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Studies on Acetylenic Compounds. LVIII.[1] Reaction of 2-Propynyl Sulfones with Methyl Acrylate

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Three 2-propynyl sulfones (VIIIa—c) reacted with methyl acrylate to give the corresponding 2-carbomethoxy-4-ethynyl-4-arylsulfonylcyclohexanones (IXa—c), respectively. Nucleophilic reaction of acetylenic sulfonyl carbanion showed ambident character depending on the nature of electrophiles which were classified into two kinds. Some discussions of the reaction and physical properties of the products are presented.

In earlier papers, we reported the reactions of aryl 2-propynyl sulfones (I) with alicyclic ketones[1] and with substituted benzaldehydes.[3] In the former reaction, the products obtained were 2-methylenoxetane derivatives (II) and β,γ-unsaturated ketones (III), and in the latter case the main products were 1,3-dioxins (IV) and α,β-unsaturated ketones (V) (Chart 1).

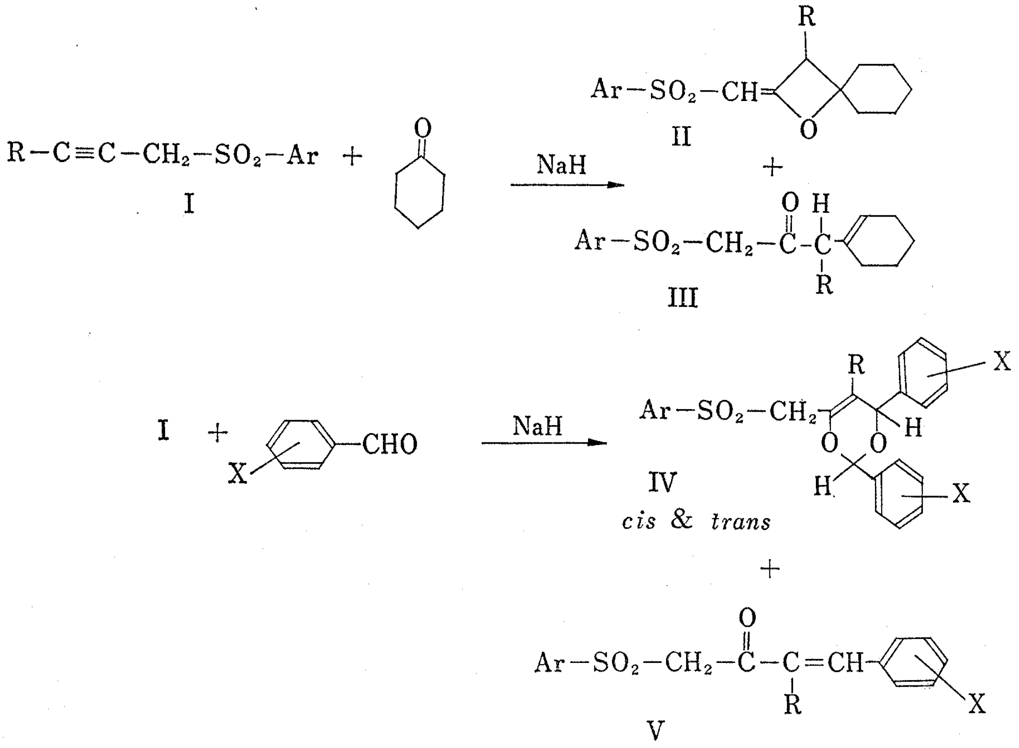

Chart 1

Considering the mechanism in view of the reaction sites initiating the nucleophilic attack on these carbonyl reagents, the firstly generated carbanion (sulfonyl ylid, VI) which was assumed to resonate with the allene carbanion (VII) and stabilized did not react with the

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[1] Part LVII: M. Yoshimoto, N. Ishida and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **19**, 1409 (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).

electrophiles in this form. The alternative ambident anion (VII) actually reacted to afford the products (II—V). In this study we wish to report the examples of VI-type reaction in which the electrophile was methyl acrylate. By the reaction sites of the carbanions electrophilic reagents were classified into E^1 (VI-type) and E^2 (VII-type). This classification was analogous to that of acyl-stabilized sulfur ylids by Johnson and Amel,[4] which had also two competing nucleophilic reaction sites and varied the course of the reaction with the nature of the electrophilic reagent.[5]

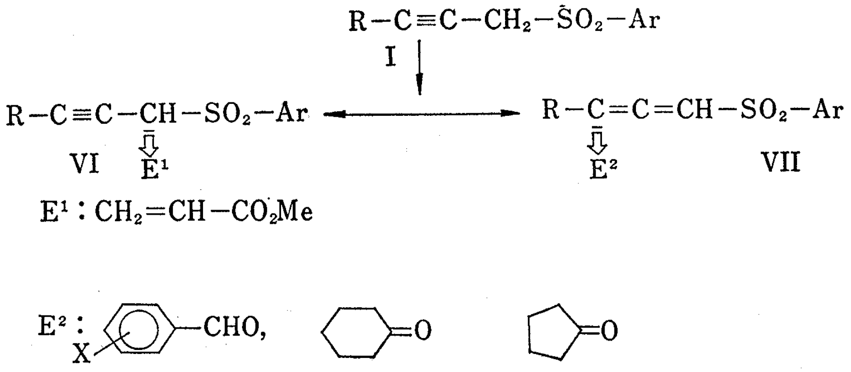

Chart 2

Julia's school[10a] and Martel's group[10b] have reported one-step syntheses of chrysanthemate by the reaction of 3,3-dimethyl-2-propenyl phenyl sulfone with senecioate derivatives, independently. With these data as background, we extended the nucleophilic reaction of acetylene sulfonyl carbanion with electrophiles to methyl acrylate, a representative of Michael acceptor.

Table I

Product	Base	Solvent	Yield (%)
IXa	*t*-BuOK	*t*-BuOH–THF (5:3)	40
IXa	NaH	THF	32
IXb	*t*-BuOK	C_6H_6–THF (5:3)	60
IXb	*t*-BuOK	*t*-BuOH–THF (2:1)	40
IXc	*t*-BuOK	*t*-BuOH–THF (2:1)	5

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[4] A.W. Johnson and R.T. Amel, *Tetrahedron Letters*, **1966**, 819; *idem*, *J. Org. Chem.*, **34**, 1240 (1969).

[5] Treatment of dimethylphenacylidenesulfurane with benzoic anhydride afforded the highly stabilized ylid, dimethyl(dibenzoylmethylene)sulfurane and acylation with benzoyl chloride resulted in an O-acylation, affording the enol benzoate of α-methylmercaptoacetophenone.[4,6] The pattern of O-acylation and C-acylation would be interesting in the cases of sulfonyl phenacylide and sulfoxonium phenacylide. Thus, the monoanion of methyl phenacyl sulfone[7] underwent O-acylation with benzoyl chloride while phenacylidenedimethyloxysulfurane[8] underwent C-acylation with benzoyl chloride. In the series of phenacyl sulfur ylids the orientation of C- or O-acylation would be reflective of the extent of delocalization of the carbanion by the two competing electron sinks attached, the vacant 3d orbitals of sulfur and the carbonyl group. This discussion would be applied to our acetylenic sulfur ylids[9] by replacing the carbonyl group with the acetylenic linkage as an electron sink.

[6] H. Nozaki, K. Kondo, and M. Takaku, *Tetrahedron*, **22**, 2145 (1966).

[7] N.M. Carroll and W.I. O'Sullivan, *J. Org. Chem.*, **30**, 2830 (1965).

[8] H. Konig and H. Metzger, *Chem. Ber.*, **98**, 3733 (1965).

[9] *a*) Sulfonyl ylids: This paper, 1) and 3); *b*) Sulfonium ylids: A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 490, 497, 991, 2507 (1970).

[10] *a*) M. Julia and A.G. Roualt, *Bull. Soc. Chim. France*, **1967**, 1411; *b*) J. Martel and C. Huynh, *ibid.*, **1967**, 985; J. Martel and G. Nomine, *Compt. Rend.* (*C*), **1969**, 2199.

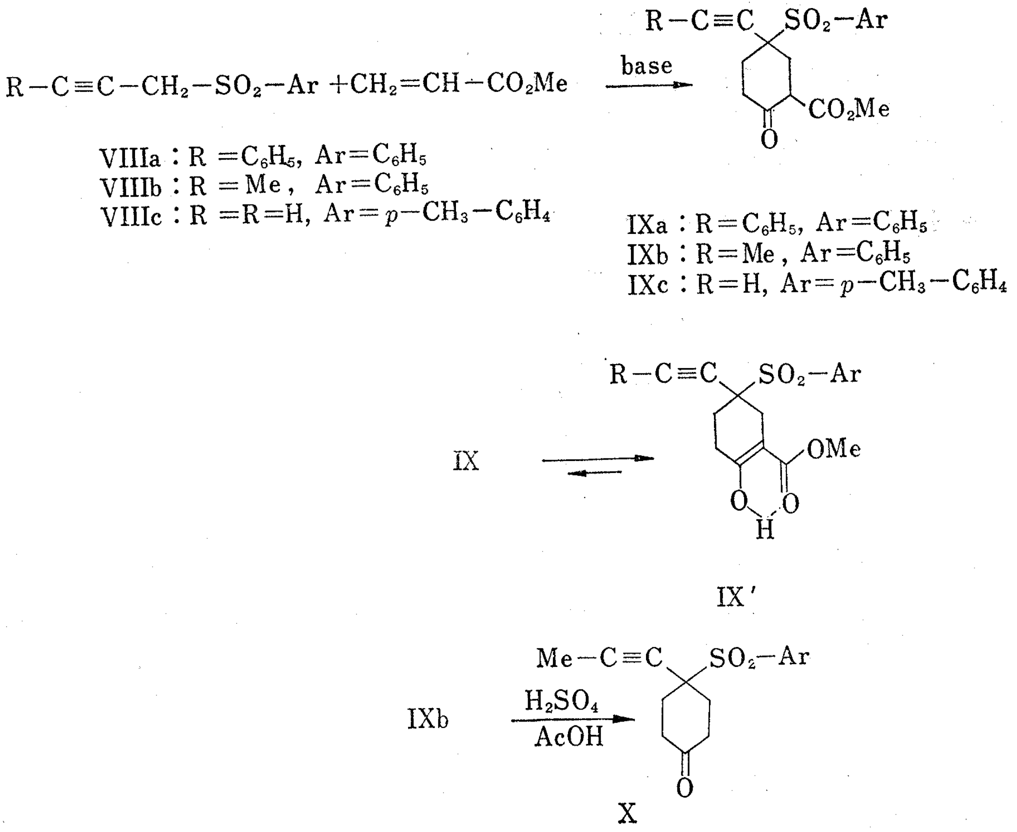


Chart 3

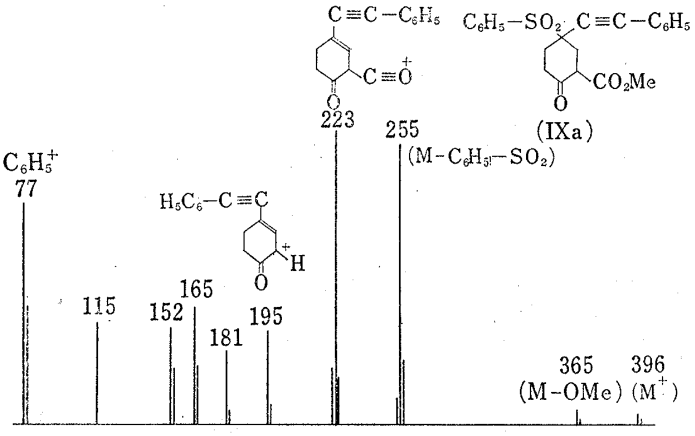


Fig. 1. Mass Spectrum of (IXa)

A mixture of phenyl 3-phenyl-2-propynyl sulfone (VIIIa) and methyl acrylate in appropriate solvents was treated with the specified base (Table I and Chart 3). A usual work-up (see Experimental) and column chromatography on silica gel gave a sole product, which was assigned to 2-carbomethoxy-4-phenethynyl-4-phenylsulfonylcyclohexanone (IXa) from the following. Molecular formula was determined as $C_{19}H_{18}O_4S$ from the elemental analysis and mass spectrum (MS, Fig. 1); m/e=396 (M^+), from which the product was shown to be methanol-

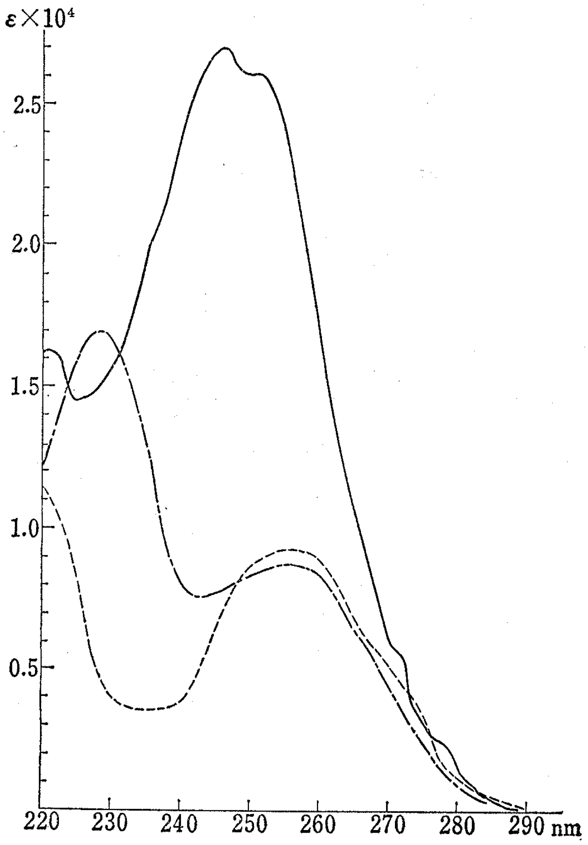


Fig. 2. UV Spectrum of (IX)

———: IXa -------: IXb —·—·—: IXc

elimination compound from the 1:2 adduct of VIIIa and methyl acrylate respectively. The ultraviolet (UV) spectrum (Fig. 2) indicated the retention of phenethynyl group (centered at 250 nm, $\varepsilon=1.5\times10^4$) and another strong absorption based on β-ketoester. The infrared (IR) spectrum exhibited more clearly the all functional groups; C≡C (2230 cm^{-1}), β-ketoester (1667, 1614, 1213), SO_2 ($\nu_{\mathrm{asym.}}$: near 1300, $\nu_{\mathrm{sym.}}$: near 1150). The nuclear magnetic resonance (NMR) spectrum showed six methylene protons, a methoxy peak, two phenyl absorption and an enolic hydrogen (Chart 3), from which IX was suggested to be equilibrated exclusively to IX′. VIIIb and VIIIc afforded also correspondingly IXb and IXc.

Table II. Spectral Data of IX

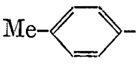
Compd.	R	Ar	IR $\nu_{\mathrm{max}}^{\mathrm{Nujol}}$ cm^{-1}					NMR δ ppm in $CDCl_3$				
			C≡C	β-ketoester		$-SO_2-$		CH_2	OMe	Ar	R	OH
IXa	C_6H_5	C_6H_5	2230	1667	1614	1286 1307	1145 1151	2.0—3.3 (6H, m)	3.78 (3H, s)	7.4—8.2 (5H, m)	7.33 (5H, s)	12.22 (1H, s)
IXb	Me	C_6H_5	2260	1662	1614	1285 1310	1155	1.9—3.0 (6H, m)	3.77 (3H, s)	7.5—8.1 (5H, m)	1.77 (3H, s)	12.18 (1H, s)
IXc	H	Me–  –	2120 3250(C≡C–H)	1667	1620	1285	1155	2.0—3.0 (6H, m)	3.77 (3H, s)	7.4—7.9 (4H, ABq) 2.50 (3H, s)	2.42 (1H, s)	12.20 (1H, s)

Table III. Melting Points and Combustion Analyses of IX

Compd.	mp (°C)	Analysis						Formula
		Calcd.			Found			
		C	H	S	C	H	S	
IXa	137—138	66.66	5.09	8.09	66.43	5.08	8.22	$C_{22}H_{20}O_5S$
IXb	120—122	61.06	5.43	9.59	60.87	5.67	9.72	$C_{17}H_{18}O_5S$
IXc	162—164	61.06	5.43	9.59	61.20	5.18	9.51	$C_{17}H_{18}O_5S$

The structure of IX was confirmed by the following experiment and the mechanistic consideration. Treatment of IXb with conc. sulfuric acid in acetic acid gave 4-phenylsulfonyl-4-(1-propynyl) cyclohexanone (X). The IR of X exhibited six-membered ketone (1720 cm^{-1}), triple bond and sulfonyl group. The MS supported the structure of X: $m/e=$ 276 (M^+), 135 ($M-C_6H_5SO_2$). Therefore IX possessed the cyclohexanone skeleton and the β-ketoester moiety. In the structure of IX the sulfonyl group and ethynyl group were assumed to locate geminally since there was no low-field methine proton neighboring at sulfonyl group, and each singlet of propynyl methyl (IXb) and ethynyl hydrogen (IXc) indicated no proton at another end of acetylenic linkage.

Contrary to our expectation from the analogy to the French works[10] no cyclopropane derivatives, which were later given by the reaction of the propargyl sulfonium ylids with acrylate,[11] were isolated and detected even by gas chromatography despite multi-fold experiments in varied conditions (Table I).

Recently Russell and Ochrymowycz[12] reported the synthesis of cyclohexanone derivatives by the reaction of β-keto sulfoxide with acrylate, which was considered to be very similar to our results.

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11) M. Yoshimoto, N. Ishida, and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **19**, 863 (1971).
12) G.A. Russell and L.A. Ochrymowycz, *J. Org. Chem.*, 34, 3624 (1969).

Considering the mechanistic pathway from VIIIa to IXa, the firstly generated sulfonyl carbanion (XIa), which resonates with allene carbanion (XIb), would react with two moles of methyl acrylate in double Michael reactions and then underwent Dieckmann condensation to give the product. Our first purpose was to obtain a cyclopropane compound and the failure would be due to the weak leaving ability of phenylsulfonyl group in a possible intermediate (XII). The extension of this reaction to methyl vinyl ketone and acrylonitrile as electrophiles resulted in obtaining intractable reaction products.

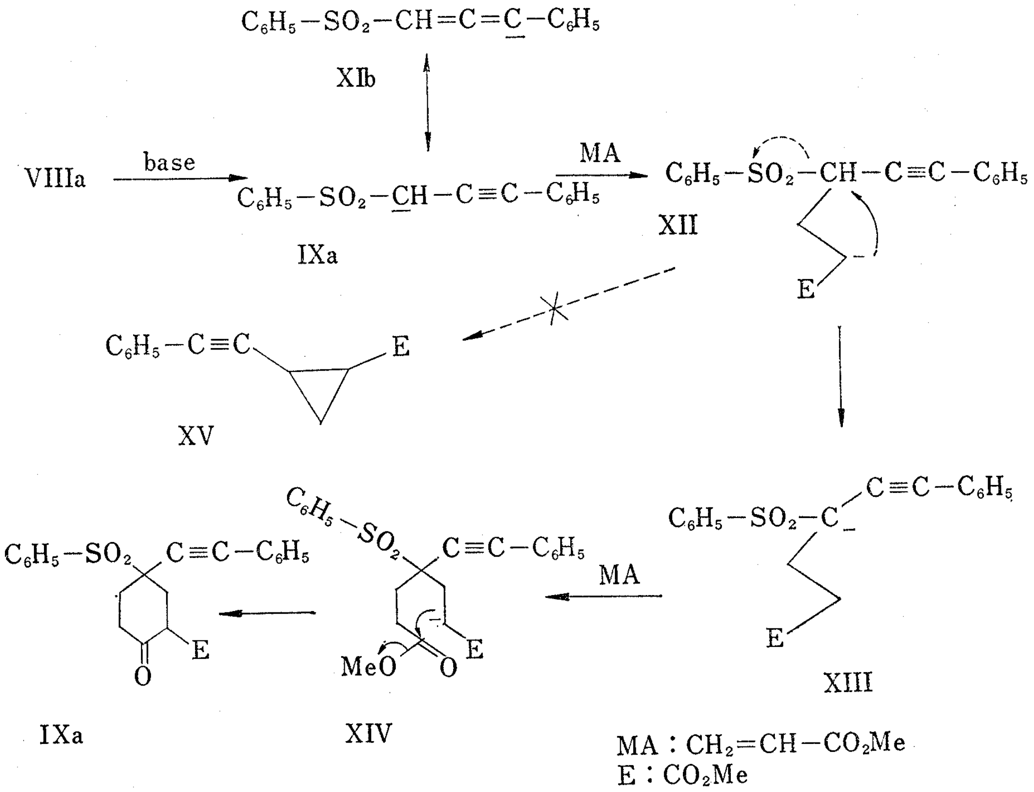

Chart 4

Experimental[13]

Reactants——Propargyl sulfones (VIII) were prepared according to the published procedures[14] as described in the preceding reports.[1,3]

General Procedure for the Reaction of Propargyl Sulfones (VIII) with Methyl Acrylate——a) To a stirred mixture of *t*-BuOK and *t*-BuOH (prepared from 780 mg of potassium and 100 ml of *t*-BuOH) was added dropwise a mixture of each 2-propynyl aryl sulfone (VIII) (10 mmole), methyl acrylate (1.72 g, 20 mmole) and dry THF (60 ml) for 1.5 hr at room temperature (r.t.: 20—25°) under N_2 atmosphere. Stirring was continued for additional 2 hr and the resulted mixture was poured into 500 ml of ice–water. The aqueous mixture 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 was purified by column chromatography on silica gel (50 g). Elution with benzene and recrystallization from EtOH gave each 4-arylsulfonyl-4-ethynyl-2-carbomethoxycyclohexanone (IX).

b) To a stirred mixture of phenyl 3-phenyl-2-propynyl sulfone (VIIIa) (2.56 g, 10 mmole), methyl acrylate (1.72 g, 20 mmole) and dry THF was added 50% NaH (0.48 g, 10 mmole) in several portions below 5° in ice–bath under Ar atmosphere. Stirring was continued for 2 hr in ice–bath, and the resulted mixture was allowed to stand at r.t. overnight and poured into 500 ml of ice–water. The aqueous mixture 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 was purified by column partition chromato-

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[13] All melting points are uncorrected. NMR spectra were obtained in the specified solvents on a Varian A-60 spectrometer with tetramethylsilane as an internal standard.

[14] G. Pourcelot and P. Cadiot, *Bull. Soc. Chim. France*, **1966**, 3024.

graphy on silica gel (100 g). Elution with benzene and recrystallization from EtOH afforded 4-phenylethynyl-4-phenylsulfonyl-2-carbomethoxycyclohexanone (IXa).

c) To a stirred mixture of *t*-BuOK (prepared from 1.17 g of potassium and 50 ml of *t*-BuOH) and dry benzene (50 ml) was added dropwise a mixture of 2-butynyl phenyl sulfone (VIIIb) (2.91 g, 15 mmole), methyl acrylate (2.58 g, 30 mmole) and dry THF (30 ml) for 0.5 hr below 10° under N_2 atmosphere. Stirring was continued at 10° for additional 0.5 hr and at r.t. for 1.5 hr, and the resulted mixture was poured into 300 ml of ice–water. The aqueous mixture was extracted with AcOEt and the combined extracts were washed with satd. NaCl solution, dried over Na_2SO_4 and evaporated to dryness. Recrystallization of the crude crystalline product (4.2 g) from EtOH afforded pure 4-phenylsulfonyl-4-(1-propynyl) 2-carbomethoxycyclohexanone (IXb, 3.0 g) of mp 120—122°. No expected cyclopropane derivative was detected by TLC and GC referring from the standard substance.[11]

Conversion[15] of 4-Phenylsulfonyl-4-(1-propynyl)2-methoxycarbonylcyclohexanone (IXb) to 4-Phenylsulfonyl-4-(1-propynyl)cyclohexanone (X)——A mixture of IXb (0.5 g), AcOH (10 ml) and conc. H_2SO_4 (0.5 ml) was heated under reflux for 6 hr. The AcOH was evaporated at reduced pressure and the residue was diluted with AcOEt. The organic solution was washed successively with satd. $NaHCO_3$ solution and satd. NaCl solution, dried over anhyd. Na_2SO_4 and evaporated to dryness. The residue was purified by TLC (silica gel: benzene) and recrystallization from EtOH to afford the title compound (X) of mp 122—123°. Yield: 0.38 g (92%). *Anal.* Calcd. for $C_{15}H_{16}O_3S$: C, 65.19; H, 5.84; S, 11.62. Found: C, 64.83; H, 5.80; S, 11.43. Mass Spectrum: $m/e=276$ (M^+), 135 ($M-C_6H_5SO_2$), 134 ($M-C_6H_5SO_2H$). UV $\lambda_{\max}^{\text{EtOH}}$ nm ($\log \varepsilon$): 259 (2.97), 266 (3.10), 273 (3.04). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2250 (C≡C), 1720 (C=O), 1305 ($-SO_2-$, ν_{asym}), 1150 ($-SO_2-$, ν_{sym}). NMR δ ppm in $CDCl_3$: 1.90 (3H, singlet, $-CH_3$), 2.0—2.8 (8H, multiplet, methylenes), 7.5—8.1 (5H, multiplet, C_6H_5-).

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[15] G.R. Allen Jr., J.F. Poletto, and M.J. Weiss, *J. Org. Chem.*, 30, 2897, 2910 (1965).