A Simple, General Preparation of *S*-Alkyl and *S*-Aryl Ynethiol Ethers

Pascal Nebois, Nina Kann, and Andrew E. Greene*

Université Joseph Fourier de Grenoble, Chimie Recherche (LEDSS), Domaine Universitaire, BP 53X, 38041 Grenoble Cedex, France

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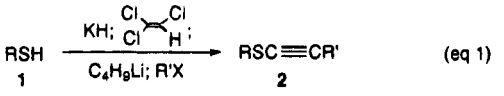
S-Alkyl and *S*-aryl ynethiol ethers are potentially interesting compounds for organic synthesis. That they have to date seen so little application can certainly be ascribed, at least in part, to the lack of simple, efficient methods for their preparation.[1] In this note we report an exceedingly facile yet versatile, high-yield synthesis of *S*-alkyl and *S*-aryl ynethiol ethers from the corresponding thiols.

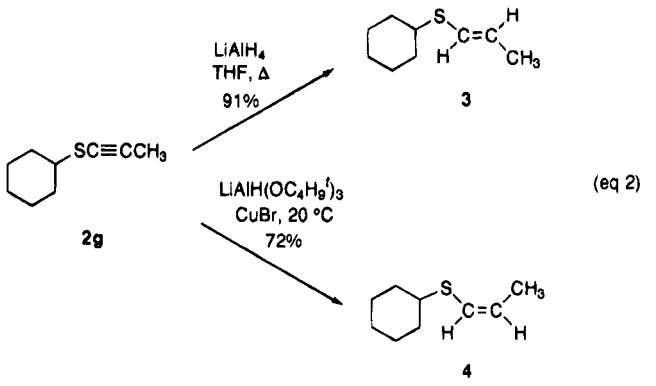
The approach effectively sequences *in one pot* the following transformations: thiol → thiolate → dichloro enethiol ether → ynethiol ether (eq 1).[2] As shown in



(eq 1)

Table 1, excellent results have been obtained with primary, secondary, and tertiary thiols, as well as with thiophenol. The intermediate acetylides can be readily protonated, silylated, and alkylated, which confers additional flexibility to the method. Significantly, it has been observed that with the inclusion of a catalytic amount of methanol to promote the *in situ* generation of dichloroacetylene,[3] an intermediate in this process, the synthesis is highly reliable irrespective of scale (entry 7). In that all of these thiol → ynethiol ether conversions are essentially spot to spot transformations, the final products can generally be isolated in analytically pure form by simple evaporative distillation.

As a consequence of this effective approach (average yield 83%), ynethiol ethers should find expanded application in synthesis. They may, for example, prove interesting as Pauson-Khand cyclization[4] substrates; also, the readily derived pure (≥95%) *E* and *Z* enethiol ethers[5] (eq 2) may be useful ketenophiles.[6]



(eq 2)

These areas, as well as other possible applications of these now readily available compounds, are currently under study.

Experimental Section

Tetrahydrofuran was distilled from sodium–benzophenone, and trichloroethylene and hexamethylphosphoric triamide were distilled from calcium hydride. Thin-layer chromatography was performed on Merck $60F_{254}$ (0.2 mm) sheets, which were visualized with molybdophosphoric acid in ethanol. Merck 70–230 silica gel 60 was employed for column chromatography. ^1H and ^{13}C NMR spectra were taken in $CDCl_3$ solution, and IR spectra were recorded neat.

General Procedure. To a well stirred suspension of 22.5 mmol of oil-free potassium hydride in 20 mL of anhydrous tetrahydrofuran under argon was added, over 10 min, 15 mmol of the thiol in 22.5 mL of tetrahydrofuran. After the hydrogen evolution was complete (15 to 120 min), the mixture was cooled to −50 °C and treated dropwise over 5 min with 1.5 mL (16.7 mmol) of trichloroethylene in 15 mL of tetrahydrofuran, followed by 40 μL of anhydrous methanol. The reaction mixture was subsequently allowed to warm to 20 °C and then stirred until gas evolution was complete (ca. 1 h). The resulting brown mixture was cooled to −70 °C and treated over 15 min with 13.2 mL (33.0 mmol) of a 2.5 M solution of *n*-butyllithium in hexanes. After 0.5 h at −70 °C, the mixture was warmed to −40 °C over 0.5 h and then treated dropwise over 10 min with 45 mmol of the electrophile in 5 mL of hexamethylphosphoric triamide (except in the case of methanol). The reaction mixture was stirred at 20 °C for 1 h, quenched slowly with 3 mL of methanol, and then poured into 60 mL of saturated aqueous ammonium chloride solution. The reaction product was extracted with 3 × 40 mL of pentane, which was washed with 4 × 30 mL of water and then dried and concentrated by rotary evaporation to yield the crude ynethiol ether, which was purified by bulb-to-bulb distillation under reduced pressure.

(Octylthio)ethyne (2a).[7] Obtained from 19 mmol of 1-octanethiol with methanol as the electrophile in 91% yield after evaporative distillation (90–110 °C, 4 torr): IR 3308 (s), 2044 (m) cm^{-1}; ^1H NMR (200 MHz) δ 2.72 (s, 1 H), 2.71 (t, J = 7.3 Hz, 2 H), 1.79–1.65 (m, 2 H), 1.49–1.11 (m, 10 H), 0.86 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz) δ 81.6, 74.7, 35.1, 31.7, 29.1 (2x), 29.0, 28.2, 22.6, 14.0; mass spectrum (EI), m/z 171 (M^+ + 1, 1.5%), 170 (M^+, 0.5%), 43 (100%). Anal. Calcd for $C_{10}H_{18}S$: C, 70.52; H, 10.65. Found: C, 70.64; H, 10.88.

1-(Octylthio)-1-propyne (2b). Obtained from 19 mmol of 1-octanethiol with iodomethane as the electrophile in 98% yield after evaporative distillation (110–130 °C, 0.7 torr): IR 2202 (vw) cm^{-1}; ^1H NMR (200 MHz) δ 2.64 (t, J = 7.3 Hz, 2 H), 1.93

* Address correspondence to Dr. Andrew E. Greene (tel: (33) 76-51-46-86; FAX: (33) 76-51-43-82; e-mail: Andrew.Greene@ujf-grenoble.fr).

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(2) Cf. Moyano, A.; Charbonnier, F.; Greene, A. E. *J. Org. Chem.* **1987**, *52*, 2919–2922. See also: Normant, J. *Bull. Soc. Chim. Fr.* **1963**, 1876–1887. Although there is normally no interest in doing so the intermediate dichloro enethiol ether can be isolated and converted with C_4H_9Li/R'X in a second operation to the ynethiol ether (e.g., thiol **1d** → dichloro enethiol ether (90%) → ynethiol ether **2g** (92%)).

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Table 1. Transformation of Thiols to Ynethiol Ethers[a]

Entry	RSH (1)	R'X	RSC≡CR' (2)	yield,[b] %
1	*n*-$C_8H_{17}SH$ (1a)	(CH_3OH)	*n*-$C_8H_{17}SC{\equiv}CH$ (2a)[c]	91
2	*n*-$C_8H_{17}SH$ (1a)	CH_3I	*n*-$C_8H_{17}SC{\equiv}CCH_3$ (2b)	98
3	$C_2H_5CH(CH_3)CH_2SH$ (1b)	C_2H_5I	$C_2H_5CH(CH_3)CH_2SC{\equiv}CC_2H_5$ (2c)	81
4	$C_2H_5CH(CH_3)CH_2SH$ (1b)	$(CH_3)_3SiCl$	$C_2H_5CH(CH_3)CH_2SC{\equiv}CSi(CH_3)_3$ (2d)	69
5	$C_2H_5CH(CH_3)SH$ (1c)	*n*-C_3H_7I	$C_2H_5CH(CH_3)SC{\equiv}CC_3H_7^n$ (2e)	81
6	$C_2H_5CH(CH_3)SH$ (1c)	*n*-$C_6H_{13}I$	$C_2H_5CH(CH_3)SC{\equiv}CC_6H_{13}^n$ (2f)	76
7	*c*-$C_6H_{11}SH$ (1d)	CH_3I	*c*-$C_6H_{11}SC{\equiv}CCH_3$ (2g)	92, 85[d]
8	*c*-$C_6H_{11}SH$ (1d)	$(CH_3)_3SiCl$	*c*-$C_6H_{11}SC{\equiv}CSi(CH_3)_3$ (2h)	87
9	$C_6H_5CH(CH_3)SH$ (1e)	C_2H_5I	$C_6H_5CH(CH_3)SC{\equiv}CC_2H_5$ (2i)	83
10	$(CH_3)_3CSH$ (1f)	CH_3I	$(CH_3)_3CSC{\equiv}CCH_3$ (2j)[e]	88
11	C_6H_5SH (1g)	(CH_3OH)	$C_6H_5SC{\equiv}CH$ (2k)[f]	72

[a]For procedure, see Experimental Section. [b]Yields are for reactions run on 10 to 30 mmol (except for entry 7) and are based on chromatographically and spectroscopically homogeneous, analytically pure material. [c]Reference 7. [d]Yields are for reactions run on 38 and 1 mmol, respectively. [e]Reference 8. [f]Reference 9.

(s, 3 H), 1.76–1.62 (m, 2 H), 1.46–1.17 (m, 10 H), 0.86 (t, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz) δ 89.2, 67.5, 35.3, 31.7, 29.2, 29.1, 29.0, 28.2, 22.6, 13.9, 4.8; mass spectrum (EI), m/z 184 (M^+, 16%), 41 (100%). Anal. Calcd for $C_{11}H_{20}S$: C, 71.67; H, 10.93. Found: C, 71.59; H, 11.13.

1-[(2-Methylbutyl)thio]-1-butyne (2c). Obtained from 15.4 mmol of 2-methyl-1-butanethiol with iodoethane as the electrophile in 81% yield after evaporative distillation (60–80 °C, 4 torr): IR 2193 (vw) cm^{-1}; ^1H NMR (200 MHz) δ 2.70 (dd, J = 12.6, 5.8 Hz, 1 H), 2.48 (dd, J = 12.6, 7.5 Hz, 1 H), 2.27 (q, J = 7.5 Hz, 2 H), 1.80–1.64 (m, 1 H), 1.59–1.39 (m, 1 H), 1.34–1.17 (m, 1 H), 1.11 (t, J = 7.4 Hz, 3 H), 0.97 (d, J = 6.6 Hz, 3 H), 0.88 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (63 MHz) δ 94.5, 68.3, 42.6, 34.5, 28.2, 18.4, 13.9, 13.7, 11.2; mass spectrum (EI), m/z 156 (M^+, 100%). Anal. Calcd for $C_9H_{16}S$: C, 69.16; H, 10.32. Found: C, 69.21; H, 10.31.

1-[(2-Methylbutyl)thio]-2-(trimethylsilyl)ethyne (2d). Obtained from 15.4 mmol of 2-methyl-1-butanethiol with chlorotrimethylsilane as the electrophile in 69% yield after evaporative distillation (90–110 °C, 13 torr): IR 2094 (s) cm^{-1}; ^1H NMR (300 MHz) δ 2.77 (dd, J = 12.4, 6.0 Hz, 1 H), 2.57 (dd, J = 12.6, 7.5 Hz, 1 H), 1.78–1.69 (m, 1 H), 1.56–1.42 (m, 1 H), 1.32–1.20 (m, 1 H), 0.99 (d, J = 6.4 Hz, 3 H), 0.89 (t, J = 7.3 Hz, 3 H), 0.15 (s, 9 H); ^{13}C NMR (75 MHz) δ 99.4, 95.7, 42.9, 34.7, 28.2, 18.4, 11.1, −0.6; mass spectrum (EI), m/z 200 (M^+, 22%), 115 (100%). Anal. Calcd for $C_{10}H_{20}SSi$: C, 59.93; H, 10.06. Found: C, 59.83; H, 10.02.

1-[(1-Methylpropyl)thio]-1-pentyne (2e). Obtained from 19.3 mmol of 2-butanethiol with 1-iodopropane as the electrophile in 81% yield after evaporative distillation (60–80 °C, 4 torr): IR 2191 (vw) cm-1; ^1H NMR (250 MHz) δ 2.80 (sextet, J = 6.8 Hz, 1 H), 2.27 (t, J = 7 Hz, 2 H), 1.74–1.45 (m, 4 H), 1.33 (d, J = 7.2 Hz, 3 H), 0.97 (t, J = 7.5 Hz, 3 H), 0.96 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (63 MHz) δ 95.2, 66.9, 45.5, 29.0, 22.2, 22.0, 20.5, 13.3, 11.5; mass spectrum (EI), m/z 156 (M^+, 100%). Anal. Calcd for $C_9H_{16}S$: C, 69.16; H, 10.32. Found: C, 69.36; H, 10.30.

1-[(1-Methylpropyl)thio]-1-octyne (2f). Obtained from 19.3 mmol of 2-butanethiol with 1-iodohexane as the electrophile in 76% yield after column chromatography (silica gel pretreated with 2.5% v/v of triethylamine) with pentane followed by evaporative distillation (90–110 °C, 0.05 torr): IR 2190 (vw) cm^{-1}; ^1H NMR (200 MHz) δ 2.80 (sextet, J = 6.7 Hz, 1 H), 2.29 (t, J = 6.8 Hz, 2 H), 1.33 (d, J = 6.7 Hz, 3 H), 1.80–1.27 (m, 10 H), 0.97 (t, J = 7.3 Hz, 3 H), 0.86 (t, J = 6.5 Hz, 3 H); ^{13}C NMR (100 MHz) δ 95.6, 66.9, 45.6, 31.3, 29.2, 28.8, 28.5, 22.5, 20.5, 20.2, 14.0, 11.6; mass spectrum (EI), m/z 198 (M^+, 23%), 41 (100%). Anal. Calcd for $C_{12}H_{22}S$: C, 72.66; H, 11.18. Found: C, 72.42; H, 11.15.

1-(Cyclohexylthio)-1-propyne (2g). Obtained from 38.4 mmol of cyclohexanethiol with 1-iodomethane as the electrophile in 92% yield after evaporative distillation (80–100 °C, 4 torr): IR 2203 (vw) cm^{-1}; ^1H NMR (200 MHz) δ 2.92–2.76 (m, 1 H), 1.96 (s, 3 H), 2.11–1.17 (m, 10 H); ^{13}C NMR (50 MHz) δ 90.9, 66.2, 46.8, 32.9, 26.0, 25.4, 5.1; mass spectrum (EI), m/z 156 (M^+, 1%), 55 (100%). Anal. Calcd for $C_9H_{14}S$: C, 70.07; H, 9.15. Found: C, 69.67; H, 9.16.

1-(Cyclohexylthio)-2-(trimethylsilyl)ethyne (2h). Obtained from 18.8 mmol of cyclohexanethiol with chlorotrimethylsilane as the electrophile in 87% yield after evaporative distillation (80–100 °C, 0.2 torr): IR 2091 (s) cm^{-1}; ^1H NMR (200 MHz) δ 2.99–2.82 (m, 1 H), 2.10–1.07 (m, 10 H), 0.15 (s, 9 H); ^{13}C NMR (50 MHz) δ 101.7, 93.7, 47.4, 32.7, 26.0, 25.4, 0.1; mass spectrum (EI), m/z 212 (M^+, 60%), 43 (100%). Anal. Calcd for $C_{11}H_{20}SSi$: C, 62.19; H, 9.49. Found: C, 62.49; H, 9.53.

1-[(1-Phenylethyl)thio]-1-butyne (2i). Obtained from 10 mmol of 1-phenyl-1-ethanethiol with 1-iodoethane as the electrophile in 83% yield after column chromatography (silica gel pretreated with 2.5% v/v of triethylamine) with pentane followed by evaporative distillation (110-130 °C, 0.3 torr): IR 2192 (vw) cm^{-1}; ^1H NMR (200 MHz) δ 7.35–7.24 (m, 5 H), 4.20 (q, J = 7 Hz, 1 H), 2.29 (q, J = 7.5 Hz, 2 H), 1.73 (d, J = 7 Hz, 3 H), 1.11 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz) δ 141.6, 128.3, 127.5, 127.2, 98.0, 67.2, 47.6, 21.0, 13.8; mass spectrum (EI), m/z 190 (M^+, 17%), 105 (100%). Anal. Calcd for $C_{12}H_{14}S$: C, 75.74; H, 7.41. Found: C, 75.53; H, 7.41.

1-[(1,1-Dimethylethyl)thio]-1-propyne (2j).[8] Obtained from 19.5 mmol of 2-methyl-2-propanethiol with iodomethane as the electrophile in 88% yield after evaporative distillation (50–70 °C, 12 torr): IR 2197 (vw) cm^{-1}; ^1H NMR (200 MHz) δ 1.98 (s, 9 H), 1.36 (s, 3 H); ^{13}C NMR (100 MHz) δ 92.4, 66.6, 46.6, 30.0, 4.9; mass spectrum (EI), m/z 128 (M^+, 93%), 57 (100%).

(Phenylthio)ethyne (2k).[9] Obtained from 15.6 mmol of thiophenol with methanol as the electrophile in 72% yield after evaporative distillation (40–60 °C, 0.1 torr): IR 2047 (m) cm^{-1}; ^1H NMR (200 MHz) δ 3.24 (s, 1 H), 7.48–7.19 (m, 5 H); ^{13}C NMR (75 MHz) δ 131.4, 129.2, 126.7, 126.6, 86.8, 71.0.

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