[Chem. Pharm. Bull.
18(12)2528—2534(1970)]

UDC 547.314.2.04 : 547.279.04 : 547.571.04

Studies on Acetylenic Compounds. LV.[1] Reactions of Phenyl 2-Propynyl Sulfone and Phenyl 3-Phenyl-2-propynyl Sulfone with Substituted Benzaldehydes

MASAFUMI YOSHIMOTO and YUKICHI KISHIDA

Central Research Laboratories, Sankyo Co., Ltd.[2]

(Received June 30, 1970)

Phenyl 2-propynyl sulfone (IV) and five kinds of benzaldehyde derivatives were treated with sodium hydride to give the corresponding 1:1 addition products, respectively. The structures were assigned to 1-phenylsulfonyl-4-substitutedphenyl-*trans*-3-buten-2-ones (V) based on the spectroscopic data. The confirmation of the elucidated structure was made by an alternative unambiguous synthesis which consisted of treating methyl phenyl sulfone and ethyl cinnamate with sodium hydride, affording V and 1-phenylsulfonyl-4-phenyl-3-penten-2-one (VI). When phenyl 3-phenyl-2-propynyl sulfone (VII) was treated with the five substituted benzaldehydes, were obtained similar products to V, 1:1 addition compounds of VII and benzaldehydes. These were assigned to be 1-phenylsulfonyl-3-phenyl-4-substitutedphenyl-3-buten-2-ones (VIII) by the spectroscopic data and the comparison with V. The plausible mechanism of the reaction and the physical properties of these products are presented in some detail.

In the preceding paper,[1] the authors reported the reactions of 2-butynyl phenyl sulfone with substituted benzaldehydes. Six kinds of products were isolated, and their physical properties and the mechanism of the reaction were presented in some detail.

On the other hand the reactions of the propargylic sulfonium ylids, which were prepared from dimethyl 2-propynylsulfonium bromide (Ia)[3a)] and dimethyl 3-phenyl-2-propynylsulfonium bromide (Ib),[3b)] with various benzaldehyde derivatives were extensively studied in this laboratory. The reaction products were 1,5-diphenyl-*trans*-4,5-epoxy-*trans*-1-penten-3-one (II) for Ia and 2-oxo-3,4-diphenyl-*cis*-3-butenylide (III) for Ib as indicated in Chart 1.

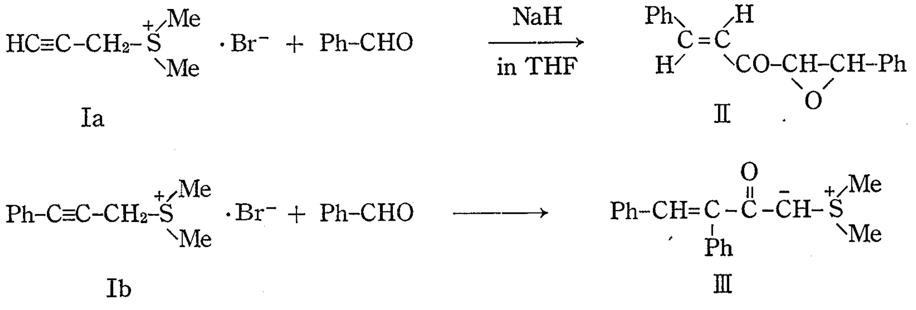


Chart 1

This paper deals with the reaction of phenyl 2-propynyl- and phenyl 3-phenyl-2-propynyl sulfone with some substituted benzaldehydes as a continuation of the chemistry of acetylenic sulfone[1].

A mixture of phenyl 2-propynyl sulfone (IV),[4] benzaldehyde and tetrahydrofuran (THF) was treated with sodium hydride and then poured into ice-water. The usual work up gave

---

[1] Part LIV: M. Yoshimoto and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 2518 (1970).

[2] Location: *2-58, 1-chome, Hiromachi, Shinagawa-ku, Tokyo.*

[3] *a)* A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 497 (1970); *b)* *Idem, ibid.*, **18**, 490 (1970).

[4] G. Pourcelot, P. Cadiot and A. Willemart, *Compt. Rend.*, **252**, 1630 (1961); G. Pourcelot and P. Cadiot, *Bull. Soc. Chim. France*, **1966**, 3025; W.E. Parham and P.L. Stright, *J. Am. Chem. Soc.*, **78**, 4783 (1956).

a sole product which was found an adduct of each one mole of IV and benzaldehyde based on the elemental analysis and mass spectrum (MS) ($M^+=286$). The depicted structure, 4-phenyl-1-phenylsulfonyl-*trans*-3-buten-2-one (Va) was presented from the following spectroscopic data. The infrared (IR) spectrum showed the existence of cinnamoyl (1686 cm^{-1} for C=O and 1606 for ph–C=C) and sulfone group (1300—1337 for ν_{asym} and 1153 for ν_{sym}), and the ultraviolet (UV) absorption maxima appeared at 219 nm and 301 (cinnamoyl group). The nuclear magnetic resonace (NMR) spectrum exhibited the absorptoin of *trans*-cinnamoyl group (7.65 ppm; 1H, doublet, $J=16.2$ Hz and 6.78; 1H, doublet, $J=16.2$) and a very low field methylene (4.40; 2H, singlet), which was assumed to attach to strong electron-attracting groups, in addition to aromatic protons (7.3—8.0; 10H).

$$\underset{\text{IV}}{Ph\text{-}SO_2\text{-}CH_2\text{-}C\equiv CH} + Ph\text{-}CHO \xrightarrow[\text{in THF}]{\text{NaH}}$$

$$\underset{\text{Va}}{Ph\text{-}SO_2\text{-}CH_2\text{-}CO\text{-}CH\text{=}CH\text{-}Ph}$$

Chart 2

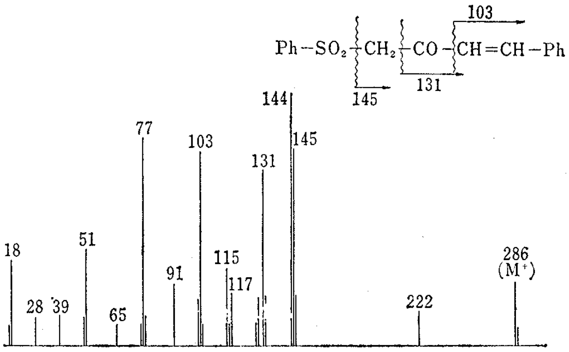


Fig. 1. Mass Spectrum of Va

The MS supported the structure as shown in Fig. 1. The confirmation of the structure was accomplished by an independent unambiguous synthesis. The condensation of ethyl cinnamate and phenylsulfonyl methyl carbanion gave two products, one of which was the ordinary Claisen condensation product[5] and identified with Va by comparison of IR and mixed melting point test. The second reaction product, 4-phenyl-1-phenylsulfonyl-3-penten-2-one (VI) was structually elucidated from the following spectroscopic data. The IR and UV were very similar to those of Va (see Experimental), but NMR exhibited a methyl group in

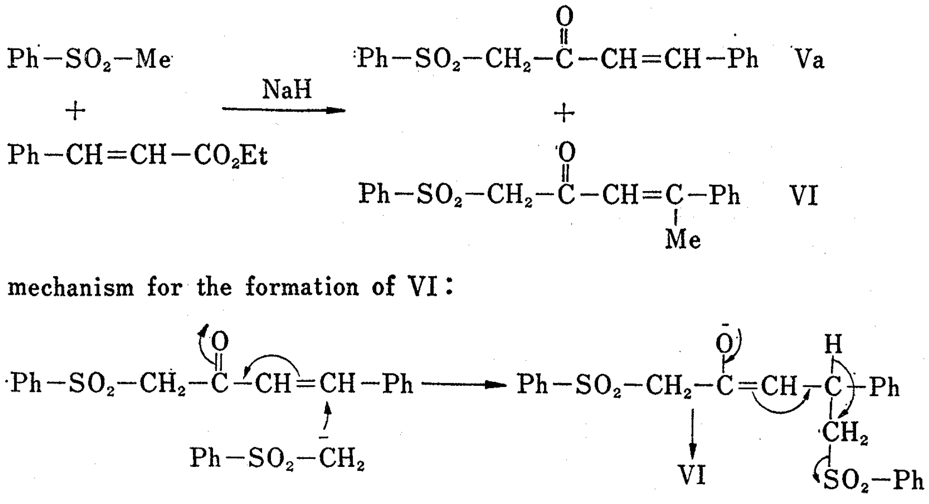


Chart 3

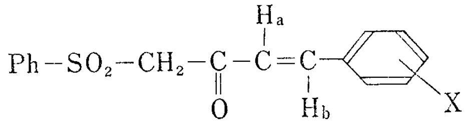
---

[5] The condensations of esters and sulfonyl carbanions are well known: W.E. Truce and R.H. Knopse, *J. Am. Chem. Soc.*, 77, 5063 (1955); H.D. Becker and G.A. Russel, *J. Org. Chem.*, **28**, 1896 (1963).

place of β-proton on α,β-unsaturated ketone system in Va. The presented structure was reasonable also from a mechanistic viewpoint[6] as shown in Chart 3.

Likewise, the reaction of phenyl 2-propynyl sulfone (IV) with various substituted benzaldehydes gave the corresponding 1:1 addition products and the results are summarized in Table I and II.

Table I. Spectral Data of V



Compound	X	UV: λ_{max}^{EtOH} nm (log ε)	IR: ν_{max}^{Nujol} cm^{-1} C=O	C=C	-SO$_2$- *asym.*	-SO$_2$- *sym.*	NMR (δppm) -CH$_2$-	H$_a$	H$_b$	J_{ab}(Hz)
a	H	301 (4.36)	1686	1606	1295—1337	1153	4.40	6.78	7.65	16.2
b	*o*-Cl	296 (4.27)	1687	1603	1295—1330	1155	4.37	6.82	7.92	16.0
c	*m*-OMe	299 (4.30)	1683	1608	1285—1325	1155	4.39	6.95	7.73	16.2
d	*p*-Me	307 (4.295)	1679	1595	1290—1330	1152	4.45	6.98	8.07	16.4
e	*p*-Br	310 (4.44)	1645	1623	1294—1320	1153	4.85	6.88	7.63	16.3

a—d: determined in CDCl$_3$, e: determined in DMSO-d$_6$

Table II. Yields, Melting Points and Elemental Analyses of V

Compound	X	Yield (%)	mp (°C)	Formula	Analysis(%) Calcd. C	H	S	Cl, Br	Found C	H	S	Cl, Br
a	H	15.7	93—94	$C_{16}H_{14}O_3S$	67.12	4.93	11.20		66.95	4.94	10.86	
b	*o*-Cl	16.6	124—125	$C_{16}H_{13}O_3SCl$	59.88	4.11	10.00	11.05	59.92	4.07	9.87	11.36
c	*m*-OMe	31.6	144—145	$C_{17}H_{16}O_4S$	64.55	5.10	10.14		64.68	5.16	10.11	
d	*p*-Me	18.0	118—119	$C_{17}H_{16}O_3S$	67.99	5.37	10.68		67.97	5.41	10.54	
e	*p*-Br	15.1	146—148	$C_{16}H_{13}O_3SBr$	52.62	3.59	8.62	21.86	52.62	3.66	8.66	21.96

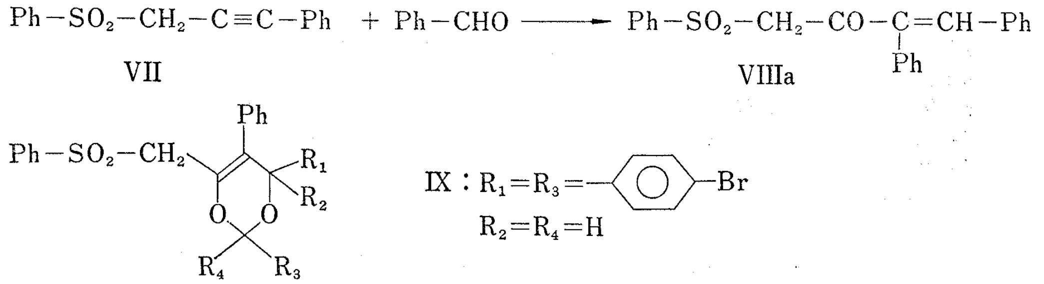
The reaction of phenyl 3-phenyl-2-propynyl sulfone (VII) with benzaldehyde gave a very similar product to Va, which again consisted of each one mole of VII and benzaldehyde. The presented structure, 3,4-diphenyl-1-phenylsulfonyl-3-buten-2-one (VIIIa) was based on the following data. The usual work up of the reaction mixture afforded colorless prisms from acetone or ethanol, which showed a conjugated ketone (1656 cm^{-1}) and a sulfone group (1296—1330 for ν_{asym} and 1155 for ν_{sym}) in the IR. The UV maximum appeared at 308 nm and the shape was closer to that of *cis*-stilben than *trans*-stilben as shown in Fig. 2,[7] and thus the two

---

[6] We presented the mechanism referring to the following literatures dealing with the methylation by dimethyl sulfoxonium methylide: V.J. Traynelis and J.V. McSweeney, *J. Org. Chem.*, **31**, 243 (1966); E.J. Corey and M. Chaycovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965). T. Durst, "Advances in Organic Chemistry: Methods and Results," Vol. 6, ed. by E.C. Taylor and H. Wynberg, Interscience Publishers, Inc., New York, N.Y., 1969, pp. 339—340.

[7] Spectra of *trans*- and *cis*-stilben: H. Suzuki, *Bull. Chem. Soc. Japan*, 33, 381 (1960); H.H. Jaffe and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley & Sons, Inc., 1962, p. 277 and p. 425.

phenyl groups of VIIIa was assumed to possess *cis* orientation. On the other hand the configuration of the double bond of the corresponding product (III)[3b)] from dimethyl 3-phenyl-2-propynylsulfonium bromide (Ib) and benzaldehyde was tentatively assigned to be *trans* in comparison with *trans*-stilben in the UV spectra. That the ethynyl hydrogen in the original system (IV), was situated in *cis* to the phenyl group in the product system (Va), also suggested the *cis* configuration of the two phenyl groups in VIIIa. The NMR exhibited a singlet at 4.45 ppm (2H) due to the methylene protons and multiplets at 7.3—8.0 (16H) assigned to three phenyl groups and the β-olefinic proton of the α,β-unsaturated system.



$$Ph{-}SO_2{-}CH_2{-}C{\equiv}C{-}Ph + Ph{-}CHO \longrightarrow Ph{-}SO_2{-}CH_2{-}CO{-}\underset{Ph}{C}{=}CH{-}Ph$$

Chart 4

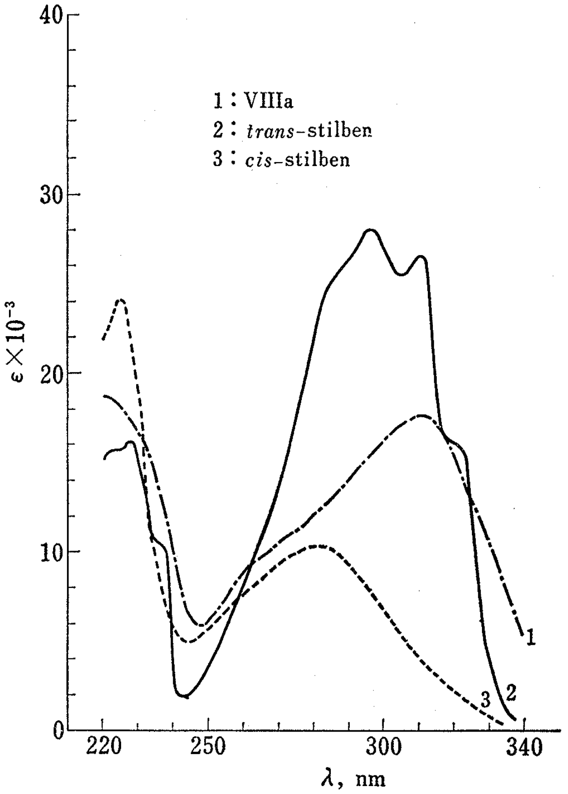


Fig. 2. UV Spectra of VIIIa, *trans*- and *cis*-Stilbens

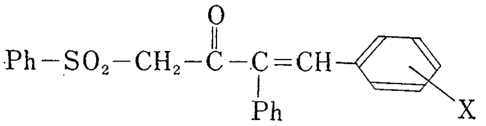
The reactions of VII with various benzaldehyde derivatives gave the corresponding 1:1 adducts (VIIIb—e), whose physical and spectroscopic properties (summarized in Table III and Table IV) were similar to those of VIIIa. However in the reaction of VII with p-bromobenzaldehyde was isolated a small amount of 1:2 adduct in addition to the 1:1 product (VIIIe). The 1:2 reaction product, $C_{29}H_{22}O_4SBr_2$, exhibited IR bands for a sulfone (ν_{asym} 1290—1330 and ν_{sym} 1168) a double bond (1670) and no carbonyl. The $\lambda_{\max}^{\mathrm{EtOH}}$ 253 nm (log ε=4.11) in the UV shifted to 313 nm, suggesting that an original 1,3-dioxin compound degradated to VIIIe and p-bromobenzaldehyde. A proposed structure, 2,4-di-p-bromophenyl-5-phenyl-6-phenylsulfonylmethyl-1,3-dioxin (IX) was based upon very close spectroscopic data to those of the 1,3-dioxin compounds described in the preceding paper.[1)] IX was found to be a mixture of *cis*- and *trans*-isomer by the NMR (see Experimental). Considering the mechanistic pathway, this 1,3-dioxin may play an important role in the formation of VIIIe.

The plausible mechanism for the formation of V and VIII is presented in Chart 5 and is very similar to that reported in the earlier paper.[1)] The firstly formed propynyl carbanion

---

8) C.J.M. Stirling, *J. Chem. Soc.*, **1964**, 5856; I. Iwai, "Mechanisms of Molecular Migrations," Vol. 2, ed. by B.S. Thyagarajan, Interscience Publishers, Inc., New York, N.Y., 1969, pp. 78—84.

Table III. Spectral Data of VIII



Compound	X	UV: λ_{max}^{EtOH} nm (log ε)	IR: ν_{max}^{Nujol} cm^{-1} C=O	C=C	−SO₂− asym.	sym.	NMR (δppm) −CH₂−
a	H	308 (4.25)	1656	1620	1296—1330	1155	4.45
b	*o*-Cl	306 (3.99)	1650	1618	1290—1330	1156	4.50
c	*m*-OMe	307 (4.17)	1658	1622	1296—1325	1156	4.38
d	*p*-Me	317 (4.30)	1655	1622	1295—1330	1154	4.37
e	*p*-Br	313 (4.28)	1662	1614	1285—1320	1147	4.37

Table IV. Yields, Melting Points and Elemental Analyses of VIII

Compound	X	Yield (%)	mp (°C)	Formula	Anlysis (%) Calcd. C	H	S	Cl, Br	Found. C	H	S	Cl, Br
a	H	72	164—165	$C_{22}H_{18}O_3S$	72.92	5.01	8.85		73.33	5.04	8.72	
b	*o*-Cl	27	142—144	$C_{22}H_{17}O_3SCl$	66.57	4.32	8.08	8.93	66.13	4.20	8.11	8.91
c	*m*-OMe	58	120—121	$C_{23}H_{20}O_4S$	70.40	5.14	8.16		70.21	5.04	8.31	
d	*p*-Me	34	171—172	$C_{23}H_{20}O_3S$	73.39	5.36	8.50		73.22	5.39	8.64	
e	*p*-Br	68	179—180	$C_{22}H_{17}O_3SBr$	59.90	3.89	7.27	18.11	57.94	4.04	7.18	17.80

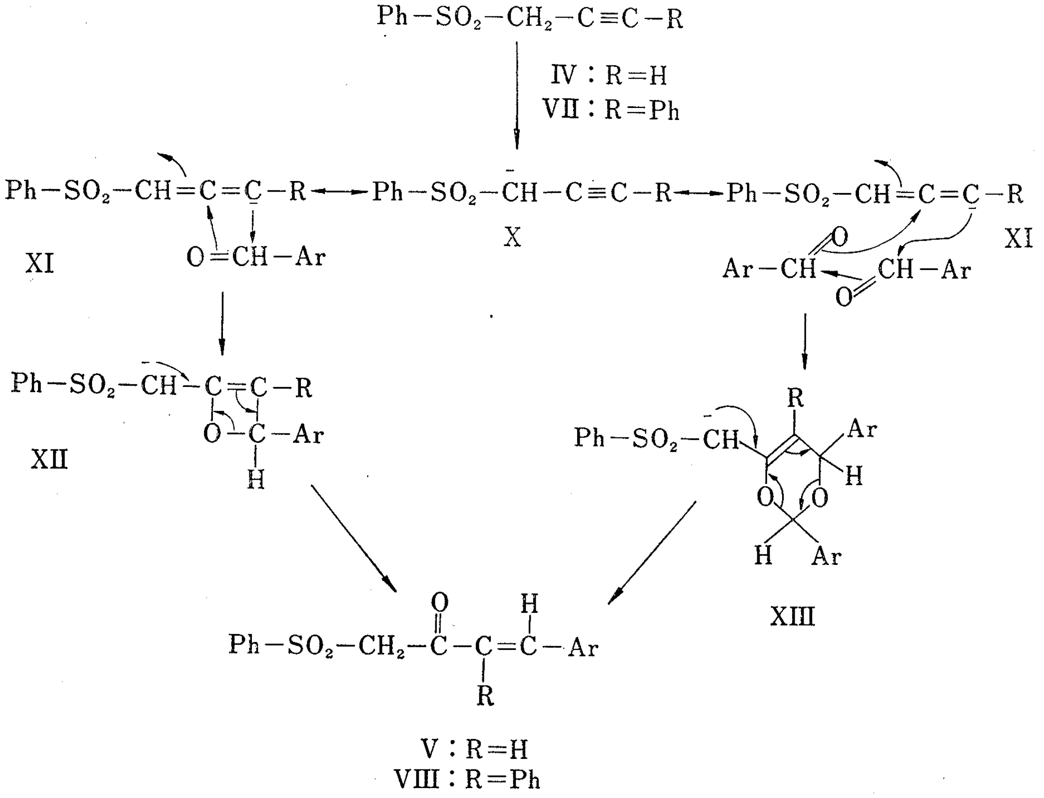


Chart 5

(X), which would be stabilized by the sulfone and acetylenic likage might isomerize to a more stable allene carbanion (XI).[8] The probable intermediate, XI might react with the substituted benzaldehydes to afford the corresponding 1-phenylsulfonyl-3-buten-2-ones (V, VIII) *via* an oxetene intermediate XII and/or the dioxin intermediate XIII as shown in Chart 5. The possible existence of XIII was exemplified by the isolation of IX and by many analogous compounds reported earlier.[1] On the other hand the pertinent evidence for the intermediate, XII, was also indicated by isolating the corresponding compound in the reaction of 2-propynyl *p*-tolyl sulfone with cyclohexanone. The reaction of 2-propynyl sulfones with cyclohexanone and cyclopentanone will appear in the near future.

Experimental

Phenyl 3-Phenyl-2-propynyl Sulfide[9]——To a sodium ethoxide solution prepared from 250 ml of abs. EtOH and 9.5 g of Na was added 43 g of thiophenol. To the resulting phenylmercaptide solution was added dropwise 97 g of phenylpropargyl bromide for 2 hr. The reaction mixture was heated under reflux for 1 hr. After cooling the precipitated NaBr was removed on a glass filter and the filtrate was condensed at reduced pressure below 50°. To the residue was added ether, and the organic mixture was washed with H_2O three times until neutral, dried over anhyd. Na_2SO_4, and evaporated to dryness. The distillation of the residue gave the title compound of bp 130° (1×10^{-3} mmHg). Yield: 68 g (78%). (lit.,[9] bp 170°/1 mmHg, Yield: 81%). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 244 (4.233). IR $\nu_{\max}^{\mathrm{liquid}}$ cm^{-1}: 2190 (weak, C≡C). NMR δppm in $CDCl_3$: 3.73 (2H, singlet), 6.95—7.50 (10H, multiplet).

Phenyl 3-Phenyl-2-propynyl Sulfone[10]——To a mixture of phenyl 3-phenyl-2-propynyl sulfide (4.5 g, 20 mmole) and 50 ml of AcOH was added dropwise 9.1 g of 30% H_2O_2 under vigorous stirring at 50—55°. The resulting mixture was heated at 55° for 5 hr and then poured into 500 ml of crushed ice–water. After allowing to stand for 2 hr, precipitated solid was collected on a glass filter and washed with water. Recrystallization from ether–*n*-hexane gave prisms of mp 116—117°. Yield: 3.4 g (61%). (lit.,[10] mp 116°, Yield: 65.5%). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 244 (4.267), 249 (4.250). IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 2220 (weak, C≡C), 1321, 1309 and 1296 ($-SO_2-$, *asym.*), 1148 ($-SO_2-$, *sym.*). NMR δppm in $CDCl_3$: 4.18 (2H, singlet), 7.30 (5H, singlet), 7.52—7.78 (3H, multiplet), 7.94—8.16 (2H, multiplet).

General Procedure for the Reaction of Phenyl 2-Propynyl Sulfone (IV) with Substituted Benzaldehydes——To a mixture of phenyl 2-propynyl sulfone (1.80 g, 10 mmole), each substituted benzaldehyde (20 mmole) and dry THF (40 ml) was added sodium hydride (0.24 g, 10 mmole) in several portions with vigorous stirring under N_2 atmosphere in ice–water bath keeping the temperature at 0—10°. The resulting mixture, turning into orange and then dark red, was allowed to stand with stirring at 0—5° for 30 min and then at room temperature (r.t., 20—25°) for 1.5 hr. The mixture was poured into 500 ml of ice–water with stirring and the precipitated crystals were collected to give pure 4-phenyl-1-phenylsulfonyl-*trans*-3-buten-2-one derivative (V) by recrystallization from acetone. The aqueous filtrate was extracted with AcOEt and the combined extracts were washed with satd. NaCl solution, dried over anhyd. Na_2SO_4, and evaporated to dryness. The oily residue gave another crop of V by column partition chromatography on silica gel (100 g).

Reaction of Methyl Phenyl Sulfone with Ethyl Cinnamate——A mixture of methyl phenyl sulfone (7.8 g, 50 mmole), 10 ml of dimethylsulfoxide (DMSO), 20 ml of 1,2-dimethoxyethane and sodium hydride (1.2 g, 50 mmole) was heated to 60°, with stirring, for 1 hr and then a solution of ethyl cinnamate (4.2 g, 24 mmole) in 5 ml of 1,2-dimethoxyethane was added dropwise with stirring. After the resulting mixture had been stirred at 60° for 1.5 hr and allowed to stand at r.t. for 2 days, this was acidified with AcOH (3 ml) and then partitioned between water and $CHCl_3$. The organic layer was washed successively with aq. $NaHCO_3$ solution and aq. NaCl,. dried over anhyd. Na_2SO_4, and evaporated to dryness. The residual oil was chromatographed on 190 g of silica gel. Elution with a benzene–$CHCl_3$ (99:1) solvent system and recrystallization from ether gave needles of 4-phenyl-1-phenylsulfonyl-3-penten-2-one (VI), mp 97—98°. Yield: 2.0 g (13%). *Anal.* Calcd. for $C_{17}H_{16}O_3S$: C, 67.98; H, 5.37; S, 10.67. Found: C, 67.73; H, 5.31; S, 10.77. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 296 (4.260). IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 1670 (C=O), 1592 (C=C), 1300—1330 ($-SO_2-$, asym.), 1155 ($-SO_2-$, sym.). NMR δppm in $CDCl_3$: 2.50 (3H, doublet, $J=1.2$ Hz, $-CH_3$), 4.28 (2H, singlet, $-CH_2-$), 6.77 (1H, quartet, $J=1.2$, C=CH–), 7.4—8.1 (10H, aromatic protons). Elution with a benzene:$CHCl_3$ (97:3) solvent system and recrystallization from ether gave needles of 4-phenyl-1-phenylsulfonyl-*trans*-3-buten-2-one (Va), mp 92—93°. Yield, 2.3 g (17%). This sample was identified by mixed melting point test, TLC and IR spectrum comparison with a sample prepared from IV and benzaldehyde.

General Procedure for the Reaction of Phenyl 3-Phenyl-2-propynyl Sulfone (VII) with Substituted Benzaldehydes——To a mixture of VII (2.7 g, 10 mmole), each substituted benzaldehyde (20 mmole) and 40 ml

---

9) G. Pourcelot and P. Cadiot, *Bull. Soc. Chim. France*, **1966**, 3016.
10) G. Pourcelot and P. Cadiot, *Bull. Soc. Chim. France*, **1966**, 3024.

of THF was added sodium hydride (0.24 g, 10 mmole) in several portions with vigorous stirring under N_2 atmosphere in ice–water bath keeping the temperature at 0—10°. The resulting mixture, turning into orange and then dark red, was allowed to stand with stirring at 0—10° for 1 hr and then at r.t. for 1 hr. The mixture was poured into 500 ml of ice-water with vigorous stirring and a precipitated solid was collected to afford pure 3,4-diphenyl-1-phenylsulfonyl-3-buten-2-one derivatives (VIII) by recrystallization from acetone. The aqueous filtrate was extracted with AcOEt and the combined extracts were washed with satd. NaCl solution, dried over anhyd. Na_2SO_4, and evaporated to dryness. The oily residue gave a second crop of VIII by column partition chromatography on silica gel (50—120 g).

***p*-Bromobenzaldehyde**——The usual work up gave 4-*p*-bromophenyl-3-phenyl-1-phenylsulfonyl-3-buten-2-one (VIIIe) as small needles after recrystallization from acetone (the first crop from the precipitated solid: 2.5 g). The oily residue, which was obtained from the extracts of the filtrate, was chromatographed on silica gel (120 g). Elution with benzene and recrystallization from acetone gave prisms of 2,4-di-*p*-bromophenyl-5-phenyl-6-phenylsulfonylmethyl-1,3-dioxin (IX), mp 142—144°. Yield: 630 mg (10%). *Anal.* Calcd. for $C_{29}H_{22}O_4SBr_2$: C, 55.60; H, 3.54; S, 5.12; Br, 25.51. Found: C, 55.70; H, 3.83; S, 4.94; Br, 25.51. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 253 (4.11). IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 1670 (C=C), 1290—1330 ($-SO_2-$, *asym.*), 1170 ($-SO_2-$, *sym.*). NMR δppm in $CDCl_3$: 4.00 (1.2H, broad singlet) and 4.15 (0.8H, broad singlet) for $-CH_2-$ of *trans*- and *cis*-1,3-dioxin, 5.70 (1H, singlet), 5.75 (0.6H, singlet) and 6.10 (0.4H, singlet) due to four kinds of methine protons, 7.1—8.1 (18H, aromatic protons). Elution with a benzene- $CHCl_3$ (99:1) solvent system and recrystallization from acetone afforded a second crop of VIIIe (0.5 g).

Acknowledgement The authors are very grateful to Dr. A. Terada of this laboratory for his valuable suggestion and kind discussion, and to Mr. N. Ishida for his technical assistance. Their thanks are also due to the members of physical chemistry laboratory for the spectroscopic measurements and microanalyses.