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Studies on Acetylenic Compounds. LII.[1] Reactions of Acetylenic Sulfonium Salts with Cyclohexanone and Cyclopentanone

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Treatment of dimethyl 3-phenyl-2-propynylsulfonium bromide (I) with cyclohexanone in the presence of sodium hydride gave methyl 2-phenyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl sulfide (II), which accompanied with the rearrangement of $S_{Ni'}$ type. Similarly, I reacted with cyclopentanone to give a mixture of methyl 2-phenyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl sulfide (III) and methyl 2-phenyl-4-(1-hydroxycyclopentyl)-3-butynyl sulfide (IV). Dimethyl 2-butynylsulfonium bromide (V), likewise, reacted with cyclohexanone and cyclopentanone to afford methyl 2-methyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl sulfide (VI) and methyl 2-methyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl sulfide (VII), respectively. On the other hand, treatment of dimethyl 2-propynylsulfonium bromide (VIII) with cyclohexanone and cyclopentanone gave methyl 4-(1-hydroxycyclohexyl)-3-butynyl sulfide (X) and methyl 4-(1-hydroxycyclopentyl)-3-butynyl sulfide (XIII), respectively.

We already reported on the base-catalyzed intramolecular rearrangements ($S_{Ni'}$ reaction) of acetylenic sulfonium salts giving allenic sulfides[3] and the intermolecular reactions of acetylenic sulfonium salts with substituted benzaldehydes in the presence of base to afford stable sulfonium ylids,[4] epoxides[5] and allenic alcohol.[5] In the continuation and extension of the intermolecular reactions of S-ylid compounds, we attempted to conduct the reactions of acetylenic sulfonium salts with ketones.

It is known that the simple sulfonium ylids react with ketones to give epoxide compounds[6] as outlined in Chart 1.

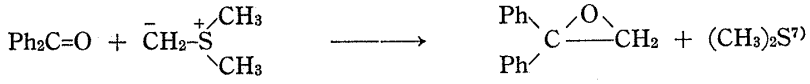

Chart 1

This paper deals with the reactions, which accompanied with the rearrangement of $S_{Ni'}$ type, of acetylenic sulfonium bromide with cyclohexanone and cyclopentanone.

Reaction of dimethyl 3-phenyl-2-propynylsulfonium bromide (I) with cyclohexanone in the presence of sodium hydride in anhydrous tetrahydrofuran gave an oil (II) ($C_{17}H_{22}OS$), bp 145—150° (0.0001 mmHg), in 43.1% yield. The infrared (IR) spectrum of II showed absorption at 3430 cm^{-1} due to the hydroxyl group and 1945 cm^{-1} for typical allenic moiety, and the ultraviolet (UV) spectrum revealed absorption maximum at 254 mμ (ε=12430). The nuclear magnetic resonance (NMR) spectrum in deuteriochloroform showed the signals at 1.67 ppm (in δ) (10H, multiplet) due to the cyclohexyl hydrogens, 2.17 ppm (3H, singlet) ascribable to the methyl group adjacent to sulfur atom, 3.64 ppm (2H, doublet, J=2 cps)

1) Part LI: A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 505 (1970).
2) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
3) A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **17**, 966 (1969).
4) A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 490 (1970).
5) A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 497 (1970).
6) A.W. Johnson, "Ylid Chemistry," Academic press New York and London, 1966.
7) V. Franzen and H.E. Driessen, *Tetrahedron Letters*, **1962**, 661.

assignable to the methylene protons attached to the allenic carbon, 5.81 ppm (1H, triplet, $J=2$ cps) for the allenic proton and an aromatic multiplet centered at 7.40 ppm (5H). From these data, the oily product, II, was concluded to be methyl 2-phenyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl sulfide.

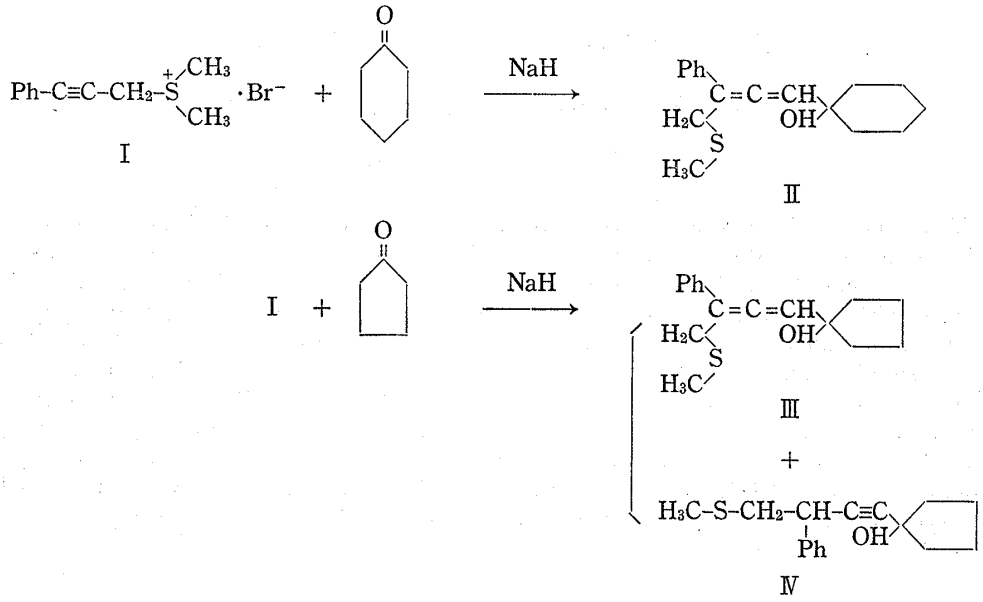

Chart 2

Similarly, treatment of I with cyclopentanone under the same conditions as described above followed by careful silica gel chromatography afforded a mixture of two oily products (III and IV) in 36.5% yield. This mixture decomposed easily and could not be purified by distillation even under highly diminished pressure (0.0001 mmHg). Comparison of the NMR spectra with that of II (Fig. 1 and 2) disclosed that this mixture was constituted of methyl 2-phenyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl sulfide (III) and methyl 2-phenyl-4-(1-hydroxycyclopentyl)-3-butynyl sulfide (IV).

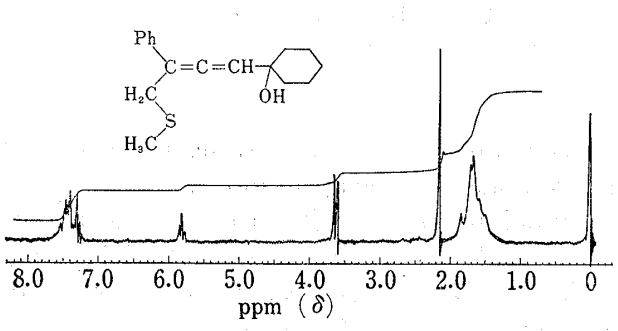

Fig. 1. II

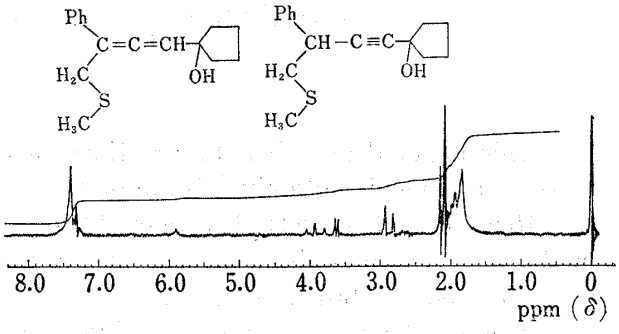

Fig. 2. III+IV

NMR Spectra (60 Mc) of II and a Mixture of III and IV in $CDCl_3$

In the NMR spectra, the signals appeared at 1.89 (multiplet), 2.10 (singlet), 2.15 (singlet), 2.88 (doublet, $J=7$ cps), 3.62 (doublet, $J=2$ cps), 3.92 (triplet, $J=7$ cps), 5.91 (triplet, $J=2$ cps) and 7.38 ppm (multiplet) for the mixture. The signals at 1.89, 2.15 (-S-CH_3), 3.62 (-S-CH_2-C=), 5.91 (=C=CH-) and 7.38 ppm were attributed to III, and at 1.89, 2.10 (-S-CH_3), 2.88 (-S-$\underline{CH_2}$-CH-), 3.92 (-CH-C≡C) and 7.38 ppm were to IV. From the intensity of the signals due to the methyl groups, the ratio of III to IV was determined to be 2:1. Further support to the above assignments was given in the IR spectra, showing a strong hydroxyl band at 3450 cm^{-1}, a characteristic triple bond absorption at 2255 cm^{-1} and a typical allenic

band at 1960 cm^{-1}. The compound of IV may be produced *via* III as will be shown in the mechanistic discussion.

Dimethyl 2-butynylsulfonium bromide (V) was likewise allowed to react with cyclohexanone under the same conditions and methyl 2-methyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl sulfide (VI) of bp 90—93° (0.01 mmHg) was obtained in 40.3% yield.

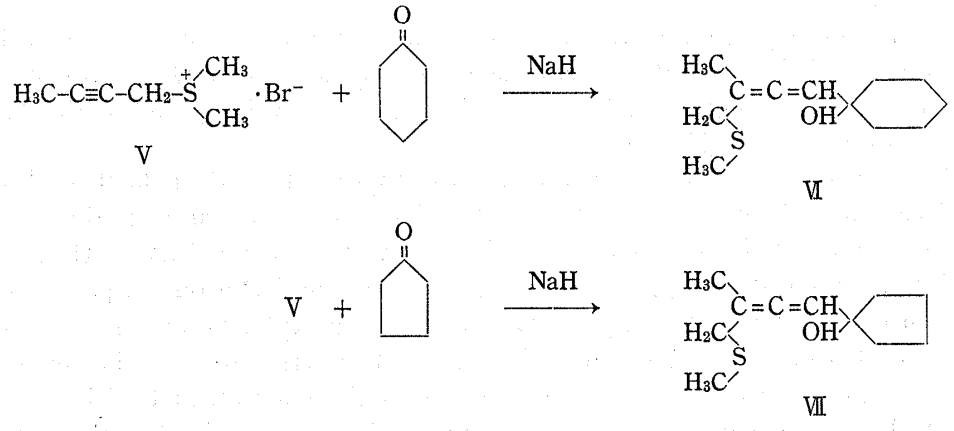

Chart 3

The IR spectrum showed an intense hydroxyl absorption at 3315 cm^{-1} and a typical allenic band at 1965 cm^{-1}. The NMR spectrum exhibited a multiplet centered at 1.58 ppm (10H) due to the cyclohexyl hydrogens, a doublet at 1.84 ppm (3H, J=2.5 cps) ascribable to the methyl group attached to the allenic carbon, a singlet at 2.10 ppm (3H) assignable to the another methyl group adjacent to the sulfur atom, a doublet at 3.10 ppm (2H, J=2 cps) assigned to the methylene protons and a multiplet at 5.31 ppm (1H) for the allenic proton.

In a similar manner, treatment of V with cyclopentanone gave methyl 2-methyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl sulfide (VII) after careful separation using silica gel chromatography in 17.2% yield. As in the case of the mixture of III and IV, this compound also could not be distilled even under highly reduced pressure (0.0001 mmHg), owing to the unstable nature. The IR spectrum showed an intense hydroxyl band at 3350 cm^{-1} and a

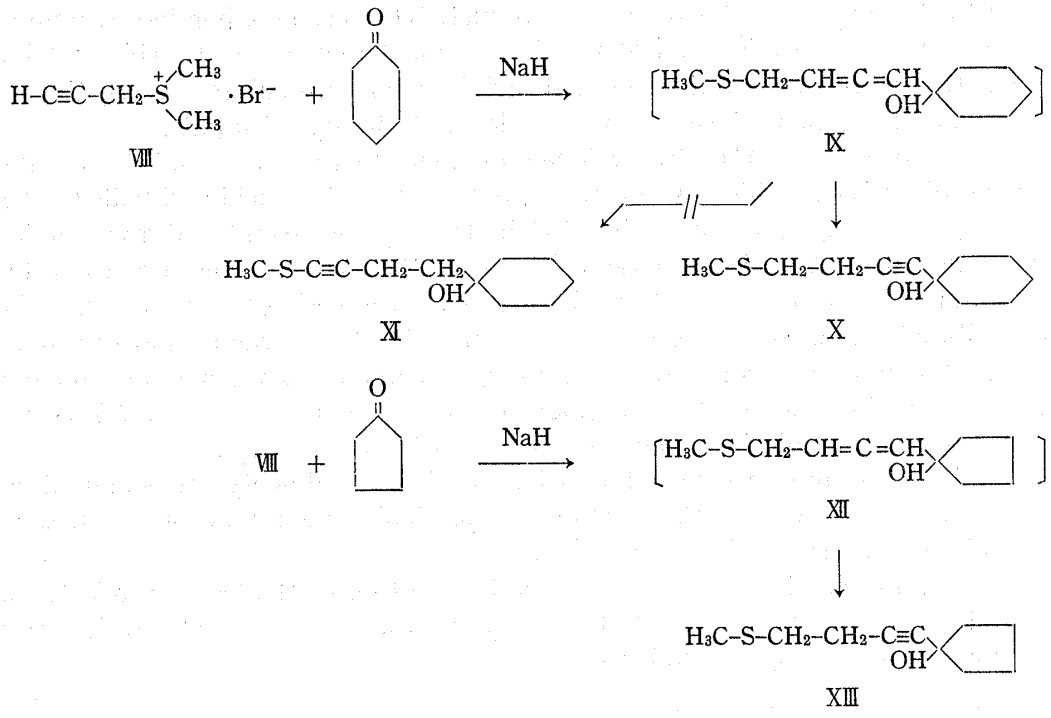

Chart 4

characteristic allenic band at 1915 cm^{-1}. The NMR spectrum exhibited a multiplet centered at 1.73 ppm (8H) due to the cyclopently protons, a doublet at 1.84 ppm (3H, J=2.5 cps) assignable to the methyl group attached to the allenic carbon, a singlet at 2.10 ppm (3H) assigned to the another methyl group adjacent to the sulfur atom, a doublet at 3.14 ppm (2H, J=2 cps) ascribable to the methylene protons and a multiplet centered at 5.42 ppm (1H) for the allenic proton.

When dimethyl 2-propynylsulfonium bromide (VIII) was treated with cyclohexanone under the same conditions as afore-mentioned, an oily substance (X) of bp 98—102° (0.03 mmHg) was obtained in 53.2% yield. The elemental analysis agreed with the empirical formula corresponding to $C_{10}H_{16}OS$.

The IR spectrum of this oil showed an intense hydroxyl band at 3380 cm^{-1} and a characteristic triple bond absorption at 2235 cm^{-1}. The NMR spectrum exhibited a multiplet centered at 1.68 ppm (10H) due to the cyclohexyl hydrogens, an A_2B_2 pattern centered at 2.04 ppm (4H), a singlet at 2.19 ppm (3H) assigned to the methyl group adjacent to the sulfur atom and a broad singlet at 2.30 ppm (1H) for the hydroxyl proton. From these results, the structure of this oil would be either X or XI. The structure, XI, however, should be excluded by the following reasons: 1). In the case of the reaction of I with cyclopentanone (see Chart 2), IV (corresponded to the structure of X) was obtained. 2). When this oil was treated with hydrogen peroxide in acetic acid, an acetylenic sulfone compound (XIV) was obtained.

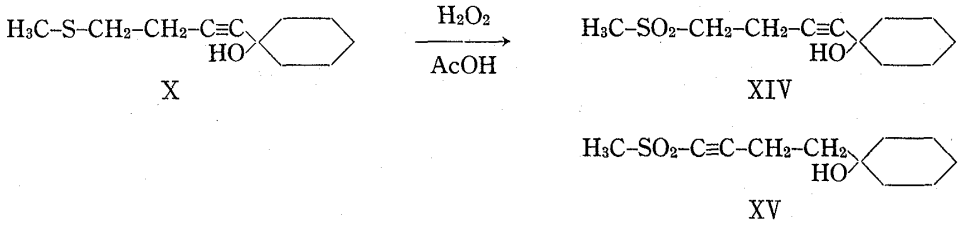

Chart 5

In the IR spectrum of XIV, the triple bond absorption (2230 cm^{-1}) showed no increase as compared to that of X. If this oxidation product, XIV has a conjugated structure such as XV, the intensity of the triple bond absorption should be enhanced.[8] This fact indicated that the structure of X was not the conjugate triple bond with sulfur. Thus, the structure of X was assigned to be methyl 4-(1-hydroxycyclohexyl)-3-butynyl sulfide.

Similarly, treatment of VIII with cyclopentanone under the same conditions as described above gave an oil (XIII). This oily substance, obtained in 11% yield and boiled at 98—105° (0.005 mmHg), was assigned to be methyl 4-(1-hydroxycyclopentyl)-3-butynyl sulfide on the basis of the following facts as in the case of X. The IR spectrum showed a strong hydroxyl absorption band at 3400 cm^{-1} and a typical triple bond absorption at 2220 cm^{-1}. The NMR spectrum exhibited a multiplet centered at 1.89 ppm (8H) due to the cyclopentyl hydrogens, a singlet at 2.19 ppm (3H) assigned to the methyl group and an A_2B_2 pattern centered at 2.62 ppm (4H). Considering the reaction mechanism, the compounds, X and XIII, would be produced *via* unstable allenic intermediate, IX and XII, respectively.

A mechanistic assumption for the formation of allenic- and acetylenic sulfide derivatives containing the hydroxyl group by the reactions of acetylenic sulfonium bromides with alicyclic ketones would be expressed as indicated in Chart 6.

The initial ylid carbanion (XVI) attacks the ketone to give the betaine (XVII), then the anion of betaine (XVII) attacks one of the methyl protons giving XVIII, which rearranges by an $S_{Ni'}$ reaction to the stable products.

8) L.H. Allan, G.D. Meakins and M.C. Whiting, *J. Chem. Soc.*, **1955**, 1874.

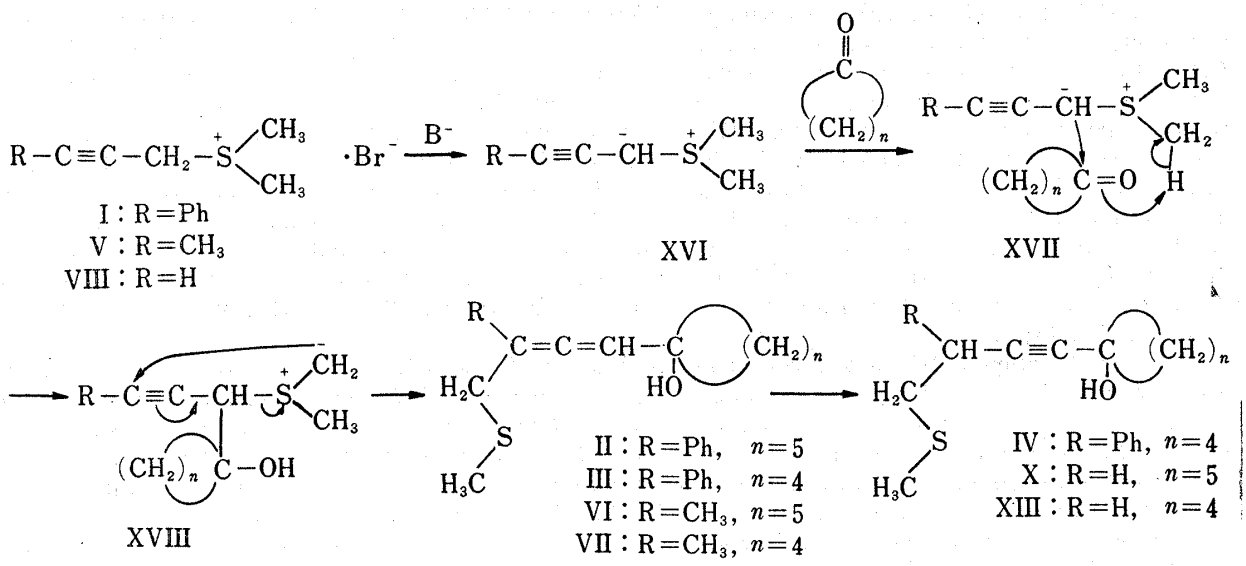

Chart 6

We should recall an earlier paper,[3] in which we have described the formation of a compound (XXI) by an $S_{Ni'}$ reaction of dimethyl 2-propynylsulfonium bromide derivatives (XIX) with base.

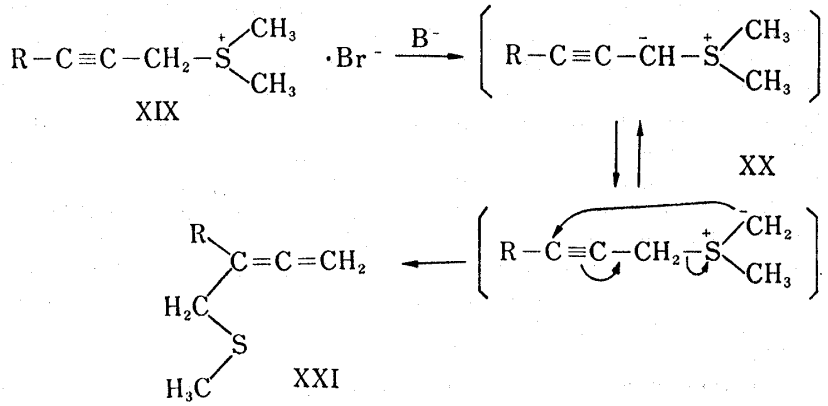

Chart 7

The reaction paths of XVIII giving II, III, VI and VII make the same analogy to that of XX giving XXI.

Experimental[9]

Methyl 2-Phenyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl Sulfide (II)——To a suspension of dimethyl 3-phenyl-2-propynylsulfonium bromide (2.6 g, 10.1 mmole) and cyclohexanone (1.0 g, 10.2 mmole) in 30 ml of anhyd. tetrahydrofuran was added in one portion 0.5 g of NaH (50% oily support) at 3—5° under N_2. Stirring was continued for 10 min at the same temperature and further 3 hr at 20—25° by external cooling. The reaction mixture was poured into 300 ml of ice-water and extracted with AcOEt. The combined extracts were washed with satd. aq. solution of NaCl until neutral to litmus, dried over Na_2SO_4 and evaporated to dryness. The oily residue (2.5 g) was chromatographed on 50 g of silica gel and eluted with benzene–hexane (2:1) to afford 1.18 g (43.1%) of methyl 2-phenyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl sulfide, bp 145—150° (0.0001 mmHg) (bath temp.). *Anal.* Calcd. for $C_{17}H_{22}OS$: C, 74.40; H, 8.04; S, 11.64. Found: C, 73.95; H, 7.93; S, 11.65.

9) All melting and boiling points are uncorrected. NMR spectra were taken using Varian A-60 and HA-100 spectrometer and the chemical shifts were expressed in ppm unit from the internal standard of tetramethylsilane.

Methyl 2-Phenyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl Sulfide (III) and Methyl 2-Phenyl-4-(1-hydroxycyclopentyl)-3-butynyl Sulfide (IV)——To a suspension of dimethyl 3-phenyl-2-propynylsulfonium bromide (2.6 g, 10.1 mmole) and cyclopentanone (0.9 g, 10.7 mmole) in 30 ml of anhyd. tetrahydrofuran was added in one portion 0.5 g of NaH (50% oily mixture) at 3—5° under N_2. Stirring was continued for 10 min at the same temperature and then 3 hr at 20—25° by external cooling. The reaction mixture was poured into 300 ml of ice-water and extracted with AcOEt. The combined extracts were washed with satd. aq. solution of NaCl until neutral to litmus, dried over Na_2SO_4 and evaporated to dryness. The oily residue (1.8 g) was chromatographed on 50 g of silica gel. Elution with benzene afforded 0.95 g (36.5%) of an oil, which was a 2:1 mixture of methyl 2-phenyl-4(1-hydroxycyclopentyl)-2,3-butadienyl sulfide (III) and methyl 2-phenyl-4(1-hydroxycyclopentyl)-3-butynyl sulfide (IV) (see Fig. 2). This oil could not be distilled even under highly diminished pressure (0.0001 mmHg). *Anal.* Calcd. for $C_{16}H_{20}OS$: C, 73.86; H, 7.69; S, 12.30. Found: C, 73.75; H, 7.75; S, 11.94.

Methyl 2-Methyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl Sulfide (VI)——To a suspension of dimethyl 2-butynylsulfonium bromide (2.93 g, 15 mmole) and cyclohexanone (1.5 g, 15 mmole) in 30 ml of anhyd. tetrahydrofuran was added in one portion 0.75 g of NaH (50% oily mixture) at 3° under N_2. Stirring was continued for 10 min at the same temperature and then 5 hr, maintaining at 25—30°. The reaction mixture was poured into 300 ml of ice-water and extracted with satd. aq. solution of NaCl until neutral to litmus, dried over Na_2SO_4 and evaporated to dryness under diminished pressure. The oily residue (2.8 g) was chromatographed on 50 g of silica gel and eluted with benzene–hexane (2:1) to give 1.3 g (40.3%) of methyl 2-methyl-4-(1-hydroxycyclohexyl)-2,3-butadienyl sulfide, bp 90—93° (0.01 mmHg) (bath temp.). *Anal.* Calcd. for $C_{12}H_{20}OS$: C, 67.86; H, 9.49; S, 15.09. Found: C, 67.63; H, 9.41; S, 14.67.

Methyl 2-Methyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl Sulfide (VII)——To a suspension of dimethyl 2-butynylsulfonium bromide (2.93 g, 15 mmole) and cyclopentanone (1.35 g, 15 mmole) in 30 ml of anhyd. tetrahydrofuran was added in one portion 0.75 g of NaH (50% oily mixture) at 3—5° under N_2. Stirring was continued for 10 min at 5° and further 5 hr at 25—30°. The reaction mixture was poured into 300 ml of ice–water and extracted with AcOEt. The combined extracts were washed with satd. aq. solution of NaCl, dried over Na_2SO_4 and evaporated. The oily residue (2.5 g) was chromatographed on 50 g of silica gel and eluted with benzene to afford 0.51 g (17.2%) of methyl 2-methyl-4-(1-hydroxycyclopentyl)-2,3-butadienyl sulfide. This oil could not be distilled even under highly diminished pressure. *Anal.* Calcd. for $C_{11}H_{18}OS$: C, 66.67; H, 9.09; S, 16.16. Found: C, 66.96; H, 8.96; S, 16.05.

Methyl 4-(1-Hydroxycyclohexyl)-3-butynyl Sulfide (X)——To a suspension of dimethyl 2-propynylsulfonium bromide (2.71 g, 15 mmole) and cyclohexanone (1.5 g, 15 mmole) in 30 ml of anhyd. tetrahydrofuran was added in one portion 0.75 g of NaH (50% oily mixture) at 3° under N_2. Sitrring was continued for 15 min and then 2 hr at room temperature. The reaction mixture was poured into 300 ml of ice-water and extracted with ether. The combined extracts were washed with satd. aq. solution of NaCl until neutral to litmus, dried over Na_2SO_4 and evaporated. The oily residue (2.7 g) was chromatographed on 40 g of silica gel and eluted with benzene to give 1.58 g (53.2%) of methyl 4-(1-hydroxycyclohexyl)-3-butynyl sulfide, bp 98—102° (0.03 mmHg) (bath temp.). *Anal.* Calcd. for $C_{11}H_{18}OS$: C, 66.62; H, 9.15; S, 16.16. Found: C, 66.43; H, 9.24; S, 16.35.

Methyl 4-(1-Hydroxycyclopentyl)-3-butynyl Sulfide (XIII)——To a suspension of dimethyl 2-propynylsulfonium bromide (2.71 g, 15 mmole) and cyclopentanone (1.3 g, 15.1 mmole) in 30 ml of anhyd. tetrahydrofuran was added in one portion 0.75 g of NaH (50% oily mixture) at 3—5° under N_2. Stirring was continued for 30 min at 5° and then 2 hr at 20—25°. The reaction mixture was poured into 100 ml of ice-water and extracted with AcOEt. The combined extracts were washed with satd. aq. solution of NaCl, dried over Na_2SO_4 and evaporated to dryness. The oily residue (2.5 g) was chromatogarphed on 50 g of silica gel. Elution with benzene afforded 0.9 g of methyl 4-(1-hydroxycyclopentyl)-3-butynyl sulfide, bp 98—105° (0.005 mmHg) (bath temp.). *Anal.* Calcd. for $C_{10}H_{16}OS$: C, 65.11; H, 8.75; S, 17.38. Found: C, 64.75; H, 8.47; S, 17.07.

Methyl 4-(1-Hydroxycyclohexyl)-3-butynyl Sulfone (XIV)——To a mixture of methyl 4-(1-hydroxycyclohexyl)-3-butynyl sulfide (0.396 g) and 10 ml of AcOH was added dropwise 1.2 ml of 30% hydrogen peroxide at 5° with stirring. After the addition was completed, stirring was continued for 5 hr at 40°. The reaction mixture was poured into 50 ml of crushed ice-water and extracted with AcOEt three times. The combined extracts were washed with satd. aq. solution of NaCl, satd. aq. solution of $NaHCO_3$, H_2O and dried over Na_2SO_4. The solvent was evaporated under diminished pressure to give an oil (0.3 g). This oil was chromatographed on silica gel (15 g) and eluted with hexane–benzene (1:3) to give 0.195 g of methyl 4-(1-hydroxycyclohexyl)-3-butynyl sulfone, bp 160—163° (0.0001 mmHg) (bath temp.). *Anal.* Calcd. for $C_{11}H_{18}O_3S$: C, 57.38; H, 7.88; S, 13.90. Found: C, 56.94; H, 7.95; S, 13.50.

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