Phthalimidosulfenyl Chloride; Part 3: A Novel and Efficient Synthesis of Alkynyl Vinyl Sulfides

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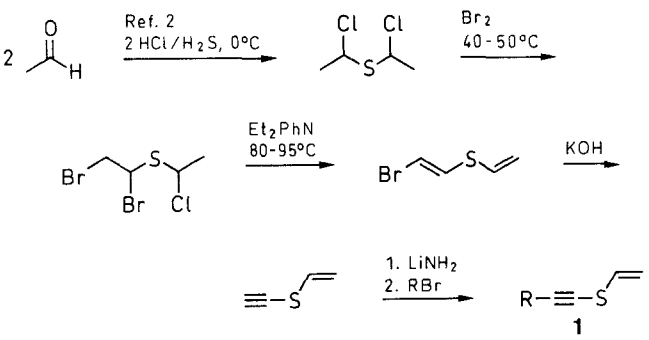
Alkynyl vinyl sulfides are prepared in good yield by reaction of lithium acetylides with the unsaturated sulfenamides **4** which in turn are easily synthesized by addition of phthalimidosulfenyl chloride to alkynes. In all cases the reaction occurs without effecting the stereochemistry of the double bond.

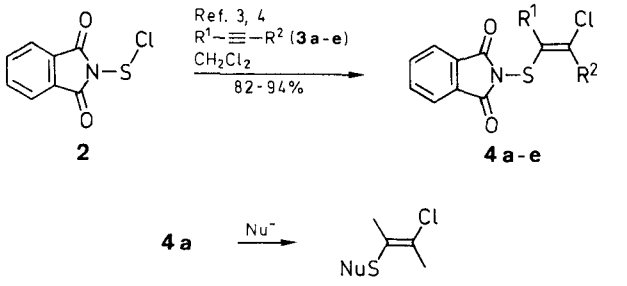
Alkynyl vinyl sulfides **1** are known compounds which have been found to have pesticide and bactericide[1] activity.

To our knowledge only one method for the synthesis of this class of compounds has been reported.[2] However, it is a multistep procedure which gives low yields of **1** and suffers from severe limitations as far as the substitution at the vinylic carbons is concerned (Scheme 1).



Scheme 1

In preliminary comunications[3,4] we reported the reaction of phthalimidosulfenyl chloride **2** with alkynes **3a–e** and the reactivity of the β-chlorovinylsulfenamide **4a** with a number of different nucleophiles which give substitution at sulfur with elimination of the phthalimido residue (Scheme 2).



3, 4	R^1	R^2	3, 4	R^1	R^2
a	Me	Me	d	*t*-Bu	H
b	Ph	Ph	e	Me	Ph
c	Me	H			

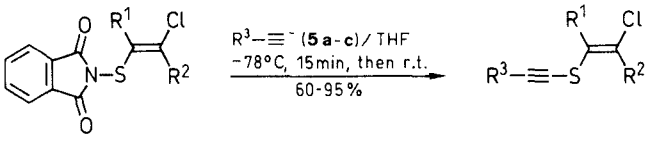
Nu = Me, Bu, *t*-Bu, Ph, $(Me_3Si)_2N$

Scheme 2

In this paper we report the use of adducts of type **4** for the synthesis of alkynyl vinyl sulfides. The addition of phthalimidosulfenyl chloride to alkynes **3** occurs with the same stereochemistry and regiochemistry observed for the reaction of other not functionalized sulfenyl chlorides.[5] The synthesis of β-chlorovinylsulfenamides **4a, 4c** and **4d** has been already described;[3,6] similarly, compounds **4b** and **4e** have been prepared.

Alkyl vinyl sulfides **6a–j** have been simply prepared by reaction of the β-chlorovinylsulfenamides **4a–e** with a appropriate lithium acetylide (Scheme 3). All reactions have been performed in dry tetrahydrofuran under nitrogen atmosphere at − 78 °C. They are complete in less than 15 minutes giving satisfactory yields of the unsaturated sulfides **6**.

Yields and physical and spectroscopic data of the products synthesized are reported in the Table. The reaction is quite general irrespective of the nature of the acetylide ion and structure of the β-chlorovinylsulfenamide **4**. A single product was obtained in each reaction so that the same stereochemistry of the sulfenamide **4** can be assigned to the alkynyl vinyl sulfides **6**.



4a-e **6a-j**

5	R^3	6	R^1	R^2	R^3	6	R^1	R^2	R^3
a	*t*-Bu	a	Me	Me	*t*-Bu	f	Ph	Ph	Bu
b	Bu	b	Ph	Ph	*t*-Bu	g	Me	Ph	Bu
c	Ph	c	*t*-Bu	H	*t*-Bu	h	Me	H	Bu
		d	Me	Ph	*t*-Bu	i	Me	Me	Ph
		e	Me	Me	Bu	j	Me	H	Ph

Scheme 3

The reactivity of **6** towards oxidation has been tested for **6e** using 1 or 2 equivalents of 3-chloroperoxybenzoic acid. As expected we obtained the sulfoxide **7** and the sulfone **8**, respectively (Scheme 4).

Vinyl and alkynyl sulfoxides and sulfones have been extensively used as dienophiles in Diels–Alder reactions or as Michael acceptors.[7,8]

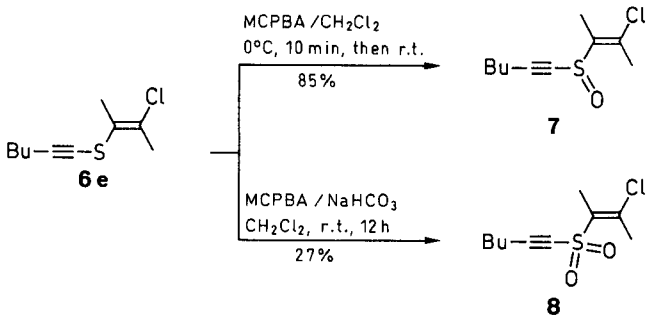
The simple access to the unsaturated sulfides **6** described here and the possibility of their transformation into sulfoxides and sulfones allow an easy entry to these classes of compounds which might be usefully employed in organic synthesis.

Table. Alkynyl 2-Chloroalk-2-enyl Sulfides **6** Prepared

Product	Yield (%)	bp[a] (°C)/mbar	Molecular Formula[b]	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
6a	80	85/0.8	$C_{10}H_{15}ClS$ (202.7)	1.24 [s, 9H, $(H_3C)_3C$], 2.20 (q, 3H, J = 1.6, CH_3), 2.23 (q, 3H, J = 1.6, CH_3)	19.65 (H_3CC=), 23.41 (=CCH_3), 28.69 [$(H_3C)_3C$], 30.58 [$(H_3C)_3\underline{C}$], 63.82 (C≡C), 105.26 (C≡C), 123.65 (C=C), 126.51 (C=C)
6b	72	oil	$C_{20}H_{19}ClS$ (326.8)	1.25 [s, 9H, $(H_3C)_3C$], 7.00–7.30 (m, 10H_{arom})	28.10 [$(\underline{C}H_3)_3C$], 30.50 [$(CH_3)_3\underline{C}$], 64.90 (C≡$\underline{C}$S), 106.00 ($\underline{C}$≡CS), 125.40 (S$\underline{C}$=C), 127.10, 128.05, 128.16, 128.40, 129.20, 129.76 (6CH_{arom}), 131.90 (SC=$\underline{C}$), 134.40, 137.95 (2C_{arom})
6c	87	90/0.9	$C_{12}H_{19}ClS$ (230.7)	1.27 [s, 9H, $(H_3C)_3C$], 1.34 [s, 9H, $C(CH_3)_3$], 6.22 (s, 1H, =CH)	28.23 [$(\underline{C}H_3)_3C$], 28.75 [$(CH_3)_3\underline{C}$], 30.30 [$(\underline{C}H_3)_3CC$=C], 36.91 [$(CH_3)_3\underline{C}C$=C], 64.86 (C≡$\underline{C}$S), 109.93 ($\underline{C}$≡CS), 110.69 (SC=$\underline{C}$), 141.64 (S$\underline{C}$=C)
6d	70	147/0.2	$C_{15}H_{17}ClS$ (264.7)	1.14 [s, 9H, $(H_3C)_3C$], 2.32 (s, 3H, CH_3), 7.26 (brs, 5H_{arom})	20.46 (CH_3C=), 28.82 [$(\underline{C}H_3)_3C$], 30.65 [$(CH_3)_3\underline{C}$], 63.98 (C≡$\underline{C}$S), 106.06 ($\underline{C}$≡CS), 125.48 (S$\underline{C}$=C), 126.97 (SC=$\underline{C}$), 128.21, 128.81, 129.07, 137.80 (4C_{arom})
6e	92	80/0.05	$C_{10}H_{15}ClS$ (202.7)	0.91 [t, 3H, J = 7.1, $\underline{C}H_3(CH_2)_3$], 1.30–1.60 (m, 4H, $CH_3\underline{C}H_2\underline{C}H_2CH_2$), 2.21 (q, 3H, J = 1.5, CH_3), 2.25 (q, 3H, J = 1.5, CH_3), 2.34 [t, 2H, J = 6.9, $H_3C(CH_2)_2\underline{C}H_2$]	13.53 [$\underline{C}H_3(CH_2)_3$], 19.79 (CH_3), 20.12 [$CH_3\underline{C}H_2(CH_2)_2$], 21.93 ($CH_3CH_2\underline{C}H_2$), 23.65 ($CH_3$), 30.60 ($CH_2\underline{C}H_2\underline{C}H_2$), 65.00 (C≡$\underline{C}$S), 97.35 ($\underline{C}$≡CS), 123.42 (S$\underline{C}$=C), 126.92 (SC=$\underline{C}$)
6f	65	180/0.4	$C_{20}H_{19}ClS$ (326.8)	0.81 [t, 3H, J = 7.0, $\underline{H}_3C(CH_2)_3$], 1.10–1.30 (m, 4H, $CH_3\underline{C}H_2\underline{C}H_2CH_2$), 2.05 [t, 2H, $CH_3(CH_2)_2\underline{C}H_2$], 7.30–7.50 (m, 10$H_{arom}$)	13.49 [$\underline{C}H_3(CH_2)_3$], 19.48 ($CH_3\underline{C}H_2CH_2$), 21.52 ($CH_2\underline{C}H_2CH_2$), 30.14 ($CH_2\underline{C}H_2\underline{C}H_2$), 65.06 (C≡$\underline{C}$S), 98.34 ($\underline{C}$≡CS), 127.51, 127.95 128.16, 128.30, 128.94, 129.10, 129.75 (6CH_{arom}), 131.91 (SC=$\underline{C}$), 137.21, 137.74 (2C_{arom})
6g	67	70/0.05	$C_{15}H_{17}ClS$ (264.7)	0.91 [t, 3H, J = 7.2, $\underline{C}H_3(CH_2)_3$], 1.30–1.60 (m, 4H, $CH_3\underline{C}H_2\underline{C}H_2CH_2$), 2.33 [t, 2H, $CH_3(CH_2)_2\underline{C}H_2$], 2.41 (s, 3H, CH_3), 7.36 (brs, 5H_{arom})	13.51 [$\underline{C}H_3(CH_2)_3$], 19.80 ($\underline{C}H_3C$=C), 20.70 [$CH_3\underline{C}H_2(CH_2)_2$], 21.90 ($CH_3CH_2\underline{C}H_2CH_2$), 30.54 [$CH_3(CH_2)_2\underline{C}H_2$], 65.06 (C≡$\underline{C}$S), 98.36 ($\underline{C}$≡CS), 125.84 (S$\underline{C}$=C), 126.93 (SC=$\underline{C}$), 128.23, 128.83, 129.08, 137.67 (4C_{arom})
6h	95	67/0.5	$C_9H_{13}ClS$ (188.6)	0.92 [t, 3H, J = 7.1, $\underline{C}H_3(CH_2)_3$], 1.30–1.61 (m, 4H, $CH_3\underline{C}H_2\underline{C}H_2CH_2$), 2.02 (d, 3H, J = 1.3, CH_3), 2.38 [t, 2H, J = 6.9, $CH_3(CH_2)_2\underline{C}H_2$], 6.18 (q, 1H, J = 1.3, CH=)	13.51 [$\underline{C}H_3(CH_2)_3$], 16.87 ($\underline{C}H_3C$=C), 19.83 [$CH_3\underline{C}H_2(CH_2)_2$], 21.92 ($CH_3CH_2\underline{C}H_2CH_2$), 30.53 [$CH_3(CH_2)_2\underline{C}H_2$], 63.61 (C≡$\underline{C}$S), 100.71 ($\underline{C}$≡CS), 112.52 ($\underline{C}$=CS), 129.99 (C=$\underline{C}$S)
6i	70	140/0.1	$C_{12}H_{11}ClS$ (222.7)	2.32 (brs, 6H, 2CH_3), 7.20–7.50 (m, 5H_{arom})	20.39 (CH_3), 23.83 (CH_3), 75.87 (C≡$\underline{C}$S), 95.54 ($\underline{C}$≡CS), 122.86, 128.21, 128.33, 128.46, 131.48 ($\underline{C}$=CS, C=$\underline{C}$S, 4C_{arom})
6j	60	90/0.05	$C_{11}H_9ClS$ (208.6)	2.12 (d, 3H, J = 1.3, CH_3), 6.31 (q, 1H, J = 1.3, CH), 7.30–7.50 (m, 5H_{arom})	17.19 (CH_3), 74.25 (C=$\underline{C}$S), 98.30 (C=$\underline{C}$S), 114.09 (SC=$\underline{C}$), 122.47 (S$\underline{C}$=C), 128.38, 128.81, 129.53, 131.59 (4C_{arom})

[a] KR distillation; uncorrected values

[b] Satisfactory microanalyses obtained: C ±0.35, H ±0.36. **6h**: C +1.02, H +1.0



Scheme 4

This new method for the synthesis of the alkynyl vinyl sulfides **6** is certainly a valid alternative to the previously known method[2] and represents a further aspect of the versatility of thiophthalimido derivatives as precursors of not easy accessible organic sulfur compounds.

All reagents were of commercial quality from freshly opened containers. BuLi (1.6 mol/L in hexane) was purchased from Aldrich. CH_2Cl_2 was washed with H_2O, dried over $CaCl_2$ and freshly distilled from $CaCl_2$; THF was freshly distilled once from Na and twice from $LiAlH_4$. Analytical TLC plates (silica gel 60 F_{254}) and silica gel 60 (70–400 mesh) were purchased from Aldrich. All melting points (Büchi 510) are uncorrected. In the case of Kugelrohr distillations (Büchi GKR 50) the oven temperature is given. Microanalysis were obtained using an Elementary Analyser 245 C Perkin-Elmer. GC/MS spectra were recorded on a Hewlett-Packard 5790 (OV1 capillary column; 30 m)/HP 5970 A instrument. IR spectra were obtained using a Perkin-Elmer Infrared 881 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were measured on a Varian Gemini 200 (200 and 50 MHz), a Varian VXR (300 and 75 MHz) or a Bruker AMX (600 MHz) spectrometer.

Alkynyl Vinyl Sulfides 6a–j; General Procedure:

To a solution of 1-alkyne **5** (1.0 mmol **5a,c**, 2.0 mmol **5b,d–j**) in dry THF (2 mL) at −78 °C under N_2 atmosphere, BuLi (1.6 mol/L in hexane, 1.0 equiv) was added dropwise via a syringe. After 5 min at −78 °C the mixture was warmed up to r.t. and kept at this temperature for 20 min. The mixture was cooled again at −78 °C

and a solution of **4a–e** (1 equiv) in dry THF (3 mL) was slowly added via a syringe. TLC analysis performed after 15 min showed the complete disappearance of **4**. The mixture was then warmed to r.t. and sat. aq NH_4Cl (20 mL) and Et_2O (20 mL) were added. The organic layer was separated, washed with brine (3 × 30 mL) and dried (Na_2SO_4).

The crude product obtained after evaporation of the solvent was diluted with pentane (30 mL) and the solid phthalimide precipitated was filtered off. Evaporation of the solvent, column chromatography (silica gel, eluant petroleum ether for **a–c, h–j** petroleum ether/Et_2O, 3:1, for **d–g**) and Kugelrohr distillation gave the sulfides **6a–j** (Table 1).

[(*E*)-(1,2-Dimethyl-2-chlorovinyl)] (1-Hexynyl) Sulfoxide (7):
To a solution of sulfide **6e** (100 mg, 0.49 mmol) in dry CH_2Cl_2 (1 mL) at 0 °C MCPBA (55%, 156 mg, 0.49 mmol) was added under stirring. After 10 min the mixture was allowed to reach r.t. Pentane (30 mL) was added, the white precipitate was filtered off and the organic layer washed with a solution of $Na_2S_2O_3$ (2 × 20 mL), NaOH 10% (5 × 20 mL), H_2O (until pH 7) and dried (Na_2SO_4). Evaporation of the solvent and chromatography (preparative TLC, eluant petroleum ether/Et_2O, 2:1) of the residue gave sulfoxide **7** as a pale yellow oil (92 mg, 85% yield).

$C_{10}H_{15}ClOS$	calc.	C 54.91	H 6.91
(218.5)	found	55.17	7.00

MS: *m/z* (%) = 119 (7); 107 (23); 91 (26); 71 (26); 53 (100); 41 (52).

^{1}H NMR ($CDCl_3$/TMS): δ = 2.34–2.46 (m, 5H), 2.20–2.24 (m, 3H), 1.30–1.64 (m, 4H), 0.89 (t, 3H, J = 7.02 Hz, CH_3).

^{13}C NMR ($CDCl_3$/TMS): δ = 138.32 (C=C), 137.78 (C=C), 104.73 (CSC), 76.01 (CSC), 29.43 [$CH_3(CH_2)_2CH_2$], 23.17 (H_3C=C), 21.80 ($CH_3CH_2CH_2CH_2$), 19.26 [$CH_3CH_2(CH_2)_2$], 13.34 (=CCH_3), 11.65 [$CH_3(CH_2)_3$].

[(*E*)-(1,2-Dimethyl-2-chlorovinyl)] (1-Hexynyl) Sulfone (8)
To a solution of sulfide **6e** (60 mg, 0.30 mmol) in dry CH_2Cl_2 (2 mL) at r.t., MCPBA (55%, 193 mg, 0.61 mmol) and $NaHCO_3$ (53 mg, 0.61 mmol) were added and the resulting mixture was stirred overnight (12 h). After this time TLC analysis showed the complete disappearance of **6e** and Me_2S (90 mL, 1.2 mmol) was added to eliminate the excess of MCPBA. Evaporation of the solvent gave a residue which was purified without any further manipulation by column chromatography (silica gel, petroleum ether/EtOAc, 5:1, as eluant). The sulfone **8** (19 mg, 27% yield) was obtained as an oil.

$C_{10}H_{15}ClO_2S$	calc.	C 51.28	H 6.41
(234.5)	found	51.61	6.52

MS: *m/z* (%) = 192 (M^+ – 42, 20.1), 129 (98.0), 91 (97.0), 53 (100).

IR (film): ν = 2860 (m); 2200 (w), 1340 (m), 1220 cm^{-1} (s).

^{1}H NMR ($CDCL_3$/TMS): δ = 2.66 (q, 3H, J = 1.6 Hz, H_3CC=C), 2.40 (t, 2H, J = 7 Hz, CH_2CS), 2.20 (q, 3H, J = 1.6 Hz, C=CCH_3), 1.30–1.60 (m, 4H, $CH_3CH_2CH_2CH_2$), 0.90 [t, 3H, J = 7.2 Hz, $CH_3(CH_2)_3$].

^{13}C NMR ($CDCl_3$/TMS): δ = 146.9 (C=C), 135.5 (C=C), 97.0 (CSC), 53.4 (CSC), 29.0, 24.7 (H_3CC=C + C=CCH_3), 22.0, 18.6, 17.3 ($CH_3CH_2CH_2CH_2$), 13.4 [$CH_3(CH_2)_3$].

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