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Studies on Acetylenic Compounds. LVII.[1] Reactions of 2-Propynyl Sulfones with Cyclic Ketones

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2-Butynyl phenyl sulfone (VI) and cyclic ketones were treated with sodium hydride to give the corresponding 1:1 addition products, respectively. The structures were assigned to 1-phenylsulfonyl-3-(1-cyclohexenyl)2-butanone (VII) and 2-phenylsulfonylmethylene-3-methyloxetane-4-*spiro*-1′-cyclohexane (VIII) in the case of cyclohexanone and assigned to 1-phenylsulfonyl-3-(1-cyclopentenyl)2-butanone (XIII) in the case of cyclopentanone, respectively. Acid treatment of VIII afforded three degradation products, VII, X and XI, which confirmed the novel structure of VIII. 2-Propynyl *p*-tolyl sulfone (XIV) and cyclohexanone with sodium hydride treatment gave also an oxetane compound, XV. A plausible mechanism of the reaction and the physical properties of the products were presented in some detail.

In the preceding papers,[3] we reported the reactions of 2-propynyl sulfones with several substituted benzaldehydes. Base treatments of 2-propynyl sulfones (I) gave propargyl carbanions (II), which would be stabilized through the conjugation with the neighboring strong electron attracting groups, sulfone and acetylenic linkage. The initiation of the reaction with benzaldehyde derivatives (generally electrophiles) was the attack of the allene carbanions (III) which were assumed to resonate with the propargyl carbanions and to be more reactive species.

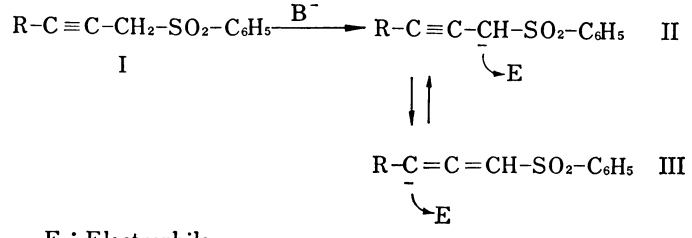

Chart 1

On the other hand the reactions of propargylic sulfonium ylids, which were prepared from corresponding 2-propynyl sulfonium salts (IV), with cyclohexanone and cyclopentanone were intensively investigated in this laboratory.[4] Propargylic ylids derived from IV reacted with cyclohexanone at the propargylic position followed by 1,5-sigmatropic rearrangement[5] of dimethyl sulfide moiety to afford allenic alcohol (V).

1) Part LVI: Y. Kishida, N. Nakamura, and N. Ishida, *Chem. Pharm. Bull.* (Tokyo), **19**, 1389 (1971).
2) Location: *2-58, 1-chome, Hiromachi, Shinagawa-ku, Tokyo.*
3) M. Yoshimoto and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 2518, 2528 (1970).
4) A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 991 (1970).
5) The 1,5-sigmatropic rearrangement of propargyl sulfonium compounds was observed by two groups, independently. A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **17**, 966 (1969); J.E. Baldwin, R.E. Hackler and D.P. Kelly, *Chem. Commun.*, **1968**, 1083.

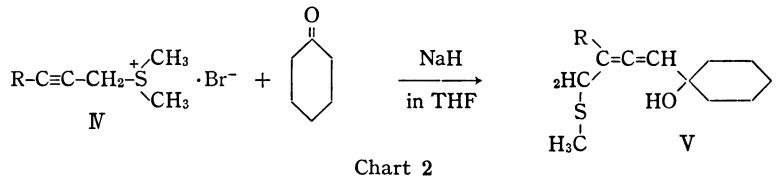

Chart 2

With these data as background, we set out to examine the reaction of 2-propynyl sulfones with cyclic ketones. A mixture of 2-butynyl phenyl sulfone (VI) and cyclohexanone was treated with sodium hydride to give two products. That the first was 1:1 reaction product of VI and cyclohexanone was indicated by the elemental analysis and mass spectrum (MS):M^+=292, and the product (VII) had a non-conjugated ketone (1710 cm^{-1}), a double bond (1655) and a sulfone group (1325, 1310, 1150) in the infrared (IR) spectrum. The ultraviolet (UV) spectrum of VII had no other chromophore but phenylsulfone group. The nuclear magnetic resonance (NMR) spectrum consisted of a doublet at 1.13 ppm (J=6.0 Hz) assignable to a secondary methyl, a pair of doublets at 4.06 and 4.44 (J=14 Hz) assigned to a non-

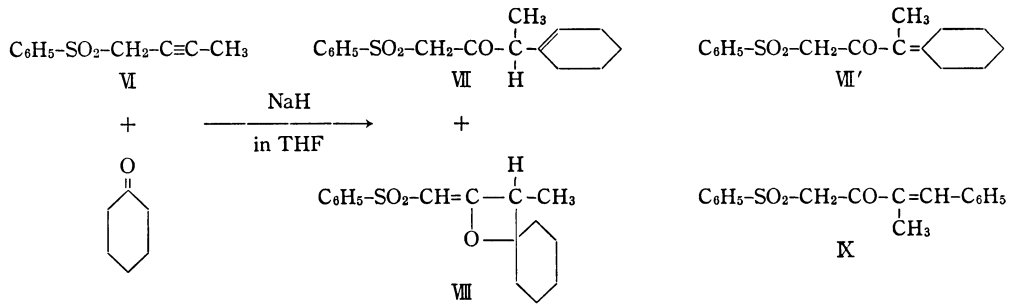

Chart 3

equivalent methylene with a proximate chiral center (-$\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}$H-), a quartet at 3.30 ascribable to a methine assumed to be coupled with the secondary methyl, a broad triplet-like singlet at 5.60 (olefinic proton), broad peaks of eight methylene protons and five aromatic protons. These data were consistent with the proposal structure (VII). In our earlier study[3] the reaction of VI and benzaldehyde gave 3-methyl-4-phenyl-1-phenylsulfonyl-3-buten-2-one (IX), which was very similar compound to VII except the position of the double bond. The formation of non-conjugated system in VII was presumably due to release of the steric hindrance of VII′, which corresponded to IX and which was never isolated. Treatments of VII with triethylamine, 1,4-diazabicyclobutane (DABCO) and sodium methoxide did not bring about the conversion to VII′. Another reaction product was also shown to be 1:1 adduct of VI and cyclohexanone by the elemental analysis and the compound (VIII) showed no carbonyl function but strong double bond absorption (1650 cm^{-1}), olefinic hydrogen (3050) and sulfone group (1300, 1140) in the IR spectrum. The UV maximum appeared at 244 nm (log ε=4.15) and the NMR spectrum comprised a doublet at 1.49 ppm (J_1=7.0 Hz) assigned to a secondary methyl, doublet of quartets at 3.50 (J_1=7.0, J_2=2.0) ascribable to a methine proton which coupled with the methyl and an olefinic proton, a doublet at 5.60 (an olefinic proton, J_2=2.0), broad peaks of ten methylene protons and five aromatic protons. These data and a mechanistic assumption which will be described later suggested the structure, VIII. The chemical character toward acid was investigated. VIII was warmed in ethanol containing a small amount of hydrochloric acid. An usual work-up and chromatography on silica gel afforded three products. The first was identified with VII by thin-layer chromatography (TLC), IR spectrum comparison and mixed melting point (mmp). The second product

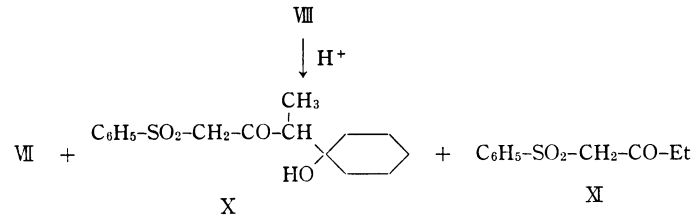

Chart 4

(X) was similar to VII in the NMR spectrum. Pointing out the difference of them, X exhibited ten methylene protons on the cyclohexane ring, while VII exhibiting eight methylene protons which had been assigned. The decisive difference was that in X tertiary alcohol group (IR: 3500 cm^{-1}, NMR: no low-field proton assignable to H-C-OH) was found in place of the olefine group in VII. From these data the structure in Chart 4 was proposed for X. The third product (XI) was very simple and identical with the hydration compound of VI, 1-phenylsulfonyl-2-butanone by IR spectrum comparison, TLC and mmp. The acid catalyzed rearrangement of VIII would be explained as described in Chart 5. The reaction would be initiated by the hydration of the double bond followed by the cleavage of the oxetane ring (VIII→XII→X). The dehydration of X would lead to VII. The original reaction of VI and cyclohexanone did not afford X, which seemed very reasonable in the non-aqueous solvent. The acid-catalyzed retro-aldol cleavage of X would afford XI and cyclohexanone.

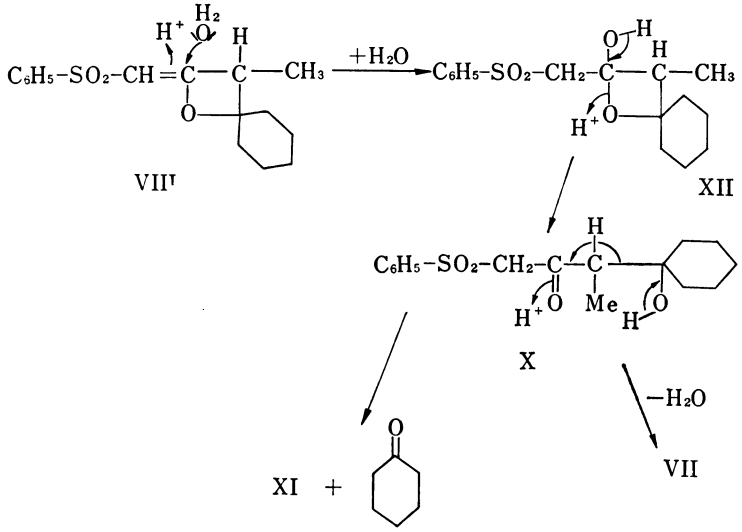

Chart 5

The reaction of VI with cyclopentanone gave only one product (XIII), which was very similar to VII in all the spectroscopic data (see Experimental) and suggested the structure in Chart 6.

2-Propynyl *p*-tolyl sulfone (XIV) was chosen for the second reagent and allowed to react with cyclohexanone to afford also only one product (XV), which was very similar to VIII in spectroscopic data and assignable to the structure in Chart 6. The clear confirmation of the proposed structure XV was based on the comparison of the mass spectrum with that of VIII. The two compounds showed the same molecular weight, 292. The brief assignments of the fragment peaks were shown in Fig. 1 and Fig. 2. In order to determine

the configuration of the double bond in XV, nuclear Overhauser effect (NOE) was investigated. Irradiation at the methylene protons on the oxetane ring induced no appreciable increment of the integrated intensity of the olefine peak. Since we noticed no example of the *cis* configuration of methylene and olefinic proton with no NOE data, the geometric structure was tentatively assumed to be *trans* as shown in Chart 6.

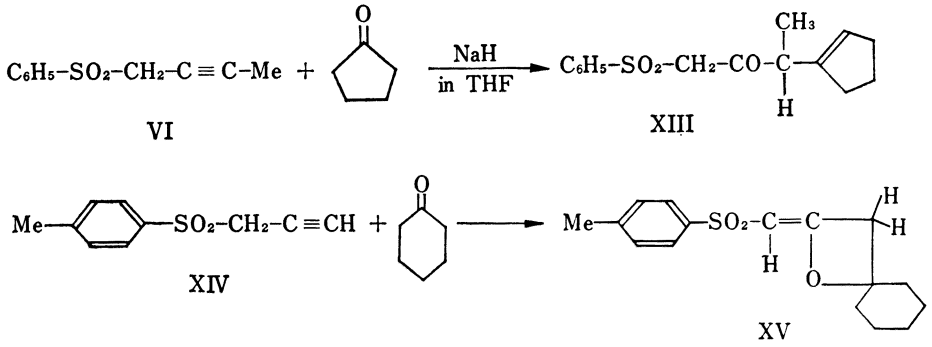

Chart 6

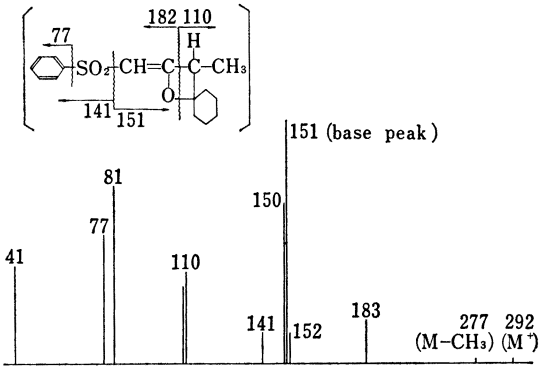

Fig. 1. Mass Spectrum of VIII

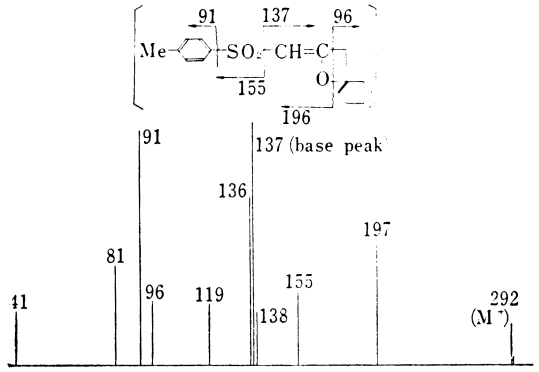

Fig. 2. Mass Spectrum of XV

Plausible mechanisms for the formation of the ketone, VII, and the oxetane, VIII, from 2-butynyl phenyl sulfone (VI) and cyclohexanone are presented in Chart 7. Thus the mechanism has an analogy to the reaction mechanism of VI and benzaldehyde derivatives which has been presented in the earlier paper.[3] The firstly formed sulfonyl carbanion (VI') might be resonated with a more reactive allene carbanion (XVI).[6] The probable intermediate would then react with cyclohexanone to afford an oxetene intermediate (XVII), which would be protonated (a) to 2-phenylsulfonylmethylene oxetane-4-*spiro*-1'-cyclohexane (VIII). While, XVII might cause the decomposition of the oxetane ring (b) to give VII followed by protonation and double bond migration of the possible intermediate, XVIII. Of course, we can not exclude the intermediacy of the 1,3-dioxin compound (XIX), although we could not detect it. The 1,3-dioxin compounds had been found in the reaction of 2-propynyl sulfones with benzaldehyde derivatives.[3] Formation of other interesting products, XIII and XV, could also be explained by a mechanism analogous to that described in Chart 7.

6) C.J.M. Stirling, *J. Chem. Soc.*, **1964**, 5856; I. Iwai, "Mechanism of Molecular Migrations," Vol. 2, ed. by B.S. Thyagarayan, Interscience Publishers, Inc., New York, N.Y., 1969, pp. 78—84; J.H. Wotiz, *J. Am. Chem. Soc.*, **72**, 1637 (1950).

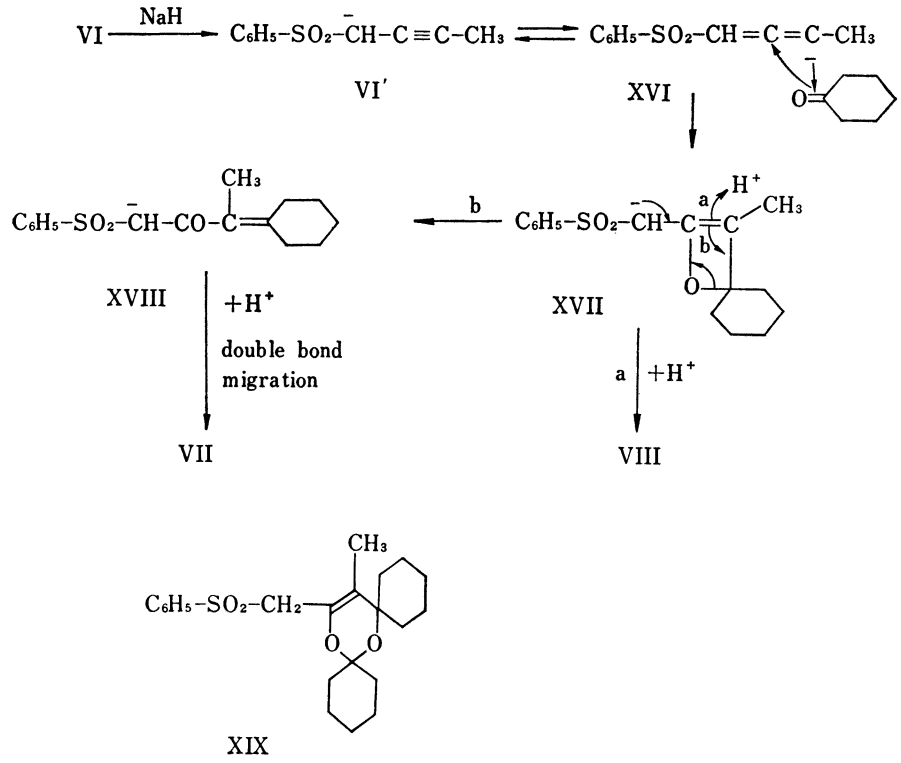

Chart 7

Experimental[7]

Reactants——2-Butynyl phenyl sulfone (VI)[3,8] and 2-propynyl *p*-tolyl sulfone (XIII) were prepared according to published procedures.[3,6,8]

2-Propynyl *p*-Tolyl Sulfide——To a sodium ethoxide solution prepared from 300 ml of abs. EtOH and Na (13.9 g, 0.605 mole) was added 75.0 g (0.605 mole) of *p*-tolyl mercaptane with 50 ml of EtOH. To the resulting mixture was added dropwise 86.0 g (0.721 mole) of propargyl bromide and then the reaction mixture was heated at 70° for 30 min. After cooling, NaBr precipitated was removed on a glass filter and the filtrate was condensed at reduced pressure below 50°. To the residue was added ether and the solution was washed with aq. NaCl and dried over anhyd. Na_2SO_4. After removal of the solvent below 50°, the distillation of the residue gave the title sulfide as a colorless oil, bp 114—115° (9 mmHg). Yield, 87.7 g (89.5%). *Anal.* Calcd. for $C_{10}H_{10}S$: C, 74.00; H, 6.21; S, 19.76. Found: C, 73.00; H, 6.29; S, 19.32. UV λ_{max}^{EtOH} nm (log ε): 220 (3.96) and 254 (3.72). IR ν_{max}^{Liquid} cm^{-1}: 3290 (H-C≡C), 2120 (C≡C), 1600, 1500.

2-Propynyl *p*-Tolyl Sulfone (XIV)——(a) To a solution of 2-propynyl *p*-tolyl sulfide (32.4 g, 0.200 mole) in 400 ml of AcOH was added dropwise 50.0 g of 30% H_2O_2 (0.441 mole) with stirring for 1 hr at *ca.* 40°. The resulting mixture was warmed at 45° for 5 hr and after cooling, poured into 2.0 liters of crushed ice-water. The precipitated needles were collected on a glassfilter. Recrystallization from MeOH afforded colorless needles of the title compound, mp 95—97°. Yield, 33.0 g (85.0%). *Anal.* Calcd. for $C_{10}H_{10}O_2S$: C, 61.85; H, 5.19; S, 16.51. Found: C, 61.80; H, 5.22; S, 16.32. UV λ_{max}^{EtOH} nm (log ε): 231 (4.13), 264 (2.95) and 274 (2.74). IR ν_{max}^{Nujol} cm^{-1}: 3280 (H-C≡C), 2130 (C≡C), 1600, 1290—1320 (-SO_2-, *asym.*), 1143 (-SO_2-, *sym.*). NMR δ ppm in CCl_4: 2.23 (1H, t, J=2.8 Hz, H-C≡C), 2.47 (3H, s, -CH_3), 3.78 (2H, d, J=2.8, -CH_2-), 7.32, 7.80 (4H, a pair of doublets, J=8.0, aromatic protons).

7) All melting points were uncorrected. NMR spectra were obtained in the specified solvents on a Varian A-60 and Varian HA-100 spectrometer with tetramethylsilane as an internal standard. Mass spectra were determined on a JEOL JMS-O1SG spectrometer.

8) G. Pourcelot and P. Cadiot, *Bull. Soc. Chim. France*, **1966**, 3025.

(b) To a solution of 2-propynyl *p*-tolyl sulfide (8.1 g, 50.0 mmole) in 200 ml of CH_2Cl_2 was added with stirring a mixture of *m*-chloroperbenzoic acid (17.3 g, 0.100 mole) and CH_2Cl_2 (200 ml) for 30 min at 0° in ice-NaCl bath. Stirring was continued for 1 hr below 10° and then the mixture was diluted with ether. The organic mixture was washed with satd. $NaHCO_3$ solution, H_2O and drid over anhyd. Na_2SO_4. Evaporation of the solvent and recrystallization from MeOH gave needles of the title compound, mp 95—97°. Yield, 8.8 g (91%).

Reaction of 2-Butynyl Phenyl Sulfone (VI) with Cyclohexanone——To a mixture of VI (5.82 g, 30.0 mmole), cyclohexanone (5.89 g, 60.0 mmole) and 80 ml of dry THF was added 1.44 g of 50% NaH (30.0 mmole) in several portions with vigorous stirring under N_2 atmosphere in ice-bath keeping the temperature at 5—10° for 30 min. The resulting mixture, turning into orange and then dark brown, was stirred below 10° for 30 min and then allowed to stand at room temperature (20—25°) for 2 hr. The mixture was poured into 1000 ml of crushed ice-water with stirring and extracted with AcOEt. The combined extracts were washed with satd. $NaHCO_3$ solution, dried over anhyd. Na_2SO_4 and evaporated. The residue (10.8 g) was separated on silica gel (500 g) by dry column chromatography method[9] using Woelm nylon tube (5 × 100 cm). The residue-adsorbent mixture was distributed on the top of the column. The developing solvent was a mixture of benzene and AcOEt (5:1). When the solvent reached the bottom of the column, development completed and the tube was sliced into six equal length portions. The extracts of the second segment from the bottom with AcOEt followed by evaporation and recrystallization from EtOH afforded 2-benzenesulfonylmethylene-3-methyloxetane 4-*spiro*-1′-cyclohexane (VIII) as colorless prisms, mp 86—87°. Yield, 3.65 g (41.7%). *Anal.* Calcd. for $C_{16}H_{20}O_3S$: C, 65.74; H, 6.90; S, 10.95. Found: C, 65.59; H, 6.98; S, 10.91. UV λ_{max}^{EtOH} nm (log ε): 244 (4.15). IR ν_{max}^{Nujol} cm^{-1}: 3050 (olefinic C-H), 1650 (C=O), 1300 (-SO_2-, *asym*) and 1140 (-SO_2-, *sym*). NMR δ ppm in $CDCl_3$: 1.49 (3H, d, J_1=7.0 Hz, -CH_3), 1.00—2.15 (10 H, broad, cyclohexyl), 3.50 (1H, doublet of quartets, J_1=7.0, J_2=2.0, 3-position methine on the oxetane ring), 5.60 (1H, d, J_2=2.0, olefinic proton), 7.30—8.00 (5H, m, aromatic protons). While, the extracts of the third segment from the bottom with AcOEt followed by evaporation and recrystallization from EtOH gave 3-(1-cyclohexenyl)1-phenylsulfonyl-2-butanone (VII) as colorless prisms, mp 75—76°. Yield, 1.80 g (20.5%). *Anal.* Calcd. for $C_{16}H_{20}O_3S$: C, 65.74; H, 6.90; S, 10.95. Found: C, 65.42; H, 6.85; S, 10.89. UV λ_{max}^{EtOH} nm (log ε): 259 (2.98), 265 (3.09), 272 (3.03). IR ν_{max}^{Nujol} cm^{-1}: 1710 (C=O), 1655 (C=C), 1310 and 1325 (-SO_2-, *asym*), 1150 (-SO_2-, *sym*). NMR δ ppm in $CDCl_3$: 1.13 (3H, d, J_1=6.0 Hz, -CH_3), 1.30—2.20 (8H, m, methylene protons on the cyclohexene ring), 4.06, 4.44 (2H, a pair of doublets, J=14.0, -SO_2-CH_2-), 5.60 (1H, broad s, olefinic proton), 3.38 (1H, q, J=6.0, H-C-CH_3), 7.30—8.00 (5H, m, aromatic protons).

Acid Treatment of 2-Benzenesulfonylmethylene-3-methyloxetane-4-spiro-1′-cyclohexane (VIII)——A mixture of VIII (500 mg, 1.71 mmole), conc. HCl (7.0 ml) and 80 ml of EtOH was refluxed for 7 hr and condensed at reduced pressure. The mixture was diluted with ether, washed with satd. aq. $NaHCO_3$ solution and then H_2O, dried over anhyd. Na_2SO_4, and evaporated. The residue was separated by preparative TLC (developing solvent; a mixture of benzene: AcOEt=9:1). The fraction near the bottom (Rf=0.2) was extracted with AcOEt. Evaporation gave an oily residue of 3-(1-hydroxycyclohexyl)-1-phenylsulfonylbutan-2-one (X) (31 mg). Mass Spectrum: M^+=310, 292 (M-H_2O), 212 (C_6H_5-SO_2-CH_2-CO-$\overset{+}{C}$H-CH_3), 183 (C_6H_5-SO_2-CH_2-C≡$\overset{+}{O}$), 155 (C_6H_5-SO_2-CH_2^+), 169 (M-$C_6H_5SO_2$)$^+$, 141 (C_6H_5-SO_2^+), 77 ($C_6H_5^+$). IR ν_{max}^{Liquid} cm^{-1}: 3500 (-OH), 1720 (C=O), 3050 and 1590 (benezne ring), 1320 (-SO_2-, *asym*), 1150 (-SO_2-, *sym*). NMR δ ppm in $CDCl_3$: 1.08 (3H, d, J=7.0 Hz), 1.2—2.1 (10H, m, methylene protons on the cyclohexane ring), 4.30, 4.50 (2H, a pair of doublets, J=14.0, -SO_2-CH_2-), 2.98 (1H, q, J=7.0), 7.3—8.0 (5H, m, aromatic protons). The fraction near the center (Rf=0.5) was extracted with AcOEt. Evaporation and recrystallization from EtOH gave colorless prisms of 1-phenylsulfonyl-2-butanone (XI), mp 48—49°, which was identified with the hydration compound of VI in TLC and IR spectrum comparison. Yield, 128 mg (35.2%). *Anal.* Calcd. for $C_{10}H_{12}O_3S$: C, 56.57; H, 5.70; S, 15.10. Found: C, 56.61; H, 5.76; S, 14.75. UV λ_{max}^{EtOH} nm (log ε): 259 (3.11), 265 (3.19), 272 (3.14). Mass Spectrum: M^+=212, 194 (M-CH_3), 183 (M-Et), 141 (C_6H_5-SO_2^+), 77 ($C_6H_5^+$). IR ν_{max}^{Nujol} cm^{-1}: 1725 (C=O), 1320 and 1310 (-SO_2-, *asym*), 1150 (-SO_2-, *sym*). NMR δ ppm in $CDCl_3$: 1.05 (3H, t, J=7.0 Hz, -CH_3), 2.72 (2H, q, J=7.0, -CO-CH_2-CH_3), 4.17 (2H, s, -SO_2-CH_2-). The fraction near the top (Rf=0.7) was extracted with AcOEt. Evaporation and recrystallization from EtOH gave colorless prism, mp 75—76°, which was identified with VII in TLC, IR spectrum comparison and mmp (no depression). Yield, 33.2%.

Reaction of 2-Butynyl Phenyl Sulfone (VI) with Cyclopentanone——To a mixture of VI (1.94 g, 10.0 mmole), cyclopentanone (1.68 g, 20.0 mmole) and 30 ml of dry THF was added 0.48 g of 50% NaH (20.0 mmole) at once with stirring under N_2 atmosphere in crushed ice-water bath at 5°. The resulting mixture, turning to orange and then dark red, was stirred at 5° for 1.5 hr. Then the mixture was poured into 500 ml of ice-water with stirring and extracted with AcOEt. The organic solution was washed with aq. NaCl solution, dried over anhyd. Na_2SO_4 and evaporated. The residue (3.2 g) was purified by column partition chromatography on silica gel (125 g). Elution with a mixture of benzene and $CHCl_3$ (19:1) and recrystalli-

9) B. Loev and K.M. Snader, *Chem. Ind.* (London), **1965**, 15; B. Loev and M.M. Goodman, *ibid.*, **1967**, 2026.

zation from EtOH afforded colorless prisms of 1-benzenesulfonyl-3-(1-cyclopentenyl)butan-2-one (XIII), mp 51—53°. Yield, 0.33 g (12%). *Anal.* Calcd. for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52; S, 11.52. Found: C, 63.88; H, 6.44; S, 11.59. UV λ_{max}^{EtOH} nm (log ε): 258 (3.17), 265 (3.23), 272 (3.15). IR ν_{max}^{Nujol} cm^{-1}: 3050 (olefinic C-H), 1715 (C=O), 1647 (C=C), 1298—1330 (-SO_2-, *asym*), 1152 (-SO_2-, *sym*). NMR δ ppm in $CDCl_3$: 1.13 (3H, d, J=7.0 Hz, -CH_3), 1.6—2.7 (6H, m, methylene protons on the cyclopentene ring), 3.65 (1H, q, J=7.0, H-C-CH_3), 4.10, 4.44 (2H, a pair of doublets, J=14.0, -SO_2-CH_2-), 5.54 (1H, broad s, olefinic proton), 7.4—8.0 (5H, m, aromatic protons).

Reaction of 2-Propynyl *p*-Tolyl Sulfone (XIV) with Cyclohexanone——To a mixture of XIV (2.91 g, 15.0 mmole), cyclohexanone (2.94 g, 30.0 mmole) and dry THF (100 ml) was added 0.72 g of 50% NaH-oil at once with vigorous stirring under N_2 atmosphere in ice bath below 5°. Stirring was continued below 5° for 2 hr and the mixture was poured into 700 ml of ice-water. Extracts with AcOEt were washed with aq. NaCl solution and drid over anhyd. Na_2SO_4. Evaporation gave 5.7 g of oily residue, which was purified by 100 g of silica gel column. Elution with a mixture of benzene and $CHCl_3$ (9:1) and recrystallization from EtOH gave colorless prisms of 2-*p*-tolylsulfonylmethyleneoxetane-4-*spiro*-1′-cyclohexane (XV), mp 132—133°. Yield, 580 mg (13.3%). *Anal.* Calcd. for $C_{16}H_{20}O_3S$: C, 65.72; H, 6.89; S, 10.96. Found: C, 65.47; H, 6.96; S, 10.89. UV λ_{max}^{EtOH} nm (log ε): 245 (4.32). IR ν_{max}^{Nujol} cm^{-1}: 3050 (olefinic C-H), 1668 (C=C), 1600, 1500, 1290—1315 (-SO_2-, *asym*), 1144 (-SO_2-, *sym*). NMR δ ppm in $CDCl_3$: 1.3—2.0 (10 H, m, methylene protons on the cyclohexane ring), 2.43 (3H, s, -CH_3), 3.32 (2H, d, J=2.0 Hz, C=C-CH_2-), 5.63 (1H, t, J=2.0), 7.35, 7.77 (4H, a pair of doublets, J=8.0, aromatic protons).