ≡CCH_2), 4.73 (2 H, t, *J* 1.8 Hz, ≡CCH_2), 5.58 (2 H, s, CH_2Cl). ^{13}C NMR: δ 20.3 (CH_3), 51.7 (≡CCH_2), 55.9 (≡CCH_2), 79.8 (≡C), 79.9 (≡C), 81.9 (CH_2Cl), 169.7 (CO), MS: 146 (1), 144 (4), 136 (4), 134 (9), 117 (10), 111 (24), 81 (100). Method B. In the reaction from **1c** cyclohexene was present; yield 82%.

cis-4-tert-*Butyldimethylsilyloxy-2-butenyl chloromethyl ether* (**2d**). Compound **2d** was obtained from **1d** in the presence of 4-bromostyrene. Yield 50%, b.p. 53–55 °C/0.01 mmHg. ^{1}H NMR: δ 0.08 [6 H, s, $(CH_3)_2Si$], 0.90 [9 H, s, $(CH_3)_3C$], 4.25–4.34 (4 H, m, 2 × CH_2C=), 5.50 (2 H, s, CH_2Cl), 5.51–5.60 (1 H, m, =CH–), 5.75–5.84 (1 H, m, =CH–). ^{13}C NMR: δ −5.3 [$(CH_3)_2Si$], 18.2 [$(CH_3)_3C$], 25.7 [$(CH_3)_3C$], 59.5 (=CCH_2), 65.0 (=CCH_2), 81.7 (CH_2Cl), 124.0 (=CH–), 134.8 (=CH–). MS (CI): 253/251 (1/4, *M*+1), 223 (4), 215 (38), 205 (10), 203 (15), 187 (10), 186 (14), 185 (100), 145 (18).

cis-*4-Acetoxy-2-butenyl chloromethyl ether* (**2e**). Compound **2e** was obtained from **1e** in the presence of 4-bromostyrene; yield 80%, b.p. 42–44 °C/0.01 mmHg. ^{1}H NMR: δ 2.00 (3 H, s, CH_3), 4.27 (2 H, d, *J* 5.4 Hz, =CCH_2), 4.59 (2 H, d, *J* 5.6 Hz, =CCH_2), 5.43 (2 H, s, CH_2Cl), 5.62–5.83 (2 H, m, 2 × =CH–). ^{13}C NMR: δ 20.5 (CH_3CO), 59.6 (=CCH_2), 64.7 (=CCH_2), 81.6 (CH_2Cl), 127.9 (=CH–), 128.3 (=CH–), 170.3 (CO).

4-Allyloxymethylphenyl chloromethyl ether (**2h**). Compound **2h** was obtained from **1h** in the presence of cyclohexene. Yield 67%, b.p. 110–112 °C/0.05 mmHg. Anal. $C_{11}H_{13}ClO_2$: C, H. ^{1}H NMR: δ 4.01 (2 H, m, *J* 5.4, 1.5 and 1.5 Hz, =CCH_2), 4.47 (2 H, s, ArCH_2), 5.20 [1 H, m, *J* 10.4, 1.5 and 1.5 Hz, =CH_2 (*trans*)], 5.30 [1 H, m, *J* 17.3, 1.5 and 1.5 Hz, =CH_2 (*cis*)], 5.85 (2 H, s, CH_2Cl), 5.94 (1 H, m, *J* 17.3, 10.4 and 5.4 Hz, =CH–), 7.0–7.4 (4 H, m, Ar). ^{13}C NMR: δ 70.8 (CH_2), 71.3 (CH_2), 77.0 (CH_2Cl), 115.9, 129.1, 133.1, 154.9 (Ar), 117.0 (=CH_2), 134.4 (=CH–). MS: 214/212 (3/7, *M*), 213 (3), 211 (5), 184 (2), 182 (8), 177 (19), 155 (72), 147 (8), 41 (100).

*5-Chloro-1-(4-styryloxy)methylpyrimidin-2(1*H*)-one* (**4**). Chloromethyl 4-styryl ether (**2f**) was prepared as a 1:1 mixture with 1-chloro-2-methylthiocyclohexane as described above from methylthiomethyl 4-styryl ether (**1f**). After the solvent had been evaporated the residue was dissolved in benzene (10 ml) and added to a solution of 5-chloro-2-tributylstannyloxypyrimidine[10] (5 mmol) in benzene (10 ml). The mixture was heated under reflux for 6 h with azeotropic removal of water, whereupon the solvent was evaporated and the residue was triturated with hexane and recrystallized from ethyl acetate; yield 63%, m.p. 167 °C. Anal. $C_{13}H_{11}ClN_2O_2$: C, H. ^{1}H NMR: δ 5.19 [1 H, dd, *J* 11.0 and 0.8 Hz, =CH_2 (*trans*)], 5.65 [1 H, dd, *J* 17.6 and 0.8 Hz, =CH_2 (*cis*)], 5.86 (2 H, s, CH_2N), 6.45 (1 H, dd, *J* 17.7 and 11.1 Hz, =CH–), 6.9–7.4 (4 H, m, Ar), 7.88 (1 H, d, *J* 3.6 Hz, H-6), 8.55 (1 H, d, *J* 3.6 Hz, H-4). ^{13}C NMR: δ 75.5 (CH_2N), 112.0 (=CH–), 113.3 (C-5), 115.5, 127.9, 133.1 (Ar), 135.6 (=CH_2), 142.0 (C-6), 153.7, 154.8 (C-2 and Ar), 166.2 (C-4). MS: 264/262 (3/10, *M*), 145 (30), 143 (100), 120 (2), 119 (2), 118 (7), 116 (24), 103 (3).

2-Allylphenyl phenylthiomethyl ether (**5g**). 2-Allylphenyl chloromethyl ether (**2g**) was prepared as a 1:1 mixture with 1-chloro-2-methylthiocyclohexane as described above from 2-allylphenyl methylthiomethyl ether (**1g**) (5.0 mmol). After the solvent had been evaporated the residue was dissolved in DMF (5 ml) and the solution was added dropwise over 5 min to a stirred solution of sodium thiophenolate (5.0 mmol) in DMF (10 ml) at 0 °C. The mixture was stirred at ambient temperature for 1 h before the solvent was distilled off under reduced pressure. The residual material

was poured onto ice–water (50 ml) and extracted with diethyl ether (3 × 30 ml). The washed and dried ($MgSO_4$) ether solution was then evaporated to leave the crude product which was purified by flash chromatography on silica gel eluting with hexane-ethyl acetate 50:1; yield 77 %, colourless liquid. ^{1}H NMR: δ 3.25 (2 H, m, *J* 6.6, 1.5 and 1.5 Hz, ArCH_2), 4.89 [1 H, m, *J* 10.8, 1.5 and1.5 Hz, $=CH_2$ (*trans*)], 4.90 [1 H, m, *J* 16.2, 1.5 and1.5 Hz, $=CH_2$ (*cis*)], 5.34 (2 H, s, OCH_2), 5.82 (1 H, m, *J* 16.2, 10.8 and 6.6 Hz, =CH–), 6.7–7.4 (9 H, m, Ar). ^{13}C NMR: δ 34.1 (ArCH_2), 72.9 (OCH_2), 113.0, 121.7, 126.88, 126.93, 128.8, 129.6, 130.1, 130.3, 135.0, 154.3 (Ar), 115.3 ($=CH_2$), 136.6 (=CH–). MS: 256 (1, *M*), 147 (7), 146 (3), 133 (2), 132 (1), 131 (3), 125 (6), 123 (100), 115 (9), 109 (4). Mol. wt., obs. 256.0918. Calc. for $C_{16}H_{16}OS$: 256.0922.

Phenylthiomethyl 4-propargyloxymethylphenyl ether (**5i**). Chloromethyl 4-propargyloxymethylphenyl ether (**2i**) was prepared as a 1:1 mixture with 1-chloro-2-methylthiocyclohexane as above from methylthiomethyl 4-propargyloxymethylphenyl ether (**1i**) (5 mmol). The subsequent reaction with sodium thiophenolate was as described above. The product was isolated by flash chromatography on silica gel eluting with hexane–ethyl acetate 5:1; yield 80 %, colouress liquid. ^{1}H NMR: δ 2.45 (1 H, t, *J* 2.4 Hz, (≡CH), 4.14 (2 H, d, *J* 2.4 Hz, ≡CCH_2), 4.54 (2 H, s, ArCH_2), 5.44 (2 H, s, CH_2S), 6.9–7.5 (9 H, m, Ar). ^{13}C NMR: δ 56.8 (≡CCH_2), 71.0 (CH_2), 73.2 (CH_2), 74.6 (*C*≡CH), 79.7 (≡CH), 116.1, 127.2, 129.0, 129.7, 130.6, 130.8, 135.1, 156.5 (Ar). MS: 284 (4, *M*), 175 (1), 129 (2), 125 (2), 123 (100), 110 (3), 109 (2). Mol. wt., obs. 284.0879. Calc. for $C_{17}H_{16}O_2S$: 284.0871.

1-Methylthiomethoxy-2-propyne (**6a**).[16]

3-(4-Chlorophenylthio)methoxy-2-propyne (**6c**). To a solution of propargyl alcohol (20 mmol) in DMF (20 ml) was added sodium hydride (80 % in paraffin; 20 mmol) at 0 °C. The mixture was stirred for 30 min before a solution of bromomethyl 4-chlorophenyl sulfide[17] (20 mmol) in DMF (20 ml) was added over 15 min, and the mixture was stirred overnight under N_2, at ambient temperature. The solution was evaporated under reduced pressure and the residual material was poured into saturated aqueous NH_4Cl (100 ml) and extracted with diethyl ether. The washed and dried ($MgSO_4$) ether solution was evaporated, and the crude product was purified by distillation; yield 77 %, b.p. 94–99 °C/0.1 mmHg. Anal. $C_{10}H_9ClOS$: C, H. ^{1}H NMR: δ 2.45 (1 H, t, *J* 2.4 Hz, HC≡), 4.36 (2 H, d, *J* 2.4 Hz, ≡CCH_2), 5.08 (2 H, s, CH_2S), 7.2–7.4 (4 H, m, Ar). ^{13}C NMR: δ 54.6 (≡CCH_2), 74.0 (CH_2S), 75.2 (≡C), 78.5 (≡C), 129.1, 131.4, 133.0, 133.8 (Ar). MS: 214/212 (6/15, *M*), 159 (22), 157 (62), 147 (20), 145 (9), 143 (20), 108 (25), 69 (100).

4-Methylthiomethoxy-2-butyn-1-ol (**7a**). To a solution of 1-methylthiomethoxy-2-propyne (43 mmol) in dry THF (20 ml) was added BuLi (1.6 M in hexane, 43 mmol) over 10 min at −40 °C and the solution was stirred for 1 h at −40 °C and allowed to reach 0 °C. Paraformaldehyde (65 mmol) was added and the mixture was stirred for 1 h at 0 °C then heated at reflux for 1 h before it was poured into saturated aqueous NH_4Cl (100 ml) and extracted with diethyl ether (3 × 50 ml). The ether extracts were dried ($MgSO_4$) and evaporated to leave the crude title product which was purified by distillation; yield 60 %, b.p. 96–98 °C/0.02 mmHg. Anal. $C_6H_{10}O_2S$: C, H. ^{1}H NMR: δ 2.15 (3 H, s, CH_3), 3.24 (1 H, br s, OH), 4.30–4.32 (4 H, m, *J* 1.2 Hz, 2 × ≡CCH_2), 4.74 (2 H, s, CH_2S). ^{13}C NMR: δ 14.0 (CH_3), 50.7 (*C*H_2C≡), 54.5 (*C*H_2C≡), 73.7 (CH_2S), 80.7 (C≡), 85.0 (C≡). MS: 116 (8), 85 (8), 73 (7), 69 (14), 68 (8), 61 (34), 52 (10), 51 (14), 41 (100).

4-(4-Chlorophenylthio)methoxy-2-butyn-1-ol (**7c**). Compound **7c** was obtained from **6c** using the procedure described for the preparation of **7a**. The crude product was purified on a silica-gel flash column eluting with hexane–ethyl acetate 3:2; yield 60 %, colourless liquid. Anal. $C_{11}H_{11}ClO_2S$: C, H. ^{1}H NMR: δ 2.5 (1 H, br s, OH), 4.70 (2 H, s, CH_2C≡), 4.80 (2 H, s, CH_2C≡), 5.47 (2 H, s, CH_2S), 7.6–7.8 (4 H, m, Ar). ^{13}C NMR: δ 50.6 (*C*H_2C≡), 54.8 (*C*H_2C≡), 73.9 (CH_2S), 80.2 (C≡), 85.2 (C≡), 128.9, 131.3, 132.8, 133.6 (Ar). MS: 244/242 (6/19, *M*), 214 (2), 212 (6), 183 (6), 181 (20), 159 (4), 157 (10), 99 (42), 69 (59), 41 (100).

4-Hydroxymethylphenyl methylthiomethyl ether (**9**). Sodium borohydride (6.3 mmol) was added to a solution of 4-formylphenyl methylthiomethyl ether (**8**)[7] (11 mmol) in 2-propanol (60 ml). The mixture was stirred for 1 h at ambient temperature before being poured onto ice–water, acidified (pH 3–4) and extracted with chloroform. The organic layer was dried ($MgSO_4$) and evaporated to leave the crude title product which was used without further purification; yield 95 %, colourless liquid. Anal. $C_9H_{12}O_2S$: C, H. ^{1}H NMR: δ 2.12 (3 H, s, SCH_3), 2.5 (1 H, br s, OH), 4.54 (2 H, s, ArCH_2), 5.12 (2 H, s, CH_2S), 6.9–7.3 (4 H, m, Ar). ^{13}C NMR: δ 14.2 (S*C*H_3), 64.4 (Ar*C*H_2), 72.3 (SCH_2), 115.8, 128.3, 134.1, 156.3 (Ar). MS: 184 (6, *M*), 167 (1), 154 (1), 153 (1), 123 (1), 111 (1), 107 (3), 61 (100).

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