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ADDITIONS OF THIOLS TO ACETYLENIC SULFONES

H. A. SELLING*
Institute for Organic Chemistry TNO,† Utrecht, The Netherlands

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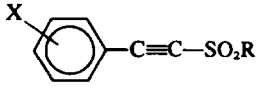
Abstract—Thiol addition to acetylenic sulfones in the 1 - methylsulfonyl - 2 - arylethyne series has been investigated. In analogy with earlier reports on thiol additions to arylsulfonyl - 1 - alkynes no violations of the *trans*-addition rule have been observed. Besides the expected nucleophilic attack on the β-C-atom, considerable α-addition occurred.

In the course of a research programme on the design of new agricultural fungicides it was found that 1-alkylsulfonyl-2-arylethynes, **1**, possess interesting fungicidal properties.[1] The presumed mode of action of these compounds,[1] viz. an irreversible reaction of thiols occurring within fungal cells,



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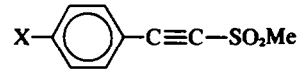
prompted us to investigate the nucleophilic addition of some model thiols. Thiol additions to acetylenic sulfones have been described earlier for alkylsulfonyl- and arylsulfonyl - 1 - alkynes.[2-5] In contrast with the addition of amines[6-8] to acetylenic sulfones, thiol addition was found to proceed in a stereospecific way, i.e. the *trans*-addition rule was followed in all instances.

In our study a set of acetylenic sulfones **2** was selected with substituents X so as to cover a wide range of Hammett σ-values.

The additions were carried out at room temperature in a 1:1 mixture of EtOH and DMF to ascertain a kinetic control of the reaction. The thiols used were methane thiol and n-butanethiol, which were added to the substrates in equimolecular quantities either as such under the catalytic influence of a piece of sodium or as their sodium salts. It was expected that only the Z-isomer, resulting from a nucleophilic attack on the β-C-atom, would be obtained. However, the base-catalysed reaction of **2a–c** with methanethiol afforded a mixture of essentially three components. Only traces of ethoxide adducts formed by reaction with the solvent could be detected.

The components were separated by column chromatography. The compound with the lowest R_f value was assigned the configuration of the "normal" thiol adduct **3**.



2a: X = H
b: X = Cl
c: X = Me
d: X = NO_2
e: X = $MeSO_2$

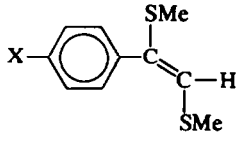
This may be envisaged by the correspondence between the chemical shifts of the olefinic protons in the NMR spectrum for compounds **3a–d** (Table 2) as compared with **5** for which the olefinic proton resonance is reported[3] to appear at 6·35 ppm.

The component with intermediate R_f value has been given structure **4**, based on the following considerations:

i. Violations of the *trans*-addition rule have not been encountered as yet for acetylenic sulfones while thiolate induced post-isomerization of the Z-isomer is not very likely under the reaction conditions.[5]

ii. The addition of butanethiol to **2d** and **2e** afforded **4e** and **4b** respectively as the sole products. This may be explained by the ability of nitro and sulfonyl groups to delocalize or stabilize an adjacent negative charge of incipient carbanion intermediates, arising after nucleophilic attack at the α-C-atom. On the contrary, the presence of a slightly deactivating group as encountered in **2c**, results in the lowest yield of compound **4** (Table 1), as compared with other substituents.

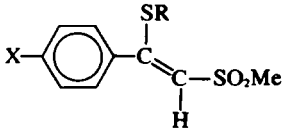
The third component in the reaction mixture which is devoid of a SO_2Me signal in the NMR spectrum has been given structure **6**.



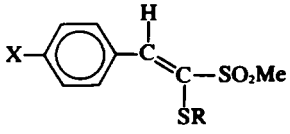
6a: X = H
b: X = Cl
c: X = Me
d: X = NO_2
e: X = $MeSO_2$

This configuration is proposed because of the close analogy of the proton signals of **6a** (Table 2) and the compound obtained by Russell and Ochrymowycz[9] from the acid-catalysed rearrangement of 1 - phenyl - 2,2 -

†Organization for Applied Scientific Research in The Netherlands.

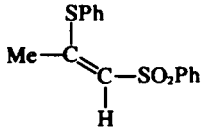


3a–c,f



4a–c,f–h

a: X = H, R = Me
b: X = Cl, R = Me
c: X = Me, R = Me
d: X = NO_2, R = Me
e: X = $MeSO_2$, R = Me
f: X = Cl, R = Bu
g: X = NO_2, R = Bu
h: X = $MeSO_2$, R = Bu



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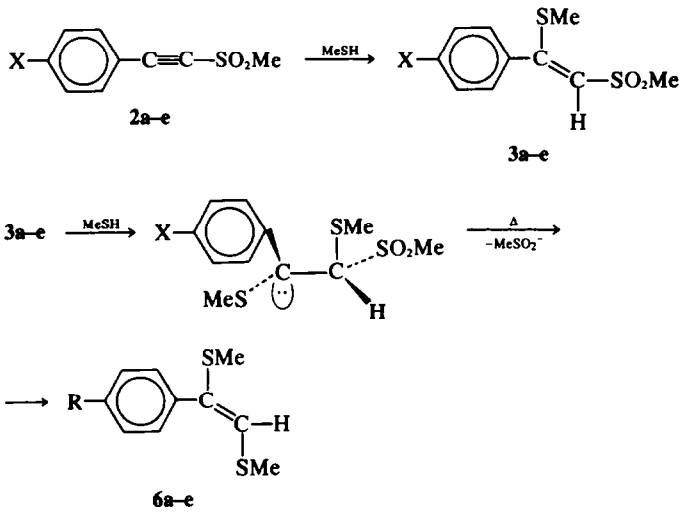


Scheme 1.

di(methylthio)ethanol [δ_{CDCl_3}: 2·02, 2·34 (MeS); 6·37 (=CH)]. This reaction is rationalized in Scheme 1.

The addition-elimination mechanism visualized in Scheme 1 is supported by the geometrical configuration of the products **6** which is predetermined by the required trans-elimination in the last step. The intermediacy of compounds **3** is demonstrated by the slow conversion of the pure compounds into **6** with sodium methanethiolate at room temperature.

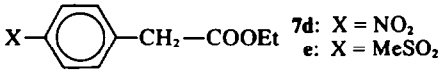
The most interesting feature of this reaction is the substitution of a methylsulfonyl group by a methylthio group. Only one account of an expulsion of alkane sulfinates from an ethylenic system under relatively mild conditions has been reported for 2-alkylsulfonyl acrylates.[10]

Thiolate addition was found to yield a mixture of products of exactly the same composition as the base-catalysed reaction which confirms the reliability of the results.

The addition of butanethiol did not proceed as far as products **6**. Probably the more bulky butylthio substituents prevent further attack of butane thiol.

The results of the thiol additions are compiled in Table 1. The composition of the crude reaction mixture has been determined by NMR analysis.

The reaction of **2d** and **2e** with methanethiol took an anomalous course. Apart from the formation of **6**, large quantities of **7** were isolated, which in the case of **7d** was proven to be identical with an authentic sample by its IR



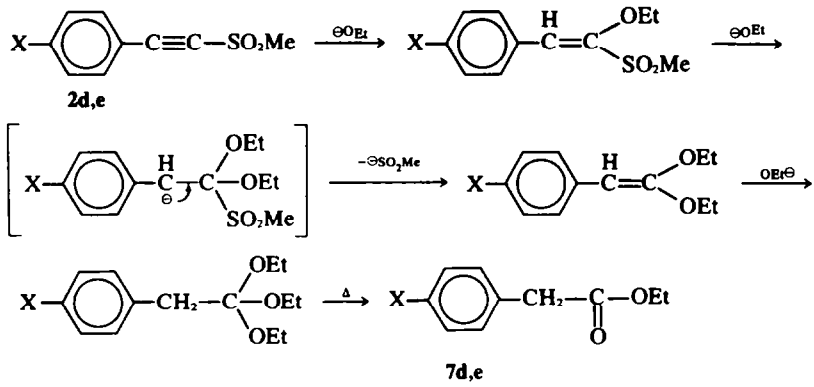
and NMR spectra. These products may have been formed by competitive addition of ethoxide according to the sequence outlined in Scheme 2.

A last indication for the correctness of the assignments of structures **3** and **4** was obtained by irradiation of the

Table 1. The reaction of RSH with $XC_6H_4C{\equiv}C\text{-}SO_2Me$

X	R	Product	Composition (%)	M.p. (recryst. from)	Microanalysis (S) calcd	Microanalysis (S) found
H	Me	**3a**	14	125–125·5° (MeOH/H_2O)	28·09	27·93
		4a	50	oil[a]	—	—
		6a	36	oil[b]	—	—
Cl	Me	**3b**	37	136–136·5° (LP/benzene)	24·40	24·56
		4b	53	105–105·5° (LP/benzene)	24·40	24·44
		6b	10	oil[b]	—	—
Me	Me	**3c**	52	107–109° (MeOH/H_2O)	26·46	26·31
		4c	44	92–96° (MeOH/H_2O)	26·46	26·29
		6c	4	oil[b]	—	—
NO_2	Me	**6d**	30	oil[b]	—	—
		7d	70	65–66° (LP)	—[c]	—[c]
$MeSO_2$	Me	**6e**	40	oil[b]	—	—
		7e	60	78–79° (LP/benzene)	—[d]	—[d]
Cl	Bu	**3f**	40	90–92° (MeOH/H_2O)	21·04	20·86
		4f	60	56–57° (MeOH/H_2O)	21·04	20·95
NO_2	Bu	**4g**	100	59–60° (MeOH)	20·33	20·31
$MeSO_2$	Bu	**4h**	100	125–125·5° (MeOH)	27·60	27·28

[a] Still contaminated with **3a**.
[b] Not completely pure.
[c] C,H-analysis: calcd 57·40, 5·30; found 57·71, 5·44.
[d] C,H-analysis: calcd 54·52, 5·82; found 54·02, 6·05.

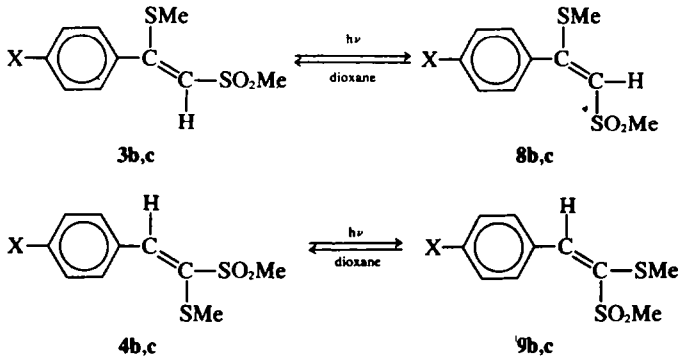


Scheme 2.

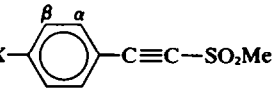
pure compounds in dioxane with a low-pressure mercury arc lamp (Vycor filter). In both cases an equilibrium mixture of stereoisomers was obtained in which the new-formed compounds were different from each of the starting compounds. This proves that **3** and **4** cannot be stereoisomers (Scheme 3).

Compounds **8** and **9** could be separated and purified by column chromatography and preparative TLC successively. NMR data of all products are summarized in Table 2.

As a conclusion we may state that thiolate addition to 1 - methylsulfonyl - 2 - arylethynes, although not giving



Scheme 3.

Table 2. NMR-data[a] of RSH adducts to 

Compound			R		$MeSO_2$	X	aryl α	aryl β	=CH	CH_2CO	COOEt	
3a X = H	R = Me	—	—	2·00	3·17		7·2–7·5 m		6·34	—	—	—
b Cl	Me	—	—	2·02	3·18	—	7·30	7·40	6·35	—	—	—
c Me	Me	—	—	2·00	3·16	2·37	7·21	7·21	6·33	—	—	—
f Cl	Bu	0·80	1·36 m	2·42	3·10	—	7·40	7·40	6·40	—	—	—[b]
4a X = H	R = Me	—	—	2·40	3·06	7·2–7·5 m; 7·8–8·0 m			8·02	—	—	—
b Cl	Me	—	—	2·45	3·10	—	7·88	7·40	8·00	—	—	—
c Me	Me	—	—	2·43	3·07	2·38	7·85	7·22	8·01	—	—	—
f Cl	Bu	0·84	1·44 m	2·96	3·03	—	7·92	7·36	7·98	—	—	—[b]
g NO_2	Bu	0·80	1·43 m	2·98	3·12	—	8·06	8·25	8·12	—	—	—
h $MeSO_2$	Bu	0·82	1·42 m	2·99	3·14	3·08	8·00	8·07	8·14	—	—	—
6a X = H	R = Me	—	2·04	2·38	—		7·2–7·5 m		6·41	—	—	—
b Cl	Me	—	2·02	2·37	—	—	7·34	7·23	6·40	—	—	—
c Me	Me	—	2·05	2·39	—	2·33	7·33	7·13	6·36	—	—	—
d NO_2	Me	—	2·38	2·42	—	—	7·68	8·14	6·60	—	—	—
e $MeSO_2$	Me	—	2·06	2·42	—	3·03	7·64	7·86	6·76	—	—	—
7d X = NO_2	R = Me	—	—	—	—	—	7·45	8·13	—	3·72	1·24	4·16
e $MeSO_2$	Me	—	—	—	—	3·02	7·47	7·88	—	3·69	1·25	4·16
8b X = Cl	R = Me	—	—	2·36	2·72	—	7·36	7·36	6·09	—	—	—
c Me	Me	—	—	2·36	2·63	2·33	7·31	7·20	6·03	—	—	—
9b X = Cl	R = Me	—	—	2·50	2·92	—	7·40	7·33	7·19	—	—	—
c Me	Me	—	—	2·50	2·90	2·34	7·39	7·17	7·31	—	—	—

[a] Values indicate chemical shifts (δ) downfield from TMS. Spectra were recorded in $CDCl_3$ unless otherwise stated.
[b] Spectrum recorded in CCl_4.

rise to products conflicting with the *trans*-addition rule, follows a course different from that in the alkyne series. The inductive effect of the phenyl group accounts for a competition between α and β addition, which may be steered so as to favour an almost esclusive α-addition by the introduction of substituents with electrondelocalizing ability. This is exemplified by BuSH addition to **2d** and **2e**. MeSH addition to the same compounds proceeds less specifically probably due to its smaller dimensions. The presence of these activating substituents makes the compounds also more prone to addition by other nucleophilic species, resulting in the formation of compounds **7d** and **7e**.

EXPERIMENTAL

General. M.ps given are uncorrected. NMR spectra were recorded in either $CDCl_3$ or CCl_4 using a Varian HA-100 spectrometer. The chemical shifts are reported in δ-values relative to TMS as an internal standard.

IR spectra were recorded as KBr pellets using a Grubb–Parsons Spectromaster or a Perkin Elmer PE 457 spectrophotometer.

Microanalyses were performed by Mr. W. J. Buis and staff of this department.

General prescription for the thiol-addition to acetylenic sulfones **2**. Methane- or butanethiol (0·02 moles) was added at 0° to a soln of **2** (0·02 moles) in 50 ml 1:1 abs EtOH/DMF by means of a hypodermic syringe. Subsequently, a catalytic amount of clean Na metal was added. Immediately a reaction set in, causing the temp. to rise to about 5°. The mixture was stirred for 30 min during which the temp. was allowed to increase to ambient values. The alcohol was distilled off *in vacuo*, and the residue poured in water (100 ml) and extracted with ether. After drying ($MgSO_4$) the solvent was removed and a sample was taken for NMR, in order to determine the product composition. The crude mixture was then separated by column chromatography and, if necessary, by successive preparative TLC, affording the products given in Table 1. Most of compounds **6** contained small amounts of persistent impurities, and were characterized solely by their NMR spectra.

General prescription for the thiolate addition to acetylenic sulfones **2**. Sodium methane thiolate (0·02 moles) was added at 25° portion-wise with stirring to a soln of **2** (0·02 moles) in 50 ml 1:1 abs EtOH/DMF under N_2. After working up as above the product composition was analysed by NMR. No differences with respect to the nature and the ratio of the components were found in comparison with thiol addition.

Photoisomerization of **3-b,c** *and* **4-b,c**. 100 Mg samples of the compounds (about 0·4 mmol) dissolved in 1 ml freshly distilled dioxane in 2 ml quartz tubes were irradiated at 25° with a low-pressure mercury arc lamp (Vycor filter) for 5 hr (**3b** and **4b**) and 40 hr (**3c** and **4c**) respectively. It was necessary to comply exactly with these reaction periods for optimal conversion without concomittant decomposition. In all cases equilibrium mixtures consisting of about 33% of the required stereoisomers **8a,b** and **9a,b** were obtained. The isomers were isolated free from their starting materials by repeated chromatographic separations over preparative silicagel plates. **8b**: m.p. 137·5–138·5° (MeOH); **8c**: m.p. 105–106° (LP/benzene); **9b**: oil; **9c**: oil; NMR data for the photo-isomerization products are compiled in Table 2.

IR spectra. The compounds (**3**, **4**, **8** and **9**) showed –C≡C– stretch vibrations of variable intensity in the region 1590–1610 cm^{-1} and strong asymmetrical S–O stretch vibrations of the SO_2 group in the region 1289–1306 cm^{-1}. Compounds **4** and **9** could be distinguished from their isomers **3** and **8** by a small shift of the symmetrical S–O stretch vibration to higher wavenumbers (ranges 1130–1139 and 1118–1131 cm^{-1} respectively).

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REFERENCES

[1]H. A. Selling, Dissertation, State University of Utrecht, The Netherlands (1973).
[2]L. Maioli and G. Modena, *Ricerca Sci* **29**, 1931 (1959).
[3]C. J. M. Stirling, *J. Chem. Soc.* 5856 (1964).
[4]E. N. Prilezhaeva, V. I. Laba, V. I. Snegotskii and R. I. Shekhtman, *Izv. Akad. Nauk SSSR Ser. Khim.* 1602 (1970).
[5]W. E. Truce and G. J. W. Tichenor, *J. Org. Chem.* **37**, 2391 (1972).
[6]C. J. M. Stirling, *J. Chem. Soc.* 5863 (1964).
[7]W. E. Truce and D. G. Brady, *J. Org. Chem.* **31**, 3543 (1966).
[8]W. E. Truce and L. D. Markley, *Ibid.* **35**, 3275 (1970).
[9]G. A. Russell and L. A. Ochrymowycz, *Ibid.* **35**, 764 (1970).
[10]W. E. Truce and F. E. Roberts Jr., *Ibid.* **28**, 593 (1963).