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THE REACTION OF 3-METHYL-2-BUTENYL PHENYL SULFIDE WITH ALDEHYDES AND KETONES.* APPLICATION TO THE SYNTHESIS OF 2,2-DIMETHYLCYCLOPROPANECARBALDEHYDES

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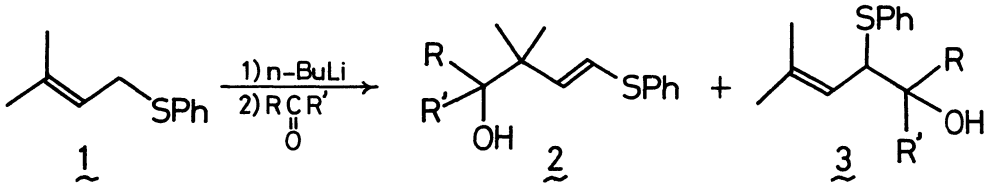
The base promoted addition of 3-methyl-2-butenyl phenyl sulfide to aldehydes and ketones occurred selectively on the γ-position of the allylic moiety. The product was converted to the methanesulfonate. Treatment of the resulting homoallylic ester with nucleophiles induced the cyclization to give cyclopropane derivatives in excellent yields.

Regioselective alkylation of allylic sulfides has successfully been applied to the synthesis of physiologically interesting natural products by ourselves[1] and others.[2] Very recently, Biellmann and his associates reported the reaction of 3-methyl-2-butenyl phenyl sulfide with acetone and observed that the position of the alkylation depends on the reaction condition.[3] In this communication, we wish to report our own findings on the related problem as well as the application of the product to the synthesis of cyclopropanecarbaldehydes.

When the lithiated 3-methyl-2-butenyl phenyl sulfide was allowed to react with aldehydes or ketones,[4] the addition occurred selectively on the γ-position of the allylic moiety, though alkylation with alkyl halides or epoxides proceeded exclusively on the α-position.[2] Some of the results are summarized in Table 1. The data clearly demonstrate that exclusive γ-addition occurs when the reaction is applied to the aldehydes.

The observed regioselectivity as well as the unique structure of the product stimulated us to device a new synthetic reaction as follows. If the hydroxyl group in 4 could be eliminated by heterolysis, the homoallylic electrondonating participation of the



1 2 3

Table 1. The reaction of 3-methyl-2-butenyl phenyl sulfide with carbonyls

carbonyls		total yield (%)	2(%) : 3(%)	
propionaldehyde	(R=Et, R'=H)	85	~100	0
benzaldehyde	(R=Ph, R'=H)	92	~100	0
cyclohexanone	(R=R'=-$(CH_2)_5$-)	85	95	5
acetone	(R=R'=Me)	70	91	9

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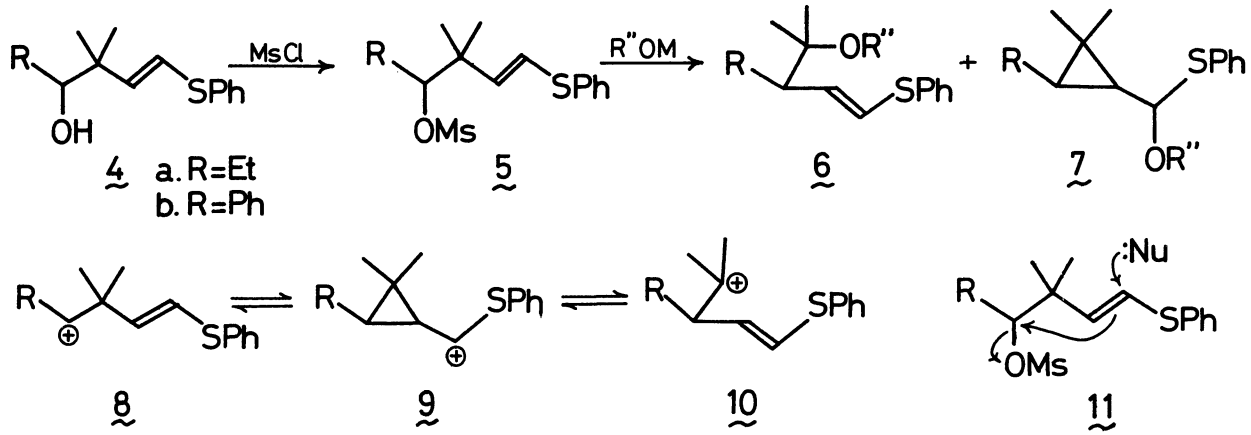
sulfur atom would induce cyclization to form a cyclopropane ring. In order to realize the idea, the addition products 4 were firstly converted to the methanesulfonates 5. Contrary to our expectation, treatment of 5a and 5b in MeOH at room temperature afforded no desired cyclopropanes 7 but rearranged products 6a(R"=Me) and 6b(R"=Me) in 75 and 70% yields, respectively. Acetolysis of 5a also produced 6a(R"=Ac) in 70% yield. In the case of 5b, however, the cyclopropane 7b(R"=Ac) was obtained in 35% yield along with the rearranged product 6b(R"=Ac, 40%). The formation of 6 can be rationalized by assuming the presence of an equilibrium between open-chain cations 8 and 10 through the cyclized cation 9. The structure of the product suggests that the carbonium ion 10 is the most stable species in the system and thus has been quenched selectively in this form.

The direct nucleophilic substitution of the mesyloxy group in 5 would be highly hindered as it has a neopentyl-type structure. Therefore, if a nucleophile could favorably attack on the α-carbon of the vinyl sulfide linkage as formulated in 11, it might also be possible to obtain the desired cyclopropanes. The methanesulfonates 5 were now treated with an equimolar amount of MeONa in MeOH at room temperature. Usual work-up of the reaction mixture afforded the cyclopropanes 7a(R"=Me) and 7b(R"=Me) exclusively in 77 and 92% yields, respectively. Similarly, treatment of 5b with AcOK in t-BuOH or DMF gave the cyclization product 7b(R"=Ac) in excellent yield. The resulting monothioacetals 7(R"=Me) were converted to the corresponding cyclopropanecarbaldehydes by treating with $HgCl_2$ in MeCN-H_2O in the presence of $CaCO_3$ (73-82% yields). In the case of 7(R"=Ac), the aldehyde was generated by alkaline hydrolysis. Attempted deacetalization of 7(R"=Me) under acidic condition again induced the rearrangement to produce 6(R"=H or Me).



References and Notes

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2) J. F. Biellmann and J. B. Ducep, Tetrahedron Lett., 5629 (1968); J. F. Biellmann and J. B. Ducep, Tetrahedron, 27, 5861 (1971); K. Narasaka, M. Hayashi, and T. Mukaiyama, Chem. Lett., 259 (1972); K. Hirai and Y. Kishida, Heterocycles, 2, 185 (1974).

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4) In a typical procedure, n-BuLi(3.9ml, 6 mmol) was added to dry THF solution of 1 (1.07g, 6 mmol) at -78°C. After 2hr, substrate (6 mmol) was added at -78°C and reaction mixture was stirred for 3hr.

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