182. A Convenient Synthesis of Vinyl Sulfides

by **Alan R. Katritzky***, **Amir S. Afridi**, and **Wojciech Kuzmierkiewicz**

Department of Chemistry and Center for Heterocyclic Compounds, University of Florida,
Gainesville, Florida 32611-2046, USA

(24.VI.91)

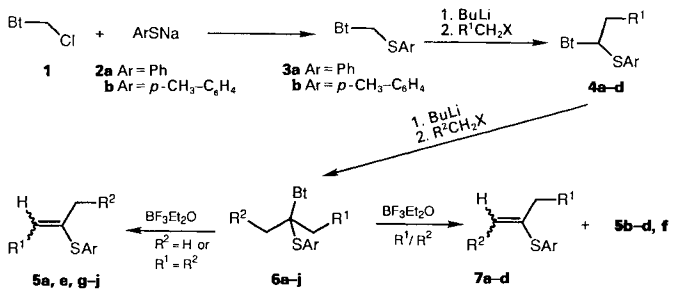
tert-Alkyl sulfides, with an α-(1*H*-benzotriazol-1-yl) group **6** and **13**, are readily prepared from *N*-[(arylthio)methyl]-1*H*-benzotriazoles **3** and *N*-(**11**), respectively, by reaction with BuLi and then with the appropriate electrophile. The *tert*-alkyl sulfides **6** and **13** are smoothly converted by $BF_3 \cdot OEt_2$ into vinyl sulfides **5**, **7** or **12**, respectively, in satisfactory yields.

Introduction. – Vinyl sulfides are useful synthetic intermediates [1]. Routes to molecules having C=C–S structural units are thus of considerable interest, and several have been described: *i*) Vinyl sulfides have been prepared by the direct treatment of cyclic ketones with thiols in the presence of strong acids (P_2O_5, TsOH, $AlCl_3$) [2–5]; however, acyclic ketones give poor yields. *ii*) The addition of thiols to acetylenes in the presence of a base [6–9]. *iii*) The *Wittig* reaction of suitable phosphoranes with carbonyl compounds [10], as well as the related phosponate olefins synthesis can lead to vinyl sulfides [11]. Thus, diethyl(methylthio)methyl phosphonate is alkylated by successive treatments with BuLi and an alkyl iodide to give the corresponding 1-(methylthio)alkyl-phosphonate esters. Their lithio derivatives react with aldehydes or ketones to form α-alkoxy-phosphonate adducts, which decompose upon heating at 50° (in THF) to form substituted methyl vinyl sulfides. Vinyl sulfides are accessible also through the reaction of (alkylidene)triphenylphosphoranes with thiolesters [12]. *iv*) Pyrolysis of thioacetals is a well-established route to vinyl sulfides [13]. An alternative procedure involves the conversion of dithioketals by using the Et_2Zn/CH_2I_2 reagent [5] [14].

Recently, we have reported [15] that *tert*-alkyl sulfides can be readily prepared by displacement of 1*H*-benzotriazole from α-benzotriazole sulfides with *Grignard* reagents. In the present paper, we report a new synthetic route to vinyl sulfides of the type Ar–S–C=C by the elimination of 1*H*-benzotriazole from *tert*-alkyl sulfides.

Results and Discussion. – *Preparation of* N-*[α-(Arylthio)alkyl]-1*H*-benzotriazoles* **6a–j** *and* **13a–c**. Using the methodology previously developed in our laboratories, *tert*-alkyl sulfides of type **6** were prepared in good yield from 1-[(phenylthio)methyl]-1*H*-benzotriazole (**3a**) [16] or 1-{[(4-methylphenyl)thio]methyl}-1*H*-benzotriazole (**3b**). The benzotriazoles **3a** and **3b** are readily available from 1-(chloromethyl)-1*H*-benzotriazole (**1**) and the appropriate thiophenol **2a, b**. Compounds **3a** and **3b** formed anions with BuLi at −78° (*Scheme 1*) which, with $PhCH_2Br$ and 4-methylbenzyl chloride, gave the expected alkylated products **4a–d** in 83–89% yield (*Table 1*). Treatment of *sec*-alkyl sulfides **4a–d** with more BuLi readily afforded the α-lithio derivatives, which reacted with MeI, 1-iodoethane, 1-iodobutane, 1-bromoheptane, benzyl chloride, and 4-methylbenzyl bromide to provide the corresponding *tert*-alkyl sulfides **6a–j** with an α-benzotriazolyl

Scheme 1



4	Ar	R^1
a	Ph	Ph
b	Ph	p-CH_3–C_6H_4
c	p-CH_3–C_6H_4	Ph
d	p-CH_3–C_6H_4	p-CH_3–C_6H_4

6	Ar	R^1	R^2
a	Ph	Ph	H
b	Ph	Ph	Me
c	Ph	Ph	Pr
d	Ph	Ph	C_6H_{13}
e	Ph	Ph	Ph
f	Ph	Ph	p-CH_3–C_6H_4
g	Ph	p-CH_3–C_6H_4	p-CH_3–C_6H_4
h	p-CH_3–C_6H_4	Ph	H
i	p-CH_3–C_6H_4	Ph	Ph
j	p-CH_3–C_6H_4	p-CH_3–C_6H_4	p-CH_3–C_6H_4

5,7	Ar	R^1	R^2
5a	Ph	Ph	H
5b	Ph	Ph	Me
5c	Ph	Ph	Pr
5d	Ph	Ph	C_6H_{13}
5e	Ph	Ph	Ph
5f	Ph	Ph	p-CH_3–C_6H_4
5g	Ph	p-CH_3–C_6H_4	p-CH_3–C_6H_4

5,7	Ar	R^1	R^2
5h	p-CH_3–C_6H_4	Ph	H
5i	p-CH_3–C_6H_4	Ph	Ph
5j	p-CH_3–C_6H_4	p-CH_3–C_6H_4	p-CH_3–C_6H_4
7a	Ph	Ph	CH_3
7b	Ph	Ph	C_3H_7
7c	Ph	Ph	C_6H_{13}
7d	Ph	Ph	p-CH_3–C_6H_4

Table 1. *Preparation of the Sulfides* **3**, **4**, **6**, **11**, *and* **13**

Compound (Formula)	Electrophile	Yield [%]	M.p. [°C][a])	Solvent[b])
3b ($C_{14}H_{13}N_3S$)	–	80	101–103	EtOH
4a ($C_{20}H_{17}N_3S$)	$PhCH_2Br$	79	108–110[c])	MeOH
b ($C_{21}H_{19}N_3S$)	p-$CH_3C_6H_4CH_2Cl$	74	98–100	MeOH[d])
c ($C_{21}H_{19}N_3S$)	$PhCH_2Br$	81	60–62	E-PE
6a ($C_{21}H_{19}N_3S$)	MeI	88	100–102	MeOH
b ($C_{22}H_{21}N_3S$)	EtI	70	96–98	MeOH
c ($C_{24}H_{25}N_3S$)	BuI	86	110–112	MeOH
d ($C_{27}H_{31}N_3S$)	$C_7H_{15}Br$	86	83–85	MeOH
e ($C_{24}H_{19}N_3S$)	$PhCH_2Br$	83	138–140[e])	MeOH
f ($C_{28}H_{25}N_3S$)	p-$CH_3C_6H_4CH_2Cl$	90	136–138	MeOH
g ($C_{28}H_{27}N_3S$)	p-$CH_3C_6H_4CH_2Cl$	80	111–113	MeOH
h ($C_{22}H_{21}N_3S$)	MeI	81	60–62	MeOH
i ($C_{28}H_{25}N_3S$)	$PhCH_2Br$	90	55–57	E-PE
j ($C_{30}H_{29}N_3S$)	p-$CH_3C_6H_4CH_2Cl$	82	65–67	E-PE[c])
11 ($C_{19}H_{14}N_3S$)	–	35[f])	81–82	E
13a ($C_{21}H_{18}N_3S$)	EtI	75	126–128	MeOH
b ($C_{23}H_{23}N_3S$)	BuI	80	127–129	MeOH
c ($C_{26}H_{21}N_3S$)	$PhCH_2Br$	95	128–130	EtOH

[a]) All compounds gave satisfactory elemental analyses.

[b]) E: Et_2O, PE: petroleum ether.

[c]) [16]: m.p. 103–105°.

[d]) Initially purified by column chromatography (hexane/$CHCl_3$ 2:1).

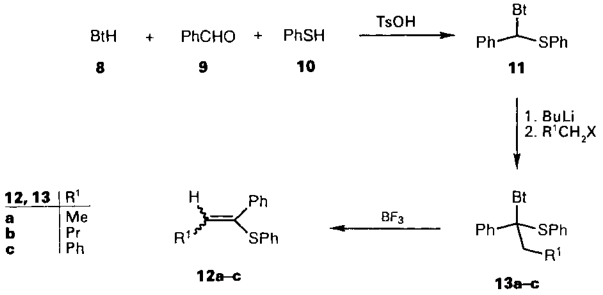
[e]) [16]: m.p. 140–142°.

[f]) The yield was calculated only for the 1*H* isomer.

group in good yields. Products **6a–j** were purified by recrystallization or column chromatography followed by recrystallization (*Table 1*).

In an alternative approach, condensation of benzotriazole (**8**), benzaldehyde (**9**), and benzenethiol (**10**) in the presence of catalytic TsOH in refluxing toluene with azeotropic removal of H_2O, formed α-(benzotriazolyl)alkyl sulfide **11** as the 1*H* isomer contaminated with a trace of the 2*H* isomer. The 1*H* isomer was easily separated from the mixture by recrystallization from Et_2O. The sulfide **11** was lithiated by BuLi at −78°, and the carbanion formed trapped with electrophiles to give *tert*-alkyl sulfides **13** (*Table 1* and *Scheme 2*).

Scheme 2



Synthesis of Vinyl Sulfides **5a–j**, **7a–d**, *and* **12a–c**. The *tert*-alkyl sulfides with an α-(1*H*-benzotriazol-1-yl) group, **6a–j** and **13a–c**, were smoothly transformed into the corresponding vinyl sulfides on stirring in dry THF in the presence of an equivalent amount of $BF_3 \cdot OEt_2$ at 20° for 4 to 8 h. The vinyl sulfides were isolated in good yields (*Table 2*). In the cases of **6c**, **d** and **6f**, mixtures of two isomeric vinyl sulfides **5** and **7** were formed due to the presence of two different active α-H-atoms (*Scheme 1* and *Table 2*).

Table 2. *Preparation of Vinyl Sulfides* **5**, **7**, *and* **12**

Compound[a])	Substrat	Yield [%]	M.p [°C][b])
5a	**6a**	60	oil[c])
b, 7a	**6b**	75	oil
c, 7b[d])	**6c**	62	oil
d, 7c	**6d**	70	oil
e	**6e**	85	60–62
f, 7d	**6f**	83	54–56
g	**6g**	80	79–81
h	**6h**	52	oil
i	**6j**	91	71–73
j	**6j**	90	82–84
12a	**13a**	92	42–43[e])
b	**13b**	71	oil
c	**13c**	71	63–64[f])

[a]) Vinyl sulfides **5** and **7** were obtained as a mixture of (*Z*)- and (*E*)-isomers.
[b]) All compounds gave satisfactory elemental analyses.
[c]) B.p. 137–140°; [17]: b.p. 138–140°.
[d]) From compounds **6b–d** and **6f** mixtures of two types of vinyl sulfides **5** and **7** were obtained.
[e]) [17]: m.p. 42–43°.
[f]) [17]: m.p. 63–64°.

When $R^2 = H$ or $R^1 = R^2$, precursor **6** gave only a mixture of (*Z*)- and (*E*)-isomers of **5**. *tert*-Alkyl sulfides **13** gave vinyl sulfides **12** in good yield as (*Z*/*E*)-mixtures.

Compound **6f** was also converted into vinyl sulfide **5h** upon reaction with PhMgBr. After 24-h treatment of **6f** with NaH in boiling THF or toluene, *ca.* 50% of the starting material was recovered. HCl was also used for the transformation of **6** into vinyl sulfides. However, yields were lower than the BF_3 reactions due to the partial hydrolysis of **6** to the ketones.

Thus, the elimination of 1*H*-benzotriazole from *tert*-alkyl sulfides with an α-benzotriazolyl group in the presence of $BF_3 \cdot OEt_2$ provides a convenient route to the synthesis of a variety of vinyl sulfides in good-to-excellent yields.

The most appropriate method for the preparation of vinyl sulfides of the type described in this paper, was the *Emmons-Horner* phosphonate reaction [11], described in the *Introduction*. This also involves a three-step sequence with yields (*ca.* 50%) which are comparable with our method in several instances, but in some cases (acetophenone, cyclopentanone) only traces (up to 10%) of the products were formed.

^1H- and ^{13}C-NMR Spectra. The structure of all the compounds were determined on the basis of their ^1H- and ^{13}C-NMR spectra. It is interesting to note that in the ^1H spectra of *sec*-alkyl sulfides **4**, the two methylene protons and the N–C*H* proton connected to the asymmetric C-atom resonate as *ABX* systems. The CH_2 protons of benzylic substituents in **6** $R^1 \neq R^2$ resonate as two *doublets* with large geminal coupling constants of *ca.* 14–15 Hz. H–C(4) and H–C(7) of the 1-substituted 1*H*-benzotriazole moieties are shifted to *ca.* 7.95 and 7.60 ppm in the case of **4** and to *ca.* 8.30 and 8.10 ppm for **6**, respectively. The ^{13}C-NMR spectra revealed typical patterns for 1-substituted 1*H*-benzotriazoles.

^1H-NMR Spectra of vinyl sulfides showed two *singlets* corresponding to the (*Z*)- and (*E*)-vinylic protons (*ca.* 6.80 and 6.70 ppm), clearly assignment of configuration from this is not possible. In the cases of vinyl sulfides of types **5** and **7**, the isomeric ratios were close to 1:1, but for compounds **12** the ratios were all *ca.* 4:1. ^{13}C-NMR Spectra of vinyl sulfides also indicated (*Z*)- and (*E*)-isomer formation.

We are grateful to the USAID/AED officials Islamabad and Washington D.C. for financial support to *A. S. Afridi* and to the Education Department N.W.F.P. Pakistan for his leave.

Experimental Part

General. M.p.: determined on a hot-stage apparatus, uncorrected. ^1H- (300 MHz) and ^{13}C- (75 MHz) NMR spectra were recorded on a *Varian-VXR-300-MHz* spectrometer; $CDCl_3$ as solvent, TMS as the internal standard. THF was distilled from sodium-benzophenone prior to use. Column chromatography was performed with MCB silica gel (230–400 mesh). 1-(Chloromethyl)-1*H*-benzotriazole (**1**) [18] and 1-[(phenylthio)methyl]-1*H*-benzotriazole (**3a**) [16] were prepared by the literature method quoted.

*1-{[(4-Methylphenyl)thio]methyl}-1*H*-benzotriazole* (**3b**). To an ice-cold soln. of 4-methylbenzenethiol (12.4 g, 0.1 mol) in MeOH (200 ml) was added Na metal (2.3 g, 0.1 mol). After complete dissolution of the metal, 1-(chloromethyl)-1*H*-benzotriazole (16.7 g, 0.1 mol) was added in small portions over 10 min. The soln. was allowed to warm to r.t. and stirred 6 h. The solvent was removed under reduced pressure to give a solid which was triturated with H_2O (3 × 50 ml). The resulting solid was collected and washed with 50% $EtOH/H_2O$ (2 × 50 ml) to give **3b** (20 g) (*Table 1*).

*1-[Phenyl(phenylthio)methyl]-1*H*-benzotriazole* (**11**). A mixture of 1*H*-benzotriazole (24 g, 0.2 mol), benzaldehyde (21.2 g, 0.2 mol), benzenethiol (20.6 ml, 0.2 mol), and TsOH (0.2 g) in toluene (200 ml) was refluxed for 14 h with azeotropic removal of H_2O. The mixture was stirred with 5% NaOH (500 ml), extracted with Et_2O (3 × 50 ml), washed with H_2O (3 × 50 ml), dried ($MgSO_4$), and the solvents were removed under reduced pressure to give an oily residue which was recrystallized from Et_2O (100 ml) (*Table 1*).

α-Substituted and α,α-Disubstituted Sulfides **4a–d**, *and* **6a–j** *and* **13a–c**, *Resp. General Procedure.* To a soln. of the appropriate sulfide **3**, **4**, or **11**, (0.01 mol) in dry THF (30 ml), BuLi (0.01 mol in hexane) was added slowly *via* a syringe at −78° under N_2. The mixture was stirred for 1 h at −78°, and a soln. of the electrophile (0.01 mol) in dry THF (5 ml) was slowly added. The resulting mixture was stirred for 2 h at −78° and for 15 h at r.t. The product was quenched with aq. NH_4Cl, extracted with Et_2O (3 × 30 ml), the Et_2O layer washed with H_2O dried ($MgSO_4$), and the solvent removed. The product was purified by recrystallization (*Table 1*).

Vinyl Sulfides **5a–j**, **7a–d**, *and* **12a–c**. *General Procedure.* $BF_3 \cdot OEt_2$ (3 mmol) was added to a soln. of the appropriate *tert*-alkyl sulfide **6a–j** or **13a–c** (3 mmol) in dry THF (20 ml) and the product stirred at r.t. under N_2 for 2–5 h. The solvent was evaporated and the residue dissolved in Et_2O and washed with 10% Na_2CO_3 soln., H_2O, and dried ($MgSO_4$). The Et_2O was removed under reduced pressure and the oil purified by column chromatography (hexane) followed by recrystallization from MeOH.

REFERENCES

[1] 'Organic Compounds of Sulphur, Selenium, and Tellurium', The Chemical Society, Burlington House, London, 1970–79, Vol 1–5.

[2] D. J. Peterson, *J. Org. Chem.* **1968,** *33,* 780.

[3] F. A. Carey, A. S. Court, *J. Org. Chem.* **1972,** *37,* 939.

[4] B. M. Trost, D. E. Keeley, *J. Am. Chem. Soc.* **1976,** *98,* 248.

[5] B. M. Trost, A. C. Lavoie, *J. Am. Chem. Soc.* **1983,** *105,* 5075.

[6] R. A. Raphael, 'Acetylenic Compounds in Organic Synthesis', Academic Press, New York, 1955, pp. 43.

[7] S. V. Amosova, N. I. Ivanova, B. A. Trofimov, *Zh. Org. Khim.* **1977,** *13,* 458.

[8] R. N. Kudyakova, A. N. Volkov, *Zh. Org. Khim.* **1977,** *13,* 934.

[9] S. R. Buzilova, I. D. Sadekov, T. V. Lipovich, T. M. Filippova, L. I. Vereschagin, *Zh. Obshch. Khim.* **1977,** *47,* 1999.

[10] G. Wittig, M. Schlosser, *Chem. Ber.* **1961,** *94,* 1373.

[11] E. J. Corey, J. I. Shulman, *J. Org. Chem.* **1970,** *35,* 777.

[12] T. Kumamoto, K. Hosoi, T. Mukaiyama, *Bull. Chem. Soc. Jpn.* **1968,** *41,* 2742.

[13] A. S. Atavin, B. A. Trofimov, A. I. Mikhaleva, I. P. Vasilev, *Izv. Akad. Nauk SSSR, Ser. Khim* **1972,** 2014.

[14] A. D. Rodriquez, A. Nickon, *Tetrahedron* **1985,** *41,* 4443.

[15] A. R. Katritzky, S. Perumal, W. Kuzmierkiewicz, P. Lue, J. V. Greenhill, *Helv. Chim. Acta* **1991,** *74,* 1924.

[16] A. R. Katritzky, S. Rachwal, K. C. Caster, F. Mahni, K. W. Law, O. Rubio, *J. Chem. Soc., Perkin Trans. 1* **1987,** 781.

[17] E. Campaigne, J. R. Leal, *J. Am. Chem. Soc.* **1954,** *76,* 1272.

[18] J. H. Burckhalter, V. C. Stephens, L. A. R. Hall, *J. Am. Chem. Soc.* **1952,** *74,* 3868.